Externalising behaviour and the neural correlates of reward in adolescence.

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Declaration

I, James G. Sheffield, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm this has been indicated in the thesis.

For the project reported in the first two empirical chapters, I was solely responsible for EEG data pre-processing and relevant scripts, statistical analysis, and writing of both chapters.

For the project reported in the second two empirical chapters, I was involved in the initial ethics application and inputting questionnaire data from the original START project. I was solely responsible for several ethics amendments, programming one of the behavioural tasks and editing the other, recruitment and data collection, creating and processing questionnaire database, EEG and behavioural data pre-processing, statistical analysis, chapter writing and image creation.

Abstract

Externalising problems are some of the most common disorders in childhood and adolescence, and predict worse criminal, social, and academic outcomes during adulthood. These externalising behaviours have been associated with an imbalance between approach/reward systems and avoidance/punishment systems. This imbalance is thought to express itself as behavioural disinhibition, empathic blunting, and reward dominance. However, whilst recent neuroimaging studies have begun to investigate functional changes surrounding externalising behaviours, we know little about the underlying neural mechanisms these changes reflect. This is especially true of feedback processing where the literature has been limited to haemodynamic methodologies, which may blur distinct events related to feedback processing. The primary aim of this thesis was to investigate differences in reward and punishment processing associated with externalising behaviour amongst both normative and clinical samples. Electroencephalogram (EEG) recordings were taken during feedback tasks and analysed in both the time domain and time-frequency domain. Results from typically developing participants revealed that high externalising was associated with increased motivational salience of reward feedback compared to punishment feedback, and deficits in error monitoring processes. By comparison, high externalising behaviour amongst clinical participants was associated with differences in EEG signals of error-monitoring, but no differences in the motivational significance of reward and punishment. However, given the social elements of the Taylor Aggression Paradigm, where participants competed against fictitious opponents, these results may partially reflect differences in the ecological validity of the tasks used. This lack of consistency between normative and clinical samples highlight the need for research investigating externalising related changes in approach and avoidance behaviours in both social and non-social circumstances.

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This thesis is dedicated to my dad; an administrator by position, but an academic at heart.

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Chapter 1

General Introduction

1. Introduction

Externalising behaviours represent a highly prevalent and heterogeneous set of behaviours that breach the age appropriate norms for their culture (Keil & Price, 2006). These can include behaviours such as physical, destructive, and relational aggression, theft, deceitfulness, drug and alcohol use, and temper tantrums. In both children and adolescents (Althoff et al., 2014; Reef, van Meurs, Verhulst, & van der Ende, 2010; Sayal, Washbrook, & Propper, 2015), regular engagement in externalising behaviours predicts poorer social and criminal outcomes in adulthood (Odgers et al., 2008). Even in children as young as 4 years of age, the presence of externalising behaviours have been found to predict poorer life outcomes (Reef et al., 2010) and further externalising psychopathology in adolescence and adulthood (Bennet et al., 1998; Caspi et al., 1995; Kellam et al., 2008).

Moreover, these consequences are not limited to the individual, but instead extend to the societal level. As it stands, conservative cost estimation work with one extreme example of externalising psychopathology, Conduct Disorder, has placed costs of providing interventions and treatment to a single child at an average of £5,960 per annum, the majority of which is at the expense of the family (Romeo, Knapp & Scott, 2006). Other studies have placed these figures at similar or greater amounts (Foster & Jones, 2005; Knapp, Scott & Davis, 1999; Scott et al., 2001), with comparable estimated costs for ADHD (Pelham, Foster, & Robb, 2007). This excludes the costs of less tangible factors associated with externalising behaviours, such as victim pain and suffering resulting from violent crime (Dolan et al., 2005).

In this introduction, I will briefly describe the social and neurological development associated with adolescents. Followed by a description of what is commonly meant by externalising behaviour, its developmental characteristics and associated outcomes. I will then provide a synopsis of theories that propose that motivational imbalances (e.g., between approach and avoidance) may underlie externalising behaviour, and examine the evidence supporting hypotheses regarding a putative imbalance of motivational systems amongst children and adolescents with externalising problems. Finally, because this thesis relies on electroencephalography (EEG), I will outline this method in detail and summarise the advantages and

disadvantages of EEG techniques, before providing an overview of the thesis and its primary research questions.

1.1. Adolescence

It is well established that adolescence is a period of social development. Specifically, ingratiation with a social group is a method to achieve social status, and values and behaviours of the desired group are likely to influence an individual's behaviour (see Brechwald & Prinstein, 2011, for a review). Peer influence has been shown to effect externalising behaviours including aggression (Berger & Rodkin, 2011; Mrug et al., 2014), smoking (Mercken, Steglich, Sinclair, Holliday, & Moore, 2012; Valente, Fujimoto, Soto, Ritt-Olson, & Unger, 2013), drug and alcohol use (Allen, Chango, Szwedo, Schad, & Marston, 2012; Huang et al., 2014; van Ryzin, Fosco, & Dishion, 2012), and delinquency (Mrug et al., 2014; Tilton-Weaver, Burk, Kerr, & Stattin, 2013), as well as non-externalising behaviours, such as disordered eating (Ferguson, Munoz, Garza, & Galindo, 2013) and self-harm (Prinstein et al., 2010). This may be especially true in early adolescence, where an individual's resistance to influence is relatively low compared to older groups, as resistance to peer influencing increases over the late adolescent period (Steinberg & Monaham, 2007), potentially related to development of self-identity (Collins & Steinberg, 2006).

Whilst peer group association and influence is a potential risk for deleterious behaviour, peer acceptance itself can have large beneficial effects. Brady, Dolcini, Harper, and Pollack (2009) found that adolescents with low levels of peer support were more prone to risk-taking behaviours than those with high levels of peer support. Similarly, Telzer, Fuligni, Lieberman, Miernicki, & Galvan (2014) found an inverse relationship between peer support and risk-taking behaviours amongst adolescents, and that peer support mediated the relationship between peer conflict (as measured by a diary) and risk taking behaviour on a Balloon Analogue Risk Task. This also appears to also be true for internalising disorders. Nilsen, Karevold, Røysamb, Gustavson, and Mathiesen (2013) found that poor social skills in girls was related to changes in depressive symptoms over adolescence, but that this relationship was mediated by social support they received from their friends. More recently, Frenkel et al. (2015) conducted a longitudinal study over a 20-year period and found that children who demonstrated high levels of behavioural inhibition were more prone to anxiety in

adulthood. However, this relationship was mediated by peer social support for those with high levels of behavioural inhibition - participants who reported high levels of social support during adolescence demonstrated less social anxiety than those who reported lower levels.

Alongside changes in social processing, adolescence is also characterised by large structural reorganisation in the brain. Grey matter volume decreases significantly over adolescence (Blakemore & Mills, 2014), beginning in the sensory and motor regions before progressing to the frontal regions (Shaw et al., 2008), a process that continues into early adulthood (Petanjek et al., 2011). This is accompanied by significant increases in white matter (Peters et al., 2012), though this demonstrates a logarithmic growth, rapidly changing in early adolescence and tailing off in adulthood (Lebel & Beaulieu, 2011). However, adolescent neurodevelopment is not limited to structural changes, but also functional changes. A recent review of the literature by Ernst, Torrisi, Grillon, and Hale (2015) highlighted 3 significant functional changes occurring over adolescence: a shifting from local to global connections; changes in the relative strength of networks; and reorganisation occurring within networks, allowing more flexibility and efficiency in processing.

A number of investigators (e.g. Casey & Jones, 2010; Geier & Luna, 2009; Steinberg, 2007) have suggested a dual systems model to explain increases in approach behaviours seen during adolescence, reflecting a developmental imbalance between top-down control systems, responsible for inhibition, and bottom-up motivational systems. The earlier development of the reward systems compared to frontal systems involved in inhibition and cognitive control leads to period where adolescents demonstrate greater approach behaviours. However, whether this is related to hypo- or hypersensitivity is still debated, though most evidence converges to support hypersensitivity (see Galvan, 2010, for a review).

Several neuroimaging studies have observed altered reward signalling in adolescents when compared against adults and children. Both Cohen et al. (2010) and Van Leijenhorst et al. (2010) found that adolescents demonstrated increased activity in the ventral striatum (VS) following reward cues when compared against both children and adults. Geier, Terwilliger, Teslovich, Velanova, and Luna (2009) observed heightened VS activation during the reward anticipation phase of a modified anti-

saccade task, but noted blunted VS response when viewing a cue indicative of whether the trial would result in a reward or not. Similarly, Braams, van Duijvenvoorde, Peper, and Crone (2015) found a quadratic effect of age on nucleus accumbens (NAcc) activity following reward, peaking in adolescence, in a sample of participants ranging from 8 to 25 years old. This enhanced reward sensitivity extends to social situations. In a recent study by Braams, Peters, Peper, Guroglu, and Crone (2014) asked participants to complete a random gambling task in which they could win money for themselves, a friend, or an antagonistic peer. They found that participants demonstrated greater VS activation following reward compared to punishment when they won money for either themselves or their friend. This effect did not remain when they won money for the antagonistic peer.

Whilst inhibitory control findings appear to increase from childhood, over adolescence, into adulthood (e.g. Crone, 2009; Grose-Fifer, Rodrigues, Hoover, & Zottoli, 2013; Tottenham, Hare, & Casey, 2011), adolescents demonstrate difficulty in maintaining control in the presence of emotional stimuli. Cohen-Gilbert and Thomas (2013) found that younger adolescents demonstrated poorer inhibitory control than older adolescents or adults in the presence of negatively valence stimuli during an affective Go/No-Go task. Similarly, Somerville, Hare, and Casey (2011) found adolescents, but not children or adults, demonstrated greater numbers of false alarm errors towards positively-valenced cues, but not neutral cues. Regarding neural activation, Vetter, Pilhatsch, Weigelt, Ripke, and Smolka (2015) found greater activation in the left anterior insula, an area thought to be important for response inhibition in adults (Smith et al., 2014), amongst 16 year olds compared to 14 year olds whilst attending to positive stimuli and ignoring stimuli. Maturation of white matter integrity in neural structures important for inhibition and impulse control appears to play a role in the decline of reward driven behaviours. Recently, using a longitudinal design, Achterberg, Peper, van Duijvenvoorde, Mandl, and Crone (2016) asked adolescent participants to complete a delayed discounting task. As expected, they found a preference for delayed discounting as participants increased in age, however, this relationship was fully mediated by white matter integrity over the frontostriatal tract. Moreover, frontostriatal white matter connectivity could significantly predict delay discounting two years later.

Given that adolescents are more socially motivated than adults, it is perhaps unsurprising that adolescents also demonstrate differential activations to social stimulus when compared against adults. Both Burnett, Bird, Moll, Frith, and Blakemore (2009) and Sebastian et al. (2012) found greater activation in medial prefrontal cortex (mPFC) amongst adolescents in comparison to adults when participants were presented with mentalising tasks (reading scenarios and passively viewing cartoons, respectively). Similarly, Moor et al. (2012) asked both adolescents and adults to make judgement about a person's emotions whilst only viewing their eyes. They found that whilst both groups demonstrated equivocal activation in the posterior superior temporal sulcus, mPFC activation was only seen in the adolescents. Van den Bos, Cohen, Kahnt, and Crone (2011) had both adult and adolescent participants play as the receiving player in a trust game, and observed the increasing temporoparietal junction (TPJ) and dorsolateral prefrontal cortex activation with age, areas associated with perspective taking and self-orientated impulse control, respectively.

Furthermore, this increased social sensitivity of adolescence may influence approach behaviours in adolescence. Using the Stopping task, Gardner and Steinberg (2005) found adolescents, undergraduates, and adults differed in their risk-taking behaviour when accompanied by their peers. Adolescents, and to a lesser extent, undergraduates, demonstrated increases in risk-taking behaviours, which was not seen in the adult group. Both O'Brien, Albert, Chein, and Steinberg (2011) and Weigard, Chein, Albert, Smith, and Steinberg (2014) found that older adolescents demonstrated greater reward discounting when they were being observed by peers compared to when they were alone, regardless of whether they knew their observers (O'Brien et al., 2011) or not (Weigard et al., 2014). Similarly, when adolescents thought that they were being observed by a peer, they were significantly more likely to gamble on a probabilistic gambling task compared to adolescents who played alone, even in trials with low win probability (Smith, Chein, & Steinberg, 2014). At the functional level, Chien, Albert, O'Brien, Uckert, and Steinberg (2011) found greater activation in the orbitofrontal cortex and VS amongst adolescents when accompanied by their peers compared to when they were alone, whilst the adults did not demonstrate this effect. Building on this Peake, Dishion, Stormshak, Moore, and Pfeifer (2013) ask adolescent participants to complete a Stoplight task after playing a game of Cyberball, a task designed to elicit a feeling of social exclusion. Following social exclusion, participants who reported a low

of resistance to peer influence recruited the TPJ more and the anterior cingulate cortex less during risk decision making, suggesting more consideration of others perspective and lower error monitoring procedures during risk decision making in these participants. However, work investigating peer influence on risk behaviours outside the laboratory has been limited. Simons-Morton et al. (2011) used vehicle-mounted instruments to monitor risky driving and collisions amongst teenagers. They found that having other teenagers in the car was negatively associated with risk driving in adolescents, similar to having an adult presence in the car. The only social factor increasing risky driving was the number of risk-taking friends, which is consistent with previous literature suggesting that deviant peers are associated with increases in the amount of risky and externalising behaviours amongst adolescents (Cox, 2014; Hinnant, Erath, Tu, & El-Sheikh, 2015; Hou et al., 2013).

Thus, whilst the literature is indicative of motivational changes in adolescence, and the importance of social factors in influence approach behaviours amongst adolescents, there remain inconsistencies in the direction of effect. This may be related to the large amounts of variance in the studies used to investigate motivational response in adolescence with age and gender make-up of the samples, the comparison group, and the motivational period of interest (e.g. anticipation vs. receipt of reward) differing between studies. Moreover, several studies only used adult samples for comparison, making it impossible to draw conclusions about the developmental trajectory of motivational circuits peaking in adolescence, as these are usually between group comparisons, and are only able to describe a linear relationship between adolescent and adult groups. Ideally, a comparative child group (or potentially two adolescent groups; a younger and older group), or quadratic age term during analysis would aid in understanding the changes in feedback processing over adolescence.

Furthermore, these studies primarily focus on reward sensitivity, comparing it against neutral or non-reward stimuli. Few studies have actively investigated whether adolescents demonstrated increased sensitivity to punishment as they do to reward, and those that have done so demonstrate somewhat mixed findings (Eppinger, Mock, & Kray, 2009; Hammerer, Li, Muller, & Lindenberger, 2011; Santesso, Dzyundzyak, & Segalowitz, 2011; Galvan & McGlennen, 2013). Potentially, these inconsistencies in results may reflect same inconsistencies in study design seen in developmental research

regarding motivation in general, as well as the operationalisation of punishment sensitivity. Yet, without a clearer understanding of adolescent punishment sensitivity relative to child and adult samples, we cannot be certain that adolescence is not associated with an indiscriminate increase in feedback sensitivity.

It is also worth noting that the majority of adolescent studies investigating social effects in a laboratory setting have focused on the presence or observation of peers, and few have investigated adolescent reward response in the face of provocation from an antagonistic peer. However, past literature suggests that inhibition amongst adolescence is weakest in emotionally salient, "hot" scenarios. Therefore, investigating social provocation and its effects on approach behaviour, may be imperative for understanding adolescent externalising behaviour. By investigating the influence of both peer presence and social context on reward and inhibition, we may gain a more thorough understanding of their underlying neural circuits, better informing approach behaviours *in vivo*.

1.2. Externalising Behaviour

After anxiety disorders, externalising disorders represent the second most common type of mental disorder amongst young samples, with a prevalence rate of around 20% (Merikangas et al., 2010), and referral rates of between 28-45% (NICE, 2013). Externalising disorders common in childhood and adolescence include Conduct Disorder (CD), Oppositional Defiant Disorder (ODD), Substance Use Disorder, and Attention-Deficit Hyperactivity Disorder (ADHD). On average, the age of onset for behavioural disorders is thought to be around 11 years of age (Merikangas et al., 2010), though fluctuations exist depending on the specific disorder, with disorders such as ADHD and ODD occurring earlier (Lavigne et al., 2001; Kieling et al., 2010), and substance abuse occurring later (Ormel et al., 2015).

Specifically, this thesis will be primarily focused on externalising behaviours characteristic of CD and ODD, classified together as Disruptive Behaviour Disorders. The DSM-IV diagnostic features of CD include aggression to others, destruction of property, deceitfulness, theft, and rule violation (such as running away from home). There needs to be 3 or more of these behaviours present for a duration of at least 6 months, with significant impact on the young person's social, academic, or occupational

function for diagnosis (American Psychiatric Association, 2000). By comparison, the diagnostic criteria for ODD is arguably less severe, focusing on hostile or defiant behaviours, including defiance, loss of temper, touchiness, spitefulness, argumentativeness, and deliberate intention to annoy others. However, similar to CD, these behaviours must cause significant impairment in the child's social, emotional, or academic environment to meet the necessary criteria for diagnosis (American Psychiatric Association, 2000). It is important to note that whilst a combination of these behaviours over time leading to significant impairment is necessary for a diagnosis of either CD or ODD, a lot of these behaviours (such as oppositional defiance, rebelliousness, and aggression) are common amongst normative samples (Kisicki & French, 2011).

1.2.1. Gender and externalising behaviour

In general, evidence indicates that externalising behaviours are more common amongst males than females. In a developmental longitudinal study, Lahey et al. (2006) found that maternally rated conduct problems were higher in males compared to females, and this difference increased over childhood, but began to diminish over the prepubertal period. Even amongst children as young as 45 months, there is a higher prevalence of externalising behaviours in males compared to females (Crick, Casas, & Mosher, 1997; Ostrov & Keating, 2004). Similarly, Maughan et al. (2004) found that female conduct problems remained low compared to males over childhood, but increased significantly over early adolescence. Furthermore, males are at a substantially greater risk for developing externalising disorders such as CD (Maughan et al., 2004; Nock et al., 2006), Substance Use Disorder (Duncan et al., 2015), and ADHD (Polanczyk et al., 2007) than girls. Moreover, the life-course persistent form of Conduct Disorder (Conduct Disorder beginning in childhood and continuing through adolescence to adulthood) is somewhere between 10-15 times more likely to be observed in males compared to females (Moffitt, 2006), and Maughan and colleagues (2004) suggests that childhood-onset CD is markedly more prevalent in males than females.

However, despite the consistency of these findings, it is possible that differences in the presentation of externalising behaviour may at least partially explain the apparently lower prevalence rates in females compared to males. Whilst physical and destructive aggression does appear to be more common in males, reports of relational

aggression (a socially mediated form of aggression, including actions such as threatening to end a friendship or socially excluding another; Crick and Gropeter, 1995) are typically higher in females (Card et al., 2008). Crick and Grotpeter (1995) found that relational aggression was almost nine times as common amongst girls than boys in a sample of five hundred elementary school children. Crick, Casas, & Mosher (1997) found that even in a group of pre-schoolers, teachers reports of aggression indicated that boys were more prone to overt aggression whereas girls were more likely to engage in relational aggression. Therefore, the difference in prevalence rates of externalising disorders, such as CD, may in part reflect a bias in the clinical criteria towards physical and destructive aggression, which are more common in males than females (Crick & Zahn-Waxler, 2003; Moffitt et al., 2008). This is reinforced by Crick and Zahn-Waxler (2003) who noted that without reports of relational aggression used in Crick and Grotpeter (1995), the study would have failed to identify 80% of female externalisers. Arguably, this bias may lead the research literature to have under-represented a set of externalising behaviours with its own set of risks and developmental antecedents. Relational aggression appears to be related to higher peer rejection and negative peer acceptance (Crick, 1996; Crick & Grotpeter, 1995), and to higher self-reported loneliness and depression scores (Crick & Grotpeter, 1995).

1.2.2. Developmental changes in externalising behaviour

As might be expected, the expression of externalising behaviours changes over childhood and adolescence. In 2004, Bongers, Koot, van der Ende and Verhulst investigated the prevalence rates over childhood and adolescence of 4 different types of externalising behaviour: aggression; oppositionality; property violations; and status violations (e.g. obscene language, truancy, or substance use). Both aggressive and oppositional behaviours decreased as participants got older, with males starting at higher values, but decreasing at a faster rate than females until they converged in adulthood. Property violations similarly decreased over childhood and adolescence. However, males and females did not converge, and males continued to show more property violations than females at 18 years of age. Finally, status violations decreased in the preadolescent years, but rose rapidly over adolescence. Similarly, studies by Baillargeon et al. (2007) and Tremblay et al. (2000) have both found that direct aggression decreases from childhood. In a large, longitudinal study of 1,161 boys by

Nagin and Tremblay (1999), they found that majority of children (approximately 95% of the sample) demonstrated a reduction in physical aggression between ages 6 and 15. They also identified a group (the remaining 5%) who demonstrated high physical aggression during childhood, which persisted throughout adolescence, who also demonstrated considerably higher reports of physical violence, theft, and juvenile infractions in later adolescences (17-18 years old). Côté, Vaillancourt, LeBlanc, Nagin, and Tremblay (2006) reported a similar decrease in physical aggression over childhood in a larger cohort (approximately 10,500 children), though their high persistent aggressing group was much larger (16.6% of the sample). However, a general decrease in physical aggression may not be the case for all types of physical aggression. Work by Loeber and Slot (2007) found that severe forms of physical aggression, such as homicide, sexual assault, or assault with a weapon increases over adolescence, peaking in mid-to-late adolescence.

1.2.3. Outcomes

Consistently, increased externalising behaviour has been associated with worse life outcomes (Bongers et al., 2004; Maughan et al., 2014; Nagin & Tremblay, 1999; Timmermans, van Lier, & Moot., 2008). Bongers, Koot, van der Ende, and Verhulst (2008) found that externalising behaviour in childhood and adolescence was predictive of greater social functioning impairment in later life, such as greater chance of educational expulsion, unemployment and substance use, with males reporting more severe impact than females in all areas except relationship problems. Furthermore, different types of externalising behaviours were associated with different outcomes. High levels of oppositional behaviours were associated with poorer relationship outcome and low achievement. By comparison, status violations (drug use, theft, and vandalism) were associated with poor academic attainment and substance abuse. By comparison, Timmermans, van Lier and Moot (2008) found that physical aggression and property violations both uniquely predicted later adult substance abuse and risky sexual behaviour. In contrast, status violations only predicted smoking and soft drug use, and oppositionality did not significantly predict either when other externalising behaviours were controlled for. However, in a study by Reef, Diamantopoulou, van Meurs, Verhulst, and van der Ende (2011), oppositional behaviours were found to be predictive of disruptive disorders and anxiety disorder in adulthood. Further, similarly

to Timmermans and colleagues' (2008) findings, status violations were associated with substance dependence, but also mood and anxiety disorders.

Individuals with externalising disorders in childhood and adolescence are at risk for significantly worse outcomes when compared against their typically developing counterparts. Odgers et al. (2008) found that the age of onset and the trajectory of CD predicted variations in outcomes. Those with a life course persistent trajectory (CD diagnosis in childhood that was persistent throughout adolescence) were at the most risk compared to those with consistently low antisocial behaviour, scoring worse on nearly all measures of academic, economic, violence, and mental and physical health measures. Maughan et al. (2014) found that these health risks can extend to over 50 years later, as participants with high levels of self-reported conduct problems at 13 to 15 years of age were at significantly higher risk for cardiovascular disease and cancer. In another study, alcohol abuse in adolescence was associated with high levels of criminal activity, substance abuse, and worse academic achievement and familial relationships at the age of 21 (Hill et al., 2000).

1.2.4. Comorbidity

Within the externalising disorders, comorbidity (co-occurrence of other disorders) appears to be the rule rather than the exception (Angold, Costello, & Erkanji, 1999). CD, for example, is often comorbid with another externalising disorder (e.g. ADHD or Substance Use Disorder) or internalising disorder (e.g. anxiety or depression; Angold, Costello, & Erkanji, 1999). CD comorbid with ADHD is a highly prevalent presentation, and the comorbidity of the two has been reported to represent between 42-93% of CD cases (Jensen, Martin, & Cantwell, 1997), though Nock et al. (2006) found that in 75% of comorbid cases individuals developed ADHD first, followed by CD. Furthermore, this comorbid group is thought to be more prone to reoffending than either non-comorbid CD or ADHD samples alone (Cohn et al., 2012), and demonstrates greater risk-taking behaviour under experimental conditions than either 'pure' CD or ADHD groups (Humphrey & Lees, 2011).

Though not as pervasive as comorbid CD+ADHD, CD comorbid with depression is common amongst both children and adolescents (Vander Stoep et al., 2012), with prevalence between 15-24% (Zoccolillo, 1992). Comorbid CD and Major

Depressive Disorder (MDD) can have a particularly poor prognosis in later life, increasing risk of suicide and suicidal ideation (Vander Stoep et al., 2011; Foley et al., 2006), severe and violent crime (Copeland et al., 2007) and adversely affecting academic performance (Marmorstein & Iacono, 2003). Comorbid CD+MDD has also been associated with higher scores for externalising behaviour and depressive symptoms than either disorder alone (Rockhill et al., 2009) and worse overall adjustment two years after diagnosis (Ingoldsby et al., 2006).

Similarly, comorbidity between substance use and internalising disorders is commonly seen (Chan, Dennis, & Funk, 2008; Couwenbergh et al., 2006), which may reflect the tendency of some anxious children or adolescent to self–medicate using illegal and/or addictive substances (Esposito-Smythers et al., 2008; Esposito-Smythers & Spirito, 2004; Robinson et al., 2011; though see Lembke, 2012, for a rebuttal). However, despite short-term anxiolytic effects of drug use (Battista, Stewart, & Ham, 2010), there is work to suggest that withdrawal can mimic anxiety (Fusar-Poli et al., 2009; Krystal et al., 2006), which may contribute to the persistence of chronic comorbid drug and anxiety problems. Furthermore, internalising difficulties significantly impact treatment effectiveness for substance use (King & McChargue, 2014; Rowe et al., 2004; Tomlinson, Brown, & Abrantes, 2004; however, see Godley et al., 2014 for an exception), although it is associated with favourable retention rates compared to substance use comorbid with externalising disorders (Flanzer, 2005).

There has been some debate regarding the consequences of comorbid CD with Anxiety. Specifically, questions have arisen as to whether each disorder mitigates the other, or instead leads to more a detrimental presentation (e.g. lower social functioning that is the product of both disorders; Ollendick, Seligman & Butcher, 1999). Sourander et al. (2007) found that 8 year-olds with comorbid conduct problems and anxious/withdrawal behaviours were more likely to have committed crimes between the ages of 16 and 25, and accounted for more of the crimes conducted amongst the sample. Similarly, Ensminger, Juon, and Fothergill (2002) found that males (but not females) who were rated highly on both aggressive behaviour and shyness in first grade were significantly more likely to be substance abusers at thirty-two than those who scored highly on neither, an effect not seen in those scoring highly on either scale alone. By comparison, Hofman et al. (2009) found a buffering effect of comorbid anxiety and

externalising behaviour, with comorbid individuals being less like to demonstrate alcohol and illicit substance abuse compared to pure-anxiety and pure-CD samples. However, in a more severe sample of incarcerated youths, Ollendick, Seligman, and Butcher (1999) did not find any differences between comorbid and non-comorbid CD groups in either the number or severity of criminal acts.

1.2.5. The Externalising Spectrum

Traditionally, the externalising behaviour has been divided into diagnostically discrete entities. However, there is increasing evidence to suggest that a single underlying construct contributes significantly to all externalising behaviour. Genetics studies investigating the transmission of a general externalising factor suggest that individuals inherit a liability towards non-specific externalising behaviour from their parents. Hicks et al. (2004) found the expression of externalising behaviours in twins was attributed to the heritability of a general liability, rather than disorder specific transmission from parents, and the heritability of this underlying factor appears to increase over time (Bergen, Gardner, & Kendler, 2007; Young et al., 2009). Furthermore, as noted already, co-occurrence of externalising behaviour is considerably higher than chance, with reported 50% comorbidity rates of substance abuse and disruptive behaviour disorders (Armstrong & Costello, 2002) and correlations between different externalising behaviours ranging from 0.3 and 0.7 (Kessler et al., 2005), suggesting that a general predisposition underlies much of the variability in specific forms of externalising behaviour.

Similarly, statistical models comparing categorical and continuous accounts of externalising behaviours have favoured a continuous model of externalising behaviour over a discreet disorders model. For example, Krueger et al. (2007) conducted a 3-wave iterative procedure for collecting questionnaire data related to various psychometric constructs (for example, construct domains included aggression, antisocial behaviour, impulsivity, and substance use, amongst others) associated with externalising behaviours, and then performed exploratory structural equation modelling on the responses. A model comparison approach indicated that a hierarchical model fitted the data best, with a single general externalising factor contributing to all measured behaviours, with two sub-factors; one related to inter-personal antisocial behaviour

(relational and destructive aggression, and empathy), and the other related to substance use (marijuana and drug use).

These findings have been further supported by confirmatory factor analysis. Both Cosgrove et al. (2011) and Lahey, Van Hulle, Singh, Waldman and Rathouz (2011) conducted confirmatory factor analysis investigating genetic and environmental influences on externalising and internalising behaviours in twin and non-twin participants, with similar results. Both studies found that a two-factor model with a broad externalising and a broad internalising factor explaining variance in genetic and non-shared environment was preferable, with little to no influence from shared environment. In addition to contribution of these broad externalising and internalising factors, each disorder was also associated with unique genetic and environmental variance. Furthermore, Cosgrove et al. (2011) identified a global factor explaining a significant proportion of the genetic variance for both externalising disorders and internalising disorders, suggesting the possibility of a general genetic predisposition to disorders that span the externalising/internalising spectrum.

Within the behavioural literature, this latent externalising factor has been directly associated with behavioural disinhibition. Young et al. (2009) found that a latent variable representing externalising behaviour ('EXT' factor) was significantly associated with response inhibition in a series of inhibition tasks at both age 12 and age 17. Both Bobova et al. (2009) and Finn, Gunn, and Gerst (2014) found that higher scores on the EXT factor lead to higher discounting rates in a delay discounting task, with no differences in discounting rates associated with any individual domain of the EXT factor alone (Bobova et al., 2009). Using psychometric measures, Taubitz, Pedersen, and Larson (2015) found that EXT was positively related with behavioural approach scores and negatively related to behavioural inhibition scores using Carver and White's (1994) BIS/BAS scales.

However, this is not to under-estimate differences between externalising behaviours. Burt (2009) found that there was a significantly greater genetic contribution to aggressive conduct disorder compared to non-aggressive conduct disorder in a meta-analysis of 103 twin and adoption studies, and Brendgen et al. (2005) found evidence to suggest that relational aggression is less heritable than physical aggression in young children. Similarly, Barker et al. (2011) found that aggression and theft, both

characteristics of Conduct Disorder, were associated with different personality profiles. Moreover, confirmatory statistical analysis run by Cosgrove et al. (2011) and Lahey et al. (2011) found that, whilst the genetic variance in externalising disorders was largely attributable to a global externalising factor, the effect of non-shared environment was unique to each disorder.

Therefore, current evidence suggests that genes may provide a general predisposition to externalising problems (and psychopathology in general; Lahey et al., 2011), but how the genes are expressed is determined in part by an individual's non-shared environment. However, little is known about what personality trait, or constellation of traits, this general underlying factor is linked to. Whilst it does appear to be associated with disinhibition (e.g. Finn, Gunn, & Gerst, 2014; Young et al., 2009), other recent behavioural studies suggest that it is related to a broader motivational imbalance and increased behavioural approach (Bobova et al., 2009; Endres, Donkin, & Finn, 2014; Gudiño, Nadeem, Kataoka, & Lau, 2012; Iacono, Malone, & McGue, 2008; Taubitz. Pedersen, & Larson, 2015). Motivational imbalance has long been considered a potential trait underlying externalising behaviour, and a substantial evidence base has built up to support it.

1.3. Motivational Imbalance

In 1987, Gray described a neuropsychologically-driven three-system model outlining septo-hippocampal system functioning in anxiety disorders (see *fig. 1.1*). According to Gray (1987) behavioural regulation was driven by three interacting motivational systems, each receptive to certain stimuli. The Behavioural Inhibition System (BIS) is responsible for inhibition of response and passive avoidance behaviour, and is sensitive to punishment and non-reward stimuli. Diametrically opposed, the Behavioural Activation System (BAS) is sensitive to reward stimuli, and is responsible

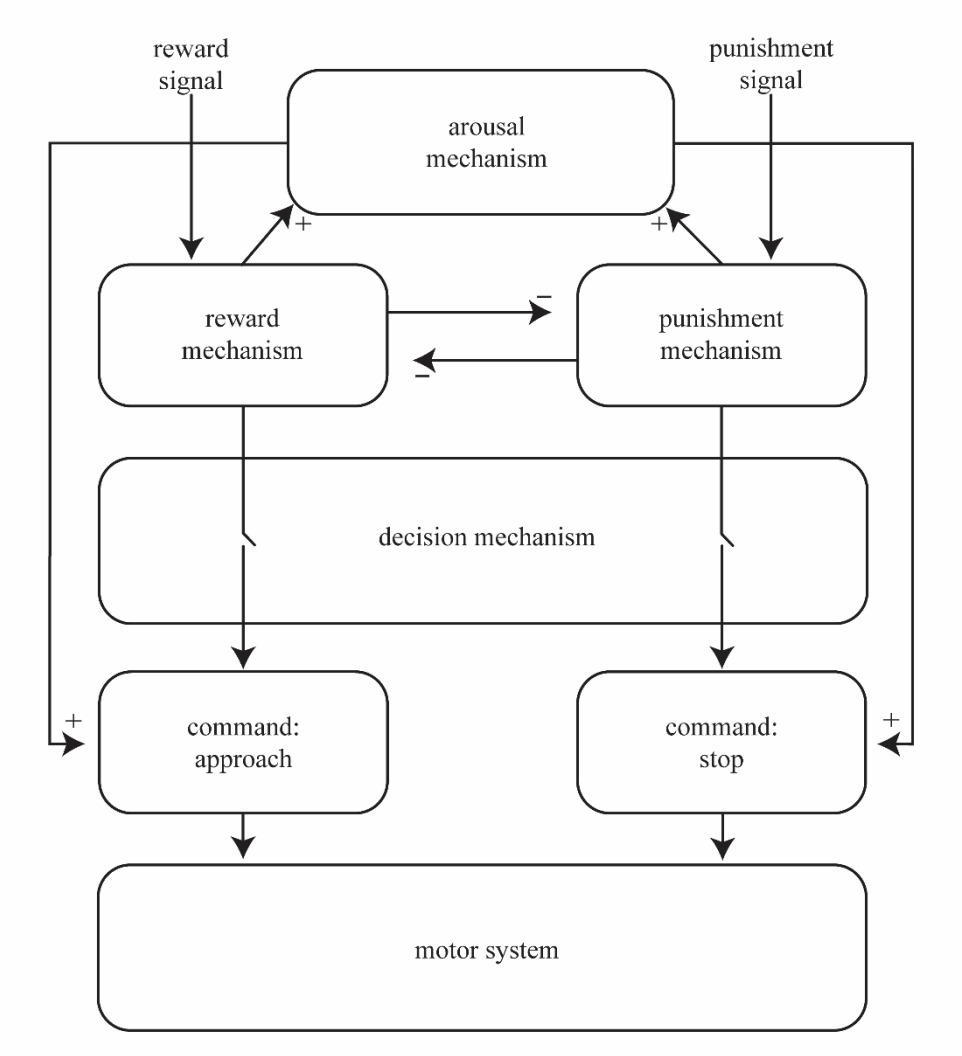

Figure 1.1. *The Gray and Smith model of conflict and discrimination learning. Reproduced from Gray (1987).*

for approach behaviour and active avoidance. These two systems are mutually inhibitory and compete to produce a behavioural response. Finally, the Fight or Flight system (F/F) is activated by nonspecific, unconditioned stimuli and is suppressed directly by the BIS, and indirectly by the BAS through consummatory mechanisms. He posited that anxiety is a product of imbalance between these motivational systems; greater BIS activation compared to BAS activation would lead to inhibited, punishment sensitive behavioural profiles typically seen in anxious samples.

Since the publication of Gray's (1987) model, two neurobiologically driven theories accounting for externalising behaviour, particularly psychopathy, have been proposed building on his framework. Quay (1993) suggested that externalising

behaviours result from an overactive BAS with a normal or underactive BIS. Greater activation of the BAS results in greater approach driven behaviour and increased salience of reward-related environmental cues. This dominant BAS activity overpowers inhibitory action from the BIS and leads to disinhibition and a relatively higher sensitivity to reward compared to punishment. A more recent model grounded in neuroendocrinology presents a similar idea. The Dual-Hormone Serotonergic model discussed in papers by van Honk and colleagues (Terburg, Morgan, & van Honk, 2010; Montoya, Terburg, Bos, & van Honk, 2012) suggests that an imbalance between testosterone and basal cortisol levels produces an imbalance between reward-driven approach behaviours and punishment-sensitive inhibitory behaviours mirroring that proposed by Quay (1993). Previous work has associated higher testosterone with increases in social approach behaviour (van Honk et al., 1999; van Honk et al., 2001) and heightened reward sensitivity (van Honk et al., 2004; Hermans et al., 2010), reflecting the BAS in Gray's (1987) model. Conversely, increased cortisol leads to increased social avoidance when presented with angry faces (van Honk et al., 1998), and is associated with increased punishment sensitivity. Moreover, the association between testosterone and aggression appears to be mediated by cortisol levels, with low levels of cortisol (leading to BAS dominance) predictive of increased aggression (Alink et al., 2008; Gordis, Granger, Susman, & Trickett, 2006; McBurnett, Lahey, Rathouz, & Loeber, 2000).

Newman and Wallace (1993) presented an alternative motivational theory. Instead of one system being dominant, in this account the behavioural approach and behaviour avoidance systems are equally sensitive to their respective stimuli. However, externalising behaviour arises due to a deficit in the integration of BIS and BAS. Specifically, the ability of the BIS to interrupt BAS activity in the middle of a dominant behaviour set is reduced. This deficit in response modulation leads to a poorer ability to fine-tune behaviour in response to incoming environmental information in externalising individuals. Furthermore, both the BIS and BAS innervate the Nonspecific Arousal System (NAS) when activated, which in turn sends outputs increasing behaviour in the already active motivational system. As the BIS is unable to interrupt the BAS, an incoming punishment stimulus does not act to inhibit BAS activity through BIS activation. Instead, the BIS activates the NAS, leading to increased activity in approach behaviours during a dominant behaviour set.

Whilst these theories propose imbalances hypothesised to exist in severe externalising populations, the behaviours the models describe or seek to explain are observable in a wide range of externalising groups, including normative samples that score highly on externalising measures. While these models describe neural and motivational processes thought to be involved in externalising behaviour, higher-level cognitive and affective traits, perhaps underpinned by differences in BIS-BAS activity, are also generally considered important. Key examples include disinhibition, reduced empathic ability, and reward dominance.

1.3.1. Disinhibition

Deficits in inhibition are one of the most commonly described features of externalising disorders and symptoms. Primarily, work investigating inhibition amongst externalisers has focused on ADHD samples, with limited work in other externalising disorders (Wright et al., 2014). Both Swann et al. (2009) and Belsky, Fearon, and Bell (2007) found that antisocial behaviour was associated with a higher number of commission errors on a modified continuous performance task, amongst adults and young children, respectively. Moreover, a meta-analysis conducted by Oosterlaan, Logan, and Seageant (1998) on ADHD, CD, comorbid ADHD+CD, and anxious children suggests that inhibition problems appear to be consistent across all forms of externalising behaviour. When examining stop inhibition tasks, they found that whilst externalisers differed significantly from control participants, AHDH, CD and comorbid groups did not differ from each other. Consistent with this, more recent work by Endres, Donkin, & Finn (2014) and Endres et al. (2011) found that externalising behaviour was associated with general disinhibition during a Go/No-Go task, which was further mediated by reduced working memory.

Furthermore, inhibitory ability appears to be predictive of future externalising behaviour. Eisenburg et al (2009) conducted a two-year longitudinal study on 185 children. Participants were measured on externalising and internalising behaviours, as well as inhibition, impulsivity, and emotionality. Those children who scored highly on externalising measures demonstrated poorer inhibition than their internalising and control counterparts. Moreover, inhibitory control, along with attention and anger, was predictive of later externalising stability. Children who improved demonstrated higher inhibition scores, whereas those who increased in externalising scores demonstrated

poorer inhibition. Similarly, Bridgett and Mayes (2011) found that the number of errors on the Stroop task at 7.5 years old predicted adolescent aggression scores at 14 years, and Tarter et al. (2003), using a composite measure of parent and teacher rating of disruptive behaviour, found that disinhibition at 10-12 years of age could predict substance abuse at 19 years.

Neuroimaging work investigating inhibition in externalising behaviour has been extensive. Rubia and colleagues (2008; 2009) have sought to separate out differences in neural activity associated with pure ADHD and pure CD in relation to inhibitory function. During inhibition tasks, both externalising groups demonstrate a shared hypoactivity in temporal and parietal regions that are generally associated with performance efficiency in controls (Rubia et al., 2009), but ADHD participants demonstrated reduced activity in structures related to inhibition, whereas hypoactivation in areas associated with performance monitoring was characteristic of those with CD (Rubia et al., 2008). Using EEG, smaller inhibition-related Event-Related Potentials (ERPs), such as the N2 and P3, have been found amongst externalisers compared to controls (Albrect et al., 2005; Johnstone, Barry, & Clarke, 2013; Kim & Jung, 2014; Liotti et al., 2007), and using time-frequency analysis, Kamarajan et al. (2004) found that alcoholics demonstrated reduced frontal theta and delta oscillatory band activity during No-Go trials compared to healthy controls, frequency bands thought to underlie ERPs associated with performance monitoring (Cavanagh, Cohen, & Allen, 2009) and inhibition (Başar-Eroglu et al., 1992).

Similar to work using behavioural measures of inhibition, evidence suggests that neural activation during inhibition tasks may act as a marker for future externalising. Both Mahmood et al. (2013) and Norman et al. (2011) found that adolescents who would go on to substance use in later adolescence demonstrated lower activity in inhibitory circuitry. Aharoni et al. (2013) found that neural response during a Go/No-Go task could predict future offending in a group of male offenders, with greater anterior cingulate cortex activation being associated with lower re-arrest rates.

More recent work suggests that there may be an emotional component to disinhibition amongst externalisers. Euler, Sterzer, and Stadler (2013) presented externalising and control participants with a colour-word Stroop task interspersed with either emotionally neutral or distressing images. They reasoned that in the absence of

callous-unemotional traits (a set of traits characterised by empathic blunting, callous use of others, and reduced guilt; Frick & White, 2008), externalising individuals may be hyper-responsive to emotional stimuli, and this will interfere with cognitive control. As they predicted, externalising individuals demonstrated no differences to control participants during the Stroop task with neutral pictures. However, when emotionally distressing imagers were used, externalisers demonstrated greater interference than controls. Similarly, using an EEG paradigm, Stieben et al (2007) found that the N2, a component commonly associated with inhibition, was smaller amongst externalising individuals than controls or those with externalising/internalising comorbidity during task blocks where self-reported anger and nervousness was higher.

1.3.2. Empathic blunting

It has long been argued that some of the behaviours observed in externalising samples, especially those related to interpersonal norm violations prevalent in those with CD and Antisocial Personality Disorder, may be due to deficits in empathy for others (Redl & Wineman, 1951; Blair, 2005). Affective empathy has been found to be negatively associated with relational aggression in both male and female adolescent groups (Endresen & Olweus, 2001; Jolliffe & Farrington, 2006). Carrasco, Barker, Tremblay, and Vitaro (2006) conducted a longitudinal study on a group of 868 boys over a five-year period from 13 years old to 17 years old, and found that those who measured highly in empathy were significantly less likely to have committed aggressive acts and acts of vandalism over the next four years compared against those who scored lower on empathy measures. Similarly, in a study of five hundred adolescents, Batanova and Loukis (2011) found that participants who scored highly on affective empathy were less likely to self-report overt aggression 1 year later.

In line with the neuroendocrinological interpretation of motivational imbalance proposed by Terburg, Morgan, and van Honk (2009) and Montoya et al. (2012), both testosterone and cortisol levels have been associated with disrupted empathic processing (Eisenegger, Haushofer, & Fehr, 2011; van Honk et al., 2011; Zilioli, Ponzi, Henry, & Maestripieri, 2014). Lower foetal testosterone has been linked with lower empathic quotient scores in males (Chapman et al., 2006), worse performance in mind reading tasks in children (Auyeung, Lombardo, & Baron-Cohen, 2013), and changes in grey matter volume in areas related to empathy and other social processes (Lombardo et al.,

2012). Hermans, Putman, and van Honk (2006) measured facial mimicry in a group of female participants after being given testosterone or a placebo. Participants who were given testosterone were significantly worse at facial mimicry than those who were given a placebo.

Structural neuroimaging studies of participants with more severe forms of externalising symptoms have found grey matter reductions in the amygdala and anterior insula, areas associated with empathy (Craig, 2009; Janak & Tye, 2015). Fairchild et al. (2011) investigated differences in the grey matter volumes of the amygdala associated with early-onset and adolescent-onset CD, and found that adolescent-onset CD participants demonstrated diminished grey matter volumes in the amygdala, bilaterally. By comparison, early-onset participants demonstrated a significant reduction in the right amygdala, and a trend towards smaller volumes in the left amygdala. Similar results were reported by Sterzer et al. (2007) in a smaller sample of adolescent males, who also noted reduction in anterior insula volume amongst externalisers. Furthermore, anterior insula volume was positively correlated with self-reported empathy. Expanding on these findings, Fairchild et al. (2013) investigated gender differences in empathy associated neural structures, and found that CD was associated with reduced bilateral amygdala grey matter volumes. Sex differences in the CD group were observed in the anterior insula, where CD females demonstrated smaller volumes compared to gender-matched, health controls, and CD males demonstrated larger volumes compared to gender-matched, healthy controls, though the authors note that this counterintuitive effect (larger anterior insula volumes in CD males) may be attributable to differences in where the reduction occurred (ventral vs. dorsal sites). Similarly, functional studies have found altered responsivity in externalising samples. Marsh et al. (2008) and Sterzer et al. (2005) both found reduced BOLD signal amongst CD participants in the anterior insula cortex and amygdala when viewing negatively-valenced images. Similarly, Lockwood et al. (2013) found that conduct problems were associated with reduced BOLD response in the bilateral anterior insula, anterior cingulate cortex, and the inferior frontal gyrus compared to typically developing controls when viewing images of other's pain (though opposite results were found by Decety et al., 2009, in a much smaller sample). Using EEG, Cheng, Hung, and Decety (2012) found that offenders demonstrated decreased empathic response to viewing others in pain as measured by the late positive potential.

However, reduced empathy is not characteristic of all externalising samples. In fact, groups externalising behaviour in the absence of high level of aggression do not appear to consistently be differentiated from normative controls. During their longitudinal study, Carrasco et al. (2006) found that empathy at 13 years old did not predict participant theft across adolescence, and Waller, Hyde, Grabell, Alves, and Olson (2015) found that empathy was not associated with oppositional defiant behaviours, but instead was selectively related to callous-unemotional traits. Nor do empathic difficulties associated with externalising problems show consistent effects across different emotions. Both behavioural (Eisenberg et al., 2001) and physiological (Wied, Gouden, & Matthys, 2005) work has suggested that externalising samples demonstrate reduced empathic responsivity to negatively-valenced emotions, but do not differ from controls when viewing positive emotions. Furthermore, other forms of empathy might not demonstrate the same relationship to externalising behaviour as affective empathy. For example, Caravita, Di Blasio, and Salmivalli (2009) found that high cognitive empathy (perspective taking) was positively associated with bullying behaviours in adolescent girls, and Batanova and Loukis (2011) found that self-reported relational aggression scores were higher amongst those with higher perspective taking abilities.

A key issue in understanding some of these apparent discrepancies may be the extent to which externalising individuals show high or low Callous-Unemotional (CU) traits, as lack of empathy for others is a characteristic component of this set of traits (Frick et al., 2003). Specifically, previous work has found that individuals with CU traits demonstrate diminished emotional empathy, reporting lower emotional induction from sad or fearful faces compared to both control groups and other externalisers (Jones et al., 2009; Pardini, Lochman & Frick, 2003; Schwenk et al., 2012) and a decreased ability to recognise facial and body cues of pain (Wolf & Centifanti, 2014). Similarly, in a review of the literature, Blair (2010) found that those with psychopathic traits were more likely to demonstrate altered amygdala and orbitofrontal cortex activity, and Lockwood et al. (2013) found unique blunting of anterior insula and anterior cingulate cortex response when viewing pain unique to callous-unemotional traits. Moreover, when controlling for participant conduct problems, Sebastian et al. (2012) found a negative relationship between CU traits and amygdala reactivity which did not exist when conduct problems were not accounted for. However, this characteristic blunting

effect appears to be limited to affective empathy, whilst cognitive empathy (Theory of Mind) appears to be relatively intact when compared to typically-developing controls (Jones, Happé, Gilbert, Burnett, & Viding, 2010).

1.3.3. Reward Dominance

Along with increased approach behaviours, excessive activation of the BAS relative to the BIS would also lead to an imbalance between reward and punishment sensitivity, known as reward dominance (Quay, 1993). Whilst originally considered to be driven by increases in sensitivity to reward stimuli (e.g. Quay, 1993), reward dominance could also exist through lower levels of punishment sensitivity, which in theory would create a similar level of imbalance.

Variants of Siegel's (1978) Card Playing task have frequently been used to test the hypothesis of an imbalance between reward and punishment sensitivity in relation to externalising behaviour. In this task, participants draw cards for either reward or punishment with the chance of punishment increasing the longer the game is played. Newman, Patterson, and Kosson (1987) argued that perseverative behaviour of drawing cards past the point where punishment outweighs reward is indicative of greater reward-driven behaviour and reduced sensitivity to punishment. In agreement with Newman and colleagues' proposition, both high externalising normative samples (Belmore & Quinsey, 1994; Seguin et al., 2002) and CD samples (Daugherty & Quay, 1991; O'Brien & Frick, 1996) play a greater number of cards than low externalising controls, despite the increasing chance of punishment. Other behavioural measures also demonstrate support for increased reward sensitivity (relative to punishment sensitivity) in externalisers. Studies using the Iowa Gambling Task have found that samples with high psychopathic traits (Blair, Colledge, & Mitchell, 2001), pathological gambling addiction (Cavedini et al., 2002), and Disruptive Behaviour Disorders (Ernst et al., 2003) choose more cards from high reward/high punishment decks compared to low reward/low punishment decks, even though they result in a net-loss. Over several task blocks, control groups demonstrated learning, increasing the number of cards selected from advantageous decks over time, while externalising groups did not demonstrate such feedback-based learning. Furthermore, performance on perseveration tasks may help identify different externalising groups. Van Goozen et al. (2004) tested ODD, ADHD and typically developing adolescents on a series of behavioural tasks, including

measures of inhibition and reward sensitivity (Stroop Colour-Word Test and Door Opening Task, respectively). ADHD and ODD participants did not differ in performance in the inhibition task, but there were significant differences in the Door Opening Task (a variant of the Card Playing Task), and performance on the Door Opening Task was the best predictor group assignment (ODD, ADHD, or control groups), suggesting that reward sensitivity may act as a marker specific to delinquent externalising behaviour as opposed to kinetic or inattentive externalising.

More recently, the Risky Choice Task (RCT) has been used to test reward sensitivity amongst externalising populations by investigating gambling behaviour following feedback. Fairchild et al. (2009) used the RCT to investigate differences in risk-taking and reward sensitivity behaviour amongst those with early-onset conduct disorder, adolescent-onset conduct disorder, and healthy controls. They found that the early-onset conduct disorder participants demonstrated greater reward seeking behaviour than either the adolescent-onset or healthy control groups following small gains than either other group, whereas they were no different to other groups following either large gains or either level of punishment, suggesting a lower threshold needed to encourage further reward seeking behaviours after approach tendencies are activated. Similarly, Syngelaki, Moore, Savage, Fairchild, and van Goozen (2009) found that young offenders gambled more following a small win or a small lose than the healthy controls using the RCT, but did not differ in other indicators of global executive function, suggesting deficits restricted to motivational processes. However, Hartung, Milich, Lynam, and Martin (2002) found that boys, but not girls, with CD demonstrated higher numbers of errors during a Go/No-Go task during a mixed feedback contingency condition (including both reward and punishment) compared to when only a punishment contingency was used, suggesting a further impact of rewarding stimuli on inhibitory functions.

Physiological work has also demonstrated aberrant feedback processing amongst those who score high in externalising measures, though the results are less clear. Low physiological response to fear stimuli may reflect altered functioning of the amygdala (Fanselow & Gale, 2003), which in turn may lead to deficits in punishment sensitivity (Hahn et al., 2010), impacting learning contingencies based on fear response and punishment processing. Consistent with that, those who score highly on externalising

measures demonstrate lower physiological responses than their typically developing counterparts on measures of SCR/EDS/startle reflex (Beauchaine, Katkin, Strassberg, & Snarr, 2001; Gao, Raine, Venables, Dawson, & Mednick, 2010; Herpertz et al., 2005; Vaidyanathan, Hall, Patrick, & Bernat, 2011). Fairchild, van Goozen, Stollery, and Goodyer (2008) found that CD participants (both early and adolescent onset groups) demonstrated impaired differential fear conditioning and attenuated startle reflex to acoustic probes during an affective picture task. In a more recent study, Syngelaki, Fairchild, Moore, Savage, & van Goozen (2013) found that conduct problems were associated with lower startle responses than healthy controls in general, and were significantly related to startle response during fearful slides even when controlling for psychopathic traits.

Similarly, cortisol level is also thought to index punishment sensitivity, given its association with the hypothalamic-pituitary-adrenal axis, a vital part of the body's stress response (Chrousos & Gold, 1992). In line with this, low basal cortisol levels have been associated with increased externalising and reward seeking behaviour in adults (van Honk, Schutter, Hermans, & Putman, 2003). Moreover, blunted cortisol reactivity to punishment has been observed in externalising participants (Snoek, van Goozen, Matthys, Buitelaar, & van Engeland, 2004). Saliva alpha amylase (sAA), a protein exuded from the salivary glands, is a non-invasive measure of sympathetic nervous system activity, and increases during periods of stress (Granger, Kivlighan, El-Sheikh, Gordis, & Stroud, 2007). Susman et al. (2010) found that sAA hypoactivity was associated with aggression and general antisocial behaviours in pre-adolescent boys, but not girls, and Spinrad et al. (2009) found that sAA reactivity was negatively associated with dispositional anger in preschool girls, but not boys. Hormonal support for the imbalance between approach and avoidance systems has been seen in studies investigating the relationship between cortisol, and testosterone, which is associated with increases in reward driven approach behaviours. For example, Portnoy et al. (2015) found that cortisol response to stress predicted rule breaking and aggressive behaviours amongst adolescent males, but only amongst males with low 2nd finger to 4th finger (index to ring finger) length ratios, thought to be an indicator of high levels of prenatal testosterone (Turanovic, Pratt, & Piquero, 2017).

An alternative physiological measure, the heart pre-ejection period (PEP), has been argued to measure reward sensitivity due to its modulation by the sympathetic nervous system (Beauchaine, et al., 2001). However, contrary to expectations, several studies have reported that children and adolescents high in externalising behaviour demonstrate reduced PEP responsivity following reward, suggestive of lower sympathetic nervous system innervation following reward stimuli (Beauchaine et al., 2001; Beauchaine, Hong, & Marsh, 2008; Crowell, Beauchaine, Gatzke-Kopp, Sylvers, & Mead, 2006). Overall, physiological work points towards a general hyporesponsivity in individuals prone to externalising behaviour, but, perhaps arguing against a reward dominance account, they demonstrate lower physiological reactivity to both punishment and reward.

The majority of neuroimaging work investigating associations between reward sensitivity and externalising behaviour has used fMRI. Finger et al. (2011) used a passive avoidance task to test differences in feedback sensitivity amongst 15 CD boys compared against 15 typically developing adolescents. By comparison to the normative adolescents, those with CD demonstrated reduced activation in the orbitofrontal cortex in response to reward and the parahippocampal gyrus when presented with punishments, areas associated with reward expectancy and punishment sensitivity, respectively. Similar findings were reported by Völlm et al. (2007) in a small group of participants with antisocial and personality disorders, and by Rubia et al. (2009) in a sample of participants with CD who were not comorbid for any other disorder. In contrast, Bjork et al. (2010) did not find reduced activity in the OFC amongst externalising adolescents, but instead found externalisers demonstrated increased ventral striatum activation after reward compared to the typically developing counterparts, and White et al. (2013) found reduced caudate response to reward stimuli and increased caudate activation to punishment amongst those with disruptive behaviour disorders compared to normative adolescents. Furthermore, Cohn et al. (2014) investigated whether persistence of externalising behaviour over the early adolescent period (approximately 10 to 14 years) was associated with altered activity in reward circuitry. Participants who persisted in externalising behaviour over time demonstrated reduced ventral striatum activation following reward feedback, and increased activation of the amygdala following punishment, when compared against both the desisting group and the healthy controls. In contrast, Castellanos-Ryan et al.

(2014) found no unique relationship between either ADHD or CD participant neural activity and reward, instead finding deficits in reward processing amongst those reporting substance misuse. However, this was only during reward anticipation, and not receipt of reward, and thus may reflect problems with reinforcement learning or reward prediction instead of reward sensitivity.

Alternative to fMRI, a small number of recent studies have used EEG to test reward responsivity in externalisers. Gao et al. (2016) compared adolescents with CD against healthy controls in a simple outcome gambling task where outcome was random, with win and loss occurring half the time. They found that CD participants demonstrated significantly lower P2 amplitudes to punishment feedback than their typically developing counterparts, and that their N2 response did not differentiate between rewards and punishment, unlike in the healthy controls. Given the role of the N2 in stimulus evaluation (Patel & Azzam, 2005), and the P2s role in processing the motivational value of stimuli (Riis et al., 2009), these may reflect deficits in distinguishing outcomes in feedback tasks, and lower valuations attributed to punishment upon receipt. However, it is important to note that in both studies externalising participants also demonstrated general reductions in the N1 and P3, which are thought to be attentional in nature (Röder et al., 1999; Polich, 2007), and therefore these findings may reflect poorer attention in the externalising group. Salim, van der Veen, van Dongen, and Franken (2015) identified a high psychopathy (top 5%) and low psychopathy (bottom 5%) group of students and had them complete a Passive Gambling Task. High psychopathy participants demonstrated significant larger P2 for predicted, but not unpredicted stimuli, and smaller P3b peaks in general, suggesting that there were no significant differences in the processing of valence associated with psychopathic traits.

A further factor worth considering is temporal discounting, as this may reflect increase strength of reward circuitry relative to normative adolescence through greater behavioural approach. Currently, whilst other externalising groups such as those with ADHD (Demurie, Roeyers, Baeyens, & Sonuga-Barke, 2012; Scheres, Lee, & Sumiya, 2008) and substance abusers (MacKillop et al., 2012) demonstrate increased discounting compared to healthy controls, and the severity of discounting can be used to predict treatment responsivity (Stanger et al., 2012), little work has been done related to

conduct problems. Petry (2002) sought to investigate how antisocial personality disorder influenced behavioural choices in adults with substances abusers, and found that individuals with both substance use and antisocial personality disorder discounted rewards at a much higher rate than both those with substance use disorder alone and healthy controls. In a more recent study focused on adolescents with CD, White et al. (2014) found that participants with CD demonstrated greater temporal discounting than age matched healthy controls, even when controlling for both IQ and psychopathic traits. Moreover, this effect is not solely limited to temporal discounting of reward, but also social discounting. Sharp et al. (2011) asked a sample of adolescents to write a list of people in order of how socially close they felt to them. They then provided participants with a series of hypothetical choices between keeping a sum of money offered to themselves, or sharing with someone from their list. They found that adolescent boys who scored highly in self- and parent-reports of externalising behaviour demonstrated greater social discounting, being much less willing to share money with participants they felt less socially close to. However, it is important to consider that this may not be purely related to reward sensitivity. Sonuga-Barke (2014) suggests that this may be due to psychosocial factors instead of reward seeking and impulsivity. High levels of home chaos are seen amongst those with externalising problems (Dumas et al., 2005), increased levels of social rejection (Rudolph et al., 2014), parent-child hostility (Richmond & Stocker, 2006), as well as lower levels of family cohesion (McKelvey, Conners-Burrow, Mesman, Pemberton, & Casey, 2015; Richmond & Stocker, 2006) when compared to typically developing children and adolescents. This may then limit the amount CD children are willing to "gamble" on potentially receiving a reward in the future, as well as limiting the social circle with which they are willing to share any rewards they receive as they may not feel there is a high likelihood of return on their investment. Therefore, these increased levels of discounting seen amongst externalising samples may reflect the lack of reliability and certainty of social circumstances in their lives, as opposed to aberrant motivational processes.

In a recent review of the literature, Byrd, Loeber, and Pardini (2014) observed that whilst the relationship between externalising and punishment sensitivity appears consistent, with antisocial youths demonstrating blunted responses in the face of punishment, results related to reward responsivity are less clear. They note that whilst the behavioural literature indicates a primarily reward driven behavioural pattern

characteristic of approach, it can also be explained by a lack of punishment related learning due to lowered punishment sensitivity, as highlighted by research in the behavioural and physiological domain. Thus, the lack of punishment sensitivity may lead to poor association between action and outcome in experimental paradigms (leading to reward dominance), but also in everyday circumstances, reinforcing reward behaviours (both pro- and antisocial), but failing to make association between their antisocial actions and received punishments. However, learning is comprised of several stages, and the authors note the importance of future work in identifying whether deficits exist in the encoding of feedback stimuli, the associative paring of stimulus and outcome, or the extinction of already existing pairings.

Overall, findings across several areas reinforce the hypothesis of deficits in feedback processing, with externalising samples demonstrating differential activity in outcome processing under several task conditions. Despite general differences between externalising and non-externalising samples, and the consistent reduction of punishment sensitivity in antisocial youths, reward responsivity findings remain largely heterogeneous, with different results obtained depending on whether a behavioural, physiological, or neurological response was measured, and the composition of the sample studied.

Some of the heterogeneity in findings are likely to be reflective of the variance of tasks used across studies. Even within domains, disparate tasks are used to evoke reward responsive behaviour or neural activity. Whilst each task has its advantages, potential confounds arising from task choice are not always considered in the experimental discussions, yet may impact the interpretation of results. Across the broad range of the early behavioural literature, variants of the Card Playing Task (Siegel, 1978) are used to measure reward seeking behaviour; its interpretation is dependent on the assumption that perseveration is a proxy for increased reward sensitivity. However, the task design obfuscates the underlying mechanism, making it difficult to differentiate between perseveration as a result of increased reward sensitivity, decreased punishment sensitivity, poor inhibitory control, or deficits in behavioural shifting. All could be indicative of motivational imbalance, but not all give us a clear understanding of externalising behaviours associated with feedback sensitivity.

The inclusion of probability in both the Risky Choice Task (RCT) and the Passive Avoidance Task (PAT) makes it difficult to draw conclusions regarding altered feedback sensitivity in relation to externalising, as both investigate feedback processing as a function of probability. In the RCT, choice is represented as an expected value, a valuation of feedback stimulus based on the valence of the feedback, the magnitude of the feedback, and the likelihood of the feedback. Therefore, feedback processing activity related to the outcome may encode additional information related to task choice. Similarly, the PAT has only been used to measure prediction error amongst externalisers, as opposed to feedback sensitivity in general. As prediction error generation depends on both the internal representation of probability of outcome and the interpretation of current feedback, and is then used to update the current prediction model, it may be difficult to understand feedback sensitivity, especially when using neuroimaging methodologies with low temporal resolution.

The rewarded Continuous Performance Task (CPT; Rubia et al., 2009) and the Target Selection Task (TST; Völlm et al., 2007) both provide feedback independent of probability, and do not alter participant expectation between action and outcome. However, both tasks included a rewarded performance element, where participants received positive or negative feedback related to their ability to respond quickly to a specified cue. As the brain uses both endogenous and exogenous markers of performance, imaging methodologies (such as those used in both Rubia and colleagues, and Völlm and colleague's studies) with low temporal resolution may not be able to differentiate between these markers. Moreover, neither task compared differently valenced feedback against each other, instead choosing to compare valenced feedback against non-valence feedback. Without the comparison of both positively- and negatively-valenced feedback, we cannot be sure that these tasks did not evoke an altered feedback sensitivity autonomous from the valence of the feedback cue.

By comparison, the Monetary Incentive Delay (MID) task used by Bjork et al. (2010) and Cohn et al. (2014) has numerous advantages. Whilst feedback differs in both magnitude and valence, the task design allows either to be analysed separately. Furthermore, the task includes both positively- and negatively-valenced feedback cues, as well as including a non-feedback trial type (outcome resulted in neither net gain or loss). One potential confound of the MID tasks is the inclusion of a delay period prior to

the presentation of the feedback cue. This may influence externalising group differences if there are differences in participant anticipatory or attentional mechanisms the pre-stimulus period before receipt of feedback.

Thus, whilst the literature appears relatively consistent in demonstrating disparity between high and low externalising samples' response to feedback, the large variance in task selection prevent us from drawing strong conclusions regarding feedback valence sensitivity in externalising groups. In the future, a greater consistency across studies may aid in determining how these groups diverge in their response to feedback cues. Moreover, a more robust understanding of feedback processing mechanisms may be gained by designing tasks that evoke activity associated with individually segregated processes in the feedback processing stream. To better understand how feedback valence is processed, simple gambling tasks implemented by studies such as Gao et al. (2016) or Salim et al. (2015) are useful as neural activity associated with performance, learning, and non-valence related feedback characteristics are minimised.

Across the literature and regardless of the methodology favoured, punishment sensitivity appears to be decreased amongst externalising samples, but findings related to reward sensitivity appear inconsistent. However, key questions remain unanswered. We are still unsure about what part of reward processing is impacted, and research is unclear whether it is attentional, motivational, or learning signals that demonstrate deficits in those with externalising problems. Secondly, little imaging work has been done to investigate feedback responsivity both in social contexts. Given the negative influence that peer presence can have on adolescent risk-taking (Albert, Chein, & Steinberg, 2013), investigating how peer presence influences approach-related motivational circuits may further advance our understanding of externalising behaviours in real-life situations.

1.3.4. Conclusion

Overall, the current literature appears to support the idea that externalising behaviour is linked to motivational imbalance. However, whilst there is some consistency in the literature regarding the broad domains of neurocognitive function deemed important, studies often measure only one of several plausible, and probably

correlated, candidates, thereby hampering efforts to identify distinct mechanisms or pathways. This is particularly relevant to the reward/punishment sensitivity literature where most work is conducted using the BIS/BAS scale questionnaire, and Seigel's (1978) Card Playing Task in behavioural research. Given the BAS component of the BIS/BAS scale designed by Carver and White (1994) to measure trait BIS/BAS activity is made up of three factors (drive, fun seeking, and reward responsiveness), it is highly notable that the scale is rarely broken down during analysis. Therefore, how observed findings are attributable to changes in reward sensitivity per se is usually ambiguous.

As it stands, current neuroimaging studies have demonstrated some differences in the activation of several neural structures amongst individuals prone to externalising behaviour. Nevertheless, the findings are remarkably mixed, and are complicated by differing methodologies and different sampling strategies and definitions (CU traits, externalising dimensions, diagnoses). These studies have also primarily deployed fMRI as the method for investigating differences. Whilst these studies are important in elucidating changes in activation patterns associated with risk for antisocial behaviour, the low temporal resolution prevents us from easily separating rapidly occurring and interlinked processes involved in interpreting feedback cues, such as attention, motivation, and encoding.

Despite the potential value of Electroencephalography (EEG) for indexing reward signal processing and inhibitory activity, research using this approach in relation to externalising behaviours is limited. EEG is a potential powerful methodology in that context as EEG components associated with these processes are already well established, and recent advances in methods for analysing oscillatory activity allow for more sophisticated analysis of neural signals. Therefore, EEG research could make a valuable contribution to our understanding of the neural mechanisms associated with reward processing in externalisers. In the following sections, two EEG techniques (Event-Related Potentials and Event-Related Spectral Perturbations) are reviewed in detail, as they form the basis for the research approach taken in this thesis. Together, these two techniques cover analysis in both the time and frequency domains, allowing for a broad understanding of how differences in delinquent behaviour elicit changes in neural mechanism associated with the processing of feedback cues.

1.4. Electroencephalogram

Electroencephalogram (EEG) was first reported by Hans Berger in 1929 during his search for a tool to investigate psychic energy in humans (Millet, 2001). In this seminal paper, Berger reported voltage fluctuations from two electrodes placed on the human scalp using a double-coil galvanometer. The activity that he reported, two different frequencies of oscillations around 10Hz and 20Hz, were named alpha (also known as the "Berger Wave") and beta activity, which he proposed reflected cognitive and cortical metabolic processes, respectively. Whilst initially met with scepticism, reproduction of his work by Adrian and Matthews (1934) lead to greater acceptance of the technique. Since then, three more oscillatory bands commonly associated with the cognitive domain have been identified: delta (1-4Hz; Walter, 1936); theta (4-8Hz; Jung & Kornmüller, 1938); and gamma (30-100Hz; Stumpf, 1965). Over the last 86 years, advances in computing and mathematics have provided a wealth of techniques for the application and analysis of EEG.

1.4.1. Electrophysiology

EEG measures the difference in scalp-recorded electrical activity between one electrode site and a reference electrode over time. However, the activity recorded at an electrode reflects the spatial summation of innumerable electrical events occurring both near and far from the electrode site. All types of electrical activity in, and occasionally outside of, the brain contribute to the ongoing EEG activity – including rapid action potentials and calcium ion (Ca^{2+}) spikes (Buzsáki, Anastassiou, & Koch, 2012). However, EEG activity primarily captures the summed excitatory and inhibitory postsynaptic potentials of Pyramidal cells (Cohen, 2014; Luck, 2014). Moreover, the signal measured at the scalp is mostly composed of activity from 10,000-50,000 superficial cortical neurones (Murakami & Okada, 2006), with less contribution from deep brain structures.

The activity measured at the scalp is brought about as neurotransmitters bind to postsynaptic receptors, which causes an influx of ions into the neurone, creating a small dipole in the cell. However, EEG sensors are not sensitive enough to register the dipole of a single cell. Instead, a more visible signal is generated when a large number of similarly aligned neurons depolarise simultaneously. The activity of unaligned neurons will cancel each other out (with respect to scalp voltage), and lack of synchrony reduces

the strength of what is known as the equivalent current dipole – an aggregate measure of all individual dipoles.

Expressed on the scalp, an individual source (a patch of aligned neurons firing in synchrony) will be positive on one side and negative on the other, with a zero line separating the two (*fig. 1.2*). The fact that it is possible to measure the activity of these individual sources at the scalp level is a result of volume conduction – the transmission of an electrical charge across conducting media, which includes both white and grey matter, cerebrospinal fluid (CSF), the skull, and the scalp (Makeig & Onton, 2011). However, whilst this allows us to non-invasively measure neural activity, boundaries where a difference in the electrical conductivity of two media exists distorts the propagation pattern, leading to a widespread projection of dipole source activity on to the scalp.

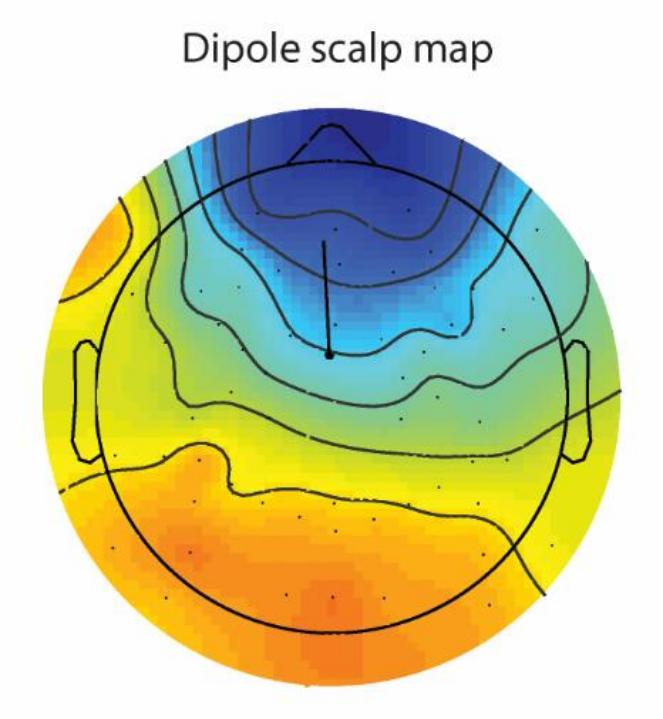

Figure 1.2. *Scalp map of a dipole demonstrating the dipole moment (indicated by a black line) and the positive and negative poles (indicated by blue and orange areas, respectively).*

1.4.2. The advantages of EEG

Arguably, the most fundamental advantage of EEG is its high temporal resolution. Both EEG and Magnetoencephalography (MEG) allow the observation of electrical activity in the brain, measuring electrical or magnetic fields, respectively. Thus, they measure neural activity on the time scale at which it occurs, with modern EEG systems being able to take readings once every millisecond (though sampling once every 2-4 milliseconds is more common). Cognitive processes can occur and end within a few hundred milliseconds, which haemodynamic methods (e.g. PET or fMRI), that are somewhere between 2 and 3 orders of magnitude slower, may miss (Cohen, 2014). This is more critical when researching sensory rather than cognitive activity, where early neural activity can occur as rapidly as 10ms after presentation (e.g. Musacchia, Sams, Nicol, & Kraus, 2006), but remains useful for cognitive research as it can be used for investigating functionally separate, but temporally contiguous, neural processes.

Furthermore, EEG has a well-developed collection of techniques available to answer a broad range of questions directly related to neural activity. Multi-site recorded EEG data is multi-dimensional, encompasses information in the space, time, frequency, power, and phase domains, and thus, using the appropriate techniques, we can examine information in one domain or several.

Aside from these functional advantages, there are some practical advantages to EEG as well. EEG systems take up less space than MEG or MRI and, though it can be advantageous, it does not require shielding. Moreover, portable EEG systems exist, allowing for EEG recordings to be taken at a participant's home. As EEG is non-invasive and quick to set up, it is useful in developmental and clinical populations where attention may be limited, and does not require the participant to lie in an enclosed space (as in MRI), which some find aversive. Moreover, EEG is less sensitive to participant movement than fMRI and MEG, where head movements can impair localisation, demanding less proprioception of individuals during tasks. The recording process itself is silent, which is ideal for the presentation of audio stimuli or for participants who are easily distracted or prone to inattention or anxiety. Finally, as no magnetic fields or radioactive isotopes are used, there are fewer physical limitations that could lead to participant exclusion.

1.4.3. The disadvantages of EEG

Whilst EEG has its advantages, all neuroimaging techniques should be considered in light of their disadvantages. Perhaps the most recognised limitation of EEG is its poor spatial resolution. Due to volume conduction, and the distortion of propagation patterns across the boundaries of conductive media, we cannot infer the location of activating sources from the recorded scalp distribution. We can project the summation of a known number of intracerebral sources onto the scalp with an accurate model of volume conduction; this is known as the Forward Problem (Hallez et al., 2007). However, doing the reverse (inferring brain sources from scalp activity) is an ill-posed problem with a high number of possible solutions and is sensitive to fluctuations in noise; this is known as the Inverse Problem (Grech et al., 2008). Instead, activation patterns are often defined with broad generalisations to areas on the scalp (e.g. parietal midline activation or right frontal asymmetry). However, source localisation techniques are becoming more common in EEG research with promising results (see Grech et al., 2008, for a review), though they depend on accurate head models (Cuffin, 1996).

Null results are particularly troublesome in EEG research. Whilst null findings may reflect an absence of effect between two or more conditions or a lack of statistical power to correctly detect a difference, with EEG, we cannot be certain that non-significant effects are not due to the spatial layout of neural structures responding to experimental stimuli (Otten & Rugg, 2005). If the arrangement of the activating neurones gives rise to a closed field (where there is minimal spatial separation between the positive and negative poles of the dipole) rather than an open field (substantial separation between the two poles), then the activity will cancel out before it is captured by scalp electrodes. Similarly, activity generated across opposing sides of a sulcus will also cancel out.

Another important limitation of EEG is its relative inability to measure activity from deep brain structures compared to other neuroimaging techniques. This is due to two reasons. Firstly, the voltage amplitude of a dipole source measured at the scalp is the inverse square of the distance between the electrode and the source (Buzsáki, Anatassiou, & Koch, 2012). Secondly, the EEG signal is dominated by large patches of similarly aligned neurones. In deep brain structures, neurones demonstrate less alignment resulting in reducing the power of patches of cells. Moreover, cells in deep

brain structures are more likely to generate a closed field, where the source (or sink[1]) are spatially close to the return current of the dipole. This is due to the spherical symmetry of the cells, as the dendritic branches extend in an approximately uniform pattern around the cell body. This results in deep brain structures contributing smaller amounts of activity to the summed scalp potential (Cohen, 2014). While it is not impossible to measure activity from deep brain structures using EEG (see Stone et al., 2009), the number of trials needed for reliable ERP measurement is greater than that needed to measure cortical ERPs.

1.4.4. Event-Related Potentials

Over the past 50 years, the analysis of Event-Related Potentials (ERPs) has become the most ubiquitous method of investigating neural activity in response to stimulus presentation (Bastiaansen, Mazaheri, & Jensen, 2011). ERPs are a series of positive and negative peaks in the waveform that differ in several characteristics (polarity, latency, and duration) that occur in relation to stimulus presentation, and are typically named as such; the N170 and P300 reflecting a negative peak occurring at 170ms and a positive peak occurring at 300ms in the waveform, respectively (*fig. 1.3*). Whilst some ERPs are visible in the raw EEG data, such as the first ERP observed by Davis (1939), most ERPs reflect relatively small changes in the scalp activity that are dominated by ongoing neural activity, as well as biological and non-biological noise. Instead, ERP analysis typically works on the principle that over a large enough number of data trials, task independent fluctuation in EEG activity will average to zero, leaving only task-dependent information (Makeig et al., 2002).

Currently, the processes involved in generating ERPs are not well understood, and three theoretical mechanisms have been identified (Cohen, 2014). The first is the signal plus noise (SPN; also known as the additive power model) model – ERPs reflect distinct fixed-latency activations (occurring at approximately the same time following stimulus) that are independent of current ongoing oscillatory activity, but add to it (Jervis, Nichols, Johnson, Allen, & Huson, 1983). Over a large enough number of trials, task-independent ongoing EEG averages to zero, whereas the task-dependent activity superimposed on top of it remains. Thus, one of the assumptions of this model is that

[1] Sources and sinks refer to the location on a neuronal membrane where the positive charge flows out of or in to the neurone, respectively.

the ERP activity is completely independent from the ongoing EEG activity. Early work by Jasiukaitis and Hakerem (1988) has found that pre-stimulus alpha activity was predictive of post-stimulus ERPs, suggesting that ERPs are not entirely independent of the ongoing EEG activity. More recently, Min et al. (2007) demonstrated that the amplitude of early visual ERPs was affected by the alpha activity occurring prior to stimulus presentation. However, they discuss the possibility that pre-stimulus alpha activity is indicative of readiness for coming stimuli and therefore plays a functional role in neural processing. Therefore, whilst the SPN model may not completely explain ERP generation, their results suggest it may be partially responsible for it.

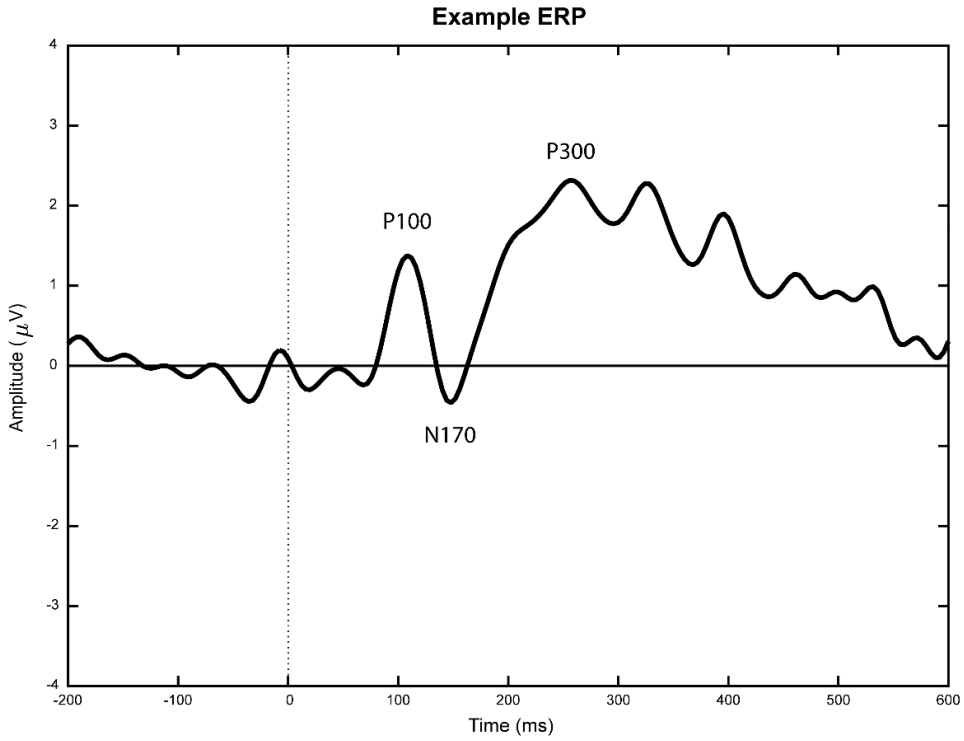

***Figure 1.3**. An example ERP waveform demonstrating positive and negative going peaks and their associated names.*

An alternative model is the Phase Resetting Model of ERP generation (Makeig et al., 2002). Instead of being independent events that add peaks to the ongoing oscillatory activity, ERPs are generated when the ongoing EEG activity resets in phase, the alignment of several frequency peaks leading to ERPs in the waveform. A few studies have demonstrated increases in phase locked oscillatory activity synchronous with ERP generation (Makeig et al., 2002; Klimesch et al., 2004). However, a few

assumptions implied by this model do not seem to hold true. Firstly, if phase resetting occurs, then the standard deviation of all frequency bands must drop simultaneously to zero just prior to the ERP, indicating complete phase organisation. However, when investigating the oscillatory activity underlying ERPs, Mäkinen, Tiitinen, and May (2005) found that the standard deviation in any oscillatory band's power does not change over the course of a trial. Secondly, the phase-locking factor, a measure of oscillatory phase alignment, should increase during phase resetting. However, a similar increase in phase-locking factor would also be seen if the ERP has a fixed latency and polarity across trials, regardless of whether it was generated through signal-plus-noise or phase-resetting. Finally, Shah et al. (2004) highlights that the strictest interpretation of the phase-resetting model requires there to be no increase in power of the ERP's dominant frequency, as an increase in power in any frequency band would reflect an evoked potential added to the ongoing activity (regardless of whether it is reset or not), in line with the signal–plus noise model. However, they found an increase in dominant frequency power as well as an increase in phase concentration around the ERP, suggesting that phase-resetting alone cannot explain ERPs.

Finally, there is some suggestion that some slow-wave ERPs may be due to differences in the modulation of peaks and troughs of ongoing oscillatory activity. Mazaheri and Jensen (2008) suggest, using alpha oscillatory activity as an example, that alpha peaks and troughs are modulated differently by visual stimuli (one is more strongly modulated that the other). This creates an asymmetrical distribution above or below zero depending on whether the peaks or troughs are more heavily modulated. After trial averaging and baselining (subtracting the pre-stimulus activity for the trial, so the pre-stimulus activity occurs at zero), this evoked asymmetry would cause slow field drifts that could account for slow-wave cognitive components. Testing this amongst a small sample of adults, they found that an asymmetry between posterior alpha peaks and troughs, and that this asymmetry was strongly correlated with slow wave changes in the Event-Related Field (the magnetoencephalographic equivalent of ERPs) over the same sites. Though these results are supportive of this model, more work needs to be conducted investigating oscillatory asymmetry to understand whether this extends beyond sensory alpha. Overall, whilst there appears to be support for all three models, the field is still undecided regarding which mechanism best explains ERP generation.

The ERP technique has a few advantages as a method for analysing EEG data. Firstly, limited use of filters compared to those used in frequency domain analysis provides high temporal precision, as filtering acts to smooth the waveform, blunting peaks and troughs in the data (Luck, 2014). This means ERPs allow for a more precise estimation of the time course of neural activity compared to other EEG analysis techniques. Secondly, compared to other techniques, the pre-processing involved to create and analyse ERPs is minimal. Thus, they are easily accessible, are quicker to compute, and can be used as a method for testing data quality. Finally, the ERP technique has an extensive literature (over 124,000 papers on PubMed alone, with the earliest dating from 1947, 8 years later than Davis' seminal paper). This provides a large evidence base aiding in the design of experiments, limiting the need for exploratory analysis and minimising type I error. Furthermore, the interpretation of results can be aided through previous work using similar evoking paradigms.

However, ERPs encompass a relatively small amount of information about the neural activity occurring in response to stimulus presentation. By averaging across data trials, all non-phase locked (induced) information should sum to zero leaving only evoked activity. Furthermore, investigating ERPs ignores activity related to other dimensions of time-signal (EEG) data, as they are unable to provide information on the frequency, power, and phase of the ongoing EEG data. However, rhythmic oscillatory activity is common in neural systems and appears to play a role in memory, sensory, and cognitive processes (Ermentrout & Chow, 2002). Thus, exclusive use of ERPs overlooks a large portion of event-related neural activity.

Overall, ERPs provide a quick and easy method for analysing EEG data. Its extensive literature has identified a broad dictionary of ERPs providing researchers with a wide range of options for study design, and decades of research has built a strong evidence base to draw upon for interpretation. Moreover, the high temporal precision allows researchers to track neural processes in the timescale in which they occur, which can be used to investigate neural mechanisms occurring rapidly in sequence. Furthermore, whilst the processes that generate ERPs are still debated, a growing literature of source localisation of ERPs further aids in drawing links between EEG research and other neuroimaging techniques. Finally, whilst often overlooked, ERPs also offer a useful tool for testing the quality of data prior to more time and

computationally demanding analysis. As they are quick to compute by creating a average of a channel's activity over all trials, we can create an ERP for channels of interest at each stage of data pre-processing to ensure no artefacts remain in the data, or have arisen as a result of pre-processing, that may influence the final analysis. Overall, ERPs remain a technique widely applicable to answer questions in the sensory and cognitive domains, whilst being a time and computationally cheap method for investigating experimental effects.

1.4.5. Event-Related Spectral Perturbations

Over the last two decades, more complex methods for analysing EEG data have been seeing increased popularity. Specifically, more researchers have been moving from analysing data in the time domain (ERPs), and instead begun investigating changes in frequency band activity over time. These methods are known as time-frequency analysis. Changes in frequency band power in response to stimulus presentation are known as Event-Related Spectral Perturbations (ERSPs; Makeig, 1993).

In EEG research, the most common method for achieving this is Complex Wavelet Analysis, which involves convolving the EEG signal with a complex wavelet; a brief windowed oscillation that begins and ends at zero, or near zero, and has an average value of zero. The most commonly used wavelet for EEG is a Morlet wavelet (also known as a Gabor wavelet; Sinkkonen, Tiitinen, & Näätänen, 1995), which is created through point-by-point multiplication of a sine wave with a Gaussian window (see *fig. 1.4*). Typically, a family of wavelets are chosen that conform to a common waveform but differ in the frequencies of the sine waves used to create them, allowing for analysis across multiple frequencies.

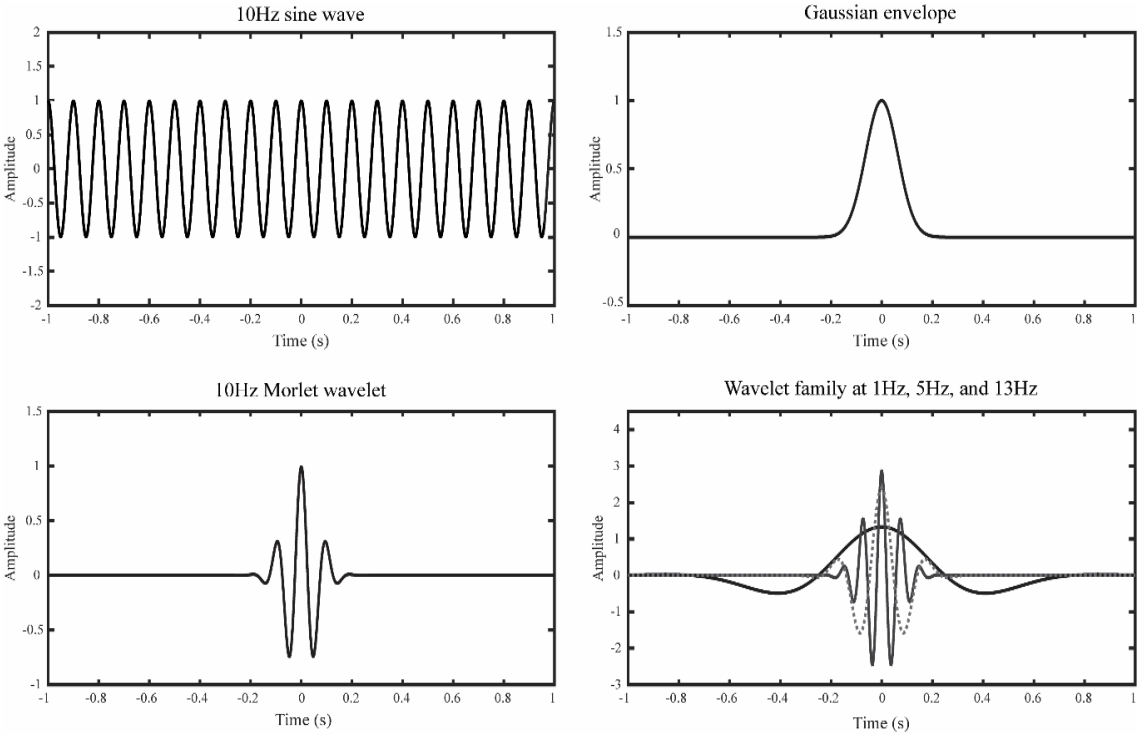

Figure 1.4. *An example wavelet and its constituent parts.*

Compared to ERPs, ERSPs provide a more complex image of the event-related neural activity. By running wavelet analysis on averaged trial data, we can investigate the phase-locked oscillatory changes in the EEG signal, similar to the activity underlying the ERP. However, by convolving the individual trials using wavelets and averaging the convolved data, it is possible to extract non-phase locked data that is not reflected in the averaged ERP. When combined with the increased dimensionality of time-frequency decomposition (space-time-frequency-power compared to the space-time-amplitude of ERPs), which allows us to understand temporally and spatially overlapping oscillations, ERSP provide a considerably larger source of information on neural activation than ERPs (Cohen, 2011b).

An additional advantage of ERSPs is that they are more intuitively understood—or biologically plausible—compared to ERPs, whose generators are still a matter of active debate, as we know that oscillations primarily reflect rhythmic excitatory-inhibitory cycling in populations of neurones (Wang, 2010). We also have a better understanding of their role in neural communication (Schnitzler & Gross, 2005) and synchronisation (Steriade, 2006), and evidence is beginning to emerge suggesting a role for oscillatory activity in neural plasticity (Assenza, Pellegrino, Tombini, Di Pino, & Di

Lazzaro, 2015). Additionally, their links across other disciplines such as neural modelling (e.g. Kozma & Puljic, 2015; Zandt, Haken, van Dijk, & van Putten, 2015) and animal inter-neuronal recording (e.g. Sheridan, Moeendarbary, Pickering, O'Connor, & Murphey, 2014) offer a broad but comprehensive evidence base to draw interpretations from.

However, whilst ERSPs provide a more complex image of event-related neural activity, the processing of EEG data in the frequency domain limits the temporal precision of the data. This is due to the tapering of the wavelet, which allows the frequency power to be located in time, but the frequency power value will include any time points where the wavelet value does not equal zero. Therefore, low frequency wavelets will usually have worse temporal precision than high frequencies (as can be seen in the bottom right box of *fig. 4*). Furthermore, there is a trade-off between temporal and frequency accuracy, following Heisenberg's uncertainty principle, particularly in wavelet analysis. Time and frequency precision are both dependent on the number of cycles in the wavelet, but their relationship with the number of cycles are opposed: increasing the number of cycles decreases the temporal resolution but increases the frequency resolution This is because increasing the number of cycles also increases the time it takes for the wavelet to taper to zero. Currently, this is frequently combatted by having the cycle number change as a function of frequency, allowing for a balance between temporal and frequency precision. Moreover, advanced methods for time-frequency analysis, such Matching Pursuit (Durka & Blinowska, 1995), which offer better resolution in both domains, are beginning to be implemented more commonly in EEG research.

Statistical problems can also arise from use of time-frequency decompositions. Depending on the parameters defined by the experimenter, the number of data points resulting from time-frequency analysis can be substantial. Assuming 2 seconds of recorded data sampled at 500Hz, wavelet analysis using 30 linearly spaced frequencies can lead to 30,000 data points at each electrode site, significantly increasing chances of Type 1 error making exploratory analysis difficult. Therefore, familywise error rate corrections are vital in the absence of *a priori* hypotheses. Due the high level of autocorrelation between contiguous time-frequency points, correction methods such as Bonferroni correction or False Discovery Rate (FDR; Benjamini & Hochberg, 1995)

can be overly conservative. However, pixel based methods, such as pixel-level correction (Cohen, 2014) or cluster-level correction (Maris & Oostenveld, 2007) can prevent overcorrection. In these methods, two conditions are compared, and all significant pixels or clusters of pixels are extracted. Then permutation testing is conducted, and from each permutation, the most significant effect at the pixel or cluster level is extracted, and this is used to build up a null distribution. All significant pixels or clusters from the test of interest are compared to the null distribution, and those with an effect size greater than a predefined threshold (e.g. in the top or bottom 2.5% for a *p*-value of 0.05) are considered significant. As contiguous pixels are likely to contain very little unique information, they will fall into similar places on the null distribution. This is compared to other methods of correction where neighbouring pixels would be treated as completely independent, potentially leading to Type II errors.

It is important to note that, whilst they are not covered here, numerous other techniques exist for the analysis of time-frequency data in EEG. ERSPs offer perhaps the most simplistic view of the data, reflecting the projection of event-related oscillatory activity to the scalp, independent of oscillations in other frequency bands or spatial projections. Though ERSPs are not without merit, more advanced techniques such as phase-amplitude coupling or inter-site coherence can provide a robust image of neural response to stimuli.

1.4.6. Conclusions

EEG is an invaluable tool for analysing neural activity during cognitive-behavioural paradigms, and represents an attractive method for working with externalising participant groups as it places much lower demand on the participant, than functional MRI or Magnetoencephalogram (MEG). The ability to measure activity in neuronal populations in their appropriate time scale coupled with the large amount of information available from EEG recordings provides a number of possible of avenues of investigation. Furthermore, as EEG, and especially ERP work, has a well-developed literature, there is a large evidence base to draw upon to interpret task-related findings.

As with all neuroimaging techniques, EEG is limited in the questions it can answer, and experiments should be designed with that in mind. However, with the

advances in the signal decomposition, source localisation, and time-frequency analysis techniques that have occurred over the last twenty years, the weight of these limitations has been lifted somewhat, broadening its applicability.

1.5. This Thesis

This thesis seeks to investigate how neural mechanisms associated with the processing of reward-related feedback are different between high and low externalising adolescents – specifically, how the processing of both reward and punishment feedback cues are associated with externalising behaviour. Following this introduction chapter is a chapter outlining the methodologies used across the empirical chapters of this thesis. In the third chapter, findings from a study investigating the effects of self-reported externalising behaviour amongst typically developing adolescents on two ERPs previously associated with reward feedback processing are reported. These results are then further expanded upon in the fourth chapter using time-frequency decomposition to understand how oscillatory activity in frequency bands previously associated with feedback may be altered in those reporting high levels of externalising problems. In the fourth and fifth chapters, the feedback related components and time-frequency responses identified in the previous two chapters are tested in a group of adolescents with a clinical history of externalising behaviour problems. This is done using the Taylor Aggression Paradigm (Taylor, 1967), a method for investigating how frustration and social competition can influence behaviour, and reward processing in particular, allowing us to further investigate how high and low externalisers' neural response to feedback is modulated under different levels of social provocation. Furthermore, the effects of therapeutic intervention (Multisystemic Therapy; Henggeler & Borduin, 1990) are tested to investigate whether neural changes in response to reward signals occur following therapy. Finally, these results are discussed in relation to the current literature, and potential avenues for future research are outlined.

Chapter 2

Methodology

2.1. Methods

The results of two separate studies are reported in this thesis. The first study involved a sample of normative adolescents and the second recruited participants with a history of externalising behaviour problems. The first study, known as The Adolescents Thoughts and Feelings project, was a cross-sectional study of normative adolescents recruited from local schools. The neuroimaging results from a reward task that participants in this study were asked to complete are reported in the first two empirical chapters (chapters 3 and 4). The second project, the START EEG project, was an offshoot of a currently ongoing follow-up of a randomised clinical trial investigating the effects of Multisystemic Therapy amongst at-risk adolescents. The results from a reward task involving social provocation are reported in the second two empirical chapters (chapters 5 and 6). In each project, the data were analysed using two EEG methods - Event Related Potentials (ERPs) and Event-Related Spectral Perturbations (ERSPs). Here, I will outline the methodologies used in each project, and these will then be briefly recapped in the respective empirical chapters.

2.2. Study 1

The primary aim of this study was to investigate whether externalising behaviour was associated with already established neural mechanisms of rewards. A further aim was to investigate whether any changes in feedback-evoked oscillatory activity could act as a neural marker for externalising behaviour for future investigation amongst clinical samples.

Chronologically, both the ERP and ERSP analyses from this study were completed before any data analysis for the START EEG project had begun.

2.2.1. Adolescent Thoughts and Feelings project

The Adolescent Thoughts and Feelings project was a cross-sectional developmental study conducted at the Anna Freud Centre in North London aimed at investigating developmental effects on individual differences. As a part of the project, the participants completed four neurocognitive assessments whilst undergoing high-density EEG, as well as a battery of self-report questionnaires to ascertain clinical, personality, and demographic information.

This study was approved by the UCL Graduate School Ethics Committee (application number: 1908/001).

2.2.2. Participants

105 typically-developing participants were recruited to take part in the Adolescent Thoughts and Feelings project (52 females) from local high schools surrounding the Anna Freud Centre (AFC). 82 of these participants provided sufficient EEG data from the reward task for both ERP and ERSP analysis (more than 15 trials per condition), 78 of whom had completed the externalising measure (see below) and were included in the final analysis. Participants ranged in age from 11 to 18 years old (mean = 14.5 years, S.D. = 1.7). Participants were considered eligible to take part in the study if they reported having normal, or corrected to normal, vision, fluency in English, had no difficult using their hands, did not have a latex or shampoo allergy, and did not have a hairstyle that impeded EEG measurement. Further exclusion criteria included a history of, or current treatment for, traumatic brain injury, epilepsy, seizure, alcohol/drug abuse, or hallucinations. To take part, adolescents younger than 16 gave signed assent to take part, whilst their parents gave informed consent. Participants 16 and older gave informed consent.

2.2.3. Reward Task: MoneyMaker

The MoneyMaker (Crowley et al., 2009) is a modified version of the Balloon Context Task reported in Holroyd, Nieuwenhuis, Yeung, and Cohen (2003). In each trial, participants were presented with four coloured balloons appearing randomly in one of four positions along a row horizontally centred on the screen. The aim of the task was to select one balloon to win virtual monetary rewards that were later converted into performance-based remuneration (cumulative with the £20 they received for participating). Participants were asked to select the balloon they thought would mostly likely result in a reward using a 4-option response pad. After selecting one of the balloons, participants either saw a green Pound sign representing a 25 pence reward, or a red cross indicating a 25 pence loss.

Each trial begun with a fixation cross presented for 500ms followed by a black screen for 500ms (*fig. 2.1*). Balloon stimuli were then presented for up to 2000ms in which participants could make their response. Following participant response, feedback

was delayed for either 1000ms for the short delay condition, or between 1400-2200ms in the long delay condition. During this delay period, participants were presented with a black screen. Feedback stimuli were presented for 800ms, and then participants were presented with a blank screen for 700ms before the next trial began.

Participants played a total of 140 trials (35 per condition), 50% of which resulted in reward, taking approximately 20 mins to complete. Outcome was random so

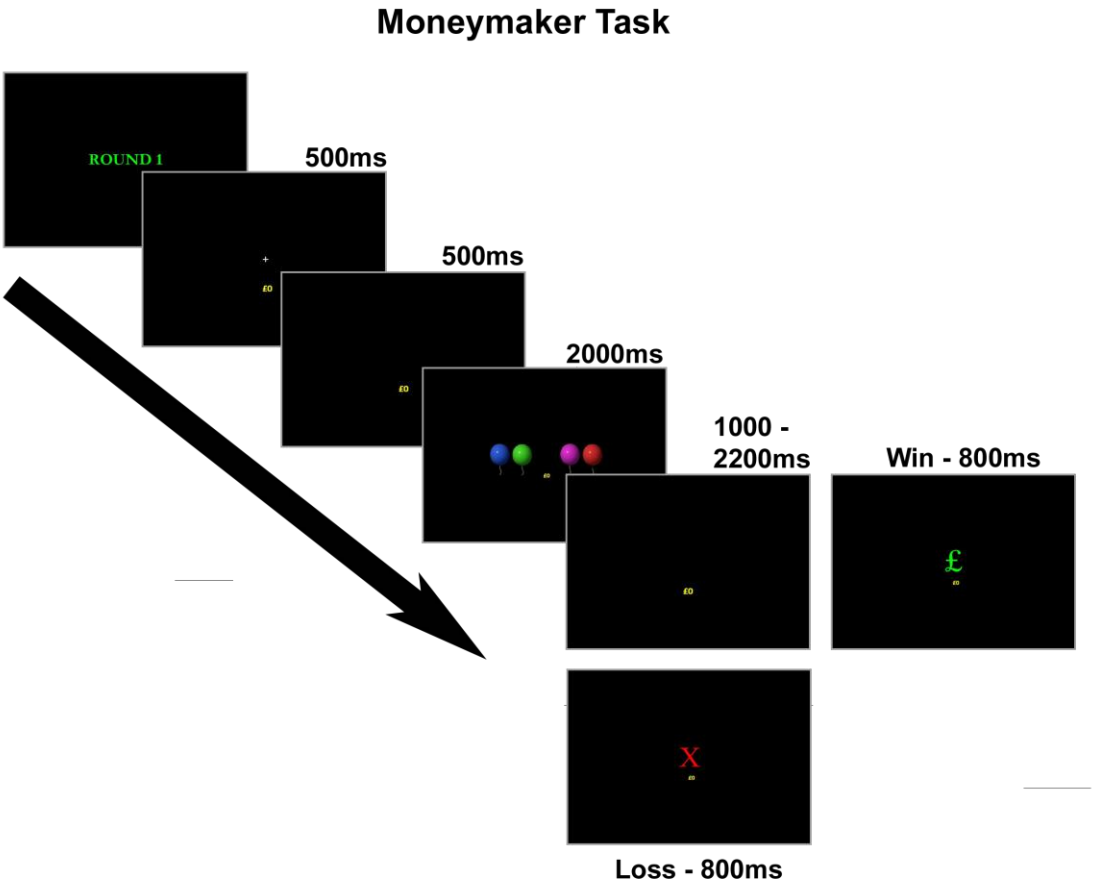

Figure 2.1. *Slides seen by participants in the MoneyMaker task and their presentation times.*

that no pattern between a specific balloon colour and outcome could be established. However, as part of the instructions, participants were led to believe that for some people it was possible to "figure out the pattern some of the time". Earnings were displayed at the bottom of the screen during the task, and were summarised at the end of each block. The task was comprised of four blocks of trials, each with 35 trials, with the balloons changing colour every 50 trials. Each block started with 10 to 12 practice trials, 75% of which resulted in a win to ensure that participants always had a winning

balance.

2.2.4. Externalising measure

Participants completed a shortened version of the Externalizing Disorder Inventory (EDI, Krueger et al., 2002; Krueger, Markon, Patrick, Benning, & Kramer, 2007) comprising 46 items covering scales for physical, destructive, and interpersonal aggression, rebelliousness, theft, alcohol use, drug use, cannabis use, and honesty. Cronbach's alpha for the total scale was acceptable ($\alpha = .79$). The total scale in the shortened version correlated $r = 0.97$ with the total from the original scale based on data provided by the EDI authors. Participants' externalizing score was calculated as the sum of all items. Participants were included in the final analysis if they answered at least 80% of all items. Final analyses were carried out on 78 participants.

2.2.5. Procedure

After giving informed consent, participants were seated approximately 24 inches in front of a 17-inch Dell LCD monitor. Head circumference was measured, and an appropriate sized net was soaked in a solution of potassium chloride (KCl; to act as an electrolyte) and baby shampoo (to break up grease on the scalp) for 5 minutes. Whilst the net was soaking, the vertex was determined as the intersecting point between lines running from the nasion to the inion, and the two preauricular notches. EEG data were collected using the NetStation v.4.4.2 software package (EGI, Inc., Eugene, OR) and an EGI Series 300 high impedance amplifier, sampling at 250Hz. Data were record with an online bandpass filter set at 0.1-100Hz. Impedances for all electrodes remained below 70kΩ as measured by the NetStation inbuilt impedance tool both prior to, and upon completion of, the task.

2.2.6. ERP analysis

Offline filtering using a 0.3-40Hz bandpass filter was applied using the NetStation inbuilt filtering tools, and then epoched around the feedback stimulus using a 100ms pre-stimulus and 600ms post-stimulus window. The data were then exported from NetStation to EEGLAB (Delorme and Makeig, 2004) for further processing. Bad channels were identified using automated methods. Channels were considered bad if their average variation in amplitude was greater than 3 standard deviations around the

median of all electrodes. These electrodes were then interpolated using EEGLABs spherical interpolation method (Delorme and Makeig, 2004). All marked channels were visually inspected and verified before interpolation to verify their selection was not a false positive. Trials containing more than 10 marked channels were rejected. Blinks were identified using a template-based correlative method, in which a stereotyped blink was selected from each individual data case. Using a moving window of 80ms, any trial in which an eye channel demonstrated greater than a .97 correlation with the template led to the trial being marked as a blink, and following visual inspection, was rejected. Artifact rejection was performed by eye due to non-stereotypical noise in some data files, which was not adequately picked up by automated methods. To check for consistency of the manual artifact detection, 20 cases were independently checked for artifact by another researcher, yielding a 79% concordance rate ($\kappa = 0.82$). Participants with greater than 15 trials in each condition and who had externalising data were included in the statistical analyses (n = 78). After artifact rejection, the average number of trials per condition were: Win, short delay = 28 trials (S.D. = 5.0); Win, long delay = 27 trials (S.D. = 5.4); Lose, short delay = 25 trials (S.D. = 5.1); Lose, long delay = 27 trials (S.D. = 5.7). Epochs underwent baseline correction using the 100ms pre-stimulus period, then data were re-referenced from the vertex (Cz) to the average of all electrodes.

Data were extracted from two electrode clusters using a peak+window measure, in which the peak was identified, and then the mean activity from 16ms either side of the peak was taken. Previous work with adolescents has extracted the FRN from frontal sites, specifically frontal mid-line sites (Crowley et al., 2009). The FRN was measured from a frontal mid-line cluster of 5 electrodes (electrodes 11 [Fz], 15, 16 [FPz], 10, and 18; see *fig. 3.1*) as the most negative inflection between 250 - 400ms following feedback presentation. By comparison, the P3b has been previously extracted from parietal mid-line sites in adolescents (Ferdinand, Becker, Kray, & Gehring, 2016; Gatzke-Kopp et al., 2015; Ma et al., 2016). Consistent with this, the P3b was defined as the most positive inflection in the 270 - 420ms windowing feedback presentation in the parietal mid-line electrodes (electrodes 62 [Pz], 61, 67, 78, 72, 77, 54, and 79).

2.2.7. ERSP analysis

Prior to ERSP analysis, the data were exported using the NetStation file

exporting tool, and imported into EEGLAB (Delorme and Makeig, 2004). Offline high-pass filtering was then conducted using the EEGLAB filtering function (*eegfilt*) set at 0.1Hz. In contrast to the ERP analysis, EEGLAB filtering tools were chosen for this analysis as EEGLAB filters are designed to prevent phase delay in oscillatory data. As larger segments of the data were required to allow processing in the theta frequency bands, signal decomposition using Independent Component Analysis (ICA; Delorme, Sejnowski, & Makeig, 2007) was used to clean the data. In preparation for ICA, the continuous data were visually inspected and periods of non-stereotyped noise were removed. Infomax ICA was then run using EEGLABs *runica* function. The continuous component data were then visually inspected to identify and further remove any non-stereotyped occurring across components, and a second Infomax ICA was run. The components were then examined visually, and those demonstrating scalp map topographies and power spectra characteristics of stereotyped artifacts (e.g. eye blinks, lateral eye movements, or heart artifacts) were removed.

To remove non-stereotyped artifacts, dipole fitting was run on the remaining components using the DIPFIT toolbox (Oostenvelt, Delorme, & Makeig, 2003) for EEGLAB. Firstly, electrode layout was manually co-registered with the standard BESA model available provided in the toolbox. The net was warped to align the net's mid-line electrodes with the model's mid-line electrodes, and then resized to align the non-midline electrodes. Next, the auto fit function was used to run both coarse and fine fitting of the dipole to the independent components. Any components that were fitted with a dipole outside of the head, or had a dipole with 100% residual variance were rejected from further analysis as these were likely to be artifacts.

Epochs were extracted around feedback presentation with a 500 pre-stimulus and 1500 post-stimulus window. The epochs were convolved with the EEGLAB *newtimef* function, using Morlet wavelets, beginning with 1 cycle at the lowest frequency band and increasing to 12.5 cycles at the highest frequency. Frequency band power was scaled in decibels (dB; computed as the $10*\log^{10}$ of the power), and changes in frequency band power was calculated relative to the -200 to stimulus presentation window using a gain approach (Delorme & Makeig, 2004).

Previous work investigating feedback related theta activity has extracted feedback from frontal midline sites (Bernat et al., 2011; Crowley et al., 2013), and in

line with the ERP study, frontal oscillatory activity was extracted from Fz (electrode 11; *fig. 4.1*). Similarly, as Bernat et al. (2011) extracted feedback related delta activity from Pz and Marco-Pallares et al. (2008) found that feedback related parietal theta activity was greatest at Pz, parietal oscillatory activity was extracted from Pz.

Frequency band power was defined as the average activity in a time-frequency window. For frontal theta (4 – 8Hz) and beta (13 – 20Hz) activity, this was the 250-400ms and 500-800ms time windows, respectively. Over parietal sites, the delta (2 – 4Hz), theta (4 – 8Hz), and beta (13 – 20Hz) time windows were 200-400ms, 250-400ms, and 500-800ms post feedback, respectively.

2.2.8. Statistical analyses

For the behavioural analysis, an anova was run with target selection time (time taken for participant to chose the balloon) as the dependent variable. Participant gender was entered as a factor with two levels (male and female), and participant age and self-reported externalising behaviour were included as continuous variables.

Mixed-effects models were used for both ERP and ERSP analyses. Mixed-effects models were run via the *xtmixed* function in the STATA 13 statistical package (StataCorp, LP). In the ERP analysis, two separate models were run, with the FRN and P3b amplitudes as the dependent variables. In each model, feedback valence (reward and punishment) and feedback delay (long and short) were included as within-subjects factors, with reward and short delay used as the reference categories, respectively. Gender was included as a between-subjects factor, with males used as the reference group. However, as gender did not correlate with externalising behaviour, nor did it demonstrate any significant main or interaction effect on either ERP, it was dropped from the analyses. Both age and externalising behaviour were centred and included in the model as between-subjects continuous variables. Finally, participant ID was included as a random effect in the model.

Similar models were used for the ERSP analysis. Frequency band power (measured in dB) was the dependent variables. As in the ERP models, feedback valence and delay were used as within-subjects factor variables, with reward and short delay used as the reference categories. Gender was included as a between-subjects factor variable, with males used as the reference group. Age and externalising scores were

centred and included as between-subjects continuous variables. Participant ID was included as a random effect in the model.

In the mixed-effect models, all significant interaction terms containing a continuous variable were investigated using the STATA *margins* function. This runs a post-estimation test using the predictive marginal means for the dependent variable estimated from the current model at 1 standard deviation above and below mean of the continuous variable (Aiken & West, 1991).

In addition to the mixed effects model, further exploratory correlative analyses were conducted on the ERSP data. Participant externalising score was correlated against the valence difference in spectral activation in the feedback window (150 - 600ms) between the frequency bands of interest (4 - 30Hz). These results were then corrected across all time-frequency points in the 2-30Hz 150-600ms time-frequency window using False-Discovery Rate (FDR) correction (Benjamini & Hochberg, 1995), a method of family-wise error rate correction aimed at computing the number of falsely rejected null hypotheses in a set of statistically significant tests. For a series of tests, all p-values from the test are sorted in ascending order. Those lower than a specified threshold are deemed to be significant. The threshold is calculated using a*(t/n), where a is the defined alpha threshold (typically 0.05), n is the total number of tests to be corrected over, and t is place of the p-value in the ascended order (e.g., for the 3rd smallest p-value, t would equal 3). Here, each correlation between a time-frequency point and self-reported externalising behaviour was considered one test with the intention of minimising the number of false-positive significant correlations. This was applied via the MATLAB *fdr_bh* function, with an adjusted significance threshold of $p < 0.05$.

2.3. Study 2

Following from the first study, the primary aim of this study was to understand whether relationship between externalising behaviour and feedback processing amongst more severe externalising samples was the same as that indicated in the typically-developing sample presented in study 1. Further aims of the study were to understand whether Multisystemic Therapy (an intensive, family based therapy), which has demonstrated some success in treating reducing externalising behaviours in American

samples, leads to changes in the reward-related neural correlates of externalising behaviour not seen in those who received Management-As-Usual (MAU). Similarly, whether participant improvement following therapeutic intervention was associated with any changes in feedback-evoked neural markers.

The analyses conducted for this study was conducted after those conducted for the Adolescents Thoughts and Feelings Project. Therefore, some of the differences in methodologies between the two studies reflect techniques learnt between the two sets of analyses.

2.3.1 START project

Participants for this study were recruited from an ongoing, nationwide Randomised Controlled Trial (RCT), the START project. The START project is being conducted in 9 sites across England (Greenwich; Peterborough; Hackney; Leeds; Merton and Kingston; Barnsley; Reading; Trafford; and Sheffield) investigating the potential benefits of Multisystemic Therapy (MST), a home- and family-based therapy, compared to MAU. Given the somewhat inconsistent international findings associated with MST efficacy (van der Stouwe, Asscher, Stams, Dekovic, & van der Laan, 2014), the START trial sought to understand whether MST would be an effective treatment program in the UK. The primary aim of the START trial was to test whether MST offered any advantages over MAU amongst at-risk adolescents in reducing out-of-home placement, with secondary and tertiary aims focused on participant outcome and cost-benefit analysis.

To do this, adolescent referrals from Youth Offending Teams (YOTs), Children's Services, Educational Services, and Child and Adolescent Mental Health Services (CAHMS) were subject to multiple screening procedures to ensure they met the appropriate criteria for the trial. A potential participant’s eligibility was discussed at 3 points: firstly, by a multi-agency panel (YOTs, CAHMS, and social care and education services); then by the MST supervisor and trial coordinator, based on their referral; and finally, by the MST supervisor and trial coordinator after their initial home visit by the clinical and research teams. Participants were considered eligible to take part in the original START project if they were aged between 11 and 17 years of age, were considered to be at high risk of school exclusion, had a history of offending, were

at risk for offending, or if there was risk for being removed from the family home, and were not currently receiving any other forms of intervention. Participants were excluded if they had any past reports of psychosis, or an IQ lower than 65, if they presented risk of injury to the therapist or researchers, or if they primarily identified as being at risk due to substance abuse or sexual offending.

A total of 700 participants were recruited across the 9 sites, and then randomly assigned to either MST or MAU groups by the UCL Clinical Trials Unit. The randomisation algorithm used the following stratification factors: treatment site, participant gender, participant age group (either 11-14 or 15-17), and age of Conduct Disorder onset (2-11 or 11 and older).

The project used a longitudinal design, in which participants completed a series of baseline assessments, and then received their assigned intervention for 6 months. Afterwards, participants were followed up every 6 months until the 18-month follow-up time point. After 18 months, participants were followed up once in each 12-month window, either 6 months or 12 months after their last follow-up interview. At each follow up point, both parents and children completed questionnaire packs with the help of a research assistant either in their own homes, or a public place in situations where the participants did not wish to take part at home.

Full details of the study procedure can be found in Fonagy et al. (2013).

Multisystemic Therapy: Multisystemic Therapy was delivered by a single, full-time generalist who was available to the family for 24 hours a day, 7 days a week, over a course of 3-5 months. Individual MST packages were tailored to the families' specific needs, and incorporated a range of modalities. These treatment teams had already been set up for a period of 12-18 months prior to the START project to increase adherence to the MST therapeutic model. To further this adherence, MST therapists were licensed by MST services Inc. (Charleston, SC, USA), and received weekly supervisions with an MST supervisor, weekly consultations with an MST expert, quarterly booster sessions, and a biannual review with an MST expert.

Management-As-Usual: MAU represents the standard care offered to those in a similar position to the participants in the study, and can be highly variable, with therapeutic interventions offered as needed, but dependent on what is deemed necessary

by the local authority. Typically, these interventions aim at reducing reoffending, and may deliver interventions to help with anger management, victim awareness, or substance misuse. They may also be aimed at reintroducing the young person with education. Unlike MST, these are not likely to be delivered by a single person, but a team of therapists, social workers, and probation officers, and may take place separate from a family context.

2.3.2 START EEG project

For the START EEG project, participants were initially approached by a research assistant from the original START project during one of their follow-up appointments. At the end of the appointment, the research assistants explained the START EEG project, and if the participant expressed interest in being involved, their contact details were collected and passed on to a START EEG researcher. Following a period of several days intended to give participants time to consider their involvement in the project, they were contacted by an experimenter from the START EEG project to explain the task, and if they still expressed interest, to book an appointment. All participants were recruited from one of the three London sites (Greenwich, Hackney, or Merton-Kingston) or the Reading site. All participants were approached at either their 18-month follow-up time point or later, with the latest being recruited at the 48-month follow-up (M = 27 months, S.D. = 7.1 months). The follow-up interview in which participants were recruited varied due to the broad initial recruitment window for the original START project, however, there were no significant differences between the two clinical groups (MST vs. MAU) in their average follow-up time point ($t(58) = 0.815$, $p = -0.49$).

To take part in the START EEG project, participants were brought to the Developmental Neuroscience Unit at the Anna Freud Centre in North London to take part in the project. As this study was cross-sectional, participants were brought in for a single 2.5 hour long testing session, consisting of 2 behavioural tasks conducted whilst collecting high-density EEG data, a measure of resting state EEG, and 3 questionnaire measures. This thesis is focused on the results from one of the behavioural tasks - the Taylor Aggression Paradigm (TAP). Financial remuneration for involvement in the project was £30 plus their winnings from the TAP task (an average of £5).

This study received ethical approval from the London Queens Square NHS ethics committee (ref: 12-LO-0733).

2.3.3. Participants

60 participants aged between 13 and 20 years (mean age = 16.23; S.D = 1.75) were recruited from the original START project. Given the stringent criteria needed for inclusion in the original study, no further eligibility criteria were included in the START EEG project, and no criteria were specified for participant selection for this project. The first 60 participants to attend and complete a testing session were used for analysis. Across the 4 sites recruited from for this study, 4 participants were recruited from Greenwich, 27 were recruited from Hackney, 17 were recruited from Merton/Kingston, and 12 were recruited from Reading.

In total, 56 participants had useable data for both the ERP and ERSP analyses. 3 participants did not provide sufficient clean data for analysis, and 1 participant's data was lost due to technical error.

2.3.4. Tasks

Taylor Aggression Paradigm (TAP): Participants were asked to complete a modified version of the Taylor Aggression Paradigm task as the final task of the testing session. The TAP (Taylor, 1969) is a task designed to evoke aggression/retaliation in participants via the loss of desired compensation, in this case, money. Specifically, they completed a competitive Go/No-Go flanker task against two fictional opponents - a high provoking opponent and a low provoking opponent.

Before the game began, participants were told that that would be playing a competitive, online game against two opponents involved in another project at another site in which they would have the opportunity to win money or lose money based on their performance in the game. They were told they would be playing the two opponents sequentially, and they should aim to respond as quickly and as accurately as possible, as the person who got the most answers correct the fastest would win the round and gain money. The other person would be punished, and lose an amount of money decided by their opponent.

In reality, their opponents' behaviour was simulated by the computer, with trial outcome determined by the participant's performance, and feedback magnitude predetermined for each trial depending on the opponent they were playing against in that block. The high provoking opponent punished significantly more highly than the low provoker. To ensure that the participants believed the social element of the task, several steps were taken by experimenters. Prior to the start of the game, one of the experimenters would leave the room to place a phone call to the fictional lab to check their participant was ready to begin. When participants first played against each opponent, a false "connecting to webcam" screen was displayed, followed by a video of a similarly aged teenager wearing an EEG net and waving at them. Finally, participants were given a break under the guise of their opponents playing against each other.

Participants played 4 blocks of the Go/No-Go flanker; 2 blocks against each opponent. Each block was made up of 20 rounds, each of which contained 6 Go/No-Go stimuli. A round was comprised of a decision phase, a task phase, and an outcome phase. During the decision phase, participants saw a slide asking them to think about the punishment they wanted their opponent to receive if their opponent lost. They were then asked to select the punishment using a keyboard press, selecting a punishment level from 1 to 6, equivalent to a 10p, 20p, 30p, 40p, 50p, or 60p punishment. The "think" slide was presented for 1500ms before the punishment selection screen appeared, which remained until the participant chose a punishment level.

During the task phase, participants were presented with 6 Go/No-Go stimuli, with a "blink" stimulus presented half-way through for 400ms. Each Go/No-Go stimulus was one central, coloured arrow surrounded by 8 grey arrows in a 3 x 3 square presented for 400ms each, followed by an 800ms blank slide in which participants could make their response. Over each block, participants saw 70% Go stimuli and 30% No-Go stimuli. The "blink" stimulus was a small white box containing a blue image of an eye, indicating an appropriate time for the participant to blink, aiming to minimise the number of ocular artifacts in the task related EEG.

At the end of each round, participants were presented with two feedback slides. The first was a "valence" slide, indicating whether the participant had won or lost the round, which was presented for 2000ms. If the participant won, they saw a green circle with a tick, and if they lost, they were presented with a red circle containing a cross. The

second slide indicated the magnitude of the punishment. If the participant won, they received 35p, and were told how much their opponent would have punished them had they lost. If they lost the round, they were punished with monetary loss and an aversive sound, which increased in volume with the size of the punishment. When playing against the high provoker, participants were punished an average of 46p. By comparison, against the low provoker they were punished an average of 17p. On average, high provoker trials lead to a monetary loss, and low provoker trials lead to a monetary gain. Participants began with £3 in their bank.

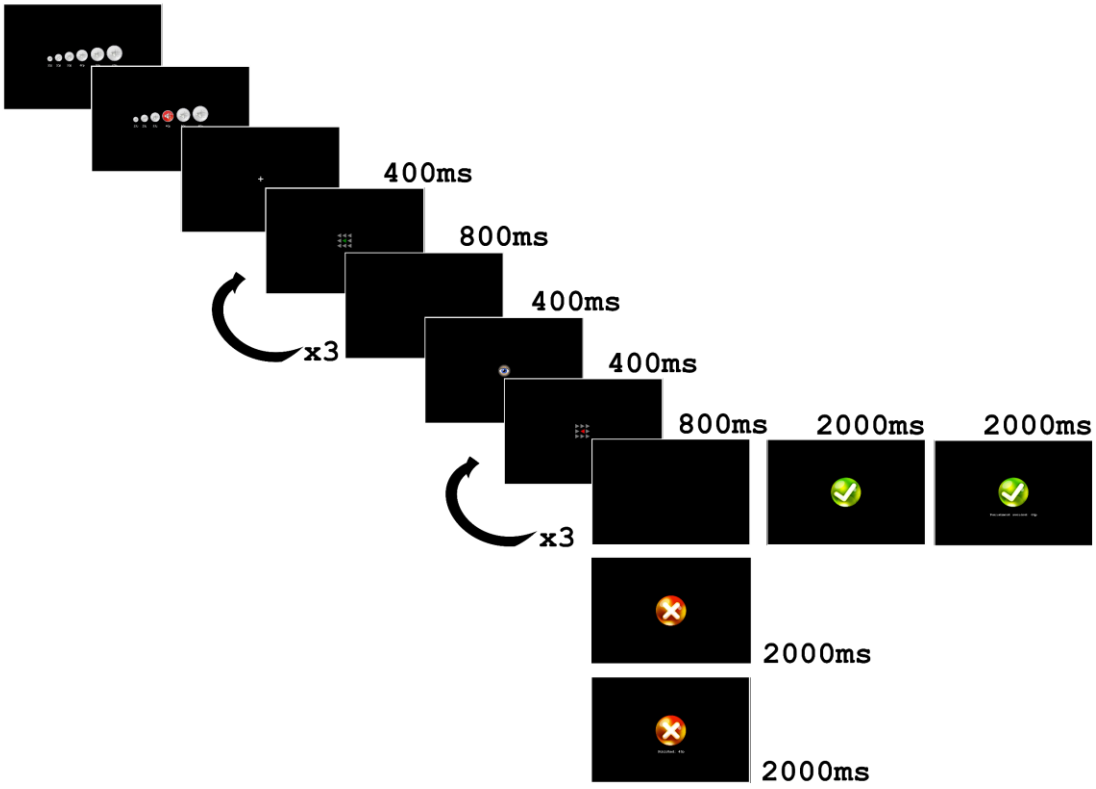

Figure 2.2. *Task progression of the START Go/No-Go Flanker task with timinings and stimuli repeats.*

Imitation-Inhibition Task (not included in this thesis, but described here for completeness): As a behavioural measure of empathy and inhibition, participants were also asked to complete a modified imitation-inhibition task (Brass, Bekkering, Wohlschlager, & Prinz, 2000). In this task, participants saw a hand resting palm down on a blue surface. They were told that a number would appear under the hand, and they had to raise a finger corresponding to the number shown as quickly as possible – a 1 indicates they need to raise the index finger, a 2 indicating the middle finger. In the

congruent condition, the hand on the screen raised the same finger as indicated by the number of the screen. In the incongruent condition, it raised the opposite finger as indicated by the number on the screen.

Each trial comprised of 500ms fixation cross, followed by a blank for 500ms and then an image of the hand resting on the blue table for 2000ms. The hand appeared to move through a series of 3 slides presented in rapid succession for 34ms each, with the number indicating which finger should be moved presented on the first slide and remaining for the rest. Following the last hand movement slide, there was a final image of the hand being held in its last position for 1240ms before a blank slide was presented for 300ms.

Participants played 3 blocks of the imitation-inhibition task. The first block contained 26 trials in which only the number was presented with no hand movement to act as a baseline, and was preceded by 6 practice trials. Following the first block, participants were given 12 practice trials in which both the number appeared and the hand moved, giving the participants a chance to see both incongruent and congruent trials. The participants then played 2 more blocks of 26 trials, each containing 13 congruent and 13 incongruent stimuli presented in a random order.

Resting State: Finally, participants also completed a resting state measure of neural activity. Participants were required to sit still for two 3-minute periods, the first with their eyes closed, and the second with their eyes open. During this time, participants were instructed to relax and asked to let their mind wander without dwelling on any one thought. In the eyes closed period, they were asked to keep their eyes closed, and wait for experimenter instruction to open their eyes again. During the eyes open period, they were asked to fixate on a white cross in the centre of the screen.

2.3.5. Measures

Self-Reported Delinquency: As part of the START project follow-up, participants were asked to report on their delinquent behaviours over the last 6 months using the Self-Reported Delinquency (SRD) scale outlined in Smith and McVie (2003). This 24-item, self-report scales asks participants to report on delinquent behaviours and conduct problems both in and out of school, and has demonstrated good internal consistency (Cronbach's $\alpha = 0.87$). This measure of externalising behaviour was chosen

over the EDI favoured in experiment 1 for two reasons. Firstly, as SRD responses were collected from each participant at all follow-up time points, using the SRD allowed identification of improvers and non-improvers (by regressing SRD scores back on time), and investigate neural changes associated with improvement. Secondly, the use of the SRD collected during their follow-up sessions with the START research assistants enabled us to reduce the study session length. This was beneficial as it minimised participant burden, and allowed us to keep the testing day shorter for participants who travelled to the Anna Freud Centre from outside London.

Substance Use: As conduct problems and substance use are known to co-occur (Brady & Sinha, 2005), and substance use is associated with changes in reward behaviours (Dawe & Loxton, 2004), participants were asked to report on the drug use over the 6 months prior to their follow-up appointment. In the same questionnaire pack as the Self-Reported Delinquency questionnaire, participants were asked to report on how frequently they used 11 real drugs and 1 fictional drug ("Semeron"). The fictional drug "Semeron" was included to control for false reporting (Riley & Hayward, 2004; Smith, Farrell, Bunting, Houston, & Shevlin, 2011), however, no participants reported its use and all participants' scores were included. This measure demonstrated reasonable internal consistency (Cronbach's $\alpha = 0.65$), however, similar to the SRD, as far as I are aware, no test-retest analyses have been conducted.

Strengths and Difficulties Questionnaire (SDQ): Both the young person, and their parent/guardian, were asked to complete the SDQ (Goodman, Meltzer, & Bailey, 1998), a 25-item questionnaire made up of 3-point Likert scales indexing hyperactivity, emotional symptoms, conduct problems, peer problems, & prosocial behaviour. The SDQ has previously demonstrated reasonable internal consistency (Cronbach's $\alpha = 0.73$; Goodman, 2001) and test-retest stability (Goodman, 2001; Stone et al., 2015). For this experiment, only the conduct problems sub-scale was used.

Demographics: Demographic information, including age, gender, ethnicity, household income, parental education, and parental profession was collected on all participants at the beginning of the original START project. Household income was operationalised into 6 bands increasing in income (State benefits/No income; less than £10,000; £10,001-£20,000; £20,001-£30,000; £31,000-£50,000; More than £51,000). Similarly, parental education level was classified into 12 bands (No qualifications; 1-4

O Levels/GCSE equivalent; 5 or more O Level/GCSE equivalent; 1 A/AS level or equivalent; 2 or more A/AS level or equivalent; Level 1 NVQ/HNC; Level 2 NVQ/HNC; Level 3 NVQ/HNC; Level 4 or 5 NVQ/HNC/HND; Other qualifications, such as City and Guilds; First Degree; Higher Degree). Finally, parental profession was operationalised into 8 bands moving from unemployed to more senior positions (Full-time student; Long-term sick/disabled; Unemployed; Homemaker; Semi-skilled or unskilled manual; Skilled manual; White collar worker; Professional).

Interpersonal Reactivity Index (IRI, not used in this thesis but described for completeness): During the START EEG project testing session, participants were asked to complete the IRI (Davis, 1980), a 28-item 5-point Likert scale questionnaire aiming to measure both affective and cognitive empathy. The IRI has demonstrated good internal reliability across adolescents of all ages (Hawk et al., 2013). The results from this questionnaire are reported elsewhere.

Reactive–Proactive Aggression Questionnaire (RPQ, not included in this thesis but described for completeness): The RPQ (Raine et al., 2006) is a 23-item 3-point Likert scale questionnaire measuring participant self-report of current proactive and reactive aggression. The RPQ demonstrates good internal reliability (Borroni, Somma, Andershed, Maffei, & Fossati, 2014; Raine et al., 2006), as well as good convergent validity with the Child Behaviour Checklist (Raine et al., 2006). The results from this questionnaire are reported elsewhere.

Borderline Personality Features Scale for Children (BPFSC, not included in this thesis but described here for completeness): Participants were also asked to complete the BPFSC (Crick, Murray-Close & Woods, 2005), a 24-item 5-point Likert scale questionnaire measuring features of Borderline Personality Disorder in children in adolescents. It has demonstrated good internal reliability and moderate test-retest reliability over 6 months (Fossanti, Sharp, Borroni, & Somma, 2016). The results from this questionnaire are reported elsewhere.

2.3.6. Combined externalising measures

Discrepancies between child-reported and parent-reported behaviour are common (De Los Reyes & Kazdin, 2005), especially related to externalising behaviour in adolescence (van der Ende & Verhulst, 2005). In order to reduce error and

incorporate both parental and self-reported externalising behaviours, latent variable modelling using the *MPlus* statistical package (Muthen & Muthen, 1998 - 2012) was used to calculate a latent externalising variable for each participant based on their score on the SRD measure, and the conduct scale from both the self-reported and parent-reported SDQ. The estimated factor scores from this model were used in the mixed effects models for both the ERP and ERSP analyses.

2.3.7. Participant Improvement

Lewis et al. (2008), investigating the effects of therapeutic change on the neural correlates of reward processing, have found changes in ERP response related to participant improvement amongst child samples. In line with this, I also investigated whether changes in externalising behaviours over the therapeutic period, for both the MST and MAU groups, were associated with post-therapy ERP and ERSP responses. Participant improvement was calculated by estimating the linear slope of participants' symptoms from baseline (pre-treatment) to the point at which they were seen for the EEG study post-treatment. This was done by regressing SRD score on time (6-month follow up time points from the baseline assessment to the follow-up preceding EEG testing taken from the original START project) using the STATA 13 *xtmixed* function, with participant ID included as a random effect. Participants with a negative or positive β coefficient demonstrate a decrease or increase in externalising behaviour over the follow-up period, respectively. The SRD was favoured over a combined measure discussed above as the SDQ was not collected at every time point. This method is preferable to defining an arbitrary cut-point on post-treatment scores for improvement as it retains the full range of levels of symptom change, and estimates improvement from all of the available data points (i.e., not just pre- and one post-treatment score).

2.3.8. Procedure

After participants provided informed consent to take part, they were measured and fitted for a net using the same procedure that was used for study 1 (section 2.2.5). After fitting, the participants were seated in the testing room, approximately 24 inches from a 17-inch Dell LCD monitor. Consistent with study 1, EEG activity was recorded using the NetStation v.4.4.2 software package (EGI, Inc., Eugene, OR) and an EGI series 300 high impedance amplifier, with online bandpass filter set at 0.1-100Hz.

Impedances were measured prior to beginning the EEG portion of the session, and between each task, using the NetStation Impedance measuring tool. For the TAP, impedances were checked at the beginning of the task, and at the half-way point. Given the expected difficulty of recruiting the clinical samples, and the plan to remove stereotyped noise from the data using ICA, acceptable impedances were set higher than the ATFP, but were kept below 100kΩ for all channels.

After the TAP was completed, an accurate measure of channel locations was taken using a Geodesic Photogrammetry System (EGI Inc.). Participants were seated in the centre of the geodesic dome so that their head was centred in all cameras. Chair and dome height were adjusted to compensate for participant height, and it was requested that participants focus on a spot on the opposite wall to prevent head movement. When the cardinal electrodes were visible in all cameras, the picture was taken. Sensor mapping was conducted using the NetStation inbuilt correspondence mapping and sensor identification algorithms (Russell et al., 2005), and manually corrected by an experimenter where needed. 3 participants did not have accurate channel position information - 2 due to participant positioning problems, and 1 due to data corruption. In these cases, the standard EGI 128-sensor location file was used.

2.3.9. ERP analysis

Data were exported from NetStation using the inbuilt file export waveform tool and was imported into EEGLAB (Delorme & Makeig, 2004) for pre-processing, along with channel location information from the photogrammetry tool. After the data were imported, the accurate channel location information was uploaded, and the data were filtered using a 0.1-30Hz band-pass filter. The data were then prepared for Infomax ICA decomposition (Delorme & Makeig, 2004) by visually inspecting the continuous data to remove any non-stereotyped noise. In contrast to the normative sample, greater noise levels were expected in the clinical sample for two reasons. Firstly, clinical participants may be expected to demonstrate lower attention and greater hyperactivity compared to typically developing participants, leading to lower quality of data through movement artifacts. Secondly, the task itself was designed to evoke frustration, and thus data loss due to reactionary movements whilst the participants played was expected. Therefore, it was important to maximise the amount of data kept. To compensate for this, ICA was used to clean the data for both ERP and ERSP analysis, as opposed to only the ERSP

analysis seen in study 1. As ICA decomposition was going to be run on this dataset, data reduction was conducted to reduce the channel number to a 64-electrode array matching the layout of the EGI 64-sensor array. This aimed to improve the stability of components by maximising the k heuristic, a multiplier relating the number of weights in the ICA matrix (equal to the number of channels) to the number of data points needed during data collection to ensure stable components (data points = $k*N^2$; where N is the number of weights; Blinowska & Zygierewicz, 2011). Typically, k = 30 is adequate to ensure stability, and thus, using 64 channels, 122,880 points are needed (approximately 8 minutes with a 250Hz sampling rate. Following ICA decomposition, the continuous components were visually inspected to remove any noise present across multiple components before a second ICA decomposition was conducted. Components demonstrating topography plots and power spectrums related to ocular movements (blinks, lateral eye movements) or other stereotyped noise (e.g. heart artifacts, line noise, bad channels) were removed from the data. The data were referenced to an average of all electrodes before being epoched around feedback presentation from 200ms pre-stimulus to 800ms post-stimulus, and baselined using the 100ms pre-stimulus period. Participants were required to have more than 14 trials per condition to be included in the analyses (n = 56). In contrast to the ATFP, DIPFIT was not used for data cleaning in the START project. As individual electrodes locations were gathered for each participant, individual electrode coregistration would need to be conducted for each individual. As there was no analysis of individual components, source estimation was unnecessary, and given the computational demand and time it takes to create individual meshes, dipole fitting was not conducted.

In contrast to ERP extraction from the Adolescent Thoughts and Feelings project, I extracted the FRN from more central locations rather than the frontal locations. The reasoning for this was 2-fold. Firstly, concurrent fMRI-EEG work by Hauser et al. (2014) who localised the FRN to ACC generators found the greatest difference in the FRN between valence conditions over central sites. Secondly, a recent meta-analysis by Sambrook and Goslin (2015) found that the majority of studies investigating valence effects in the FRN favour FCz, or FCz focused, clusters. Thus, I extracted FRN information from FCz as well. However, as results from the ATFP had been published, the analyses from the ATFP study have been reported as originally done. As I was concerned that early visual components may influence the mean FRN

activity following inspection of the ERP after pre-processing, I instead defined the FRN as the peak-to-peak differences over the 200-350ms following feedback to account for possible differences in earlier ERP peaks. As far as I am aware, no previous study using the TAP amongst adolescents has investigated the P3b during outcome. Therefore, the P3b was extracted from a similar cluster of parietal midline electrodes (33, 34, 36 [Pz], and 38) as those analysed in study 1, though an identical cluster could not be used due to differences in electrode array as a product of dimension reduction.

2.3.10. ERSP analysis

Similar to the ERSP analysis used in study 1, time-frequency information was extracted using Complex Wavelet Analysis (CWA). However, in contrast to study 1 which was completed first, custom scripts were subsequently written rather than using EEGLAB's *newtimef* function. These in-house scripts were favoured for two reasons. Firstly, the in-house scripts gave greater control over the input parameters for the convolution. Secondly, due to the more efficient technique used in the in-house script to convolve the data, it was considerably quicker than the *newtimef* function implemented by EEGLABs wavelet analysis. Prior to convolution, each data epoch was extended by appending a mirror version of the epoch to the beginning and end of the epoch. This prevented edge artifacts from contaminating the data and allowed us to convolve the data using a greater number of cycles at lower frequency bands, increasing the temporal precision of time-frequency convolution. For this CWA, a family of 40 wavelets was created, increasing linearly from 1Hz to 35Hz and from 2 to 12 cycles. This should increase the frequency precision at lower frequency bands, reducing smoothing between delta and theta frequency bands.

The wavelet convolved data were calculated by multiplying the FFT transformations of both the EEG data and the zero-padded wavelet with each other, and then taking the inverse FFT of the product of that multiplication. This is mathematically equivalent to convolution, but computationally quicker. The data epochs were then trimmed down to their original size, and the median value was taken for each condition. Unlike the ATFP, the median was selected for this analysis to minimise the influence of outlying trials, which can be particularly influential in studies with low trial number or those studies using clinical samples, both of which describe this study (Cohen, 2014). The data were then baselined using the 400-100ms pre-stimulus window using a gain

approach, and then normalised to decibel values. This shift of baseline to 100ms before stimulus presentation was to prevent any changes in frequency power occurring immediately after stimulus presentation from effecting the baseline period, which can occur as a product of the temporal smoothing associated with wavelet convolution.

To extract time-frequency information from the frequency bands of interest, a peak + window approach was used, rather than the mean window approach selected in the ATFP. A peak + window approach was favoured with this sample as it allows for individual differences in peak and frequency and time point (Cohen, 2014). Several factors that can influence peak frequencies for spectral data have been identified in the literature, including age (Grandy et al., 2013), working memory (Moran et al., 2011), GABA concentration (Muthukumaraswamy, Edden, Jones, Swettenham, & Singh, 2009), and ADHD traits (Arns, Gunkelman, Breteler, & Spronk, 2008; Lansbergen, Arns, Dongen-Boomsma, Spronk, & Buitelaar, 2011), and these have also demonstrated previous relationships with externalising behaviour and aggression (Armstrong, Lycett, Hiscock, Care, & Sciberra, 2015; Cauffman, Steinberg, & Piquero, 2005; Ende et al., 2016; Saarinen, Fontell, Vuontela, Carlson, & Aronen, 2015). Therefore, individual selection of peak activity should provide more accurate power estimates. A larger window was defined, and the peak value was found within that window. From there, the average of a 3Hz by 100ms time window centred on that peak was extracted. Whilst this approach compensates for individual differences, it requires a larger time-frequency window to be defined to compensate for individual variation in peak + window placement. For theta activity, the larger window was defined as the 200-500ms post-stimulus time window in the 3-8Hz frequency range. This window was slightly larger than that defined in the ATFP to allow for individual variation in the peak theta activity over the window expected theta window (Cohen, 2014). Similar to chapter 4, frontal beta activity was defined as the peak activity 300-600ms post-stimulus in the 13-20Hz band.

Visual inspection of the averaged time-frequency analysis across all conditions also revealed a suppression in alpha/mu activity 300-600ms post-stimulus (*fig. 6.1*), similar to that outlined by Gros, Panasiti, and Chakrabarti (2015). Therefore, in exploratory analysis, parietal alpha/mu activity was also extracted, and was defined as the peak activity 300-600ms post-stimulus in the 8-14Hz band, respectively. In line with

ERP data, frontal feedback-related activity was extracted from FCz (electrode 4), though data from the two neighbouring electrodes (7 & 54) were also taken to minimise noise, as spectral power data is heavily influenced by outlying trials (Cohen, 2014). Parietal activity was extracted from Pz and surrounding electrodes (33, 34, 36, & 38).

2.3.11. Statistical analyses

Similar to the Adolescents Thoughts and Feelings project, the main statistical analyses for both ERP and ERSP datasets were conducted using the STATA 13 statistical package (StataCorp, LP.) mixed effects model function, *xtmixed*. Mixed effects models were run using feedback related activity, either ERP (μV) or ERSP (dB), as the dependant variable. To test the effects of current externalising behaviour, feedback-related activity was regressed back on valence, provoker, participant age, participant gender, and the combined externalising measure. Both valence and provoker were within-subjects factor variables with two levels (punishment and reward, and high provoker and low provoker, respectively), with punishment and high provoking conditions used as reference conditions. Gender was treated as a two-level factor variable with males as the reference group. Age and externalising behaviour were normalised continuous variables.

For the analyses of treatment effects, the externalising variable was replaced by a two-factor between-subjects variable indicating which treatment group (MST or MAU) the individual belonged to. Similarly, to analyse improver effects, participants' individual SRD regression slopes (reflecting improvements in symptoms) were included in the analyses as a continuous variable, replacing the combined externalising measure.

In all ERSP analyses, in addition to the other variables included in the mixed effects model, the peak time and frequency points for the frequency being analysed were included as confounding variables to control for individual differences in spectral activity.

Any interactions including a continuous variable were further investigated using post-estimation tests of marginal mean with the continuous variable taken at 1 standard deviation above and below the mean (Aiken & West, 1991).

Further in line with study 1, exploratory analysis was also conducted on the

ERSP data. Whilst FDR was used in study 1, it does not account for the high amount of autocorrelation between contiguous time-frequency points, meaning the overall correction may be considerably more conservative than intended. Instead, permutation testing was run with cluster correction (Maris & Oostenveld, 2007) using in-house scripts. A null distribution of cluster t-values was built up over 10,000 bootstrap permutations, and a cluster was considered significant if its summed t-values fell within the top or bottom 0.025% (equivalent to a two-tailed *p* value of 0.05). Time-frequency information was then extracted and analysed using mixed effects models with the same independent variables as the windows-of-interest discussed above.

Chapter 3

Reward-related neural activity and adolescent antisocial behaviour in a community sample

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Abstract

Behavioural research has found evidence supporting reward dominance in adolescence with externalising disorders, but findings from neuroimaging studies have been largely heterogeneous. I examined the Feedback-Related Negativity (FRN) and P3b event-related potentials in relation to self-reported externalising behaviour amongst seventy-eight male and female adolescents (11-18 yrs.) during a monetary gambling task with concurrent high-density EEG. As expected, the P3b and the FRN demonstrated greater evoked activity to reward and punishment, respectively. Further, high externalising behaviour was associated with greater P3b difference and reduced FRN difference in response to reward and punishment, suggesting that externalising behaviours may be associated with both reward dominance and reduced feedback-monitoring.

Introduction

Adolescence is a key period in development characterized by major changes in youth's social, emotional, and cognitive functioning, and concurrent alterations in underlying brain structure and function (e.g. Casey, Getz, & Galvan, 2008). This period also coincides with well-documented increases in harmful risk-taking and antisocial behaviours (Steinberg, 2008). An important aim of neuroscience research is to understand the unfolding connections between developmental changes in antisocial behaviour and underlying changes in brain function during this period. Increasingly, researchers have focused on learning and decision-making processes in an attempt to understand the mechanisms involved in adolescent risk-taking and antisocial behaviour, and specifically the role of reward. Several authors suggest that the increases in antisocial behaviour observed during the adolescence may be related to heightened reward sensitivity (Gray, 1987; Quay, 1993).

Several neural systems have been implicated in reward processing, particularly dopamine projections from midbrain structures to frontal striatal areas (Haber & Knutson, 2010). Meta analytic work has found activation in response to reward feedback cues in multiple brain regions (Liu, Hairston, Schrier, & Fan, 2011), including the bilateral nucleus accumbens (NAcc), medial orbitofrontal cortex (OFC), pregenual cingulate cortex, posterior cingulate cortex (PCC), anterior cingulate cortex (ACC). Furthermore, ventral striatum/NAcc BOLD responses, probably mediated by phasic dopamine activity, appear to act as an error signalling system involved in learning processes governed by reward-punishment (Pagnoni, Zink, Montague, & Berns, 2002).

Extensive behavioural research indicates that adolescents are prone to reward-driven behaviour and choices, consistent with the idea of reward dominance in adolescence (Steinberg, 2008). For example, Smith, Xiao, and Bechara (2012) found that participants in early to mid-adolescence performed worse on the Iowa Gambling Task compared to adults. Whilst selecting cards from four decks, they favoured those with a high reward/high punishment ratio, resulting in overall net loss on the task. Neuroimaging studies also find evidence for reward hypersensitivity in adolescents, with greater activation in the nucleus accumbens for adolescents relative to young adults during a passive slot machine task (e.g. van Leijenhorst et al., 2010). However, research findings concerning the role of reward-related neural systems in antisocial behaviour are

less clear. While several studies suggest heightened reward sensitivity in adults presenting with severe antisocial behaviour (e.g. Brunelle, Douglas, Pihl, & Stewart, 2009), findings in adolescents characterised by high levels of externalising behaviour are less consistent. Previous work has yielded a heterogeneous set of findings. In existing research studies brain regions differentially activated by reward tasks in externalising adolescents, relative to controls, include the caudate (Finger et al., 2008; White et al., 2013), the ACC (Gatzke-Kopp et al., 2009; Bjork, Chen, Smith, & Hommer, 2010), the OFC (Rubia et al., 2009; Finger et al., 2011), the ventromedial prefrontal cortex (vmPFC; Finger et al., 2008), and the VS (Bjork et al., 2010). Moreover, the direction of reward responses (heightened or reduced BOLD signal in externalising adolescents) is inconsistent across studies. This may reflect subtle differences in sample characteristics, varying between 'pure' CD, CD+ADHD or psychopathic/callous-unemotional traits, and Antisocial Substance Disorder. Mixed findings regarding the neural systems differentially engaged in reward tasks among antisocial adolescents may also reflect the diverse range of tasks employed to elicit reward-related neural activity.

The majority of neuroimaging work investigating the relationship between externalising behaviour and feedback processing in adolescence has relied on functional Magnetic Resonance Imaging (fMRI). Whilst ideal for spatial localisation, the low temporal resolution of fMRI cannot readily detect rapid, short-term neuronal responses to feedback cues, thus potentially blurring distinct phases of feedback processing, such as cue-processing, task-related contextual encoding, learning and outcome evaluation. Event-related potentials (ERPs), with their high temporal resolution, represent an attractive methodology for investigating neural activity related to the processing of feedback cues. A large literature identifying ERP components related to feedback response already exists (e.g. Crowley et al., 2009; Crowley et al., 2013).

Previous ERP studies have isolated two event-related components linked to the processing of feedback cues, the Feedback-Related Negativity (FRN) and the P3b. The FRN is a negative deflection in the ERP waveform occurring approximately 300ms after feedback presentation apparent in the mediofrontal electrode sites. The FRN is typically greater in amplitude (i.e., more negative) for cues signalling non-reward or punishment, rather than reward, and therefore the FRN may primarily reflect the activity

of a reward-loss monitoring or classification system, similar to that indexed by the Error-Related Negativity (ERN; see Zendehrouh, Gharibzadeh, & Towhidkhah, 2014). Notably, concurrent fMRI-EEG work by Hauser et al. (2014) suggests the FRN originates from the ACC, the source typically associated with the ERN (Gehring & Willoughby, 2002). Alternatively, it has been suggested that the FRN may index reward prediction error (Holroyd & Coles, 2002). However, the FRN is not influenced consistently by reward magnitude (e.g. Hajcak, Moser, Holroyd, & Simons, 2006; for an exception see Wu & Zhou, 2009), and Talmi, Fuentemilla, Litvak, Duzel, and Dolan (2012) found that FRN response does not conform to all axioms of reward prediction error signals. Therefore, while the FRN is a consistent neural signal related to reward processing, the precise neural processes or computations it reflects (outcome monitoring versus reward prediction error) remain to be fully resolved.

The feedback-P3b is a positive inflection located in centroparietal channels, typically occurring between 300 and 600 milliseconds after feedback. Previous work indicates that the P3b is larger (more positive) in amplitude for rewards than for punishments, and is sensitive to the magnitude of the feedback (Hajcak, Holroyd, Moser, & Simons, 2005; Wu & Zhou, 2009). The P3b is thought to reflect evaluative processes related to the appraised motivational significance of the outcome (Nieuwenhuis, Holroyd, Mol, & Coles, 2004; Wu & Zhou, 2009). Its greater amplitude for reward than loss feedback suggests a specific role in approach motivation or the appraisal of positive reward value (Wu & Zhou, 2009). Moreover, the P3b has been localized to dipoles in the posterior cingulate cortex (Luu, Shane, Pratt, & Tucker, 2009), an area associated with, among other things, subjective valuation of reward (Rushworth & Behrens, 2008).

Relatively few developmentally-focused studies have investigated reward-related ERPs in childhood and adolescence in general, or specifically in relation to externalising behaviour. However, existing evidence indicates that FRN amplitude decreases from childhood to adulthood (Hammerer, Li, Muller, & Lindenberger, 2011) and shows reduced (though still significant) differentiation between gains and losses in children compared to adolescents and adults (Hammerer et al., 2011). Crowley et al. (2013) examined the FRN in a monetary reward task in a sample of early- (10-12 years), mid- (13-14 years) and late- (15-17 years) adolescents and found that FRN amplitudes

decreased with age even within the adolescent period, although differences between win and lose conditions did not vary by age. Recent data also indirectly suggest that externalising behaviour in adolescence may be associated with differences in the FRN. Segalowitz et al. (2012) observed reduced FRN activity in adolescent boys self-rated as high on approach motivation (Surgency - sensation seeking, positive affect, and behavioural approach) when presented with negative feedback in a peer interaction task. However, this study did not include a reward condition, leaving open the question of whether the findings reflect reduced sensitivity to punishment versus reward or a more general insensitivity to feedback. Similarly, Crowley et al. (2009) measured FRN responses in a sample of 32 high risk adolescents (foetal cocaine and other drug exposure) who were screened for high or low risk taking behaviour on the Balloon Analogue Risk Task (BART; Lejuez et al., 2002). They found that males who were characterised behaviourally as high risk-takers on the BART demonstrated smaller differences in FRN amplitudes to reward versus loss relative to males who were low risk takers, but only when feedback was presented after a short (1-second) delay and not after a longer (2-second) delay. As Nieuwenhuis, Slagter, Alting von Geusau, Heslenfeld, and Holroyd, (2005) have suggested that increasing feedback delay may diminish the motivational significance of feedback, Crowley et al.'s (2009) results indicate that motivational imbalance resulting in reward dominance is reduced with increasing feedback delay. Together, these studies suggest that approach motivation/risk-taking proclivity is associated with reduced FRN response, and therefore, it might be expected that individuals with externalising problems, who also commonly show these traits (Knyazev & Wilson, 2004), would also show reduced FRN responses to punishment (relative to rewards), and this effect will be increased in response to more immediate, motivationally significant feedback. Thus, while conceptual grounds for investigating the FRN as a candidate neural marker of risk for externalising psychopathology in adolescence are strong, few studies have done so.

To date, only one study has addressed the P3b response to reward cues in relation to externalising behaviours in young adults. Bernat, Nelson, Stelle, Gehring, and Patrick (2011) found that externalising behaviour was associated with reduced P3b amplitudes to feedback cues in a gambling task, and also found a tendency for high externalisers to show reduced P3b response to reward compared to punishment. However, in this study feedback was presented 100ms after participant response, which is an unusually short

period between choice and outcome. As previous work in other areas suggests that pre-stimulus EEG influences the P3 response through attentional mechanisms (Polich, 2007), and that activity in the anticipatory, pre-stimulus period affects P3b response (e.g. van der Molen et al., 2013), this very brief pre-stimulus period may have affected these results.

The current study examined the FRN and P3b response in relation to normative individual differences in adolescent externalising problems. Previous work suggests that adolescents with externalising-relevant traits (approach motivation, risk-taking) demonstrate reduced responsivity to punishment when measured by the FRN (Crowley et al., 2009). Thus, I expected to observe reduced FRN amplitudes for cues signalling loss relative to those signalling reward among adolescents with higher self-reported externalising behaviour scores. Similarly, I tested the hypothesis that P3b amplitude would differ based on participants' externalising scores, reflecting differences in the motivational significance ascribed to rewards and punishments. Further, as Crowley et al. (2009) found that adolescents with higher levels of externalising related traits, such as approach motivation, demonstrated smaller differences between reward and punishment FRN response, I expected to see changes in FRN amplitude amongst high externalising participants, but not low externalisers, when feedback is presented after a short delay compared to a long delay. Finally, I examined the extent to which these components change developmentally across adolescence, and whether age differences in these ERP components mirror normative trends in adolescent externalising behaviour.

Methods

Participants

For the analyses reported in this chapter and the chapter following, 78 typically-developing adolescents (ranging in age from 11-18 years; M = 14.5 years, S.D. = 1.7) were recruited from local areas, and asked to complete a random choice task whilst undergoing high density EEG. Inclusion and exclusion criteria are outlined in the methodology chapter.

Measures

MoneyMaker Task: Participants completed 140 trials (divided into 4 blocks) of the MoneyMaker Task. In each trial, participants were presented with 4 differently coloured balloons and asked to select the balloon they thought would lead to a reward. The result was predetermined and the trial would result in a 25p reward in 50% of the trails and a 25% loss in the remaining trials. Though the outcome was random, participants were told that there was a pattern that some players could "figure out some of the time".

Externalising Disorder Inventory (EDI): Participants were asked to complete the EDI, a 46-item scale measuring a several types of externalising behaviours, ranging from physical and interpersonal aggression to rebelliousness and honesty.

EEG

EEG pre-processing was conducted in EEGLAB after being exported from NetStation, and the details of the data pre-processing are outlined in the methodology chapter. ERP data for the FRN and P3b were extracted using a peak + window approach from two sites. The FRN window was centred on the most negative peak in 250-400ms post-stimulus window over frontal midline sites (electrodes 11, 15, 16, 10, and 18; see fig. 3.1). By comparison, the P3b window was centred on the maxima in the 270-420ms post-stimulus window over parietal sites (electrodes 62, 61, 67, 78, 72, 77, 54, and 79).

Statistical Analysis

The analysis of the behavioural data was conducted using an ANOVA, with target selection time entered as the dependent variable, and participant gender, age, and self-reported externalising behaviour as the independent variable.

To test the effects of externalising behaviour on EEG markers of reward processing, mixed-effects models were run using the *xtmixed* function in STATA 13. ERP amplitude was entered as the dependent variables. Feedback valence and delay were included as within-subjects factors with 2 levels. Both age and self-reported externalising behaviour were included in the model as centred, continuous between-subjects variables. Participant ID was included as a random effect in the model to account for individual variation in ERP response.

Post-estimation tests investigating significant interaction terms including a continuous term was conducted using a margins function with the dependant variable predicted from the continuous variable at 1 standard deviation above and below the mean.

Results

The results are separated into 4 sections: associations between externalising behaviour, age and gender; behavioural analysis, FRN analysis (*table 3.1*); and P3b analysis (*table 3.2*).

Similar to previous work, topographical maps revealed activity over frontal sites around 250-300ms after feedback and activity over parietal sites 300-400ms after feedback, consistent with the FRN and P3b, respectively (*fig. 3.1*).

Externalising behaviour

Pearson correlations indicated that there were no significant associations between age and externalising score (r = 0.17, p = 0.12) or gender and externalising score (r = -0.12, p = 0.28).

Behavioural analysis

There was no significant effect of participant age ($F(1,85) = 0.46$, $p = 0.49$), gender ($F(1,85) = 0.11$, $p = 0.74$), or self-reported externalising behaviour ($F(1,85) = 0.45$, $p = 0.50$) on participant target selection time.

Feedback-Related Negativity (FRN)

Within-subjects effects: There was a significant effect of feedback valence on FRN amplitude (b = -1.07, S.E. b = 0.34, z = -3.15, p = 0.002; *fig. 3.1*), with a more negative FRN amplitude in response to punishment than reward (-6.01μV vs. -4.63μV). However, no other effects reached significance.

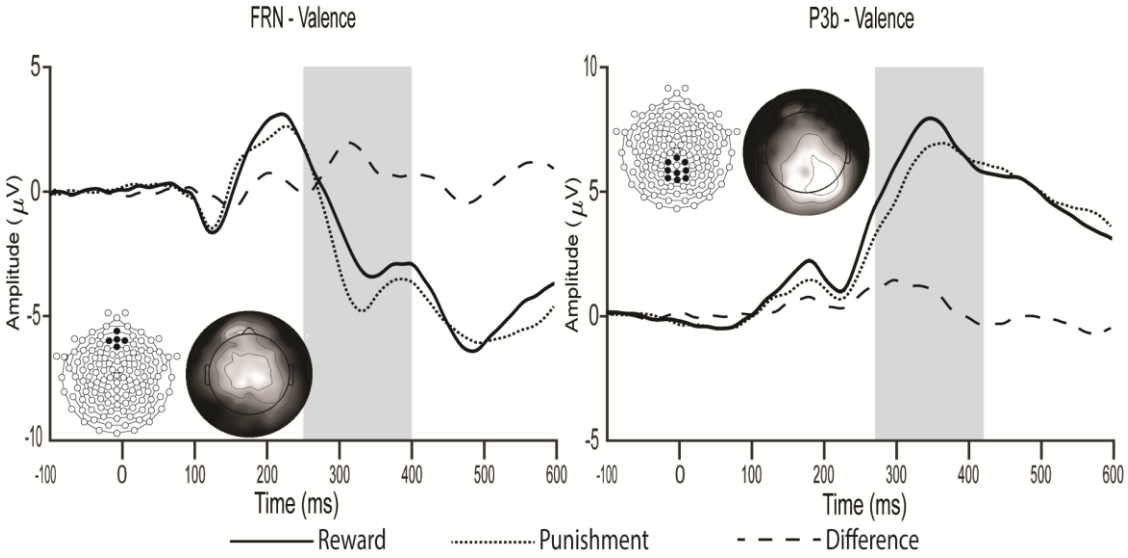

Figure 3.1. *Grand-Average Event Related Potentials waveforms for the Feedback-Related Negativity (FRN) and the P3b in response to reward and punishment stimuli. Grey area indicates the window of measurement. Sensor net layouts are inset with relevant electrode clusters highlighted in black. Also inset are topographic maps demonstrating scalp distribution at the grand average peak for the FRN (310ms) and the P3b (350ms) .*

Between-subjects effects: There were no significant main effects of age (b = 0.32, S.E. b = 0.24, z = 1.34, p = 0.18) or externalising behaviour (b = -0.02, S.E. b = 0.02, z = -1.20, p = 0.23) on FRN amplitude.

Interaction effects: There was a significant interaction between valence and externalising score (b = -0.05, S.E. b = 0.14, z = 3.23, p = 0.001; *fig. 3.2*). Post-estimation t-tests showed a significant difference in the FRN between reward and punishment in low (-1 S.D.) externalisers (t (73) = 5.35, p < 0.001, d = 0.66), with larger FRN amplitudes seen in response to punishment (-6.55μV, S.E = 0.49) compared to reward (-4.74μV, S.E = 0.49). However, high (+1 S.D.) externalisers did not demonstrate this difference (t (73) = 1.31, p = 0.19, d = 0.18), with similar amplitudes to punishment and reward (-5.52μV, S.E = 0.52 vs. -5.06μV, S.E = 0.52). Whilst visual inspection of the ERP suggests that this is driven by an attenuated FRN response to punishment amongst the high externalisers compared to the low externalisers, correlations between evoked FRN amplitudes and participant externalising score for reward and punishment stimuli did not reveal any relationship between externalising behaviour and FRN response to punishment (r = 0.21, p = 0.07) or reward (r = 0.02, p = 0.82).

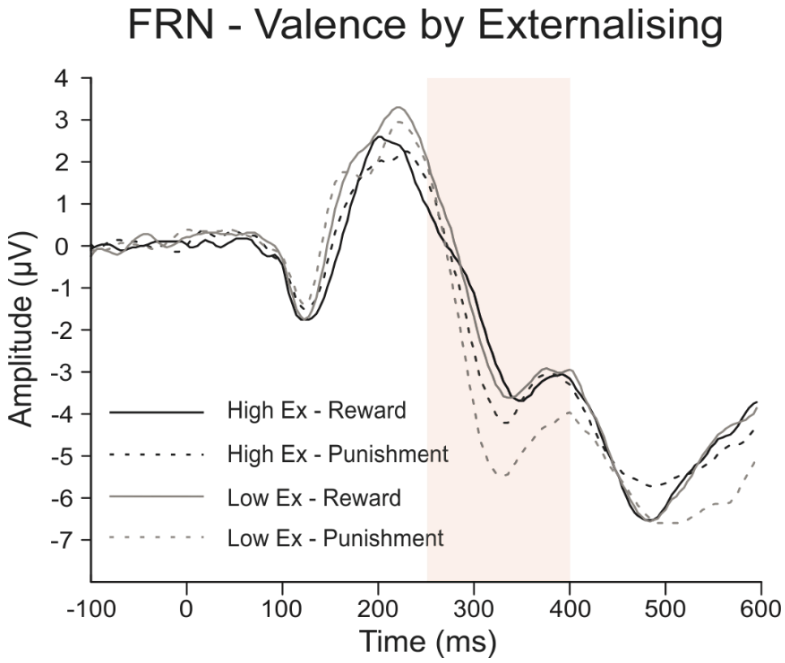

Figure 3.2. *FRN in response to reward and punishment feedback, divided by externalising group. Externalising behaviour groups were created via a median split of externalising score . Grey area highlights the window of interest.*

There was also a significant valence by age interaction (*b* = -0.52, S.E. *b* = 0.21, *z* = -2.53, *p* = 0.01). Older participants demonstrated a significant difference between valence conditions (*t* (73) = 5.20, *p* < 0.001, *d* = 0.64), with greater FRN response to punishment (-6.10μV, S.E = 0.49) than reward (-4.36μV, S.E = 0.49). Younger participants did not demonstrate this difference (punishment = -5.97μV, S.E = 0.54, reward = -5.50μV, S.E = 0.54; *t* (73) = 1.28, *p* = 0.20, *d* = 0.18).

Finally, there was a significant three-way interaction effect between valence, delay and externalising behaviour (*b* = -0.04, S.E. *b* = 0.02, *z* = -1.95, *p* = 0.05). Post estimation tests demonstrated that both low externalisers (punishment = -6.68μV, S.E = 0.54, reward = -5.34μV, S.E = 0.54; *t* (73) = 2.80, *p* = 0.005, *d* = 0.49) and high externalisers (punishment = -6.01μV, S.E = 0.58, reward = -5.03μV, S.E = 0.58; *t* (73) = 1.94, *p* = 0.05, *d* = 0.36) demonstrated a significant valence effect when feedback was presented after a long delay. After a short delay, the low externalising participants showed a significant difference between valence conditions (punishment = -6.42μV, S.E = 0.54, reward = -4.15μV, S.E = 0.54; t (73) = 4.78, *p* < 0.001, *d* = 0.83), whereas the high externalisers did not (punishment = -5.05μV, S.E = 0.58, reward = -5.09μV, S.E = 0.58; *t* (73) = 0.1, *p* = 0.94 *d* = 0.01). All other interaction effects were non-significant.

Table 3.1. *Results from the mixed effects model regressing FRN amplitude (μV) back on feedback valence, delay, participant age, and externalising activity, as well as all higher-order interactions. Reward and short delay were used as the baseline conditions.*

FRN			**Wald $\chi^2(15) = 54.14$, $p<0.00001$**	
Predictor	b	S.E. b	*z*	*p*
Valence	**-1.07**	**0.34**	**-3.15**	**0.002**
Delay	-0.57	0.34	-1.68	0.09
Age	0.32	0.24	1.34	0.18
Externalising	-0.02	0.02	-1.20	0.23
Valence * Delay	-0.07	0.48	-0.14	0.89
Valence * Age	**-0.52**	**0.21**	**-2.53**	**0.01**
Delay * Age	0.0002	0.21	0.001	0.99
Valence * Externalising	**0.05**	**0.14**	**3.23**	**0.001**
Delay * Externalising	0.03	0.01	1.74	0.08
Age * Externalising	0.02	0.01	1.62	0.11
Valence * Delay * Age	0.32	0.29	1.10	0.27
Valence * Delay * Externalising	**-0.04**	**0.02**	**-1.95**	**0.05**
Valence * Age * Externalising	0.002	0.01	0.20	0.84
Delay * Age * Externalising	-0.001	0.01	-0.10	0.92
Valence * Delay * Age * Externalising	0.004	0.01	0.37	0.71

Random Effects	Estimate	S.E.	95% Confidence Interval	
ID	2.72	0.25	2.27	3.26

P3b

Within-subjects effects: There were significant main effects of valence (*b* = -0.73, S.E. *b* = 0.30, *z* = -2.40, *p* = 0.02; *fig. 1*) and delay (*b* = 1.40, S.E. *b* = 0.30, *z* = 4.61, *p* < 0.001) on P3b amplitude. Larger P3b amplitudes were seen in response to reward (8.60μV) compared to punishment (7.96μV), and after long delays (8.96μV) compared to short delays (7.96μV).

Between-subjects effects: Neither the main effect of age (*b* = 0.02, S.E. *b* = 0.28, *z* = 0.08, *p* = 0.94) nor externalising behaviour (*b* = 0.01, S.E. *b* = 0.02, *z* = 0.62, *p* = 0.53) reached significance.

Interaction effects: The interaction between valence and externalising behaviour was significant (*b* = -0.03, S.E. *b* = 0.01, *z* = -2.23, *p* = 0.03; *fig. 3.3*). Post-estimation comparisons of marginal means showed that high externalisers demonstrated a significant difference between reward and punishment (*t* (73) = 4.64, *p* < 0.0001, *d* = 0.43), whilst the low externalisers did not (*t* (73) = 0.56, *p* = 0.58, *d* = 0.05). High externalisers demonstrated a larger P3b response to reward (9.09μV, S.E = 0.63) than punishment (7.63μV, S.E = 0.63), an effect not seen in the low externalisers (reward: 8.56μV, S.E = 0.60, punishment: 8.40μV, S.E = 0.60). No other interaction terms reached significance.

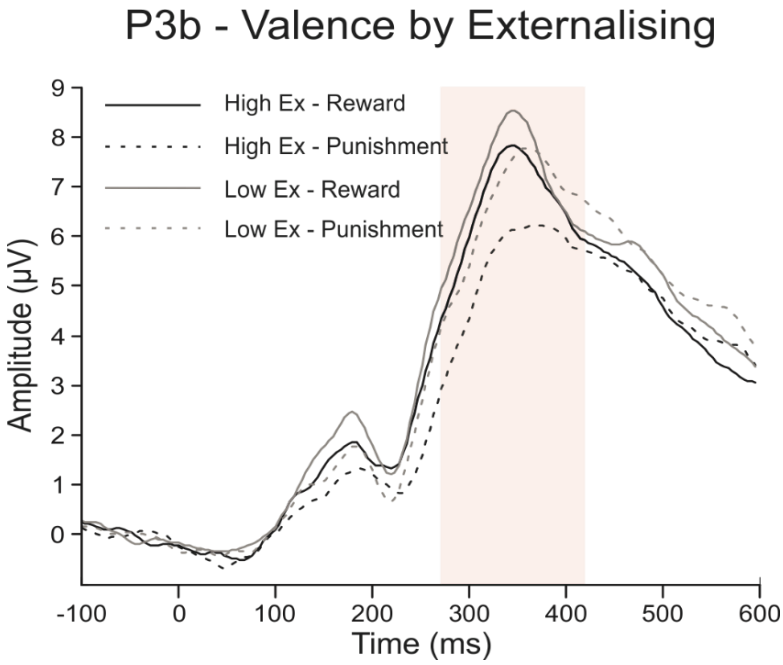

Figure 3.3. *P3b in response to reward and punishment feedback, divided by externalising group. Externalising behaviour groups were created via a median split of externalising score. Grey area highlights the window of interest.*

Table 3.2. *Results from the mixed effects model regressing P3b amplitude (μV) back on feedback valence, delay, participant age, and externalising behaviour, with all higher-order interaction terms. Reward and short delay were used as the baseline conditions.*

P3b			**Wald $\chi^2(15) = 70.29$, $p<0.00001$**	
Predictor	b	S.E. b	*z*	*p*
Valence	**-0.73**	**0.30**	**-2.40**	**0.02**
Delay	**1.40**	**0.30**	**4.61**	**0.0001**
Age	0.02	0.28	0.08	0.94
Externalising	0.01	0.02	0.62	0.53
Valence * Delay	-0.23	0.43	-0.55	0.58
Valence * Age	0.27	0.18	1.45	0.15
Delay * Age	-0.26	0.18	-1.14	0.16
Valence * Externalising	**-0.03**	**0.01**	**-2.23**	**0.03**
Delay * Externalising	-0.001	0.01	-0.10	0.92
Age * Externalising	-0.01	0.01	-1.10	0.27
Valence * Delay * Age	0.21	0.26	0.79	0.43
Valence * Delay * Externalising	0.003	0.02	0.17	0.87
Valence * Age * Externalising	0.01	0.01	0.99	0.33
Delay * Age * Externalising	0.002	0.01	0.27	0.79
Valence * Delay * Age * Externalising	0.01	0.01	0.62	0.53

Random Effects	Estimate	S.E.	95% Confidence Interval	
ID	3.54	0.31	2.99	4.19

Discussion

Adolescence is a period of development associated with maturation of reward circuitry in the brain, and significant increases in externalising behaviour. Despite the fact that several theories focus on reward sensitivity as a key mechanism in antisocial behaviour (e.g. Quay, 1993), findings from previous neuroimaging studies investigating reward-related neural activity among adolescent externalisers have been mixed. In this study, adolescents from a community sample completed a monetary reward task with

concurrent high-density EEG to assess two key ERP components related to reward processing, the FRN and the reward-related P3b. The relationship between these feedback evoked ERPs and self-reported externalising scores was then investigated.

Consistent with previous ERP studies in adults (e.g., Hajcak et al., 2005), both FRN and P3b amplitudes were influenced by feedback valence. As expected, greater amplitudes in the P3b and FRN were seen in response to reward and loss, respectively. The valence effects on these ERP components further reinforce their value as markers of reward processing in adolescence and therefore their potential as endophenotypes for externalising problems at a pre-clinical level. While several studies have examined reward versus loss effects on the FRN in adolescence (Crowley et al., 2009; 2013), less work has done so in relation to the P3b. In that regard, the findings concerning the P3b were different to those observed by Crowley et al. (2009), who found larger P3b amplitudes for loss than reward, but were consistent with the majority of studies of reward and the P3b in adults (e.g., Wu & Zhou, 2009).

The primary aim of this study was to examine feedback-related neural responses linked to self-reported externalising behaviour problems in adolescence. Consistent with expectation, both FRN and P3b amplitudes showed an interaction between externalising behaviour and feedback valence. In the FRN, adolescents scoring high on the externalising measure demonstrated smaller differences in FRN amplitude between reward and punishment feedback. Visual inspection of the ERP data suggested that his was primarily due to reduced (more positive) FRN amplitudes to punishment feedback adolescents with high externalising scores compared to those with low externalising scores. The FRN is often considered to reflect error-monitoring processes generated by the ACC. Thus, the reduced difference in FRN amplitude among those adolescents with relatively high externalising behaviour may indicate diminished error monitoring, particularly in response to punishment. An alternative interpretation of the FRN is that it reflects reward prediction errors generated by the ACC (Holroyd & Coles, 2002), though recent evidence suggests it may not display all the properties expected of a prediction error signal (Talmi et al., 2012). An alternative account suggested by the recent work of Talmi, Atkinson and El-Deredy (2013) is that the FRN reflects an unsigned prediction error, equivalent to expectation violation or surprise. The lack of differentiation between reward and punishment-evoked FRN response seen in the

sample of high externalising adolescents may therefore suggest that high externalisers fail to develop differential outcome expectations. Clearly, the precise mechanisms driving the FRN response and its role in externalising behaviour are important avenues for future research

Notably, the interaction between valence and externalising behaviour in the FRN appeared only when feedback was presented after a short delay, with no interaction effect between valence and externalising on FRN amplitude following a long delay. Past work investigating delay has been limited. Crowley et al. (2009) found that a 1-second delay period yielded a greater FRN response than a 2 second delay regardless of feedback valence, consistent with Nieuwenhuis et al.'s (2005) postulation of reduced motivational significance of feedback as time between action and feedback cue increases. However, using a block design, Weinberg, Luhmann, Bress, and Hajcak (2012) did not find a general delay effect. Instead, they found a valence difference at 1 second, with larger FRN response to punishment, which decayed when feedback was presented after 6 seconds. Similarly, these results suggest that differences in error monitoring between the high and low externalisers exist, but are only apparent during a relatively brief window following a reward-related choice.

In contrast to the FRN, *larger* P3b amplitude differences between conditions were seen in participants with higher externalising scores, with adolescents who scored highly on self-reported externalising behaviour showing larger P3b responses to reward than punishment, relative to those with low externalising behaviour scores. As the P3b is thought to reflect attentional effects associated with the motivational significance of stimuli during feedback tasks (Niuewenhuis et al., 2004; Wu & Zhou, 2009), these findings could suggest that the high externalisers demonstrated greater imbalance between the motivational significance of reward and punishment than their low externalising counterparts, with greater significance attributed to reward.

Thus, the results reported here seem to suggest that adolescents scoring highly on measures of externalising behaviour assign greater salience or motivational value to reward cues than their low-scoring counterparts (as evidenced by the P3b), consistent with reward dominance theories (Quay, 1993), but also show reduced outcome monitoring, particularly in relation to punishment. The findings indicating that high externalisers produce less reliable error signals differentiating punishment and reward,

may have implications for how we understand the role of learning impairments in externalising behaviour. With that in mind it is interesting to note that Cohen and Ranganath (2007) found that larger FRN amplitudes were associated with increased task-appropriate response switching during learning tasks; the reduced outcome monitoring I observed among high externalising adolescents might thus lead us to expect these adolescents to show poorer reinforcement learning, similar to the weaker signal discrimination seen in those with higher externalisers scores compared to lower externalising scores observed by Endres, Rickert, Bogg, Lucas, and Finn (2011).

Two additional findings of interest emerged from the data. First, a valence by age interaction in the FRN indicated greater differences between punishment and reward ERP responses in older participants versus younger participants. As the FRN is generated in the ACC (Hauser et al., 2014), this difference between younger and older externalisers may reflect the development of frontal circuitry (Giedd et al., 1999), and related functional networks (Kelly et al., 2009), known to occur over adolescence. Developmental changes across adolescence may lead to more effective classification of reward and punishment feedback given the ACCs role in feedback processing (Holroyd et al., 2004) and error-driven learning (Brown & Braver, 2005).

Second, P3b amplitudes varied as a function of feedback delay. However, unlike previous FRN findings mentioned above, P3b amplitudes increased after long delays as opposed to short delays. As the P3b is thought to be generally related to attention and motivation (Polich, 2007), the greater response seen in this sample may be indicative of anticipatory or expectancy effects, where attention increases whilst waiting for feedback.

Limitations

This study should be considered in light of its limitations. First, while the shortened EDI demonstrated reasonable to good alpha values and correlations with its full-scale counterpart, it contains too few items per sub-scale to allow for meaningful statistical comparison at the sub-scale level. Given that presentation of externalising behaviours differs between genders, sub-scale analysis would allow more precise investigation into gender differences in specific domains of externalising problems and

reward sensitivity. Future work using the full-scale EDI could help elucidate differences between sub-samples.

Moreover, given that some participants were missing data from the scale, this may have skewed results. As we cannot be sure whether participants scoring lower on the EDI measure may have been involved in less externalising behaviour, missed question, or potentially refused to answer questions regarding their involvement in certain externalising behaviours. Therefore, the results reported here should be interpreted with caution. However, this potentially highlights the need for methods designed to ensure complete participant reporting on psychometric measures. This may be especially true during experiments where participants may be uncomfortable reporting on certain behaviours, perhaps due to concerns of the experimenter reading their responses (for example, externalising behaviours amongst adolescents), or amongst samples that may be less engaged with questionnaire measures. Future work with the samples or topics may benefit from questionnaire apps or programs that prevent participants from progressing through the experiment without fully responding, but do not require the experimenter to check the responses following completion.

Secondly, the variability in the delay in the long delay condition may have influenced participant's attention to delayed feedback cues, potentially confounding results. The unpredictability of the long delay stimulus presentation may have altered long-delay elicited P3b amplitudes through attentional mechanisms, as the P3b is thought to be attentional in nature (Polich, 2007), and the related non-feedback P300 demonstrates greater amplitude to attended than non-attended stimuli (Gray, Ambady, Lowenthal, & Deldin, 2004; Spencer & Polich, 1999). Future work including a delay component should explore the effects of both fixed delay periods to avoid the influence of surprise or expectancy on P3b amplitudes, and directly assess the effects of jittered presentation of outcomes at both short and long delays.

Additionally, the findings reported here concern externalising behaviour in a normative sample, and whilst they indicate avenues of interest to investigate within clinical samples, the electrophysiological patterns may not be representative of those with clinical diagnoses of CD or other disruptive behaviour disorders. Future work will need to examine feedback processing among youth with more severe antisocial behaviour at clinical levels.

Finally, whilst these results suggest that externalisers may demonstrate attenuated feedback monitoring processes, the findings only generalize to the type of chance-based task used here. However, if this alteration in FRN response to feedback valence may impact learning, it may help to be better understand the increased behavioural approach and difficultly altering response in response reversal tasks characteristic of externalisers. Further work is needed investigating how externalising youth may differ in FRN amplitude in a learning task.

Conclusions

In summary, this study supports theories of reward dominance in adolescents with high levels of externalising behaviour (e.g. Gray, 1987; Quay, 1993). Adolescent externalisers demonstrated greater motivational imbalance between reward and punishment, as measured by the P3b, than their low externalising counterparts. Furthermore, high externalisers also demonstrated reduced differences between reward and punishment response in the FRN, indicative of a reduced prediction error response or reduced outcome monitoring, which may lead to poorer learning from feedback.

Chapter 4

Feedback induced oscillatory activity and externalising behaviour in normative adolescence.

Abstract

This is a reanalysis of the Adolescent Thoughts and Feelings project data presented in Chapter 3.

Previous work with adolescents has found differences in reward related EEG components between high and low externalisers, indicative of altered feedback related neural processing. More recently, emerging work has favoured time-frequency analysis as a method of investigating the neural processing related to feedback cues, identifying activity in the delta, theta, and beta bands as sensitive to feedback valence. Currently, little is known about the relationship between externalising behaviour and feedback-induced spectral activity, and work in adolescents has been limited to the theta band. Here, I present the results from a study on normative adolescents, who completed a monetary gambling task. Time-frequency information was extracted from the window after feedback presentation, and the relationship between self-reported externalising score and EEG activity was investigated. Participants scoring highly on externalising measures did not differ from low scorers in neural activity during predefined theta or lower beta band windows. However, exploratory analysis identified potential windows in the alpha and beta bands that may guide future research with clinical samples.

Introduction

Learning and decision making is guided by endogenous and exogenous feedback from previous decisions, and differences in motivational value attributed to different options may help to explain why risky decisions are made. Several studies have already demonstrated that adolescents are more prone to reward-driven choices than younger children or adults (Galvan et al., 2006; Smith, Xiao, & Bechara, 2012; van Leijenhorst et al., 2010). This effect may be exacerbated in high externalising adolescents. Quay (1993), building on work from Gray (1987), suggested that increase in reward-focused approach systems (Reward System; Gray, 1987), combined with a normal or ineffectual punishment-driven avoidant system (Behavioural inhibition system; Gray, 1987), may lead to greater valuation of reward, even in the face of increased punishment – an imbalance know as Reward Dominance.

Previous work on high externalising groups have found they score more highly on questionnaire measures of reward sensitivity and approach behaviours, such as the BAS scale (Colder & O'Connor, 2004; Hundt, Kimbrel, Mitchell, & Nelson-Gray, 2008; Muris, Meesters, de Kanter, & Timmerman, 2005), when compared against typically developing counterparts. Moreover, externalisers also demonstrate reward sensitivity during behavioural paradigms involving reward-related decisions. The most widely used is the Card Playing Task (CPT; Newman, Patternson, & Kosson, 1987) in which CD individuals demonstrate greater levels of perseverative behaviour compared to control individuals despite the decreasing likelihood of reward and increasing chance of punishment (Daugherty & Quay, 1991; Matthys, van Goozen, de Vries, Cohen-Kettenis, & van Engeland, 1998; O'Brien & Frick, 1996; Séguin, Arseneault, Boulerice, Harden, & Tremblay, 2002).

As previously stated, several fMRI studies investigating the relationship between externalising behaviour and feedback responsivity have identified altered reward response amongst externalisers in areas associated with reward, such as the OFC (Finger et al., 2011), VS (Bjork, Smith, Chen, & Hommer, 2010), and the ACC (Gatzke-Kopp et al., 2010), providing a strong basis for investigating externalising difference in feedback processing. Similarly, two ERPs associated with exogenous feedback processing, the FRN and the P3b (Bellebaum & Daum, 2008; Santesso, Dzyundzyak, & Segalowitz, 2011), also demonstrated altered responsivity amongst

externalising samples.

Using these two ERPs, Bernat, Nelson, Steele, Gehring, and Patrick (2011) found that externalising undergraduates demonstrated reduced P3b amplitudes in response to feedback, with a greater reduction seen in response to wins compared to losses, which they attribute to a diminished motivational effect of feedback in general, with less motivation assigned to reward. In contrast , the findings reported in chapter 3 demonstrated greater differences in P3b amplitude between reward and punishment in adolescents who scored highly on externalising measures (compared to low-scoring adolescents), with high externalisers demonstrating greater P3b amplitudes to reward compared to punishment. Furthermore, high externalising adolescents demonstrated smaller FRN amplitude differences between reward and punishment compared to the low externalisers. Contrary to Bernat and colleagues, these results seem to indicate dual-processes at play in relation to externalising problems: higher motivational value attributed to reward, and attenuated error-monitoring processes. These inconsistencies between the findings of Bernat et al. (2011) and the previous chapter may reflect differences in tasks used to elicit neural responses. Their short inter-stimulus period between participant response and feedback may have affected their P3b response as recent work suggests anticipatory, pre-stimulus activity influences P3b response (e.g. van der Molen et al., 2013). Alternatively, as I used an adolescent sample, it may be that the relationship between reward sensitivity and externalising behaviour as outlined by Quay (1993) is more applicable to adolescent rather than adult samples.

Using ERSPs to analyse feedback-evoked neural activity may be a viable alternative to ERPs, and work investigating the FRN (Cavanagh, Zambrano-Vazquez, & Allen, 2012) and the P3b (Bernat et al., 2011) suggests that these ERPs may be characterised by changes in the theta and delta band respectively. Consistently, past work has found a change in theta activity (4–8Hz) between 200-600ms after feedback presentation, with higher activation being demonstrated in response to error-related feedback (Cavanagh, Zambrano-Vazquez, & Allen, 2012; Cohen, 2011b) and monetary loss (Cohen, Elger, & Fell, 2009; Crowley et al., 2014). Early work by Luu et al. (2003) suggests that this theta activity is related to the FRN ERP, and recent time-frequency decomposition of the FRN by Bernat et al. (2011) revealed increases in theta band activity. However, by subjecting an averaged ERP component to time-frequency

decomposition, the study only reflects phase-locked theta activity. In contrast, a recent study by Cavanagh, Zambrano-Vazquez, & Allen (2012) found that changes in mediofrontal theta band activity was an encompassing feature of 4 ERPs (including the FRN, and the closely related Error Related Negativity, or ERN). Thus, whilst individual ERPs may encode separate stages of action monitoring, such as endogenous and exogenous error processing or reward prediction error, midline theta activity may reflect a more general action monitoring process. Nevertheless, similar to the FRN, feedback-induced theta demonstrates increased activity to negatively-valenced stimuli (Cavanagh, Figueroa, Cohen, & Frank, 2012; Cavanagh, Zambrano-Vazquez, & Allen, 2012; Cohen, 2011b; Crowley et al., 2014), greater activity to uncertainty (Cavanagh et al., 2012), has frontal midline topography (Cavanagh, Zambrano-Vazquez, & Allen, 2012; Cohen, 2011b), and has been localised to the ACC (Ishii et al., 2014).

Feedback induced changes in beta activity (13-30Hz) have also been documented, but less thoroughly investigated. Several papers have found an increase in beta activity following feedback cues, with larger increases in beta activity upon presentation of a reward compared to a punishment (Marco-Pallarés et al., 2008; Marco-Pallarés et al., 2009; van de Vijver, Ridderinkhof, & Cohen, 2011), but opposing results have also been reported, with greater beta band activity to punishment compared to reward observed in some studies (Banis, Geerligs, & Lorist, 2014; Cohen, Elger, & Fell, 2009). Furthermore, beta band activity appears to be sensitive to other characteristics of reward feedback. Both larger magnitude reward cues (Marco-Pallarés et al., 2008) and lower probability reward (Cohen, Elger, & Ranganath, 2007) induce greater beta band activity, whilst no such feedback effects occurred in punishment conditions.

Moreover, higher beta band activity has consistently been found in people with substance use disorder (SUD) in resting state (Rangaswamy et al., 2002). As SUD is often comorbid with antisocial behaviour (Armstrong & Costello, 2002), and epidemiological work by Kendler, Prescott, Myers, and Neale (2003) suggests that common genes contribute to both, neural oscillatory changes in those with substance abuse disorders may also be reflected in those scoring highly on externalising behaviours. Given that SUDs, similar to externalising behaviours, are thought to have their roots in altered reward systems (Volkow, Fowler, Wang, Baler, & Telang, 2009), this common factor may express itself during feedback tasks.

So far, relatively few studies have investigated oscillatory feedback responsivity in externalisers. Bernat et al. (2011) and Hall, Bernat, and Patrick (2007) have both found differences between high externalisers' and low externalisers' spectral profiles in response to feedback. Bernat et al. (2009) found externalisers demonstrated significantly lower delta activity than low externalisers. Similarly, Hall et al. (2007) found a reduction in theta activity 50-75ms after error feedback for high externalisers compared to low externalisers. However, these studies both investigated the time-frequency decomposition of the principal-component ERP waveform, and not the phase unlocked, induced oscillatory activity. If these two ERPs are products of underlying spectral activity, then performing time-frequency analysis on the ERPs themselves combines information related to both frequency band power and inter-trial coherence, making it difficult to identify which differs between externalising groups. By averaging data in the time domain (as ERPs) before spectral analysis, smaller ERP waveforms may be due to lower spectral power, lower inter-trial coherence leading to more temporally spread ERPs due to less consistency the phasic peaks in the sinusoidal waveform following feedback, or a combination of the two. Furthermore, these studies have tested undergraduate samples, not adolescent samples. Yet the rise in externalising disorders and risk-taking behaviour (Maughan et al., 2004) and developmental changes in feedback related neural oscillatory activity (Crowley et al., 2014) over adolescence highlights the importance of investigating the effects of externalising behaviour on processing of feedback cues in adolescent samples.

Methods

Participants and Externalising Measures

Both the participant sample and the externalising measure used in this chapter are the same as those reported in the previous chapter. I direct the reader back to the Adolescent Thoughts and Feelings Project subsection in the methodology chapter for a detailed explanation of the sample and externalising measure.

EEG

After the EEG data was pre-processed, time-frequency information was extracted using a family of Morlet wavelets using the *newtimef* function in EEGLAB. These wavelets increased linearly in frequency from 2 to 50Hz, and increased in cycle

number from 1 at the lowest frequency to 12.5 at highest frequency. Power was scaled to decibels (dB; computed as 10*log10 of the power), and baselined from -200 to stimulus presentation. Frontal theta and beta band power was defined as the average activity over the 4-8Hz 250-400ms and 13-20Hz 500-800ms time-frequency windows at the Fz electrode. Parietal band power was extracted for the delta (2-4Hz 200-400ms time-frequency window), theta (4-8Hz 250-400ms time-frequency window), and beta band (13-20Hz 500-800ms time-frequency window) at the Pz electrode.

Statistical Analysis

Similar to the previous chapter, hypothesis testing was conducted using mixed-effects models run in STATA 13. Frequency band power was included as a dependent variable. Both feedback valence and delay were within-subjects factors with 2-levels. Participant gender was included as a between-subjects factor with 2-levels, and age and self-reported externalising behaviour were included in the model as centred, continuous predictors.

In addition to the planned comparisons, further exploratory analyses were conducted by correlating self-reported externalising behaviour against each time-frequency point in the 2-30Hz 150-600ms post-stimulus time-frequency window. Each analysis was then corrected using False Discovery Rate correction.

Results

ERSP activity was extracted from two windows of interest: theta activity (4-8Hz) 250-400ms post stimulus; and beta activity (13-20Hz) 500-800 post stimulus. This activity was extracted from two electrodes, the Fz and Pz. Delta activity (2-4Hz) was also extracted from the Pz electrode between 200-400ms post-stimulus. Further exploratory analysis investigating the relationship between externalising behaviour and valence differences were conducted.

Relationship between externalising behaviour, age and gender.

Point-biserial correlations between externalising behaviour, age and gender revealed that there were significant but weak correlations between participant gender and self-reported externalising behaviour (r_{pb} = -0.21, p = 0.04), and participant age and

gender (r_{pb} = 0.27, p = 0.01). Females demonstrated lower EDI scores compared to males (122 vs. 133), and females were older on average than males (15.0 y.o. vs. 14.1 y.o.). The correlation between age and externalising behaviour was non-significant (r = 0.08, p = 0.46).

Oscillatory activity over frontal sites

Theta: Theta was sensitive to feedback valence (b = 0.50, S.E. b = 0.20, z = 2.48, p = 0.01; *table 4.1*). Punishment feedback resulted in larger theta activity than reward (2.08dB vs. 1.62dB). There was also a significant effect of participant age on theta response (b = 0.21, S.E. b = 0.09, z = 2.34, p = 0.02). Investigation of the marginal means found that older adolescents (+1 S.D.) show greater feedback theta response than younger adolescents (-1 S.D.) regardless of feedback valence (2.17dB & 1.55dB, respectively). No other effects reached significance.

Beta: There was a significant effect of valence on beta activity (b = 0.42, S.E. b = 0.15, z = 2.84, p = 0.004; *table 4.2*) with greater beta suppression to reward compared to punishment (-0.39dB vs. -0.10dB). No other effects reached significance at the α = 0.05 level.

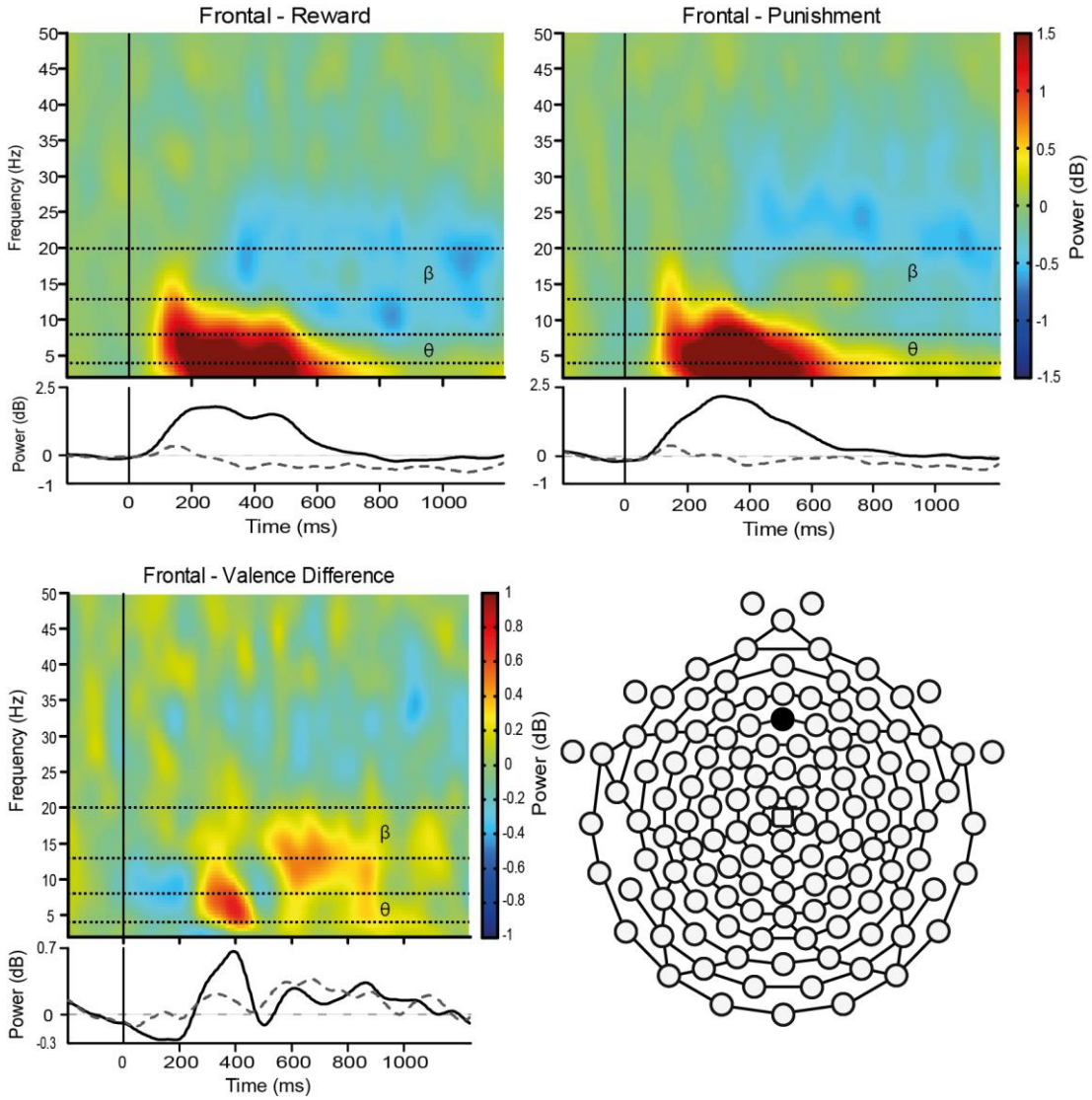

Figure 4.1. *Average time-frequency distribution for reward, punishment, and their difference, measured in decibels (dB), taken from the frontal electrode. Frequency bands for the theta (θ) and beta (β) bands are marked delineated on the contour plot. Power distributions are displayed below each time-frequency plot, demarcating changes in theta (black line) and low beta (13-20Hz; dashed grey line) over time. The electrode from which activity was extracted, electrode 11, is highlighted in black in the bottom right hand corner.*

Table 4.1. *Mixed effects model regressing frontal theta activity back on valence, delay, age, gender and externalising behaviour.*

Frontal Theta			Wald chi2(23) = 46.96, p = 0.002	
Predictor	*b*	*S.E. b*	*z*	*p*
Valence	**0.5**	**0.2**	**2.48**	**0.01**
Delay	0.29	0.2	1.41	0.16
Age	**0.21**	**0.09**	**2.31**	**0.02**
Gender	-0.5	0.3	-1.65	0.1
Externalising	-0.001	0.01	-0.08	0.94
Valence * Delay	-0.12	0.29	-0.43	0.67
Valence * Age	-0.1	0.09	-1.1	0.27
Valence * Gender	0.01	0.29	0.02	0.98
Valence * Externalising	0.005	0.01	0.61	0.54
Delay * Age	0.004	0.09	0.04	0.97
Delay * Gender	0.01	0.29	0.02	0.98
Delay * Externalising	0.003	0.01	0.38	0.7
Age * Externalising	-0.002	0.004	-0.52	0.61
Gender * Externalising	-0.001	0.01	-0.08	0.94
Valence* Delay * Age	0.08	0.12	0.67	0.51
Valence* Delay * Gender	-0.05	0.41	-0.13	0.9
Valence * Delay * Externalising	-0.01	0.01	-0.72	0.47
Valence* Age * Externalising	0	0.004	-0.09	0.93
Valence * Gender * Externalising	-0.02	0.01	-1.52	0.13
Delay * Age * Externalising	0.003	0.004	0.87	0.39
Delay * Gender * Externalising	-0.003	0.01	-0.27	0.79
Valence * Delay * Age * Externalising	-0.01	0.01	-0.98	0.33
Valence * Delay * Gender * Externalising	0.02	0.02	1.06	0.29
Intercept	1.74	0.21	8.14	0.001
Random-effects	Estimate	S.E.	95% Confidence Interval	
Identity	0.96	0.09	0.8	1.15

Table 4.2. *Mixed effects model regressing frontal beta activity back on valence, delay, age, gender and externalising behaviour.*

Frontal Beta			Wald chi2(23) = 39.02, p = 0.02	
Predictor	*b*	*S.E. b*	*z*	*p*
Valence	**0.42**	**0.15**	**2.84**	**0.004**
Delay	-0.26	0.15	-1.71	0.09
Age	-0.07	0.05	-1.28	0.2
Gender	0.05	0.17	0.31	0.76
Externalising	0.001	0.005	0.16	0.87
Valence * Delay	-0.06	0.21	-0.3	0.77
Valence * Age	0.04	0.06	0.6	0.55
Valence * Gender	-0.18	0.21	-0.87	0.39
Valence * Externalising	-0.001	0.01	-0.1	0.92
Delay * Age	-0.03	0.06	-0.39	0.7
Delay * Gender	0.39	0.21	1.86	0.06
Delay * Externalising	0.001	0.01	0.19	0.85
Age * Externalising	0	0.002	0.2	0.84
Gender * Externalising	-0.003	0.01	-0.45	0.66
Valence* Delay * Age	-0.03	0.09	-0.36	0.72
Valence* Delay * Gender	-0.08	0.3	-0.26	0.8
Valence * Delay * Externalising	0.01	0.01	0.7	0.48
Valence* Age * Externalising	-0.0002	0.003	-0.06	0.95
Valence * Gender * Externalising	0.002	0.01	0.25	0.8
Delay * Age * Externalising	-0.003	0.003	-1	0.32
Delay * Gender * Externalising	0.004	0.01	0.45	0.66
Valence * Delay * Age * Externalising	0.0002	0.004	0.05	0.96
Valence * Delay * Gender * Externalising	-0.01	0.01	-0.51	0.61
Intercept	-0.39	0.12	-3.25	0.001
Random-effects	Estimate	S.E.	95% Confidence Interval	
Identity	0.36	0.05	0.27	0.47

Oscillatory effects over parietal sites

Theta: There were significant main effects of both feedback valence (b = 0.45, S.E. b = 0.23, z = 1.94, p = 0.05; *table 4.3*) and delay (b = 0.48, S.E. b = 0.23, z = 2.06, p = 0.04; *fig. 2*) on theta activity. Theta response was larger in response to punishment stimulus compared against reward (2.25dB vs. 1.92dB), and when feedback was presented after a long delay compared to a short delay (2.18dB vs. 2.00dB). There was also a main effect of age (b = 0.25, S.E. b = 0.10, z = 2.43, p = 0.02). Similar to frontal

theta, parietal theta activity increased with age (older participants: 2.50dB, younger participants: 1.69dB). No other effects reached significance at the α = 0.05 level.

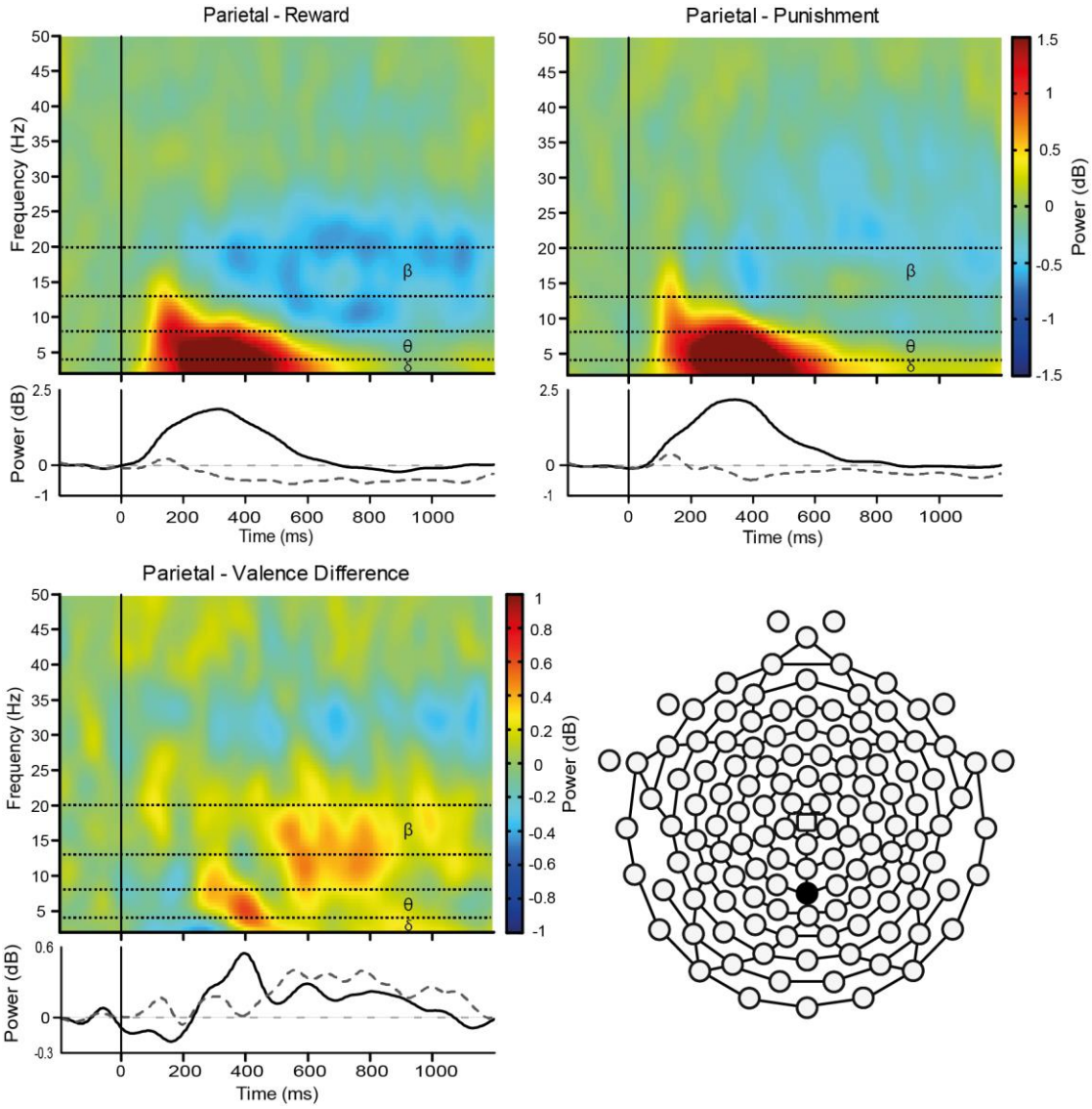

Figure 4.2. A*verage time-frequency distribution for reward, punishment, and their difference, mrsdutrf in decibels (dB), taken from the parietal electrode. Frequency bands for the delta (δ), theta (θ) and beta (β) bands are marked delineated on the contour plot. Power distributions are displayed below each time-frequency plot, demarcating changes in theta (black line) and low beta (13-20Hz; dashed grey line) over time. The electrode from which activity was extracted, electrode 62, is highlighted in black in the bottom right hand corner.*

Beta: There was a significant effect of valence on beta activity (*b* = 0.61, S.E. *b* = 0.16, *z* = 3.80, *p* = 0.001; *table 4.4*). Reward feedback induced greater beta suppression than punishment (-0.53dB vs. -0.19dB). There was also a main effect of gender (*b* = 0.36, S.E. *b* = 0.18, *z* = 1.98, *p* = 0.05), with males demonstrating greater beta suppression than females, in general (-0.51dB vs. -0.22dB). All other effects were

non-significant.

Table 4.3. *Mixed effects model regressing parietal theta activity back on valence, delay, age, gender and externalising behaviour.*

Parietal Theta			Wald chi2(23) = 43.90, *p* = 0.005	
Predictor	*b*	*S.E. b*	*z*	*p*
Valence	**0.45**	**0.23**	**1.94**	**0.05**
Delay	**0.48**	**0.23**	**2.06**	**0.04**
Age	**0.25**	**0.1**	**2.43**	**0.02**
Gender	-0.35	0.33	-1.06	0.29
Externalising	0.01	0.01	0.58	0.57
Valence * Delay	-0.38	0.33	-1.17	0.24
Valence * Age	-0.04	0.1	-0.39	0.7
Valence * Gender	-0.12	0.33	-0.38	0.71
Valence * Externalising	-0.0001	0.01	-0.01	0.99
Delay * Age	-0.002	0.1	-0.02	0.99
Delay * Gender	-0.38	0.33	-1.16	0.25
Delay * Externalising	0.01	0.01	0.68	0.49
Age * Externalising	0.001	0.004	0.29	0.77
Gender * Externalising	-0.001	0.01	-0.1	0.92
Valence* Delay * Age	0.05	0.14	0.37	0.71
Valence* Delay * Gender	0.43	0.46	0.93	0.35
Valence * Delay * Externalising	-0.01	0.01	-0.58	0.56
Valence* Age * Externalising	-0.004	0.004	-0.88	0.38
Valence * Gender * Externalising	-0.02	0.01	-1.8	0.07
Delay * Age * Externalising	0.003	0.004	0.57	0.57
Delay * Gender * Externalising	-0.01	0.01	-0.68	0.49
Valence * Delay * Age * Externalising	-0.01	0.01	-0.9	0.37
Valence * Delay * Gender * Externalising	0.03	0.02	1.62	0.11
Intercept	1.97	0.24	8.35	0.001
Random-effects	Estimate	S.E.	95% Confidence Interval	
Identity	1.03	0.1	0.85	1.24

Table 4.4. *Mixed effects model regressing parietal beta activity back on valence, delay, age, gender and externalising behaviour.*

Parietal Beta			Wald chi2(23) = 49.09, p = 0.001	
Predictor	*b*	*S.E. b*	*z*	*p*
Valence	**0.61**	**0.16**	**3.8**	**0.001**
Delay	-0.18	0.16	-1.15	0.25
Age	-0.06	0.06	-1.14	0.25
Gender	**0.36**	**0.18**	**1.98**	**0.05**
Externalising	0.01	0.01	1.32	0.19
Valence * Delay	-0.19	0.23	-0.83	0.4
Valence * Age	0.04	0.07	0.53	0.6
Valence * Gender	-0.39	0.23	-1.74	0.08
Valence * Externalising	-0.003	0.01	-0.49	0.63
Delay * Age	-0.05	0.07	-0.79	0.43
Delay * Gender	0.15	0.23	0.67	0.51
Delay * Externalising	-0.002	0.01	-0.26	0.8
Age * Externalising	0.001	0.002	0.25	0.81
Gender * Externalising	-0.003	0.01	-0.45	0.65
Valence* Delay * Age	-0.03	0.1	-0.27	0.78
Valence* Delay * Gender	0.19	0.32	0.6	0.55
Valence * Delay * Externalising	-0.005	0.01	-0.53	0.6
Valence* Age * Externalising	0.001	0.003	0.21	0.84
Valence * Gender * Externalising	0	0.01	-0.03	0.98
Delay * Age * Externalising	-0.002	0.003	-0.57	0.57
Delay * Gender * Externalising	0.001	0.01	0.09	0.93
Valence * Delay * Age * Externalising	-0.002	0.004	-0.44	0.66
Valence * Delay * Gender * Externalising	0.01	0.01	0.96	0.34
Intercept	-0.67	0.13	-5.22	0.001
Random-effects	Estimate	S.E.	95% Confidence Interval	
Identity	0.37	0.05	0.28	0.5

Delta: There was a significant effect of feedback delay (b = 0.63, S.E. b = 0.23, z = 2.78, p = 0.005; *table 4.5*), with greater delta activity being induced after a long delay (2.33dB) than a short delay (1.84dB). There was also a significant main effect of age (b = 0.26, S.E. b = 0.10, z = 2.58, p = 0.01). Older participants demonstrated greater delta activity compared to younger participants (2.50dB vs. 1.69dB). All other effects were non-significant.

Table 4.5. *Mixed effects model regressing parietal delta activity back on valence, delay, age, gender and externalising behaviour.*

Parietal Delta			Wald chi2(23) = 57.22, *p* = 0.0001	
Predictor	*b*	*S.E. b*	*z*	*p*
Valence	-0.05	0.23	-0.24	0.81
Delay	**0.63**	**0.23**	**2.78**	**0.01**
Age	**0.26**	**0.1**	**2.58**	**0.01**
Gender	-0.17	0.33	-0.51	0.61
Externalising	0.02	0.01	1.82	0.07
Valence * Delay	-0.07	0.32	-0.22	0.82
Valence * Age	-0.07	0.1	-0.74	0.46
Valence * Gender	-0.06	0.32	-0.18	0.85
Valence * Externalising	-0.01	0.01	-0.75	0.46
Delay * Age	0.01	0.1	0.06	0.95
Delay * Gender	-0.16	0.32	-0.48	0.63
Delay * Externalising	0.004	0.01	0.45	0.65
Age * Externalising	0.005	0.004	1.04	0.3
Gender * Externalising	-0.01	0.01	-0.59	0.55
Valence * Delay * Age	0.07	0.14	0.5	0.62
Valence * Delay * Gender	0.04	0.46	0.1	0.92
Valence * Delay * Externalising	0.001	0.01	0.11	0.91
Valence * Age * Externalising	-0.004	0.004	-0.81	0.42
Valence * Gender * Externalising	-0.01	0.01	-1.04	0.3
Delay * Age * Externalising	0.003	0.004	0.7	0.48
Delay * Gender * Externalising	-0.001	0.01	-0.08	0.94
Valence * Delay * Age * Externalising	-0.01	0.01	-1.08	0.28
Valence * Delay * Gender * Externalising	0.02	0.02	1.11	0.27
Intercept	1.95	0.23	8.39	0
Random-effects	Estimate	S.E.	95% Confidence Interval	
Identity	1.01	0.1	0.84	1.22

Externalising and valence difference

In the previous chapter, two-way interaction effects between valence and externalising behaviour on both the FRN and P3b was observed. However, in this study, no significant main or interaction effects of externalising behaviour on feedback induced oscillatory activity emerged. To explore potential relationships between participants' self-reported externalising behaviour and oscillatory activity, correlations were calculated between externalising score and valence difference for all time-

frequency points between 150-600ms and 4-30Hz in frontal and parietal sites (*fig. 4.3*). Over frontal sites, only a few contiguous time-frequency points reached significance at the uncorrected $p < 0.05$ level. As this was limited to a small window (0.5hz band for ~15ms), it is unlikely that it reflects meaningful oscillatory differences. By comparison, over parietal sites, this uncorrected correlation analysis suggests an effect of externalising behaviour in time-frequency windows not identified in previous studies. One alpha band window (~180 - 280ms post-feedback; *fig. 4.4*) and one beta band window (~280-420ms after feedback; *fig. 4.5*) both demonstrated negative

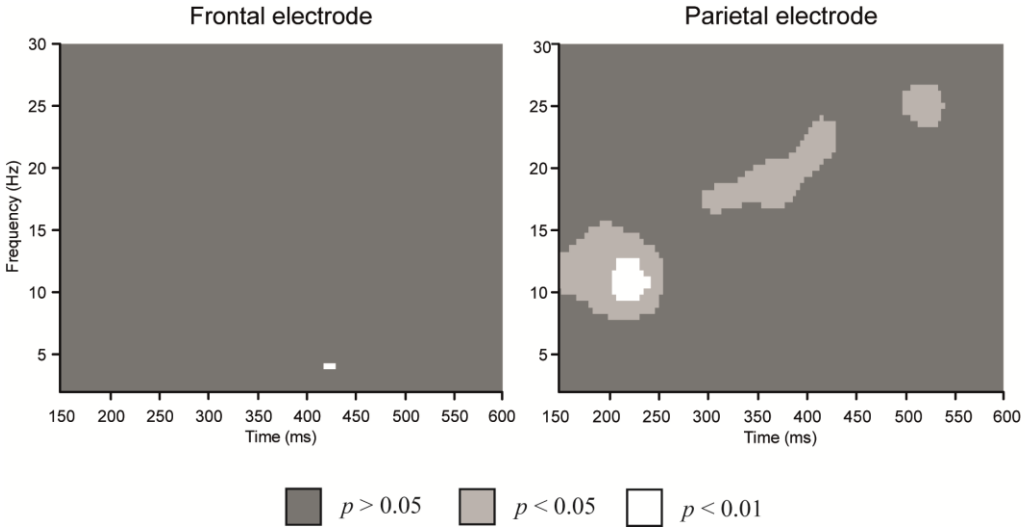

Figure 4.3. *Plots demonstrating the uncorrected significant points of correlation between self-reported externalising score and difference between reward and punishment in spectral activity over the feedback window at the frontal electrode (left) and parietal electrode (right).*

relationships with externalising behaviour. A further upper beta band window (~490-550ms post-feedback; *fig. 4.6*) also demonstrated a significant relationship with externalising behaviour scores. The mean value for each valence window was extracted and correlated with externalising score. There was no significant relationship between externalising behaviour and alpha activity following a win ($r = 0.15$, $p = 0.09$) or a loss ($r = -0.07$, $p = 0.26$). Low beta demonstrated a weak but significant positive correlation with externalising score after a reward ($r = 0.25$, $p = 0.01$), but no effect after a punishment ($r = -0.006$, $p = 0.48$). Comparatively, high beta was significantly correlated with punishment response ($r = 0.24$, $p = 0.01$), but not reward ($r = 0.04$, $p = 0.36$). However, when FDR correction was applied to all tests, no effects remained significant.

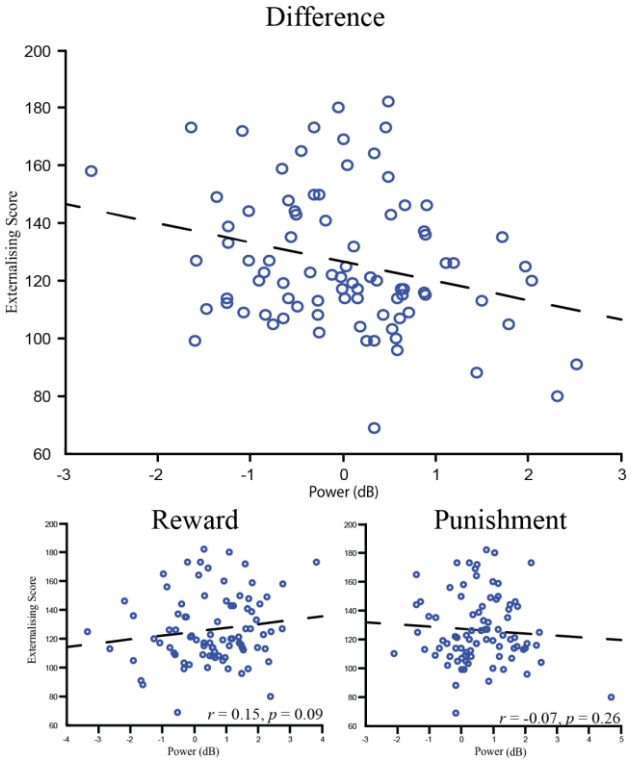

Figure 4.4. *Scatter plots demonstrating relationship between externalising score and parietal alpha activity to reward, punishment and the difference.*

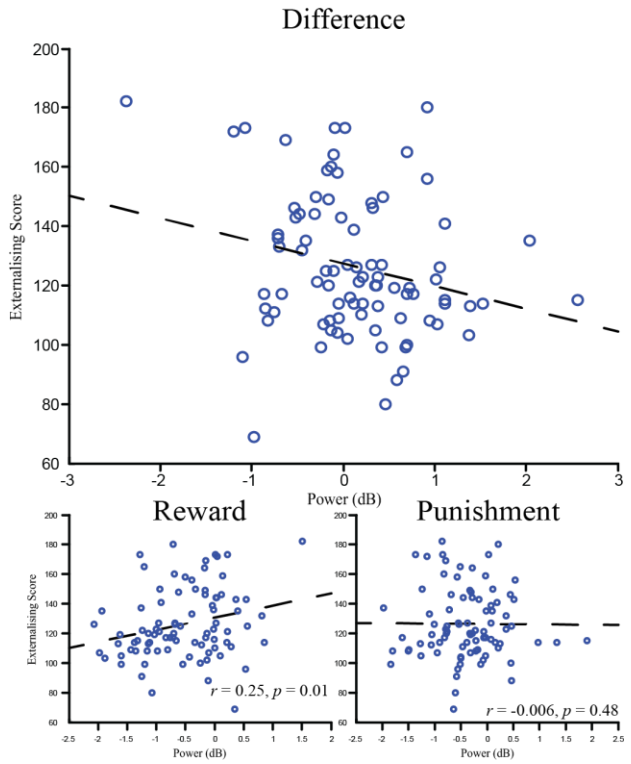

Figure 4.5. *Scatter plots demonstrating relationship between externalising score and 16-22Hz parietal beta activity (300-400ms) to reward, punishment and the difference*

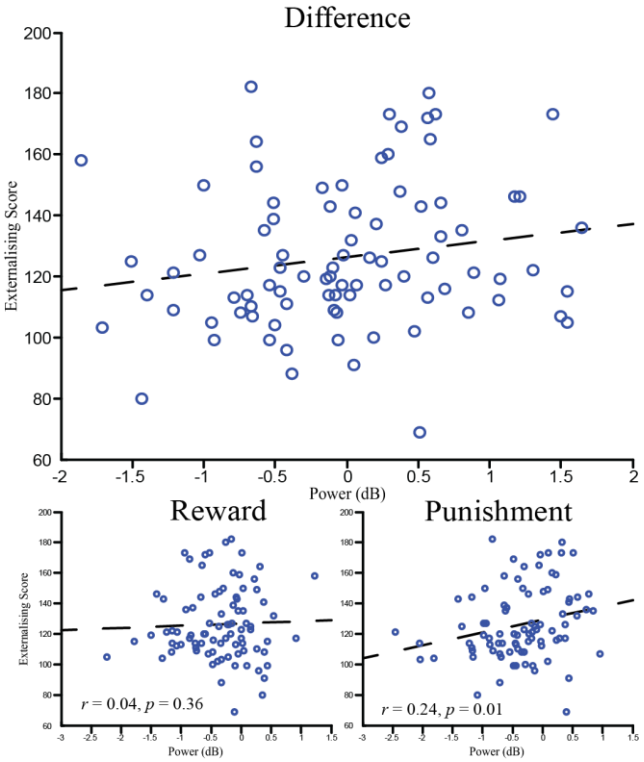

Figure 4.6. *Scatter plot demonstrating relationship between externalising score and 20-30Hz parietal beta activity (500-550ms) to reward, punishment and the difference*.

Discussion

Previous work using Event Related Potentials (ERPs) has already provided evidence for externalising-related differences in feedback-evoked neural activity in adolescence (chapter 3). However, feedback-induced changes in oscillatory activity might give a more robust picture of the neural mechanisms underpinning the processing of reward and punishment cues. In this study, a community sample of adolescents completed a gambling task, and changes in spectral powers across the theta, beta and delta frequency bands in response to feedback were analysed in relation to externalising behaviour.

Similar to previous work, theta band activity increased after participants were presented with punishment stimuli compared to reward stimuli over both frontal and parietal sites, indicating widespread responsivity to feedback in the theta band. Several studies have highlighted complementary characteristics between theta activity and Feedback- Related Negativity (FRN; Cohen, Elger, & Ranganath, 2007; Crowley et al., 2014), favouring analysis in similar time windows and topographical location. It is

possible then that cue-induced changes in the theta-band reflect common neural generators also linked to the FRN. However, a recent study by Cavanagh, Zambrano-Vazquez, and Allen (2012) suggests that theta activity underlies several event related potentials (such as the ERN, FRN, and N2) denoted by mediofrontal activation patterns, indicative of theta involvement in general error, punishment and conflict processing. Concordantly, an emerging body of evidence suggests that theta activity reflects the uncertainty generated by presented stimuli (Cavanagh et al., 2012). Positively-valenced stimuli could be argued to evoke less uncertainty, and by extension lower theta, as behavioural adjustment is not required in response to correct or rewarding stimuli.

Consistent with work by Banis, Geerligs, and Lorist (2014), punishment stimuli also elicited greater beta activity in the 13-20Hz range compared to reward. Extrapolating from a review of the sensorimotor literature outlined by Baker (2007), they suggested that greater beta power to punishment cues reflects a cognitive analogue of proprioceptive recalibration; higher beta power allows for individuals to interpret feedback cues and change their response patterns more efficiently. However, unlike Banis and colleagues, the relatively greater punishment induced beta band activity in this study was due to greater suppression of beta activity following reward feedback compared to punishment, rather than beta activation. As far as I am aware, no previous work has reported beta suppression in response to feedback. Instead, suppression of beta activity is seen during the imagination of movement (Pfurtscheller, Neuper, Brunner, & da Silva, 2006; de Lange, Jensen, Bauer, & Toni, 2008), and the planning of movement (Tzagarakis, Ince, Leuthold, & Pellizzer, 2010). Furthermore, reduced beta suppression is seen when there is more uncertainty surrounding upcoming movement (Tzagarakis et al., 2010). Along the same lines, the beta suppression may reflect participants' increased intention to act following a rewarding outcome, for example to initiate the same choices that resulted in reward previously. Moreover, Pfurtscheller et al., (2006) found that this suppression of beta activity whilst envisioning movement leads to a rebound period of beta activity, in which significant beta power increases occur. High beta band activity prior to response selection is associated with decreased reaction times (Senkowski, Moolholm, Gomez-Ramirez, & Foxe, 2005). Thus, the higher suppression seen in response to reward cues may potentially reflect a more rapid and efficient selection of goal-related action programmes triggered in response to reward cues. However, as I did not investigate reaction times in response to stimuli, I am unable to draw any

conclusions regarding beta activity in response to past feedback.

Alternatively, high beta suppression with lateral distributions have been shown to reflect higher working memory loads (Onton, Delorme, & Makeig, 2005) and retrieval from working memory (Karrasch, Laine, Rapinoja, & Krause, 2004). Onton, Delorme and Makeig (2005) found a negative correlation between working memory load and beta suppression, and Zanto & Gazzaley (2009) found that beta suppression was greater during a 4-item working memory task compared to a 2-item working memory task, but also that unsuccessfully unattended stimuli also evoked beta suppression comparable with that evoked by higher task demands. Within this task, additional working memory demands or retrieval processes may be engaged when processing reward compared to punishment, potentially reflecting retrieval of information regarding which balloon had been selected so it can be selected again, or updating of their current representation of the task reward rule. However, it remains difficult to draw conclusions regarding the interpretation of this beta activity given the task design. Participant reaction time was not recorded preventing comparison of reactions following reward and punishment, and no modulation of memory load means we cannot know how memory load affects beta suppression in this task.

It is important to note that several studies have observed the opposite effect, with increased beta activation in response to reward compared to punishment conditions (Cohen, Elger, & Ranganath, 2009; Marco-Pallarés et al., 2007; Marco-Pallarés et al., 2009). A potential explanation might be related to the tasks involved. Two of the four studies in which higher beta activity has been seen (Cohen, Elger, & Ranganath, 2007; van de Vijver, Ridderinkhof, & Cohen, 2011) have implemented tasks with a learning component. Marco-Pallares and colleagues (2008; 2009) utilised a task based on the gambling task presented by Gehring and Willoughby (2002), who noted that participants fell into risk-seeking or risk-adverse strategies. Engle and Fries (2010) suggest that during cognitive tasks with a strong top down component, beta activity acts to signal intention to maintain the current behaviour set, and feedback/learning studies have typically attributed the increased beta power to reward compared against punishment as an indication to maintain the currently rewarding response pattern. Therefore, increased beta activity to reward seen in these studies may reflect intention to maintain a strategy that is perceived to be advantageous by the individual; either

through an inbuilt learning mechanism in the task, or adopting a strategy (e.g. risk seeking/risk adverse). By comparison, the task used in this study involved random presentation of feedback stimuli, and thus behavioural response was guided largely by the bottom-up cues.

Valence difference and externalising behaviour

In a previous study, high and low externalisers differed in their feedback processing as indexed by the FRN and P3b. By comparison, in the current study, there were no observed differences between high and low externalisers in processing of reward and punishment cues in the theta and beta bands. This potentially reflects differences between the feedback-related negativity and feedback-induced theta. As mentioned above, whilst the two are linked, theta activity appears to encode a more general processing of conflict monitoring and task-evoked uncertainty (Cavanagh et al., 2012; Cavanagh, Zambrano-Vazquez, & Allen, 2012) compared to the FRN, which may encode a more specific measure of exogenous-error monitoring or reward-prediction error.

In contrast to Bernat et al. (2011), there were no significant main or interaction effects of self-reported externalising score at parietal sites. This may be related to differences in techniques utilised to measure event related oscillations. As they convolved the P3b ERP to measure delta activity, their findings may potentially reflect lower inter-trial coherence in the delta band amongst those scoring highly on externalising measures. Lower inter trial coherence would lead to delta activity averaging out over trials, lowering power in the decomposition of the ERP waveform. Therefore, high externalisers may not demonstrate any significant differences in power when compared against low externalisers, but instead demonstrate less consistent delta response over trials.

To further investigate whether there were any effects of self-reported externalising behaviour, participant EDI score were correlated against the spectral difference between reward and punishment conditions over the feedback window. There were no significant relationships between externalising behaviour and valence difference in oscillatory activity over frontal sites, but there were three bursts of activity which significantly correlated with participant externalising score.

Participant self-reported externalising behaviour demonstrated a significant positive relationship with 16 – 22Hz beta following a win, with low externalisers demonstrating larger beta suppression than high externalisers. There was no such effect in beta activity following punishment. As previously discussed, interpretation of this result is difficult given the task structure. Potentially, this may reflect a stronger intention to act amongst low externalisers than high externalisers following a reward, allowing for more efficient re-selection of previously advantageous stimuli. Alternatively, it may reflect a greater engagement of working memory amongst high externalising participants following reward. Several studies have associated weaker working memory ability with externalising behaviour (Baskin-Sommers et al., 2014; Peeters, Monshouwer, Janssen, Wiers, & Vollebergh, 2014; Schoemaker, Mulder, Deković, & Matthys, 2013), and this greater beta activity following reward may reflect the larger demand on working memory amongst externalisers to maintain or update the same task model.

A similar positive relationship between externalising score and high beta activity was seen in response to punishment in the higher beta window, with low externalisers demonstrating greater beta suppression for punishment compared to high externalisers. Previous work that has found feedback responsivity in the higher beta band (20-30Hz) has interpreted it as a signal to maintain the current cognitive status quo (see Engel and Fries, 2010, for a discussion), with greater beta activity to reward indicating a continuation of behaviour that lead to reward. Thus, the lower beta activity amongst low externalisers in response to punishment may be indicative of intention to switch to another stimulus choice.

Whilst there appeared to be a significant relationship between externalising behaviour and valence differences in early alpha activity, the individual correlation between externalising score and reward did not reach significance in either condition. Given the early window in which this difference occurred, this may be early perceptual alpha activity, possibly reflecting the P1-N1 complex which has been shown to travel from occipital sites to parietal midline sites peaking over similar time-frames (Klimesch et al., 2006). Therefore, this activity may indicate differences in the early visual processing of reward and punishment between high and low externalisers.

However, these relationships were weak overall, with average correlation coefficients

falling between 0.15 and 0.30. Furthermore, these effects became non-significant after FDR correction (Benjamini & Hochberg, 1995). Whilst this may be related to the ambitious number of tests that were corrected for (52 x 112 points), these results should be interpreted with caution. Despite this, they provide potential time-frequency windows for investigation in future studies.

Additional findings

Typically, when using whole scalp analysis, increased participant age is associated with general decreases in delta and theta frequency bands, which are replaced by activity in alpha and beta bands (Campbell & Feinberg 2009; Segalowitz, Santesso, & Jetha, 2010; Somsen, van't Klooster, van der Molen, van Leeuwen, & Licht, 1997). However, over both frontal and parietal areas, older participants demonstrated greater theta and delta power following feedback cues compared to younger participants, similar to findings from Crowley et al. (2014). Midline theta is thought to be generated in the dorsal ACC (dACC) and surrounding bilateral cortices (Ishii et al., 2014), similar to the FRN and ERN (Hauser et al., 2014). As Cohen (2011b) demonstrated that error-related theta power increases with white matter connectivity, this may reflect the increase in functional connectivity known to occur over adolescence (Kelly et al., 2009), as well as known structural brain maturation (Giedd et al., 1999).

Furthermore, males demonstrated high beta suppression compared to females over parietal sites after feedback presentation. This may suggest that males more readily prepared action following outcome cues than females, or that males were simply more involved in the task than females. However, the mechanisms underlying this are unclear, and further work needs to be conducted to understand how this might alter task reaction times and error rates.

Finally, there were significant effects of delay in the parietal electrodes on both theta and delta bands, with greater oscillatory activity after a long delay compared to short delay in both channels, similar to the delay effects on the P3b reported in chapter 3. Time-frequency decomposition of the P3b has identified power changes in the delta band (Bernat et al., 2011), and principle component analysis (PCA) of non-feedback evoked P3 components has produced components that can be convolved into changes in the delta and theta bands (Bernat, Malone, Williams, Patrick, & Iacono, 2007). As the

P3b in response to social rewards has been found to be sensitive to anticipation (van de Molen et al., 2013), it is possible that the delta and theta activity underpinning the P3b generated by monetary rewards may also be influenced by anticipation.

Limitations

Many of the limitations mentioned in the previous chapter regarding the design of the study are equally applicable to this chapter, and thus the analysis presented here must be considered in light of those limitations. However, there are additional limitations related to this analysis that need to be considered. Firstly, only spectral band power was considered. However, other methods of examining spectral bands (e.g. inter trial coherence), and the relationships between them (e.g. phase amplitude coupling), will be important for developing our understanding of feedback processing in relation to externalising behaviour.

Secondly, similar to chapter 3, the limited number of items per sub-scale in the shortened EDI meant prevented testing of the relationships between individual sub-scales and oscillatory activity. Given the previously established link between substance use and beta activity, further work needs to be conducted to disambiguated the how substance use and other forms of externalising behaviour individually contribute to spectral power. Furthermore, FDR may not be an ideal correction method for exploratory spectral analysis given the high degree of autocorrelation between contiguous time-frequency points, which is likely to be overly conservative. Instead, methods such as cluster-based (Maris & Oostenveld, 2007) or pixel-based (Cohen, 2014) correction methods which are able to compensate for high levels of similarities between neighbouring time-frequency points may be better suited for exploratory spectral analysis.

It is worth noting that broad, fixed-window methods of spectral data extraction may give poor estimations of activity due to developmentally-related changes (Whitford et al., 2007), physiological changes (Tops, van Peer, Wester, Wijers, & Korf, 2006), and individual differences (Muthukumaraswamy, Edden, Jones, Swettenham, & Singh, 2009) in both slow and fast wave bands. Future work may benefit from identifying the peak activity in a broad time-frequency window and extracting the average activity over

a smaller window for each individual, then including individual peak frequency and time as covariates to compensate for differences in spectral band power.

Finally, as little is known about potential sources for delta and beta band activity, drawing strong conclusions about the exact nature of changes in the frequency bands is difficult. Future work using source localisation or concurrent fMRI-EEG could identify possible generators for this activity.

Conclusions

Here, I reported findings suggesting that typically developing adolescents who score highly on self-reported externalising measures do not demonstrate reliable differences in feedback monitoring as indexed by theta activity when compared to low externalisers. Activity in this frequency range may be related to more general conflict monitoring processes associated with mediofrontal theta activity rather than specific mechanisms related to feedback processing, which in turn may partially explain the limited findings with respect to externalising behaviour. However, this study identified several possible windows of interest in the alpha and beta bands that may be usefully pursued in future studies of adolescent antisocial behaviour.

Chapter 5

Social provocation and Multisystemic Therapy modulate the neural correlates of reward in externalising adolescents.

Abstract

Amongst typically developing samples, we have previously observed differences in reward processing associated with self-reported externalising behaviour, suggestive of reward dominance. Yet, similar work in clinical samples is primarily limited to behavioural and fMRI studies. Emerging evidence is beginning to suggest that approach behaviours thought to underlie reward dominance are modulated by social context and participant frustration. Despite this, the effects of these factors on reward processing, particularly in clinical samples, remains relatively unknown. This study sought to understand how two event-related potentials associated with feedback processing, the Feedback-Related Negativity (FRN) and P3b, are associated with externalising behaviour under high and low social provocation, and how this relationship may be modulated by treatment. To that end, 60 participants selected from a longitudinal Randomised Controlled Trial (RCT) of Multisystemic Therapy were asked to take part in a cross-sectional study where they completed a Taylor Aggression Paradigm, playing a Go/No-Go task against a high provoking and a low provoking fictitious opponent whilst undergoing high-density EEG. Participants scoring highly on externalising measures demonstrated larger reward responsivity, as measured by the FRN, which was further sensitive to gender and provocation effects. In contrast, valence differences in the P3b were only seen amongst low externalising participants. Furthermore, participants who received Multisystemic Therapy demonstrated reduced reward responsivity compared to those from the Management-As-Usual group. These results suggest that whilst high externalising behaviour is associated with increased reward sensitivity, this relationship is influenced by gender and provocation, and is expressed through changes to error monitoring processes rather than motivational value assigned to feedback. Similarly, participant improvement (decreases in externalising behaviour from baseline, calculated using longitudinal data taken from the original RCT) was associated with reduced responsivity compared amongst those who demonstrated no improvement.

Introduction

Despite the significant negative impact that CD can have on both adult outcome (Odgers et al., 2008), as well as it significant societal costs (Foster & Jones, 2005; Romeo, Knapp & Scott, 2006), therapeutic interventions available for treating externalising behaviours have produced mixed results (Dekovic et al., 2011; Farmer, Compton, Burns, & Robertson, 2002), especially in children and preadolescents (Farmer et al., 2002).

One potential therapeutic intervention that has demonstrated promising results for externalising disorders is Multisystemic Therapy (MST; Henggeler & Borduin, 1990). MST is a short-term, intensive family treatment aimed at adolescents with severe emotional and behavioural problems. A large evidence base of Randomised Controlled Trials (RCTs) has provided positive results for MST compared against individual therapy (Henggeler, Borduin, Melton, & Mann, 1991; Sydow, Retzlaff, Beher, Haun, Schweitzer, 2013) and Management-As-Usual (MAU; Henggeler, Clingempeel, Brondino, & Pickrel, 2004) in America, and it has been shown to reduce recidivism and incarceration rates in young offenders (Bulter, Baruch, Hickey, & Fonagy, 2011; Henggeler, Melton, & Smith, 1992), chronic, violent offenders (Henggeler, Melton, Brondino, Scherer, & Hanley, 1997; Schaeffer & Borduin, 2005), substance dependent offenders (Henggeler et al., 2002), and adolescent sexual offenders (Borduin, Henggeler, Blaske, & Stein, 1990). However, studies outside the US have produced mixed results (Leschied & Cunningham, 2002; Sundell et al., 2008), and it's overall effectiveness has been called into question (Littell, Campbell, Green, & Toews, 2005). Nevertheless, whilst work investigating the improvements associated with MST has been robust, little to no work has investigated the behavioural or neurophysiological changes that may be associated with intervention, and may act as mediating mechanisms of treatment effects. Understanding such mechanisms is crucial for understanding why interventions work (or do not work), and may point the way towards more effective interventions in the future.

Over the last decade and a half, there has been an increasing acceptance that behavioural therapies may lead to biological changes (Gabbard, 2000). Several studies already demonstrated changes in neural activation patterns amongst adults with internalising problems (including anxiety, depression, and phobias) after intervention

(see Beauregard, 2007, or Frewen, Dozois, & Lanius, 2008, for reviews). Whilst there is a smaller evidence base for neural changes associated with treatment amongst externalisers, a few studies exist. Lewis et al. (2008) found that externalising children who improved after cognitive behavioural therapy demonstrated reduced prefrontal activity during an emotion induction Go/No-Go task compared to those that did not, which they attributed to changes in emotional regulation. Similarly, Woltering, Granic, Lamm, and Lewis (2011) tested inhibition-related EEG markers in externalising children who underwent cognitive behavioural therapy and compared them against typically developing controls in a Go/No-Go task. They found that externalising children who demonstrated improvement after treatment demonstrated significant differences in EEG activity during inhibition to those who did not improve, but did not differ significantly from the control participants. These studies suggest that executive function or emotional regulation may be an important set of processes linked to positive change during treatment, which is logical given their involvement in externalising behaviour (Morgan & Lilienfeld, 2000; Stringaris & Goodman, 2009). A clearer understanding of how the full range of mechanisms underlying externalising behaviour are altered by treatment may help further elucidate how MST works and for whom.

One key area highlighted by many models of externalising behaviour that has not been investigated in previous treatment studies is reward and punishment processing. Influential models by Quay (1993), and Newman and Wallace (1993), suggest that dominant behavioural approach pathways and normal or hypoactive behavioural inhibition paths underlie externalising behaviour. Based on the motivational systems outlined by Gray (1987), they propose that over arousal of the Behavioural Activation System (BAS) combined with a weaker Behavioural Inhibition System (BIS) leads to approach behaviours (e.g. reward/novelty seeking, risk-taking) in externalisers.

Certainly, behavioural results support the idea of reward dominance in externalising samples. Experiments using variants of the Card Playing Task (Siegel, 1978) have found increased reward sensitivity/decreased punishment sensitivity amongst high externalising community (Belmore & Quinsey, 1994; Seguin, Arseneault, Boulerice, Harden, & Tremblay, 2002) and clinical samples (Daugherty & Quay, 1991; O'Brien & Frick, 1996). Similarly, studies by Blair, Colledge, and Mitchell (2001) and Ernst et al. (2003) using the Iowa Gambling Task have demonstrated that participants

who score highly on externalising measures favour high reward/high punishment decks that lead to a net loss over advantageous low reward/low punishment decks, even over several trials of learning. Results from neuroimaging studies have provided a more heterogeneous set of findings. Functional Magnetic Resonance Imaging (fMRI) studies have found reward related differences between externalisers and non-externalisers in the ventral striatum (Bjork et al., 2010), orbitofrontal cortex (Finger et al., 2011; Rubia et al., 2009), anterior cingulate cortex (Bjork et al., 2010; Gatzke-Kopp et al., 2009) and the caudate (Finger et al., 2008; White et al., 2013), supporting the conclusion that externalising behaviour is associated with altered reward-punishment responsivity. However, inconsistent directions of effect and differences in the activated neural structures are abound, and may reflect differences in methodology across studies. Further, the low temporal resolution of fMRI may cause temporal smoothing of related functions making interpretation of effects difficult. EEG's high sampling rate, allowing it to track neural processes in the time frame in which they occur, as well as its established evidence base investigating feedback related activity, may help to complement the current fMRI work.

Both the FRN and the P3b have demonstrated sensitivity to several feedback characteristics, and whilst work is limited, previous research indicates altered FRN and P3b response amongst high externalising normative samples. For example, Segalowitz et al. (2012) found that adolescent males who scored highly on surgency (a composite of behavioural approach, sensation seeking, and positive affect) demonstrated reduced FRN response after task failure compared to low surgency participants. This finding was corroborated by the results from chapter 3, in which typically developing adolescents who scored highly on a self-report externalising measure demonstrated smaller differences between reward and punishment evoked FRN compared to low externalising adolescents, suggesting deficits in exogenous feedback processing.

By comparison, whilst Bernat et al. (2011) found a lack of valence effect amongst high externalising undergraduates, the results from typically developing adolescents reported in chapter 3 stood in contrast to that. Instead, adolescents reporting higher levels of externalising behaviour demonstrated a larger difference between reward and punishment evoked P3b, whilst those who reported lower levels of externalising behaviour did not demonstrate a valence effect. Critically, no research has

yet tested whether this pattern of altered reward processing (reduced FRN/heightened P3b) characterises more severe presentations of externalising behaviour problems in adolescents (e.g., those with CD), or whether such neural profiles change towards a normative pattern as a result of treatment.

Recent research has also highlighted the potentially important ways in which externalising or risk-taking behaviour and its associated neurocognitive correlates, may be influenced by the social context (Chein, Albert, O'Brien, Uckert, & Steinberg, 2011; Rodrigo, Padrón, de Vega, and Ferstl, 2014). When accompanied by peers, adolescents are more likely to engage in risk taking behaviour than their adult counterparts (Gardner & Steinberg, 2005; O'Brien, Albert, Chein, & Steinberg, 2011), and demonstrated increased reward responsivity in the following receipt of reward than when they are alone (Chein et al., 2011; Smith, Steinberg, Strang, & Chein, 2015). In a review of the literature, Anderson and Bushman (2002) highlighted that aggression is modulated by social provocation, and several previous studies using the Taylor Aggression Paradigm (Taylor, 1967) have found increased aggressive responses (higher selected punishments for their opponents) when participants play against high provoking opponents compared to low provoking opponents (Krämer, Büttner, Roth, & Münte, 2008), which may reflect increases in activation of the Behavioural Approach System. Furthermore, Tibubos, Pott, Schnell, and Rohrmann (2014) found that reward-responsivity (on the BAS scale) was associated with increased heart rate in response to anger provocation, and that verbal aggression was negatively related to behavioural inhibition (as indexed by BIS score), amongst female undergraduates. Therefore, if behavioural approach-reward systems demonstrate increased arousal, we may expect to see larger differences in reward and punishment conditions in feedback related ERPs when under high provocation compared to when participants are under low provocation. Moreover, adolescents with externalising problems, who already demonstrate hyperactivity of the Behavioural Activation System and are more prone to reactive aggression, may demonstrate changes in reward processing as a function of provocation relative to their low externalising counterparts. Given these socially driven increases in risk taking behaviour seen amongst adolescents, accompanied by a proneness towards reactive aggression characteristic of high externalising samples, a greater understanding of approach behaviours in externalisers whilst under social provocation could further our understanding of changes in approach behaviours in more realistic situations.

Here, I present the results of a cross-sectional study seeking to investigate the relationship between externalising behaviour and reward sensitivity, and how that relationship is influenced by therapeutic intervention, in a group of clinically-referred adolescents taken from a longitudinal RCT of MST. I predicted that high externalising adolescents would demonstrate smaller differences in FRN amplitude between reward and punishment feedback, indicative of poorer exogenous feedback monitoring, and greater differences between P3b amplitudes to reward, reflecting heightened reward sensitivity, compared to low externalising adolescences. As previous trials with MST have demonstrated improved recidivism and externalising rates amongst adolescents who have received MST compared to those who have received MAU, I also expected to see reduced markers of reward dominance (larger and smaller differences between reward and punishment in the FRN and P3b, respectively) amongst the MST group compared to MAU. Further, I predicted that those who improve most as a result of treatment would demonstrate improved neural responses associated with reward processing. Finally, I predicted that these anticipated findings would be most marked under conditions of high, versus low, social provocation.

Methods

Participants

Participants were 56 at-risk adolescents recruited from an ongoing Randomised Control Trial (RCT) investigating the effects the Multisystemic Therapy (MST) on externalising behaviour, ranging in age from 13-20 years of age (M = 16.23, S.D. = 1.75). These participants were approached during one of their follow-up sessions at least 18-months post-intervention to gauge their interested in being involved in this study (M = 27 months; S.D. = 7.1 months). Full description of ongoing RCT can be found in the methodology chapter.

Treatment

Participants received either MST or MAU. MST was a therapeutic intervention provided by a single generalist who was made available to the participant and their family 24 hours a day, 7 days a week, for a period of 3-5 months. This generalist would provide a range of therapies they considered beneficial to the client and their family.

Similar to previous MST studies, therapist adherence to the MST model was ensured via regular supervisions, reviews, and booster sessions with MST experts.

By comparison, those in the MAU condition may receive a regime of interventions typical for the local authority in which they were based, though the exact interventions received depend on what the local authority can provide and deems necessary for their improvement. Similar to MST, the range of potential therapies used are broad. However, in contrast, these were not provided by a single individual, and are not provided within a family context.

Measures

Taylor Aggression Paradigm (TAP): Participants were asked to complete a competitive Go/No-Go flanker task in which they played against two fictitious opponents simulated by the computer. Participants played against each opponent twice, and attempted to beat their opponents in speed and accuracy to win each trial. However, the outcome was pre-programmed so that they lost 50% of trials. If they won they trial, they would be shown a green tick indicating a reward (35p). However, if they lost, they saw a red cross and were punished by losing money. Participants were told that this loss was chosen by their opponents, and one opponent was framed to by a low provoking opponents (punishments were small; M = 17p) and the other was a high provoking opponent (punishments were large; M = 47p).

Participants played 4 blocks, 2 against each opponent, with 20 trials in each block. Each trial was comprised of 6 Go/No-Go stimuli, with 70% of the stimuli being Go stimuli. Each stimulus was comprised of 9 arrows presented in a 3x3 array, with the central arrow indicating whether it was a Go or a No-Go stimulus (a green or red arrow, respectively). In line with a typical Flanker Task, the remaining 8 arrows, which were grey, were either congruent (pointing in the same direction) or incongruent (pointing in the opposite direction) as the central arrow.

Self-Reported Delinquency (SRD): Participants completed the SRD, reporting the externalising behaviours that they had engaged in over the past 6-months.

Strengths and Difficulties Questionnaire (SDQ): Both the participants and their parents were asked to complete the SDQ, which measures behaviours associated with

externalising behaviour (such as prosocial behaviour and emotional symptoms). However, for this study, only the conduct problems subscale from both parents and young people were used

Substance Abuse Questionnaire: Participants were also asked to indicate their drug use over the past 6 months by reporting which substances they had used and how often they had used it.

Combined externalising

A combined externalising score was calculated for each participant using latent variable modelling in the *Mplus* package to reduced reporter variability. A latent externalising variable was computed for each participant from the SRD, the self-reported SDQ externalising subscale, and the parent-reported SDQ externalising subscale.

Participant Improvement

To investigate participant improvement, participant SRD score from each follow-up was regressed back on time using a mixed-effect model with participant ID included as a random effect. Participants' individual β coefficients for time were used as a proxy for improvement.

EEG

After EEG pre-processing, which is detailed in the methodology chapter, ERP data was extracted. The FRN was extracted over frontocentral sites (FCz), and was defined as the peak-to-peak difference over the 200-350ms post-stimulus window to minimise differences in earlier EEG activity. The P3b was extracted from parietal sites (electrodes 33, 34, 36 [Pz], and 38), and defined as the average activity over the 300-400ms post-stimulus window.

Statistical Analysis

Group differences between MST and MAU groups in demographic information were tested using t-test in SPSS.

Analysis of participant reaction time and punishment selection were both conducted using mixed-effects models in STATA 13 using the *xtmixed* function. Reaction time and punishment selection were entered as dependent variables. In the punishment selection models, provoker was entered as a within-subjects factor with 2 levels. Participant gender was entered as a 2 level, between-subjects factor, and participant age was a continuous, between-subjects factor. Individual models were run to test the effects of current externalising, treatment, and participant improvement; current externalising behaviour was entered as a between-subjects, continuous predictor. Treatment group was entered as a between-subjects factor with 2 levels. Participant improvement was entered as a continuous, between-subjects factor. Participant ID was entered as a random effect. Feedback valence was also included in the reaction time models as a within-subjects factor with 2 levels.

Similar to the behavioural responses, mixed-effects models were run to test the effects of valence and provocation on ERP amplitude. FRN and P3b amplitudes were entered in the models as dependent variables. However, the predictor variables were the same as those used for the reaction time models.

Post-estimation tests for interaction effects including one or more continuous predictor was conducted ising the STATA margins command to test the difference in the predicted dependent variable 1 standard deviation above and below the mean of the continuous variable.

Results

Results are separated in 8 sections. In the first section, an outline of the sample characteristics is reported. In the second section, the results of the latent variable model of externalising behaviour are outlined, and following, in the third section, the behavioural data are analysed. The next 5 sections outline the ERP results, with both FRN and P3b results reported in each. The first outlines the effects of task-related variables (valence and provocation), age, and gender on ERP amplitude. Next, ERP response in relation to participant's current externalising behaviour (as reported in the follow up preceding their EEG session) is outlined. The third and fourth sections test the relationship between treatment group and feedback related ERPs, and improver effects

on feedback related ERPs, respectively. Finally, any significant covariate effects are presented.

Sample Characteristics

The demographic characteristics of the sample are reported in table 5.1. The difference between treatment groups on self-reported delinquency approached, but failed to reach, significance (t (1, 54) = 1.95, p = 0.06), though MST participants generally reported lower levels of externalising behaviour than their MAU counterparts. No other differences between groups were significant.

Participants included in this study did not differ from those who did not take part in their level of parental education (t(40) = 1.85, p = 0.07). However, the parents of those who took part were more likely to be involved in lower skill jobs (t(91) = -2.27, p = 0.03) and fall into a lower annual wage category (t(68) = 2.00, p = 0.05) than those who did not take part. Whilst these two groups did not differ in the baseline self-reported delinquency (t(70) = 1.36, p = 0.18), those who took part demonstrated significantly lower levels of externalising behaviour at the 18 month follow-up (t(106) = 4.12, p = 0.00007).

Latent variable modelling

The self-reported Strengths and Difficulties Questionnaire (SDQ) conduct scale score had the highest loading factor on the latent externalising variable (standardised loading factor = 0.82), followed by the parent SDQ conduct scale (standardised loading factor = 0.68). The SRD had the lowest loading factor (standardised loading factor = 0.57).

Table 5.1. *Sample demographics broken down by clinical groups. Parenthetical values reflect the standard deviation or percent of group total.*

	MST	MAU	t-test results
Age	15.9 (1.75)	16.6 (1.70)	t (54) = -1.5 p = 0.13
Gender			t (54) = -0.1 p = 0.90
Males	18 (60%)	16 (61.5%)	
Females	12 (40%)	10 (38.46%)	
Ethnicity			t (53) = -1.2 p = 0.20
White (British)	21 (70%)	16 (61.54%)	
White (Other)	2 (6.67%)	2 (7.69%)	
Black or Black British (Caribbean)	6 (20%)	1 (3.85%)	
Black or Black British (African)	0 (0%)	5 (19.23%	
Asian or Asian British (Bangladeshi)	1 (3.33%)	0 (0%)	
Asian or Asian British (Other)	0 (0%)	1 (3.85%)	
Other	0 (0%)	1 (3.85%)	
Parental Education	2.56 (3.4)	2.27 (3.33)	t (30) = -0.4 p = 0.70
Household Income	1.73 (1.4)	1.81 (1.52)	t (54) = 0.3 p = 0.80
Parental profession			t (50) = -0.3 p = 0.80
Professional	3(10%)	2 (7.69%)	
White collar worker	4 (13.3%)	2 (7.69%)	
Skilled manual	0 (0%)	3 (11.54%)	
Semi-skilled/unskilled	2 (6.67%)	4 (15.35%)	
Homemaker	13 (43.33%)	10 (38.46%)	
Unemployed	5 (16.67%)	2 (7.69%)	
Unable to work	3 (10%)	3 (11.54%)	
Externalising score	6.9 (8.9)	11.8 (9.8)	t (54) = -1.9 p = 0.06
Substance use	1.4 (1.9)	1.6 (2.5)	t (54) = -0.4 p = 0.73

Behavioural Data

Participant punishment selection differed significantly by provoker condition (*b* = -1.07, S.E. = 0.19, *z* = -5.71, *p* = 0.0001), as participants selected significantly higher punishments for high provoking opponents compared to low provoking ones (51p vs. 41p). Furthermore, there was a significant effect of participant age on punishment selection (*b* = -0.28, S.E. = 0.10, *z* = -2.68, *p* = 0.007). In general, younger participants punished more highly than older participants (-1 S.D = 49p; +1 S.D = 43p). However, no other effects, including main or interacting effects of current externalising, treatment group, or improvement reached significance.

In regard to reaction time, there was a significant two-way interaction effect between provoker and current externalising score (*b* = -5.13, S.E. = 2.06, *z* = -2.49, *p* = 0.13). Individual post-estimation tests were run for high and low externalising participants investigating differences in reaction times provoker conditions. These revealed that there was a significant difference in the high externalising participants (χ^2 (1) = 4.96, *p* = 0.03), who demonstrated faster reaction times when under low provocation compared to high provocation (282ms vs. 290ms). The low externalising participants did not demonstrate any differences (293ms vs. 287ms; χ^2 (1) = 1.90, *p* = 0.17). No other main or interaction effects reached significance.

ERP data

Topoplot

Visual inspection of the waveform and topoplot was conducted to ensure that the FRN and P3b were being elicited. Consistent with expectation, and with the previous literature (e.g. Holroyd, Krigolson, & Lee, 2011; Hughes, Manthan, & Yeung, 2013), topoplots over the FRN and P3b approximate timing window demonstrated activity over central and parietal sites, respectively (*fig. 5.1*). Similarly, the waveforms were comparable to those seen in other feedback studies, and demonstrated a typical response to feedback valence.

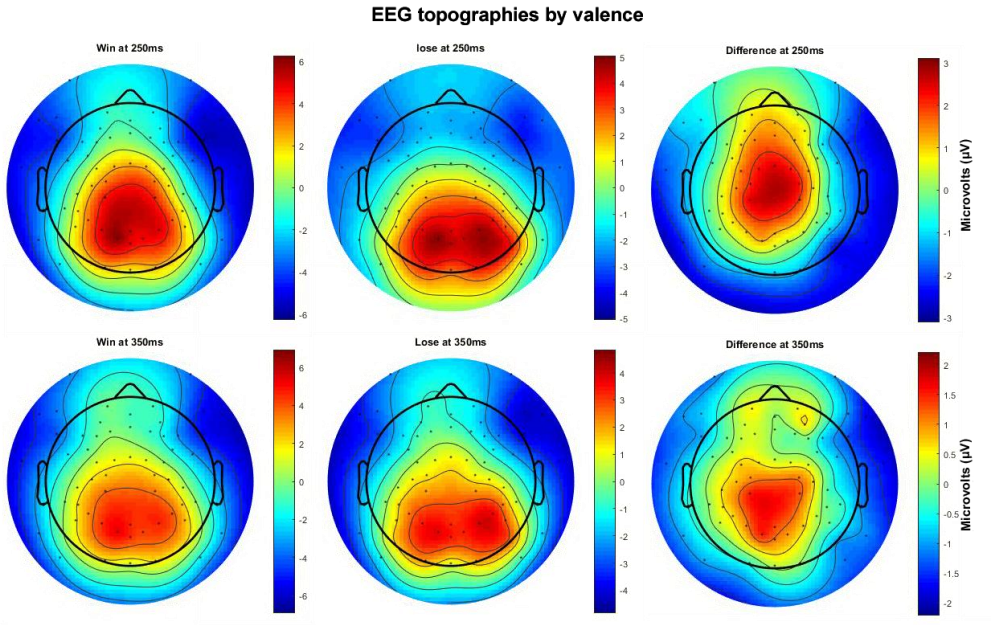

Figure 5.1. *Topoplots demonstrating distribution of electrical activity over the scalp for each valence condition, and the difference. Consistent with expectations, difference in the valence conditions appeared to peak over central sites in the middle of the FRN window. Condition averages from the P3b window indicate activity over the parietal sites, though the difference topoplot indicates a slight left laterality to the P3b response.*

Task, age and gender effects

Feedback-Related Negativity: There was a significant effect of feedback valence on FRN amplitude (b = -0.85, S.E. = 0.39, z = -2.18, p = 0.03; *fig. 5.2*). Punishment feedback generated larger (more negative) FRNs compared to reward, as measured by the peak to peak difference (5.31μV vs. 4.63μV). There was also a significant main effect of gender (b = -2.36, S.E. = 0.83, z = -2.84, p = 0.005), with male participants generating larger FRNs compared to females (5.76μV vs. 3.80μV). However, this effect was superseded by an interaction effect between provoker and participant gender (b = 1.31, S.E. = 0.65, z = 2.00, p = 0.05). Post-estimation tests revealed that whilst males demonstrated larger FRNs in general, this effect was larger under high provocation (5.85μV vs. 3.59μV; χ^2 (1) = 8.77, p = 0.003) than under low provocation (5.66μV vs. 4.02μV; χ^2 (1) = 4.62, p = 0.03).

P3b: There was a significant main effect of valence on P3b amplitude (b = 1.64, S.E. = 0.54, z = 3.00, p = 0.003; *fig. 5.2*). Reward evoked larger P3b amplitudes than

punishment (5.24μV vs. 4.09μV). There were no other significant main effects on P3b amplitude.

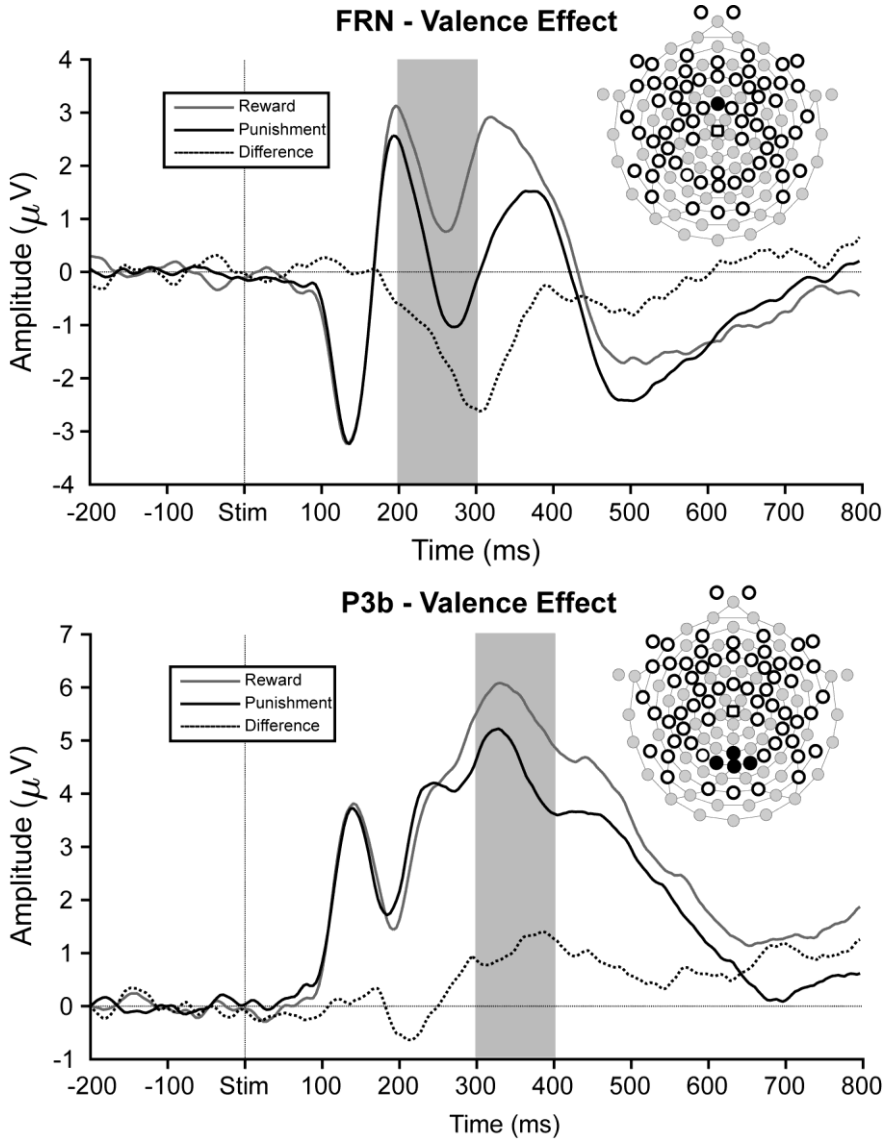

Figure 5.2. *Grand average ERPs in response to reward and punishment, and the difference wave between conditions. The area of interest in indicated by the grey window. A sensor layout map is inset, with grey electrodes indicating those removed during dimension reduction and black electrodes indicating electrode sites that ERPs are extracted from.*

Current externalising

Feedback-Related Negativity: There was no significant main effect of current externalising behaviour on FRN amplitude (b = 0.19, S.E. = 0.42, z = 0.46, p = 0.65; *table 5.2*), but there were significant interaction effects between valence and externalising (b = -0.77, S.E. = 0.33, z = -2.34, p = 0.02; *fig.5.3*) and provoker and externalising (b = -0.65, S.E. = 0.33, z = -2.00, p = 0.05). However, these effects were superseded by a three-way interaction between valence, provoker, and current externalising (b = 1.04, S.E. = 0.46, z = 2.25, p = 0.02). Post-estimation tests revealed that this effect was carried by the high externalising participants who demonstrated larger FRN amplitudes to reward compared to punishment under high provocation (5.62μV vs. 4.26μV; χ^2 (1) = 9.93, p = 0.002), which was not seen under low provocation (5.12μV vs. 4.61μV; χ^2 (1) = 1.74, p = 0.19); similarly, FRN differences were small in the low externalisers both in the high provocation (5.12μV vs. 4.91μV; χ^2 (1) = 0.23, p = 0.64) and low provocation conditions (5.47μV vs. 4.88μV; χ^2 (1) = 1.84, p = 0.17).

Finally, there was a 4-way interaction effect between valence, provoker, externalising and gender (b = -1.58, S.E. = 0.73, z = -2.16, p = 0.03). Amongst male participants, the high externalisers demonstrated a greater FRN response to punishment compared to reward when under high provocation (6.55μV vs. 4.62μV; χ^2 (1) = 9.92, p = 0.001), but did not demonstrate a valence difference under low provocation, and no differences were seen in the low externalisers. Similarly, amongst female participants, high externalising participants demonstrated significantly greater FRN response to punishment compared to reward, but only under low provocation (5.37μV vs. 3.44μV; χ^2 (1) = 6.40, p = 0.01). No differences were observed under high provocation, or amongst the low externalising participants.

Table 5.2. *Results from the mixed effects model regression FRN amplitude back on valence, provoker, age, gender, and current externalising behaviour.*

	Wald χ^2 (25) = 55.53			p = 0.0004
FRN	*b*	S.E.	*z*	*p*
Valence	**-0.86**	**0.39**	**-2.18**	**0.03**
Provoker	-0.56	0.39	-1.43	0.15
Valence * Provoker	0.75	0.55	1.34	0.18
Gender	**-2.36**	**0.83**	**-2.84**	**0.01**
Valence * Gender	0.19	0.66	0.29	0.77
Provoker * Gender	**1.31**	**0.66**	**2.00**	**0.05**
Valence * Provoker * Gender	-1.38	0.93	-1.49	0.14
Age	-0.04	0.43	-0.09	0.93
Valence * Age	-0.08	0.32	-0.24	0.81
Provoker * Age	0.45	0.32	1.41	0.16
Valence * Provoker * Age	-0.72	0.46	-1.58	0.12
Externalising	0.19	0.42	0.46	0.65
Valence * Externalising	**-0.77**	**0.33**	**-2.34**	**0.02**
Provoker * Externalising	**-0.65**	**0.33**	**-2.00**	**0.05**
Gender * Externalising	-0.04	0.66	-0.07	0.95
Age * Externalising	0.30	0.30	0.98	0.33
Valence * Provoker * Externalising	**1.04**	**0.46**	**2.25**	**0.02**
Valence * Gender * Externalising	0.90	0.52	1.74	0.08
Valence * Age * Externalising	0.13	0.24	0.55	0.58
Provoker * Gender * Externalising	0.94	0.52	1.82	0.07
Provoker * Age * Externalising	0.28	0.24	1.17	0.24
Valence * Provoker * Gender * Externalising	**-1.58**	**0.73**	**-2.16**	**0.03**
Valence * Provoker * Age * Externalising	-0.46	0.34	-1.37	0.17
Substance Use	**-0.98**	**0.38**	**-2.56**	**0.01**
Parental Education	-0.57	0.34	-1.69	0.09
Constant	**6.30**	**0.50**	**12.65**	**0.00**
Random effects	Estimate	S.E	95% CI	
Identity	2.36	0.25	1.92	2.91
Residual	1.59	0.09	1.43	1.77

P3b: There was no significant main effect of current externalising behaviour on P3b amplitude (*b* = -0.69, S.E. = 0.51, *z* = -1.35, *p* = 0.18; *table 5.3*). However, there was also significant interaction between valence and externalising behaviour (*b* = -1.19, S.E. = 0.46, *z* = -2.60, *p* = 0.01; *fig. 5.3*). Low externalising participants demonstrated significantly greater P3b amplitudes to reward compared to punishment (6.52μV vs. 4.55μV; χ^2 (1) = 20.90, $p < 0.001$), which was not seen in the high externalising participants (3.80μV vs. 4.18μV; χ^2 (1) = 0.79, *p* = 0.37). There was also a significant

interaction between age and externalising behaviour (b = 0.93, S.E. = 0.36, z = 2.54, p = 0.01). In younger participants, lower externalising behaviour was associated with larger P3b amplitudes regardless of feedback valence (7.19μV vs. 2.78μV). By comparison, amongst older participants, high externalisers demonstrated larger P3b amplitudes than low externalisers (5.21μV vs. 3.88μV).

Table 5.3. *Results from the mixed effects model regression P3b amplitude back on valence, provoker, age, gender, and current externalising behaviour.*

	Wald χ^2 (25) = 67.58			p = 0.0001
P3b	*b*	S.E.	*z*	*p*
Valence	**1.64**	**0.55**	**3.00**	**0.001**
Provoker	0.32	0.55	0.59	0.56
Valence * Provoker	-0.33	0.77	-0.43	0.67
Gender	-1.18	1.01	-1.17	0.24
Valence * Gender	-0.40	0.91	-0.44	0.66
Provoker * Gender	-0.01	0.91	-0.01	0.99
Valence * Provoker * Gender	-0.76	1.29	-0.59	0.56
Age	-0.29	0.52	-0.56	0.58
Valence * Age	0.14	0.45	0.31	0.76
Provoker * Age	-0.02	0.45	-0.05	0.96
Valence * Provoker * Age	0.05	0.64	0.07	0.94
Externalising	-0.69	0.51	-1.35	0.18
Valence * Externalising	**-1.19**	**0.46**	**-2.60**	**0.01**
Provoker * Externalising	-0.25	0.46	-0.54	0.59
Gender * Externalising	1.39	0.80	1.74	0.08
Age * Externalising	**0.93**	**0.37**	**2.54**	**0.01**
Valence * Provoker * Externalising	0.95	0.65	1.47	0.14
Valence * Gender * Externalising	0.89	0.72	1.24	0.22
Valence * Age * Externalising	0.62	0.33	1.87	0.06
Provoker * Gender * Externalising	0.01	0.72	0.01	0.99
Provoker * Age * Externalising	-0.05	0.33	-0.14	0.89
Valence * Provoker * Gender * Externalising	-1.04	1.02	-1.02	0.31
Valence * Provoker * Age * Externalising	-0.78	0.47	-1.66	0.10
Substance Use	**-0.98**	**0.44**	**-2.23**	**0.03**
Parental Education	-0.07	0.39	-0.19	0.85
Constant	4.49	0.60	7.42	0.00
Random effects	Estimate	S.E	95% CI	
Identity	2.66	0.30	2.14	3.31
Residual	2.22	0.12	1.99	2.47

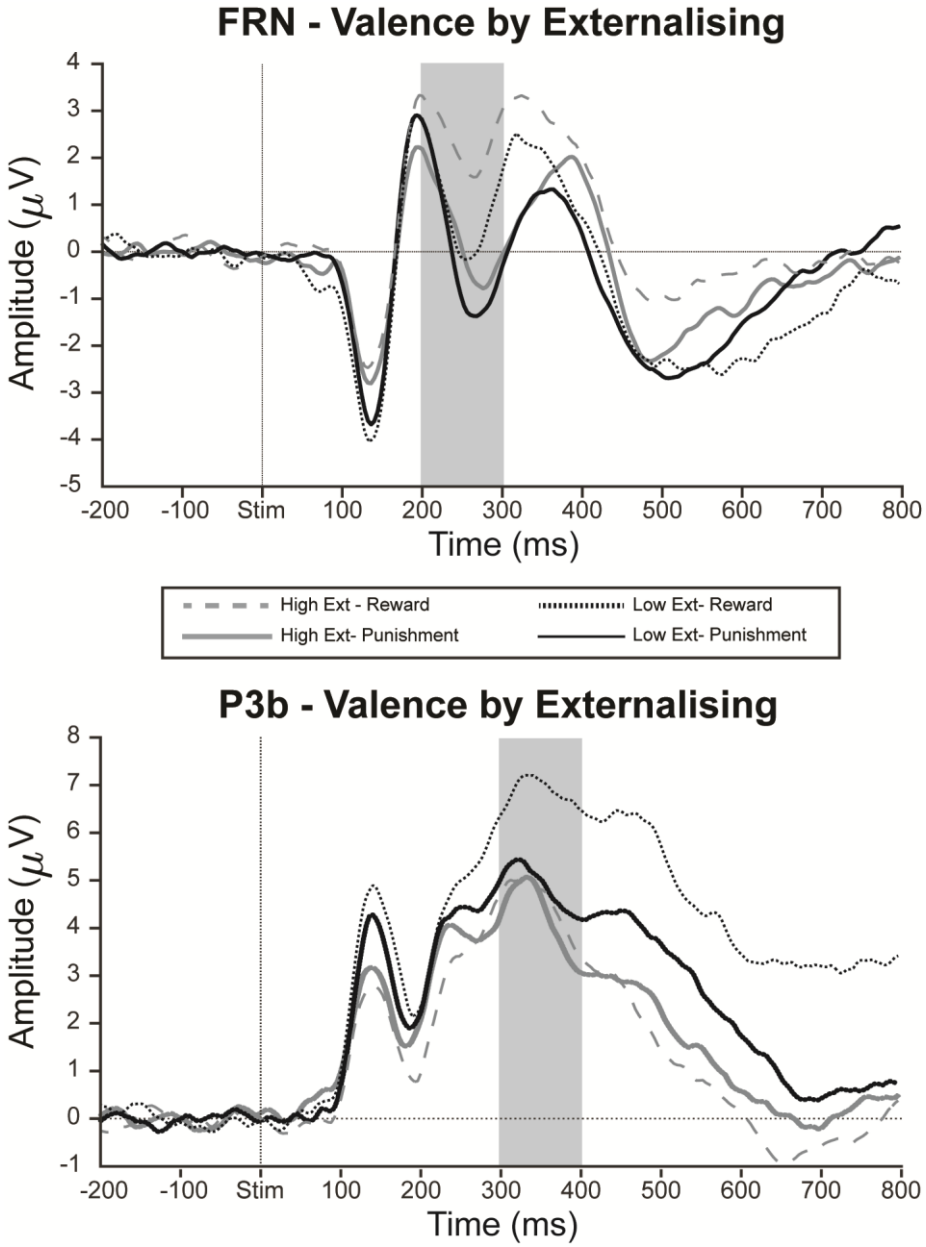

Figure 5.3. *FRN and P3b response to reward and punishment split by participant externalising behaviour. The grey box highlights the window of interest. For graphing purposes, externalising group was based on a median split of self-reported externalising*

Treatment effects

Feedback-Related Negativity: There was no significant main effect of treatment group (b = -1.38, S.E. = 1.01, z = 1.37, p = 0.17; *table 5.4*), or a significant two-way interaction between valence and group (b = -0.54, S.E. = 0.78, z = -0.69, p = 0.49; *fig. 5.4*). There was a significant 4-way interaction between valence, provoker, age, and treatment group (b = -2.55, S.E. = 0.87, z = -2.95, p = 0.003). Amongst the MST group,

there were no significant differences in FRN amplitude as a function of valence under any level of provocation, amongst either older or younger participants. However, amongst the MAU group, there were significant differences under low provocation but not high provocation. Under high provocation, neither the older (6.05μV vs. 5.10μV; χ^2 (1) = 2.86, p = 0.09) nor younger (5.52μV vs. 4.27μV; χ^2 (1) = 3.19, p = 0.07) participants demonstrated significant differences in FRN amplitude between reward and punishment feedback. Under low provocation, there was a cross over effect. Younger MAU participants demonstrated significantly greater FRN response to reward compared to punishment (3.77μV vs. 5.78μV; χ^2 (1) = 8.16, p = 0.005). By comparison, older MAU participants demonstrated greater FRN response to punishment compared to reward (6.35μV vs. 4.44μV; χ^2 (1) = 11.64, p < 0.001).

P3b: There was no significant main effect of treatment group (b = -0.42, S.E. = 1.30, z = -0.32, p = 0.75; *table 5.5*), or interaction between valence and treatment group (b = 0.73, S.E. = 1.12, z = 0.65, p = 0.51; *fig 5.4*). There was a significant two-way interaction between age and group (b = 2.52, S.E. = 1.02, z = 2.47, p = 0.01). However, neither the younger (4.85μV vs. 4.19μV; χ^2 (1) = 0.28, p = 0.60) nor older participant groups (5.71μV vs. 3.51μV; χ^2 (1) = 3.43, p = 0.06) demonstrated a treatment effect.

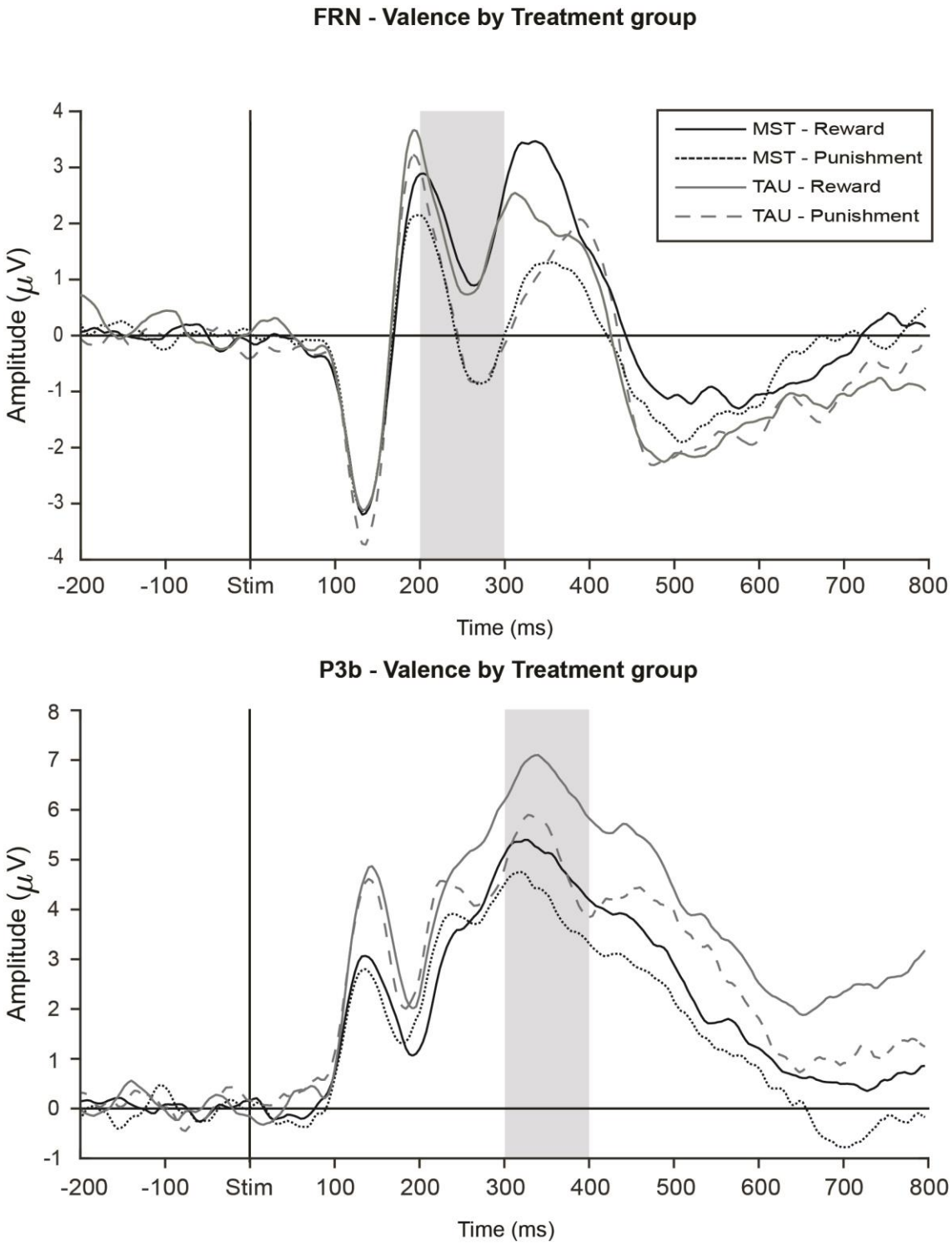

Figure 5.4. *FRN and P3b response to reward and punishment split by treatment group. The grey box highlights the window of interest.*

Table 5.4. *Results from the mixed effects model regression FRN amplitude back on valence, provoker, age, gender, and treatment group*

	Wald χ^2 (26) = 62.96			p = 0.0001
FRN	*b*	S.E.	*z*	*p*
Valence	-0.68	0.54	-1.27	0.20
Provoker	-0.18	0.54	-0.34	0.73
Valence * Provoker	0.56	0.76	0.73	0.47
Gender	-2.00	1.08	-1.86	0.06
Valence * Gender	0.03	0.83	0.04	0.97
Provoker * Gender	1.17	0.83	1.40	0.16
Valence * Provoker * Gender	-1.40	1.18	-1.19	0.24
Age	-0.37	0.56	-0.66	0.51
Valence * Age	-0.39	0.41	-0.94	0.35
Provoker * Age	0.05	0.41	0.12	0.90
Valence * Provoker * Age	0.44	0.58	0.76	0.45
Treatment Group	1.52	1.04	1.46	0.14
Valence * Treatment Group	-0.54	0.78	-0.69	0.49
Provoker * Treatment Group	-1.00	0.78	-1.28	0.20
Gender * Treatment Group	-1.25	1.58	-0.79	0.43
Age * Treatment Group	0.61	0.79	0.76	0.45
Valence * Provoker * Treatment Group	1.04	1.11	0.94	0.35
Valence * Gender * Treatment Group	0.30	1.22	0.24	0.81
Valence * Age * Treatment Group	0.54	0.61	0.89	0.38
Provoker * Gender * Treatment Group	0.03	1.22	0.02	0.98
Provoker * Age * Treatment Group	0.98	0.61	1.60	0.11
Valence * Provoker * Gender * Treatment Group	0.22	1.73	0.13	0.90
Valence * Provoker * Age * Treatment Group	**-2.55**	**0.87**	**-2.95**	**<0.01**
Externalising	-0.15	0.28	-0.54	0.59
Substance Use	**-0.85**	**0.39**	**-2.21**	**0.03**
Parental Education	-0.54	0.34	-1.59	0.11
Constant	5.60	0.70	7.99	0.00

Random effects	Estimate	S.E	95% CI	
Identity	2.37	0.25	1.93	2.91
Residual	1.56	0.09	1.40	1.74

Table 5.5. *Results from the mixed effects model regression P3b amplitude back on valence, provoker, age, gender, and treatment group.*

	Wald χ^2 (26) = 54.69			p = 0.0008
P3b	*b*	S.E.	*z*	*p*
Valence	**1.63**	**0.78**	**2.10**	**0.04**
Provoker	0.40	0.78	0.52	0.60
Valence * Provoker	-0.54	1.10	-0.50	0.62
Gender	-2.30	1.35	-1.70	0.09
Valence * Gender	-1.29	1.20	-1.07	0.28
Provoker * Gender	-0.71	1.20	-0.59	0.56
Valence * Provoker * Gender	0.48	1.70	0.28	0.78
Age	**-1.51**	**0.70**	**-2.15**	**0.03**
Valence * Age	0.77	0.60	1.30	0.19
Provoker * Age	0.35	0.60	0.59	0.56
Valence * Provoker * Age	-0.10	0.84	-0.12	0.90
Treatment Group	0.17	1.30	0.13	0.90
Valence * Treatment Group	0.73	1.13	0.65	0.52
Provoker * Treatment Group	0.06	1.13	0.05	0.96
Gender * Treatment Group	1.12	1.98	0.56	0.57
Age * Treatment Group	**2.71**	**1.00**	**2.72**	**0.01**
Valence * Provoker * Treatment Group	0.04	1.60	0.03	0.98
Valence * Gender * Treatment Group	0.57	1.77	0.32	0.75
Valence * Age * Treatment Group	-1.28	0.88	-1.45	0.15
Provoker * Gender * Treatment Group	1.45	1.77	0.82	0.41
Provoker * Age * Treatment Group	-0.89	0.88	-1.00	0.32
Valence * Provoker * Gender * Treatment Group	-1.24	2.50	-0.50	0.62
Valence * Provoker * Age * Treatment Group	-0.02	1.25	-0.01	0.99
Externalising	**-0.67**	**0.33**	**-2.03**	**0.04**
Substance Use	-0.74	0.46	-1.59	0.11
Parental Education	-0.09	0.41	-0.22	0.82
Constant	4.29	0.88	4.87	0.00

Random effects	Estimate	S.E	95% CI	
Identity	2.76	0.31	2.22	3.43
Residual	2.25	0.12	2.03	2.51

Improver status

Feedback-Related Negativity: The valence by improver interaction did not reach significance (*fig. 5.5*), but there was a significant 3-way interaction between valence, provoker, and participant improvement (b = 9.62, S.E. = 3.88, z = 2.47, p = 0.01; *table 5.6*). Under high provocation, non-improving participants demonstrated a significantly greater FRN response to punishment compare to reward (4.99μV vs. 4.01μV; χ^2 (1) =

5.64, $p = 0.02$), which was not seen amongst improving participants (5.73μV vs. 5.26μV; χ^2 (1) = 1.24, $p = 0.27$). By comparison, under low provocation, improving participants generated greater evoked FRN response to punishment than reward (5.93μV vs. 4.96μV; χ^2 (1) = 5.39, $p = 0.02$), while the non-improving participants did not (4.70μV vs. 4.63μV; χ^2 (1) = 0.03, $p = 0.87$).

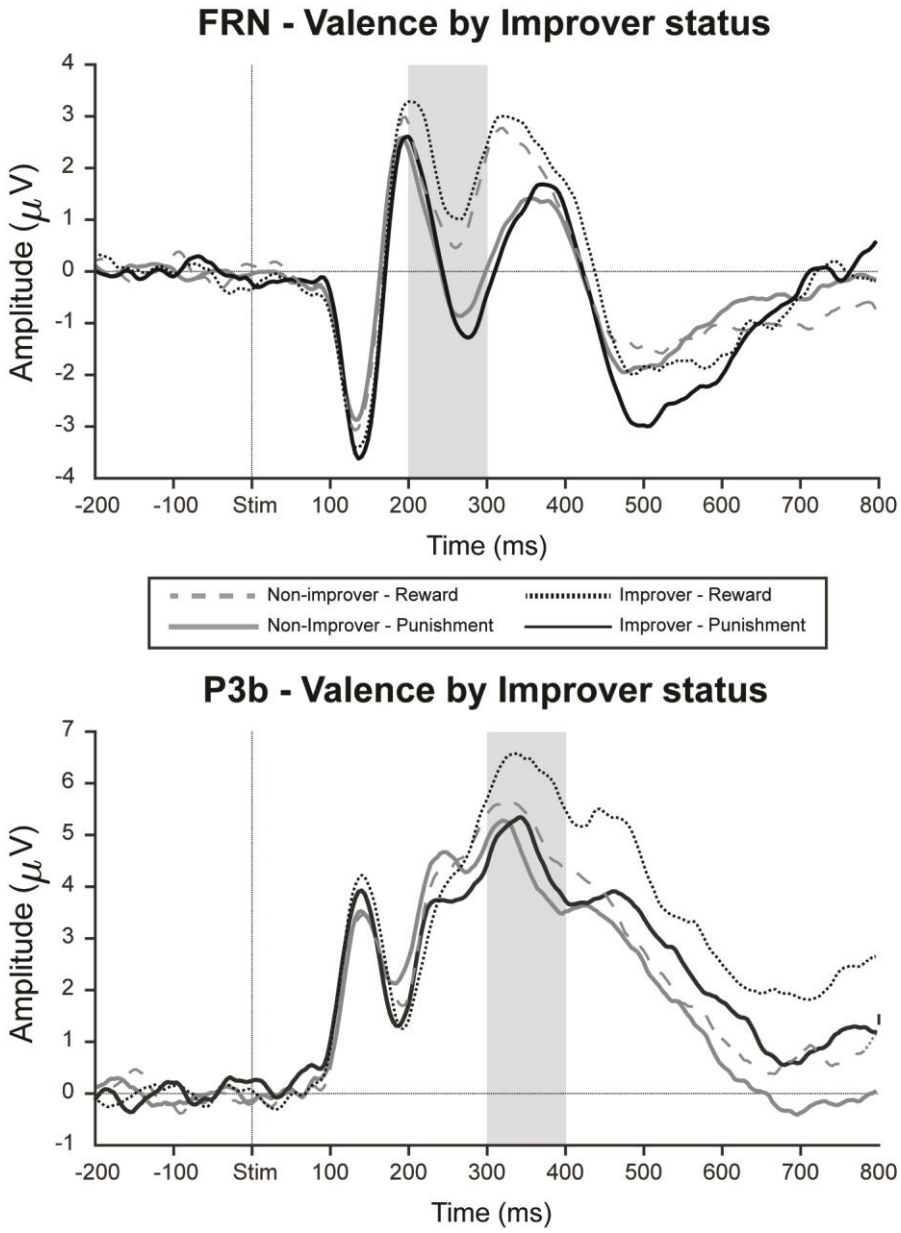

Figure 5.5. *FRN and P3b response to reward and punishment split by participant improver status. The grey box highlights the window of interest. For graphing purposes, improver status was based on a median split of participant change in externalising behaviour over time.*

There was also a significant 3-way interaction between valence, age and improvement ($b = 7.59$, S.E. = 2.42, $z = 3.13$, $p = 0.002$). Older, improving participants

demonstrated significantly greater FRN response to punishment compared to reward (5.83μV vs. 3.93μV; χ^2 (1) = 21.45, $p < 0.001$), which was not seen in younger improvers (5.81μV vs. 6.28μV; χ^2 (1) = 0.97, $p = 0.32$), or either the older (5.24μV vs. 4.80μV; χ^2 (1) = 1.05, $p = 0.31$) or younger (4.45μV vs. 3.85μV; χ^2 (1) = 2.20, $p = 0.13$) non-improvers.

Table 5.6. *Results from the mixed effects model regression FRN amplitude back on valence, provoker, age, gender, and improver status.*

	Wald χ^2 (27) = 67.20			p = 0.0001
FRN	*b*	S.E.	*z*	*p*
Valence	**-0.80**	**0.38**	**-2.12**	**0.03**
Provoker	-0.48	0.38	-1.29	0.20
Valence * Provoker	0.62	0.53	1.17	0.24
Gender	**-2.61**	**0.78**	**-3.36**	**<0.01**
Valence * Gender	0.19	0.60	0.32	0.75
Provoker * Gender	1.12	0.60	1.86	0.06
Valence * Provoker * Gender	-1.06	0.85	-1.25	0.21
Age	0.03	0.41	0.08	0.93
Valence * Age	-0.31	0.30	-1.03	0.30
Provoker * Age	0.34	0.30	1.14	0.25
Valence * Provoker * Age	-0.49	0.42	-1.17	0.24
Improvement	0.10	4.06	0.02	0.98
Valence * Improvement	-3.87	2.75	-1.41	0.16
Provoker * Improvement	-4.95	2.75	-1.80	0.07
Gender * Improvement	-6.92	5.54	-1.25	0.21
Age * Improvement	-0.54	3.23	-0.17	0.87
Valence * Provoker * Improvement	**9.62**	**3.89**	**2.47**	**0.01**
Valence * Gender * Improvement	5.18	4.30	1.20	0.23
Valence * Age * Improvement	**7.59**	**2.42**	**3.13**	**<0.01**
Provoker * Gender * Improvement	8.16	4.30	1.90	0.06
Provoker * Age * Improvement	3.83	2.42	1.58	0.11
Valence * Provoker * Gender * Improvement	-11.62	6.08	-1.91	0.06
Valence * Provoker * Age * Improvement	-6.08	3.43	-1.77	0.08
Improvement constant	-0.12	0.62	-0.20	0.84
Externalising	0.13	0.36	0.36	0.72
Substance Use	**-0.90**	**0.44**	**-2.05**	**0.04**
Parental Education	-0.50	0.34	-1.49	0.14
Constant	6.39	0.48	13.23	0.00
Random effects	Estimate	S.E	95% CI	
Identity	2.34	0.25	1.90	2.88
Residual	1.55	0.08	1.39	1.73

P3b: There were no significant main or interaction effects of participant improvement on P3b amplitude (*table 5.7*).

Table 5.7. *Results from the mixed effects model regression P3b amplitude back on valence, provoker, age, gender, and improver status.*

	Wald χ^2 (27) = 43.72			p = 0.02
P3b	*b*	S.E.	*z*	*p*
Valence	**1.78**	**0.55**	**3.21**	**<0.01**
Provoker	0.29	0.55	0.52	0.60
Valence * Provoker	-0.50	0.78	-0.63	0.53
Gender	**-2.31**	**1.02**	**-2.27**	**0.02**
Valence * Gender	-0.86	0.88	-0.97	0.33
Provoker * Gender	0.08	0.88	0.09	0.93
Valence * Provoker * Gender	-0.07	1.25	-0.06	0.95
Age	0.01	0.53	0.03	0.98
Valence * Age	0.22	0.44	0.51	0.61
Provoker * Age	-0.07	0.44	-0.16	0.87
Valence * Provoker * Age	-0.11	0.62	-0.18	0.86
Improvement	8.08	5.26	1.54	0.13
Valence * Improvement	-1.90	4.04	-0.47	0.64
Provoker * Improvement	0.47	4.04	0.12	0.91
Gender * Improvement	-1.13	7.26	-0.16	0.88
Age * Improvement	-3.50	4.22	-0.83	0.41
Valence * Provoker * Improvement	-1.96	5.72	-0.34	0.73
Valence * Gender * Improvement	-1.81	6.33	-0.29	0.78
Valence * Age * Improvement	0.84	3.56	0.24	0.81
Provoker * Gender * Improvement	-5.95	6.33	-0.94	0.35
Provoker * Age * Improvement	-0.47	3.56	-0.13	0.90
Valence * Provoker * Gender * Improvement	11.04	8.95	1.23	0.22
Valence * Provoker * Age * Improvement	3.80	5.04	0.75	0.45
Improvement constant	0.99	0.78	1.27	0.21
Externalising	-0.85	0.45	-1.87	0.06
Substance Use	**-1.27**	**0.55**	**-2.30**	**0.02**
Parental Education	-0.14	0.43	-0.32	0.75
Constant	4.77	0.63	7.54	0.00
Random effects	Estimate	S.E	95% CI	
Identity	2.89	0.32	2.33	3.58
Residual	2.28	0.12	2.05	2.54

Covariate effects

Feedback-Related Negativity: There was a significant main effect of substance use on FRN amplitude (b = -0.98, S.E. = 0.38, z = -2.56, p = 0.01). Participants reporting low substance use demonstrated greater FRN amplitudes than those reporting high substance use (-1 S.D = 5.95μV; +1 S.D. = 4.00μV).

P3b: Similar to the FRN, there was also a significant main effect of substance use on P3b amplitude (b = -0.98, S.E. = 0.44, z = -2.23, p = 0.03). Low substance use was associated with greater P3b amplitude than high substance use (-1 S.D = 5.65μV; +1 S.D. = 3.69μV).

Discussion

This study sought to investigate how feedback processing is associated with externalising behaviour in a clinical sample, and how this relationship is further influenced by therapeutic intervention (Multisystemic Therapy). Furthermore, it also set out to understand how these processes might be modulated by the social context – specifically a provocative or competitive context. To that end, participants who had taken part in a clinical trial of MST were asked to complete TAP (Taylor, 1967) against two fictitious opponents – one who punished highly, and another who punished less severely. Feedback responsivity was indexed via the FRN and P3b. Following the findings from chapter 3, high externalising participants were expected to demonstrate larger differences between reward and punishment evoked P3b response than low externalising, suggestive of motivational imbalance, and reduced valence related differences in the FRN. I also expected smaller valence related differences amongst participants who underwent MST, as well as in participants who demonstrated improvement (as indicated by a decrease in externalising behaviour over the therapeutic intervention and follow up period). Finally, I expected these reward-related differences in EEG activity associated with externalising symptoms and treatment to be most evident under conditions of high social provocation.

Unsurprisingly, participants chose punishments that were significantly larger for their high provoking opponent compared to their low provoking opponent. These findings are in line with those of Kramer et al. (2008), who used the TAP to investigate aggressive behaviour under frustration. They attributed this increase in the amount of money that participants chose to punish their fictitious high provoking opponents to participant frustration and a desire to retaliate against them. Therefore, these results would suggest that the task successfully induced retaliatory or competitive responding in this clinical sample. Notably, although there was no difference in punishment selection related to externalising psychopathology, adolescents with more externalising problems tended to respond more rapidly in the competitive game when they were

playing against the more provocative opponent. These behavioural results seem to suggest that the game engaged externalising adolescents particularly strongly, supporting the clinical rationale for choosing such a task.

Again as expected, greater FRN and P3b amplitudes were observed in response to negatively- and positively-valenced feedback, respectively, consistent with the past literature (e.g. Bellebaum, Polezzi, & Daum, 2010; Wu & Zhou, 2009), which further reinforces their validity as indicators of reward processing in adolescent clinical samples.

Current externalising behaviour

Whilst high and low externalisers differed in their ERP responses to feedback, the results observed were not consistent with those seen in chapter 3. In the current study, participants that scored highly on current externalising symptoms demonstrated greater differences between reward and punishment-evoked FRN responses compared to those with lower externalising problems. In contrast, those normative adolescents who scored relatively highly on an externalising measure in chapter 3 demonstrated *smaller* FRN differences to punishment versus reward compared to their lower-scoring counterparts. Despite the seemingly contradictory findings it is notable that the current results are broadly consistent with Kramer et al. (2008), who found that adult participants who showed high levels of experimental aggression (high value retaliations when selecting punishments for their opponents) in the TAP demonstrated larger differences in FRN amplitude between reward and punishment cues than low-aggressive participants. The findings taken together seem to imply that a social, and perhaps specifically competitive, context (and even the low provocation condition was competitive) may differentially elicit greater reward-sensitivity in aggression-prone individuals than less aggressive prone individuals.

Potentially, these findings may reflect the competitive context of the Go/No-Go task, which caused high-externalising adolescents in this sample to respond more strongly to the social context. This increased response amongst high-externalising adolescents to the social elements of the task may preferentially induced them to more closely monitor outcome cues, relative to adolescents with fewer behavioural problems, or relative to a neutral or non-social reward task. Their greater engagement in the task,

and stronger determination to win, may have positively biased their processing of reward cues. Whilst the findings reported in chapter 3 were in the opposite direction to those reported here, there is evidence from other sources that indicate that greater reward sensitivity or reward dominance is associated, or can be associated, with larger differences to reward and punishment in the FRN, in line with the findings in this study. Both high BAS scores (Lange, Leue, & Beauducel, 2012) and high extraversion (Smillie, Cooper, & Pickering, 2011), a trait associated with approach behaviour (Quilty, DeYoung, Oakman, & Bagby, 2014), have been linked to larger differences between unexpected reward and unexpected punishment. More recently, Bress and Hajcak (2013) investigated the relationship between both psychometrically and behaviourally measured reward responsivity and FRN amplitude. Behavioural reward responsivity was indexed by the participants' bias towards selecting a stimulus associated with a higher reward value, even when it was not the correct answer (and thus did not result in reward) during a signal detection task. They found that participants who demonstrated increased reward responsivity via both the questionnaire measure and behavioural response also demonstrated larger FRN amplitude differences between reward and punishment.

Another potential explanation for the apparent discrepancy between the current findings and those reported in chapter 3 is to consider difference between sample groups. The relative severity of externalising symptoms is likely to be greater amongst those reported in this sample, compared to the normative sample reported in chapter 3. However, given that the findings of Kramer et al. (2008), Lange, Leue, and Beauducel (2012), Smillie, Cooper, and Pickering (2011), and Bress and Hajcak (2013) were also based on normative samples, and showed larger FRN differences amongst those scoring highly on externalising-relevant measures, this latter explanation seems somewhat less likely than the experimental context explanation. However, the lack of comparative control group in this experiment prevents us from drawing a firm conclusion about the root of the difference.

The study also revealed gender differences that are important to consider. Importantly, amongst high externalising males, significant differences were seen between reward- and punishment-evoked FRN responses when they were playing against the high provoking opponent, but not the low provoking one. Females who were

high on externalising problems, on the other hand, showed significant valence differences under *low* provocation, but not high provocation. Assuming that larger differences in FRN to reward and punishment in this study reflect greater reward sensitivity: high externalising males appeared to demonstrate an increase in reward sensitivity under provocation, indicative of increased approach behaviours, whereas high externalising females showed reduced approach motivation under provocation, perhaps reflective of anxiety or stress, which would be consistent with work suggesting gender differences in aggressive response to provocation (Lawrence & Hutchinson, 2012).

Externalising related differences in the P3b in relation to valence were also observed, though contrary to expectations, this was due to smaller valence differences in the high externalising participants relative to the low externalisers. Whilst these results are somewhat similar to those reported by Bernat, Nelson, Steele, Gehring, and Patrick (2011), they are inconsistent with the results from chapter 3. However, neither of these studies utilized clinical samples or socially-driven, competitive tasks, making it difficult to draw direct comparison between the two sets of results. Instead, these results may also be considered similar to the P3b blunting seen in previous clinical externalising samples (Gao & Raine, 2009), which is thought to reflect limited attentional resources available to monitor all incoming information. Baskin-Sommers et al. (2014) suggests that, given the importance of the P3 in attentional processes (Polich, 2007), the sensitivity of the P3b to motivational stimuli is a downstream effect of attention. As externalising behaviour is associated with reduced working memory (Endres, Rickert, Bogg, Lucas, & Finn, 2011), and P3 response is smaller under heavy task demands (Ahmed & De Fockert, 2012), it seems likely that the lack of available attentional resources to processes motivational differences between reward and punishment feedback may account for lack of difference seen amongst high externalisers.

Differences in P3b effects between those reported here and in chapter 3 may then reflect a combination of task and population differences. Firstly, the participants involved in this study demonstrated more severe externalising symptoms than those in chapter 3. Therefore, it is possible that this is associated with greater deficits in working memory and attentional capacity, leading to diminished P3b responses amongst the high externalisers reported in this sample. Secondly, the task reported here was more

complex than the task used in chapter 3, which could further increase attention load and working memory processes. Unlike previous studies, there was more information to be processed in this task at both the trial and block level, leading to increased cognitive load. For example, within a trial, participants had to monitor their performance over 6 sets of Go/No-Go stimuli before feedback as opposed to 1 stimulus used in chapter 3. This, combined with additional information about the competitive social dynamic of the block, such as previous opponent punishment, current prediction of opponent punishment, and the participants previous and current selected punishment, would increase the working memory demands.

Treatment effects

It is noteworthy that the results reported here appear to yield partial support for treatment effects on neural systems involved in reward processing. Specifically, participants who received MST demonstrated significantly less reward responsivity compared to those assigned to the MAU group. However, this effect was modulated by both provoker condition and participant age. Amongst the older group, larger FRN valence differences were seen amongst participants who received MAU compare to those receiving MST under low levels of provocation. This supports the idea that reward responsivity is diminished amongst those receiving MST in situations of emotional arousal and remains heightened amongst older MAU participants under low social provocation. Similarly, amongst the younger participants, MST participants demonstrated less reward responsivity than the MAU group, whilst MAU participants demonstrated differences whilst under low provocation. However, the direction of the FRN effect was reversed amongst the younger MAU group, with larger FRN amplitudes seen in response to reward as opposed to punishment. This is a highly surprising finding and was not anticipated. One possible interpretation of this result though is that younger MAU participants expected to lose, and so showed greater surprise to the win cues than the loss cues. There is a growing body of evidence suggesting that the FRN may at least partially reflect an unsigned prediction error (Hauser et al., 2014; Talmi, Atkinson, & El-Deredy, 2013).

It is important to note that whilst the effect of treatment on reported externalising behaviour approached significance, there were no significant differences

in externalising behaviour between the two treatment groups, similar to other trials reported outside the US (Leschled & Cunningham, 2002; Sundell et al., 2008). Therefore, this suggests that the treatment effects on the FRN may not have been associated with changes in externalising behaviour, which is further reinforced by the fact the effects of treatment remained when controlling for current symptoms. Potentially, this may instead reflect changes in other symptomatology commonly comorbid with CD that also known to be associated with motivational changes, such as ADHD (Luman, Tripp, & Scheres, 2010) or MDD (Whitton, Treadway, & Pizzagalli, 2014). Whilst the effect of MST on non-externalising symptoms remains largely untested, there is some suggestion that it may reduce further suicide attempts in adolescents who have previously attempted suicide (Huey et al., 2004). However, without further research investigating how MST may influence non-externalising symptoms amongst externalising adolescents, I cannot draw firm conclusions.

Improvement effect

Whilst there was no difference in P3b amplitude as a function of participant improvement, there were differences in the FRN. Specifically, non-improving participants (those who demonstrated no change or an increase in delinquency over the follow-up period) showed significantly greater FRN valence differences under high provocation, whereas the improving participants demonstrated differences under low provocation. These results are consistent with the idea that treatment reduced the tendency of externalising adolescents to increase their approach tendencies or reward sensitivity under conditions of high social provocation. This might suggest that participants who have improved as a result of treatment do not demonstrate reduced reward sensitivity in general, but are less likely to increase in approach behaviour when provoked, which might suggest a mechanism by which treatment reduces the potential for interpersonal aggression. Putting this into context, if provocation came from deviant peers in the form of peer pressure, the increased reward dominance this might induce may express itself in other ways, such as non-aggressive norm violation (e.g. theft). A recent study by Centifanti and Modecki (2013) reported that individuals high in callous-unemotional traits demonstrated increased riskier decisions following punishment when in the presence of their peers, which was not seen amongst individuals with low callous-unemotional traits, suggesting that the presence of peers may influence punishment and

reward-related decision-making. However, further work is clearly needed to investigate this possibility thoroughly.

Additional findings

Unexpectedly, both feedback evoked ERPs varied as a function of participant substance use when self-reported delinquency was controlled for. Reduced amplitudes were seen in both the FRN and the P3b amongst those reporting high levels of drug taking. Previous work investigating FRN response in high substance use individuals has been limited. However, work conducted on the Error-Related Negativity (ERN), a component generated by endogenous cues of error, and thought to be related to the FRN (Cavanagh, Zambrano-Vazquez, & Allen, 2012), has found decreased ERN amplitudes in those reporting high drug use compared to low (Franken et al., 2007; Marhe, van de Wetering, & Franken, 2013). In the same vein, work with the P3b has also found smaller responses amongst substance users in general compared to non-substance users (Kamarajan et al., 2010). Moreover, emerging evidence suggests that both ERPs may index an underlying heritable neurocognitive profile. Fein and Chang (2008) found that FRN response in adult alcoholics was smaller in individuals reporting high levels of family history of alcohol use. Similarly, Euser et al. (2013) found similar results in the P3b, where adolescents whose parents demonstrated Substance Use Disorder (SUD) demonstrated smaller P3b responses in general compared to normal risk adolescents. Therefore, these results appear to be largely consistent with the current literature.

Limitations

There are several limitations of this study that must be noted. One limitation of this study relates to the measure of participant improvement. Due to the small sample size, a continuous measure of improvement was utilised, and whilst the continuous measure implemented here can identify relative increases or decreases over time, it cannot be used to define groups who did not change over time. Specifically, we are unable to assess differences that may exist between those who demonstrate relatively low levels of externalising consistently over all time points and those expressed high levels of externalising behaviour over all time points. Future work seeking to

understand improver effects may benefit from larger sample sizes or pre-screening methods targeting each improver group to ensure adequate sample size.

Building on this, this study is also limited by the variation in participant follow-up period. As participant differed in their time since intervention, ranging from 18 to 48 months, participant improvement may be attributable, at least in part, to age-related improvements in externalising behaviours. Generally, externalising participants receiving intervention, regardless of the intervention, tend to demonstrate reduction in antisocial behaviour (e.g. Butler, Baruch, Hickey, & Fonagy, 2011; Chanen et al., 2008; Weiss et al., 2013; Weiss, Han, Tran, Gallop, & Ngo, 2015). Furthermore, it is already established that a certain percentage of high externalising individuals, especially those who demonstrated marked increased in antisocial behaviour over adolescence with no childhood history of externalising, demonstrate decreases in later adolescence and early adulthood (Pardini & Frick, 2012). Combined, both these factors are likely to influence participants externalising behaviour with those who have been out of therapy for longer period demonstrating lower levels of antisocial behaviour. Future research should ensure that follow-up times across participants are equivalent to prevent possible confounding effects of both therapeutic response and age-associated changes in externalising behaviour.

Another limitation is that no baseline electrophysiological measurements were collected. Without baseline EEG activity means, it is impossible to know whether the clinical intervention lead to any changes in feedback processing, or whether the two groups demonstrated comparable improvement or deterioration from baseline. Instead of the cross-sectional designed implemented here, a much stronger understanding of neural mechanisms underlying treatment associated change could be gained using a longitudinal design with EEG measures taken at baseline and at each follow-up time point. Not only would this allow us to understand changes associated with improvement in feedback-related ERPs, but potentially allow the investigation of marker for improvement prior to intervention.

Thirdly, no information regarding CD onset or expression was collected. Given that CD is a heterogeneous disorder, this limits the study in two ways. Firstly, earlier onset of CD is associated with worse outcomes (Odgers et al., 2008), different structural

abnormalities (Fairchild et al., 2011), and risky decision making during rewarded Risky Choice Tasks (Fairchild et al., 2009). Similarly, the types of externalising behaviours that participants engage in may be associated with different electrophysiological response following feedback cues. Participants reporting high levels of aggressive behaviours may differ from those who demonstrate non-violent CD. By combining all externalising participants into one group, and not controlling for age of onset, the analysis may mask important differences in reward processing between different subsamples of externalisers. It is important that future work considers both these factors when testing investigating clinical externalisers.

Furthermore, internalising behaviours are known to both co-occur with externalising behaviour in a subset of clinical samples and have an influential effect on ERPs associated with feedback processing (Armstrong & Costello, 2002). Furthermore, internalising behaviour has been associated with higher punishment sensitivity (Santesso, Dzyundzyak, & Segalowitz, 2011) and altered ERP response to feedback (Tucker et al., 2003). Along similar lines, ADHD comorbidity is also common amongst participants with Conduct Disorder (Kessler et al., 2014). As ADHD is also associated with changes in reward processing (Luman, Tripp, & Scheres, 2010; Plichta & Scheres, 2014) Future work using high risk samples should aim to control for potential comorbidity with ADHD to more accurately desegregate neural activity associated reward processing unique to each disorder.

One further limitation of note is the differences between the participants included in the study and those who were not. Parents of participants who were included in the study demonstrated lower levels of education and reported lower annual income. Perhaps more impactful, participants themselves also reported lower levels of delinquency 18 months after the end of the intervention. Given that the participants included in this study may not be representative of the larger sample they were drawn from, the findings reported here may not be generalisable to more severe clinically externalising participants. Despite this, these participants still reported high levels of externalising behaviour, with the average score from the group indicating these participants engaged in one type of externalising behaviour nearly everyday, or several types less frequently over the previous 6 months. However, further investigation using adolescents reporting engagement in high levels of externalising behaviour at the time

the study is taking place may provide a more accurate understanding of the association between externalising and feedback processing.

In addition, the task used in this study was partially dependent on participant's ability to differentiate between colours, specifically red and green, which were used for both Go/No-Go differentiation and as part of the feedback valence indication. Whilst the valence feedback cues were distinguished by other visual cues (participants were presented with a tick mark for a reward and a cross for a punishment), the Go/No-Go stimuli differentiation was entirely dependent on the colour of the arrows (which remained the same shape and size regardless of condition). Given that approximately 8% of males report red-green colour blindness (Asenjo, Rim, & Oprian, 1994), it is possible that participants involved in the study were red-green colour blind, despite none reporting it prior to or during the task. This would inhibit their performance on the task, and potentially influence their processing of feedback due to the inability to tell whether they made a mistake. In future, studies should either use non-colour dependent stimuli or conduct colour blindness screening prior to participation.

Conclusions

In this study on clinical adolescents with a clinical history of externalising behaviour problems, I found partial support for reward dominance theories. Reward responsivity, as indexed by the FRN, appeared to be larger amongst those who scored higher on current externalising behaviour compared to those who scored lower. However, the relationship was further complicated by social provocation and participant gender. By comparison, the P3b demonstrated sensitivity to feedback valence amongst the low externalising participants, but not the high externalisers, potentially reflecting deficits in attention or working memory amongst those prone to antisocial behaviour. Importantly, these effects differed substantially from those reported in chapter 3, highlighting the need for future research investigating reward mechanisms in more socially driven contexts. Finally, differences in reward responsivity, as indexed by the FRN, were observed between participants who received Multisystemic Therapy and those who received Management-As-Usual, and between those who demonstrated a reduction in externalising behaviours over the treatment and follow up period compared

to those who did not, reinforcing previous work demonstrating changes in neural signal in response to therapeutic intervention.

Chapter 6

Feedback-related neural oscillations and social provocation amongst adolescents with a history of externalising.

Abstract

Previous work investigating feedback-induced oscillations has found that slow (theta) and fast (alpha/mu and beta) band activity is sensitive to feedback valence. Yet, work investigating the relationship between externalising behaviour and reward sensitivity in normative samples using oscillatory power as an index of reward responsivity has been mixed. Moreover, in the previous chapter, I found that the relationship between externalising behaviour and feedback related Event-Related Potentials (ERPs) activity and externalising behaviour differed substantially from those seen in normative samples. In addition, this relationship was sensitive to changes to social provocation and treatment effect. This chapter sought to understand whether externalising behaviour in clinical adolescents is associated with changes in feedback related oscillatory profiles. Furthermore, as changes in ERP activity related to treatment type (MST vs. MAU) and treatment effects (improvement vs. non-improvement) were observed in the previous chapter, I further investigated how treatment may influence oscillatory activity. To do this, participants with a clinical history of externalising behaviour taken from a MST RCT were asked to play a competitive reaction time game against two fictitious opponents - a high provoker and a low provoker, and the EEG signal following feedback presentation was analysed using Complex Wavelet Analysis. Whilst there were no significant differences associated with externalising behaviour or treatment in the expected theta, alpha/mu, or beta bands, exploratory analysis revealed a significant cluster of delta band activity that differed between high and low externalisers. Specifically, high externalising males demonstrated significant differences in punishment and reward induced delta activity following feedback. Given that delta has been previously associated with motivational processes, and more recent work indicates a role in reward prediction error, these results suggest gender specific motivational changes amongst high externalising males.

Introduction

The efficient processing of feedback resulting from one's action is vital for adjusting future behaviour (Kubanek, Snyder, & Abrams, 2015; Luft, 2014). Positive or rewarding feedback typically indicates a beneficial choice, increasing the likelihood – via learning--of the same behaviour being repeated and by contrast, negative or punishing feedback decreases the chances of a behaviour being repeated. Amongst externalising adolescents, disruptions in the motivational systems associated with the processing of feedback is thought to be indicative of increased levels of approach behaviours (Gray, 1987; Quay, 1993). Greater activation of the behavioural approach system (BAS) over the behavioural inhibition systems, responsible for reward and punishment processing, respectively, is thought to lead to a motivational state known as reward dominance (Quay, 1993). According to Quay (1993), participants who demonstrate reward dominance should demonstrate increased reward sensitivity and approach behaviours in spite of punishment signals.

Quay's theory is supported by behavioural evidence showing that externalising participants often demonstrate differences, relative to controls, in their responses to reward and punishment. Previous studies using variants of the Card Playing Task (CPT, Siegel, 1978) or the Iowa Gambling Task (IGT; Bechara, Damasio, Damasio, & Anderson, 1994) have found that both clinical externalisers, and normative participants high in externalising scores, demonstrate maladaptive strategies, favouring riskier strategies in pursuit of reward that lead to a net loss. During the CPT, externalising cohorts demonstrate perseverative behaviour, choosing to play more rounds of the game compared to low externalising participants, despite the increasing chance of punishment the more rounds played (Belmore & Quinsey, 1994; Daugherty & Quay, 1991; O'Brien & Frick, 1996; Seguin et al., 2002). In the IGT, externalising behaviour is associated with increased selection from high reward/high punishment decks that results in a net loss, as well as lower learning rates as the game is played (Blair, Colledge, & Mitchell, 2001; Ernst et al., 2003). However, these studies do not tell us directly about the neural mechanisms underlying the heightened reward sensitivity seen amongst externalisers, blurring the distinction between inhibitory and reward sensitivity mechanisms, both of which are thought to be affected by motivational imbalance (Quay, 1993).

Currently, ERP work investigating reward related mechanisms associated with externalising behaviour has been limited. One study by Bernat, Nelson, Steele, Gehring, and Patrick (2011) did not support Quay's (1993) theory of reward dominance. During a gambling task, they found valence-insensitive decreases in P3b amplitudes were associated with higher externalising scores in normative young adults, suggestive of a general decrease in the motivational salience of feedback amongst externalisers, regardless of whether it indicated reward or punishment. By contrast, the results reported in chapter 3 did reveal some support for reward dominance amongst high-externalising typically-developing adolescents. High externalising participants demonstrated increased motivational salience attributed to reward compared to punishment as measured by the P3b. Moreover, self-reported externalising behaviour was also associated with a diminished difference between punishment and reward in the FRN, which appeared to be driven by reduced FRN amplitudes to punishment stimuli amongst the high externalisers compared to low externalisers. The results appeared to indicate deficits in error monitoring associated with externalising behaviour.

However, in chapter 5, in a sample of adolescents with a clinical history of externalising disorders, those who exhibited high levels of current externalising behaviour demonstrated *larger* differences in the FRN between reward and punishment in a socially-driven task designed to elicit frustration in participants, particularly in males and in highly-socially provocative contexts. Whilst these results were different to those reported in chapter 3, similar differences were reported by Kramer, Büttner, Roth, and Münte (2008), who found larger FRN valence differences amongst participants demonstrating high experimental aggression. Work by Lange, Leue, and Beauducel (2012) and Bress and Hajcak (2013) has also found that larger differences between reward and punishment evoked FRNs are associated with high BAS scores and reward responsivity, respectively, suggestive of greater reward sensitivity amongst these higher externalising samples. Furthermore, unexpectedly, high externalising adolescents showed a smaller difference between win and loss in the P3b component. This effect may be related to differences between clinical and normative samples in attention capacity or working memory (Endres, Rickert, Bogg, Lucas, & Finn, 2011). In general, the contrasting findings seem to suggest that reward sensitivity at the level of neural response may change as a function of context, and/or may vary depending on the level of severity of antisocial behaviour.

Similar to ERP literature, event-related power changes in a couple of spectral bands have been associated with feedback response. Both frontal midline theta activity (e.g. Cohen, Elger, & Ranganath, 2007; Crowley et al., 2014) and beta band activity has also been found to been sensitive to feedback (Marco-Pallarés et al., 2008; Marco-Pallarés et al., 2009; van de Vijver, Ridderinkhof, & Cohen, 2011), though there has been considerable inconsistency in the induced activity and direction of effect in the beta band. Furthermore, recent work by Gros, Panasiti, and Chakrabarti (2015) suggests that feedback related parietal activity in the mu/beta band may be sensitive to social reward as participants demonstrated greater beta suppression when observing a smiling face with a conditioned association to reward compared to a smiling face with a conditioned association to punishment.

As far as I am aware, only two studies have investigated the relationship between externalising behaviour and feedback-related oscillations, and none have done so in a clinical sample. Bernat et al. (2011) performed wavelet analysis on principle components associated with the FRN and the P3b, relating the evoked frequency band power to self-reported externalising behaviour in a group of normative undergraduates. They found that those who reported higher levels of externalising behaviour demonstrated decreased power in the delta frequency band in general following feedback, but did not identify any difference in the theta band. In line with this, there were no observed differences in feedback theta between high and low externalisers in chapter 4 in a sample of normative adolescents, though exploratory analysis suggested that there may be some differences associated with externalising behaviour in the high alpha and beta band activity over parietal sites. The differences in these studies may be attributable to different techniques used during pre-processing. Specifically, Bernat et al. (2011) performed PCA on their data and identified two components associated with the FRN and P3b, and then ran time-frequency analysis on these components. Therefore, the oscillatory activity measured in their study only reflects that underlying these two ERPs. By comparison, the results reported in chapter 4 capture both the evoked and induced activity (the activity that is both phase-locked and non-phase locked to stimulus presentation), potentially providing a more robust image of feedback related oscillatory processes.

At this point, it is vital to note that neither Bernat et al. (2011) nor chapter 4 used a clinical population. However, as noted in chapter 5, the effect of valence on feedback related neural signals amongst clinical participants was opposite to those that were predicted based on typically developing populations. Moreover, differences between high and low externalising participants in the sample of adolescents with a history of externalising behaviour reported in chapter 5 was further modulated by whether they were under high levels of social provocation, and by participant gender, suggesting a more complicated relationship than that seen in chapter 3. Therefore, it is important to further investigated event related oscillatory activity amongst clinical populations as they may be associated with feedback related differences not evident from work in typically developing samples. In the previous chapter, changes in neural response associated with therapeutic intervention were observed, suggesting that MST (Hengeler & Borduin, 1990) may be associated with differences in reward responsivity as indexed by the FRN, compared to management as usual, although the relationships proved complex. Specifically, adolescents in the MAU condition demonstrated increased reward responsivity when under low provocation, but not high provocation, suggesting increased approach behaviour when frustration is low, though this relationship was further influenced by participant age. Moreover, participants who responded positively to therapy (regardless of which intervention they received), were less likely to show reward responsivity under high provocation than their non-improving counterparts. This increased reward responsivity may reflect increases in approach/avoidance motivational imbalance, which may lead to increased aggression when under high provocation. The results were a little clearer when examining differences between participants who improved as a result of treatment compared to those that did not. In this case, larger differences in FRN amplitude between win and loss tended, in general, to be associated with a better prognostic profile. In contrast, adolescents who responded poorly to treatment were characterised by a tendency for their reward (versus loss) FRN response to be dependent on the social context: when highly provoked their FRN differences were large; when not provoked their FRN differences were small.

Here, I present the results from a study investigating feedback induced oscillatory activity amongst a group of adolescents with a history of externalising disorders. Participants completed a competitive task against two fictitious opponents, one high punishing and one low punishing, and their neural activity was analysed in the

time-frequency domain using complex wavelet analysis. As previous work using time frequency analysis has primarily found theta and beta band activity to be sensitive to feedback characteristics, I investigated changes in these bands associated with externalising behaviour. However, as previous ERP work using a similar task (Kramer et al., 2008 and chapter 5) has demonstrated that the relationship between externalising behaviour and feedback sensitivity may be more complex when using socially driven tasks than in socially neutral tasks, no directional hypothesis is advanced. Finally, in the previous chapter, changes in FRN response related to treatment group and participant response to treatment were observed, suggesting reductions in feedback sensitivity amongst those who received MST compared to MAU, and amongst those who demonstrated reductions in externalising behaviour following treatment. Therefore, smaller differences between reward and punishment evoked oscillatory activity in MST compared to MAU, and improving participants compared non-improving participants, may also be expected.

Methods

Participants and measures

As the both the participant sample and the measures used for this study are the same as those reported in chapter 5, I refer the reader back to the previous chapter, or to the methodology chapter for an in-depth explanation of the sample and measures.

EEG

After data pre-processing, the epoched EEG data was analysed using Complex Wavelet Analysis using in-house scripts (rather than EEGLAB functions). A family of 40 wavelets increasing linearly from 1 – 35Hz and from 2 – 12 cycles, and these were convolved with the EEG data in the frequency domain, and the power was scaled to decibels (dB; calculated as the 10*log10 of the power). The frequency data was baselined using a gain function to the -500 to -200 pre-stimulus window. Frequency band power was extracted using a peak + window approach in which a larger time-frequency window was define for each frequency band, and the peak value within it was identified for each individual. Then the average activity of a 3Hz by 200ms window centred on the peak was taken. The broader frontal theta and beta windows were defined

as 3-8Hz 200-500ms post-stimulus time-frequency window and the 13-20Hz 300-600Hz post-stimulus time-frequency window, respectively, and extracted from electrodes 4 (FCz), 7, and 54. The broader parietal alpha/mu window was defined as the 8-14Hz 300-600ms window over parietal electrodes (33, 34, 36, and 38).

Statistical Analysis

Similar to the previous chapter, analyses were conducted using mixed effects models. Frequency band power was added as a dependent variable. Feedback valence and provoker block were added as within-subjects factors with two levels (reward/punishment and high provocation/low provocation, respectively). Participant gender was entered as a between-subjects factor with 2 levels. Participant age and externalising behaviour were both added as continuous predictors. To control for individual differences in participants peak within each frequency, the peak frequency and timing were both added to the model as covariates. Participant ID was added as a random effect. In the participant improvement model, participant current externalising behaviour was replaced with the participant improvement score, which was entered as a continuous variable. In the model testing group treatment effects, treatment group was included as a 2-level factor variable, and participant current externalising was entered as a covariate. Finally, to control for individual differences in participant peak frequencies within each time-frequency window, the frequency and latency of each time-frequency point was included as a continuous covariate in each model.

Exploratory analysis was conducted using permutation testing with cluster correction. A null distribution was built up over 10,000 permutations, and any cluster with a summed t-value in either 0.025% tail of the distribution was considered to be significant at the p = 0.05 level.

Results

Task, age, and gender effects

Theta activity: Contrary to expectation, there was no significant main effect of valence on frontal theta activity (b = -0.21, S.E. = 0.27, z = -0.78, p = 0.43; *figure 6.1; table 6.1*). Further, frontal theta was insensitive to provoker effects (b = -0.17, S.E. = 0.27, z = -0.63, p = 0.53). No other effects reached significance.

Beta activity: Similar to frontal theta activity, there was no significant main effect of valence on frontal beta (b = -0.33, S.E. = 0.22, z = -1.49, p = 0.14; *table 6.2.*), nor was there a main effect of provoker (b = 0.12, S.E. = 0.22, z = 0.54, p = 0.59). However, there was a significant main effect of gender (b = -0.78, S.E. = 0.32, z = -2.37, p = 0.018), with females demonstrating greater beta suppression (-2.71dB) following feedback than males (-1.98dB). No other effects reached significance.

Parietal alpha/mu activity: There was no significant main effect of valence (b = -0.27, S.E. = 0.31, z = -0.87, p = 0.39; *table 6.3.*) or provoker (b = 0.07, S.E. = 0.31, z = 0.23, p = 0.82) on parietal alpha. However, there was a significant two-way interaction between valence and age (b = -0.67, S.E. = 0.25, z = -2.62, p = 0.009). Post-estimation tests revealed that older participants demonstrated a significant difference between reward and punishment, with larger suppression relative to baseline following reward compared to punishment (-4.14dB vs. -3.26dB; χ^2 (1) = 12.58, p = 0.0004). However, younger participants did not demonstrate this difference (-3.39dB vs. -3.59dB; χ^2 (1) = 0.67, p = 0.41). No other effects reached significance.

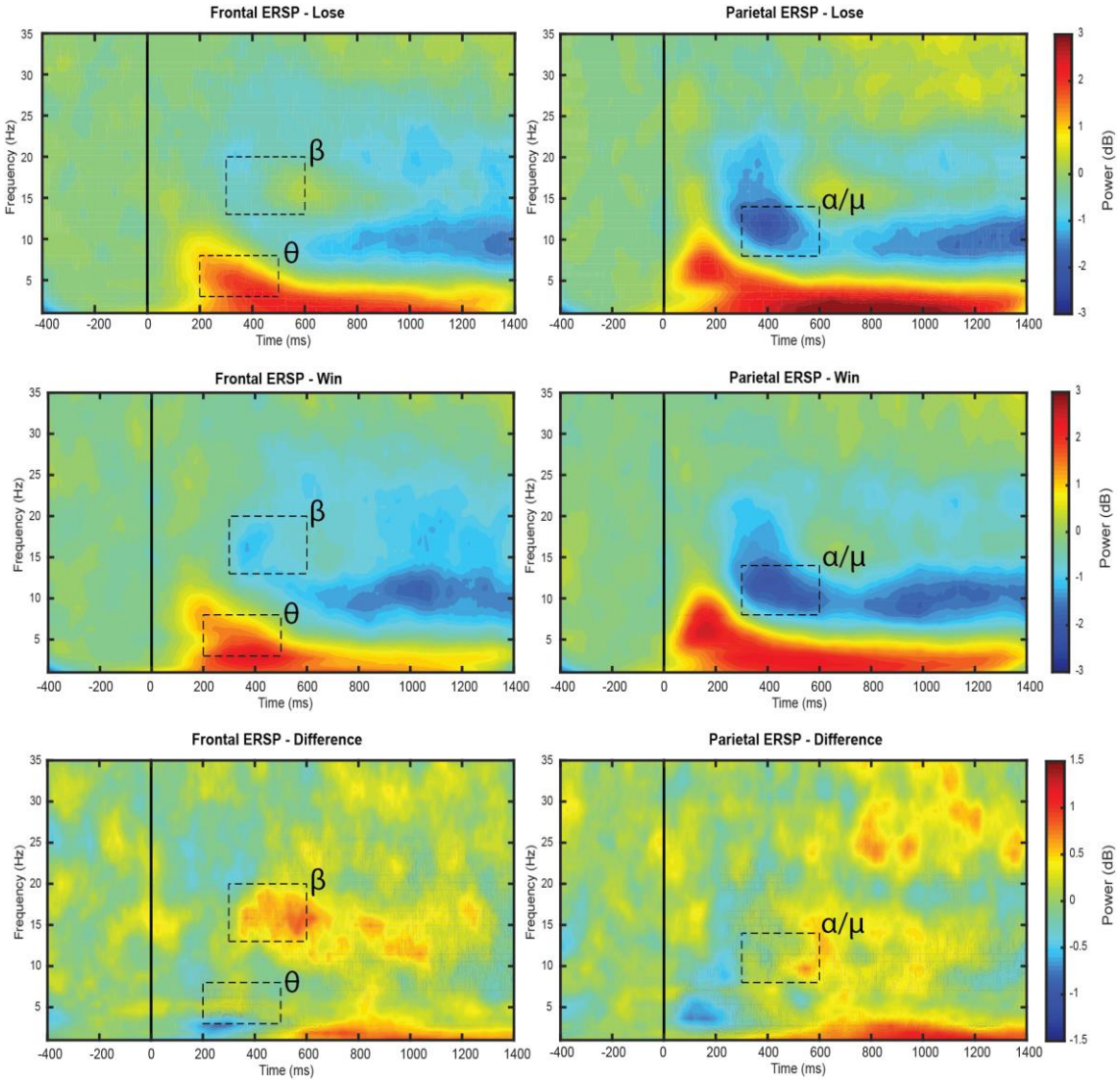

Figure 6.1. *Grand average ERSP plots for each valence condition and their differences, measured in decibels (dB), from both frontal and parietal sites. Time-frequency windows for theta (θ), beta (β), and alpha/mu (α/μ) activity are delimited using rectangles.*

Current externalising

Theta activity: The main effect of externalising behaviour approached, but did not reach, significance (b = 0.17, S.E. = 0.21, z = 1.87, p = 0.06; *table 6.1*). However, there was no interaction between valence and externalising behaviour (b = 0.17, S.E. = 0.22, z = 0.76, p = 0.44). No other effects were significant.

Table 6.1. *Results from the mixed effects model regressing frontal theta activity back on valence, provoker, age, gender and current externalising behaviour.*

	Wald χ^2 (27) = 32.18			p = 0.22
Frontal Theta	*b*	S.E.	*z*	*p*
Valence	-0.21	0.27	-0.78	0.43
Provoker	-0.17	0.27	-0.63	0.53
Valence * Provoker	0.20	0.38	0.51	0.61
Gender	-0.79	0.42	-1.87	0.06
Valence * Gender	0.04	0.45	0.09	0.93
Provoker * Gender	-0.48	0.45	-1.07	0.29
Valence * Provoker * Gender	0.74	0.64	1.16	0.25
Age	0.17	0.21	0.78	0.44
Valence * Age	-0.27	0.22	-1.20	0.23
Provoker * Age	-0.06	0.22	-0.28	0.78
Valence * Provoker * Age	0.18	0.31	0.57	0.57
Externalising	0.40	0.21	1.87	0.06
Valence * Externalising	0.17	0.22	0.76	0.45
Provoker * Externalising	0.02	0.22	0.07	0.94
Gender * Externalising	-0.34	0.33	-1.03	0.30
Age * Externalising	-0.10	0.15	-0.64	0.52
Valence * Provoker * Externalising	-0.23	0.32	-0.73	0.47
Valence * Gender * Externalising	-0.31	0.35	-0.89	0.38
Valence * Age * Externalising	0.00	0.16	-0.02	0.98
Provoker * Gender * Externalising	0.05	0.36	0.15	0.88
Provoker * Age * Externalising	0.11	0.16	0.67	0.51
Valence * Provoker * Gender * Externalising	0.42	0.50	0.85	0.40
Valence * Provoker * Age * Externalising	-0.03	0.23	-0.15	0.88
Substance Use	-0.15	0.17	-0.88	0.38
Parental Education	-0.05	0.15	-0.37	0.71
Peak Frequency	-0.08	0.05	-1.47	0.14
Peak latency	0.00	0.00	0.51	0.61
Constant	3.83	0.59	6.54	0.00
Random effects	Estimate	S.E	95% CI	
Identity	0.94	0.12	0.73	1.21
Residual	1.09	0.06	0.98	1.21

Beta activity: Current externalising behaviour had no significant main effect on frontal beta activity (b = -0.06, S.E. = 0.16, z = -0.35, p = 0.72; *table 6.2*), or interactions between valence and externalising (b = -0.26, S.E. = 0.18, z = 1.42, p = 0.16) and provoker and externalising (b = 0.09, S.E. = 0.18, z = 0.52, p = 0.61). No other effects reached significance.

Table 6.2. *Results from the mixed effects model regressing frontal beta activity back on valence, provoker, age, gender and current externalising behaviour*.

	Wald χ^2 (27) = 47.18			p = 0.009
Frontal Beta	*b*	S.E.	*z*	*p*
Valence	-0.33	0.22	-1.49	0.14
Provoker	0.12	0.22	0.54	0.59
Valence * Provoker	-0.11	0.30	-0.36	0.72
Gender	**-0.77**	**0.32**	**-2.37**	**0.02**
Valence * Gender	-0.14	0.36	-0.37	0.71
Provoker * Gender	-0.03	0.36	-0.07	0.94
Valence * Provoker * Gender	0.41	0.51	0.80	0.43
Age	0.05	0.16	0.34	0.74
Valence * Age	-0.29	0.18	-1.64	0.10
Provoker * Age	-0.22	0.18	-1.24	0.21
Valence * Provoker * Age	0.45	0.25	1.79	0.07
Externalising	-0.06	0.16	-0.35	0.72
Valence * Externalising	0.26	0.18	1.42	0.16
Provoker * Externalising	0.09	0.18	0.52	0.61
Gender * Externalising	-0.04	0.25	-0.15	0.88
Age * Externalising	0.04	0.12	0.35	0.73
Valence * Provoker * Externalising	-0.19	0.25	-0.73	0.47
Valence * Gender * Externalising	-0.37	0.29	-1.27	0.20
Valence * Age * Externalising	-0.07	0.13	-0.51	0.61
Provoker * Gender * Externalising	-0.26	0.29	-0.90	0.37
Provoker * Age * Externalising	-0.13	0.13	-0.96	0.34
Valence * Provoker * Gender * Externalising	0.66	0.41	1.62	0.11
Valence * Provoker * Age * Externalising	0.03	0.18	0.15	0.88
Substance Use	0.02	0.12	0.17	0.87
Parental Education	-0.15	0.11	-1.38	0.17
Peak Frequency	0.04	0.03	1.24	0.21
Peak latency	0.00	0.00	-1.47	0.14
Constant	-1.97	0.62	-3.16	0.00
Random effects	Estimate	S.E	95% CI	
Identity	0.65	0.09	0.49	0.85
Residual	0.87	0.05	0.78	0.97

Parietal alpha/mu activity: There was no main effect of current externalising behaviour on parietal alpha activity (b = 0.51, S.E. = 0.36, z = 1.41, p = 0.16; *table 6.3.*), nor any significant interaction between valence and externalising (b = 0.08, S.E. = 0.26, z = 0.32, p = 0.75) or between provoker by externalising (b = -0.11, S.E. = 0.26, z = -0.43, p = 0.67). There were no other significant effects.

Table 6.3. *Results from the mixed effects model regressing parietal alpha/mu activity back on valence, provoker, age, gender and current externalising behaviour*.

	Wald χ^2 (27) = 41.61			p = 0.04
Parietal Alpha/Mu	*b*	S.E.	*z*	*p*
Valence	-0.27	0.31	-0.87	0.39
Provoker	0.07	0.31	0.23	0.82
Valence * Provoker	-0.60	0.44	-1.36	0.18
Gender	-0.69	0.71	-0.96	0.34
Valence * Gender	0.04	0.52	0.07	0.95
Provoker * Gender	0.07	0.52	0.13	0.90
Valence * Provoker * Gender	1.13	0.73	1.54	0.12
Age	0.09	0.37	0.24	0.81
Valence * Age	**-0.67**	**0.25**	**-2.62**	**0.01**
Provoker * Age	0.16	0.26	0.62	0.54
Valence * Provoker * Age	0.25	0.36	0.69	0.49
Externalising	0.51	0.36	1.41	0.16
Valence * Externalising	0.08	0.26	0.32	0.75
Provoker * Externalising	-0.11	0.26	-0.43	0.67
Gender * Externalising	-0.95	0.56	-1.69	0.09
Age * Externalising	-0.42	0.26	-1.62	0.11
Valence * Provoker * Externalising	-0.19	0.37	-0.52	0.60
Valence * Gender * Externalising	0.18	0.41	0.44	0.66
Valence * Age * Externalising	0.33	0.19	1.78	0.08
Provoker * Gender * Externalising	0.56	0.41	1.37	0.17
Provoker * Age * Externalising	0.01	0.19	0.06	0.96
Valence * Provoker * Gender * Externalising	-0.15	0.58	-0.27	0.79
Valence * Provoker * Age * Externalising	0.01	0.27	0.05	0.96
Substance Use	0.21	0.33	0.61	0.54
Parental Education	-0.07	0.30	-0.22	0.82
Peak Frequency	0.06	0.05	1.29	0.20
Peak latency	0.00	0.00	-1.43	0.15
Constant	-3.18	0.96	-3.33	0.00
Random effects	Estimate	S.E	95% CI	
Identity	2.10	0.22	1.71	2.57
Residual	1.25	0.07	1.13	1.40

Treatment effects

Theta activity: There was no main effect of treatment group (b = 0.11, S.E. = 0.52, z = 0.20, p = 0.84; *table 6.4*), or interaction effects between treatment group and feedback valence (b = 0.37, S.E. = 0.54, z = 0.69, p = 0.49) or treatment group and provoker (b = -0.19, S.E. = 0.54, z = -0.35, p = 0.73). No other effects reached significance.

Table 6.4 . *Results from the mixed effects model regressing frontal theta activity back on valence, provoker, age, gender, and treatment group.*

	Wald χ^2 (28) = 40.51			p = 0.06
Frontal Theta	*b*	S.E.	*z*	*p*
Valence	-0.47	0.37	-1.29	0.20
Provoker	-0.10	0.37	-0.28	0.78
Valence * Provoker	0.32	0.52	0.60	0.55
Gender	-0.85	0.54	-1.58	0.11
Valence * Gender	0.74	0.57	1.31	0.19
Provoker * Gender	-0.12	0.57	-0.22	0.83
Valence * Provoker * Gender	0.38	0.81	0.48	0.63
Age	0.39	0.28	1.38	0.17
Valence * Age	-0.53	0.28	-1.89	0.06
Provoker * Age	-0.19	0.28	-0.69	0.49
Valence * Provoker * Age	0.41	0.40	1.04	0.30
Treatment group	-0.15	0.52	-0.29	0.77
Valence * Treatment group	0.37	0.54	0.69	0.49
Provoker * Treatment group	-0.19	0.54	-0.36	0.72
Gender * Treatment group	0.27	0.79	0.34	0.73
Age * Treatment group	-0.36	0.40	-0.90	0.37
Valence * Provoker * Treatment group	-0.09	0.76	-0.12	0.91
Valence * Gender * Treatment group	-1.34	0.85	-1.59	0.11
Valence * Age * Treatment group	0.68	0.42	1.61	0.11
Provoker * Gender * Treatment group	-0.91	0.84	-1.09	0.27
Provoker * Age * Treatment group	0.43	0.42	1.04	0.30
Valence * Provoker * Gender * Treatment group	0.65	1.19	0.55	0.59
Valence * Provoker * Age * Treatment group	-0.75	0.59	-1.26	0.21
Substance Use	-0.18	0.17	-1.06	0.29
Parental Education	-0.06	0.15	-0.40	0.69
Externalising	**0.30**	**0.12**	**2.49**	**0.01**
Peak Frequency	-0.09	0.05	-1.62	0.11
Peak latency	0.00	0.00	0.54	0.59
Constant	3.95	0.62	6.35	0.00

Random effects	Estimate	S.E	95% CI	
Identity	0.94	0.12	0.73	1.20
Residual	1.06	0.06	0.96	1.19

Beta activity: Frontal beta activity did not differ between MST and MAU participants (b = -0.54, S.E. = 0.38, z = -1.41, p = 0.16; *table 6.5*). Furthermore, there were no significant interaction effects between valence and treatment group (b = 0.22, S.E. = 0.43, z = 0.52, p = 0.60) and provoker and treatment group (b = 0.33, S.E. = 0.43, z = 0.76, p = 0.45). No other effects reached significance.

Table 6.5 . *Results from the mixed effects model regressing frontal beta activity back on valence, provoker, age, gender, and treatment group.*

	Wald χ^2 (28) = 54.98			p = 0.002
Frontal Beta	*b*	S.E.	*z*	*p*
Valence	-0.38	0.30	-1.27	0.20
Provoker	-0.14	0.29	-0.46	0.65
Valence * Provoker	0.03	0.42	0.07	0.95
Gender	**-0.87**	**0.41**	**-2.11**	**0.04**
Valence * Gender	-0.35	0.46	-0.76	0.45
Provoker * Gender	0.16	0.46	0.34	0.73
Valence * Provoker * Gender	0.07	0.65	0.11	0.92
Age	0.19	0.21	0.90	0.37
Valence * Age	-0.04	0.23	-0.19	0.85
Provoker * Age	-0.43	0.23	-1.91	0.06
Valence * Provoker * Age	0.40	0.32	1.25	0.21
Treatment group	-0.55	0.39	-1.41	0.16
Valence * Treatment group	0.23	0.43	0.53	0.60
Provoker * Treatment group	0.33	0.43	0.76	0.45
Gender * Treatment group	0.09	0.60	0.15	0.88
Age * Treatment group	-0.07	0.30	-0.24	0.81
Valence * Provoker * Treatment group	-0.25	0.61	-0.41	0.68
Valence * Gender * Treatment group	0.48	0.67	0.71	0.48
Valence * Age * Treatment group	-0.51	0.34	-1.50	0.13
Provoker * Gender * Treatment group	0.01	0.67	0.01	0.99
Provoker * Age * Treatment group	0.38	0.34	1.13	0.26
Valence * Provoker * Gender * Treatment group	0.58	0.95	0.61	0.54
Valence * Provoker * Age * Treatment group	-0.15	0.47	-0.31	0.75
Substance Use	-0.01	0.12	-0.11	0.91
Parental Education	-0.16	0.11	-1.50	0.13
Externalising	0.01	0.09	0.14	0.89
Peak Frequency	0.03	0.03	1.11	0.27
Peak latency	0.00	0.00	-1.22	0.22
Constant	-1.72	0.65	-2.64	0.01
Random effects	Estimate	S.E	95% CI	
Identity	0.65	0.09	0.49	0.85
Residual	0.86	0.05	0.77	0.95

Parietal alpha/mu activity: The main effect of treatment group on parietal alpha did not reach significance (*b* = -1.14, S.E. = 0.87, *z* = -1.32, *p* = 0.19; *table 6.6*). Furthermore, there was no significant two-way interaction between valence and treatment group (*b* = -0.69, S.E. = 0.64, *z* = -1.08, *p* = 0.28) or provoker and treatment group (*b* = 1.06, S.E. = 0.63, *z* = 1.68, *p* = 0.09). No other effects reached significance.

Table 6.6. *Results from the mixed effects model regressing parietal alpha/mu activity back on valence, provoker, age, gender, and treatment group.*

	Wald χ^2 (28) = 43.74			p = 0.03
Parietal Alpha/Mu	*b*	S.E.	*z*	*p*
Valence	0.13	0.44	0.30	0.77
Provoker	-0.39	0.43	-0.90	0.37
Valence * Provoker	-0.32	0.61	-0.52	0.61
Gender	-0.43	0.91	-0.47	0.64
Valence * Gender	-0.70	0.67	-1.03	0.30
Provoker * Gender	0.57	0.67	0.85	0.40
Valence * Provoker * Gender	0.85	0.95	0.89	0.37
Age	0.58	0.47	1.23	0.22
Valence * Age	**-0.70**	**0.34**	**-2.08**	**0.04**
Provoker * Age	0.01	0.33	0.03	0.98
Valence * Provoker * Age	0.31	0.47	0.66	0.51
Treatment group	-1.44	0.88	-1.63	0.10
Valence * Treatment group	-0.68	0.64	-1.07	0.29
Provoker * Treatment group	1.06	0.63	1.68	0.09
Gender * Treatment group	0.11	1.33	0.08	0.93
Age * Treatment group	-0.64	0.67	-0.95	0.34
Valence * Provoker * Treatment group	-0.71	0.89	-0.80	0.43
Valence * Gender * Treatment group	0.91	0.99	0.92	0.36
Valence * Age * Treatment group	0.43	0.50	0.85	0.40
Provoker * Gender * Treatment group	-1.10	0.99	-1.12	0.26
Provoker * Age * Treatment group	-0.14	0.50	-0.28	0.78
Valence * Provoker * Gender * Treatment group	0.67	1.39	0.48	0.63
Valence * Provoker * Age * Treatment group	0.19	0.70	0.27	0.79
Substance Use	0.06	0.33	0.17	0.87
Parental Education	-0.12	0.29	-0.42	0.68
Externalising	0.33	0.24	1.40	0.16
Peak Frequency	0.09	0.05	1.86	0.06
Peak latency	0.00	0.00	-1.63	0.10
Constant	-2.74	1.04	-2.63	0.01

Random effects	Estimate	S.E	95% CI	
Identity	2.04	0.21	1.66	2.50
Residual	1.26	0.07	1.13	1.40

Improver effects

Theta activity: There was no significant difference in theta activity associated with participant improvement (b = -0.46, S.E. = 2.02, z = -0.23, p = 0.89; *table 6.7*). Furthermore, there were no significant interactions between valence and improvement

(*b* = -1.20, S.E. = 1.93, *z* = -0.62, *p* = 0.53) or provoker and improvement (*b* = -1.01, S.E. = 1.97, *z* = -0.51, *p* = 0.61).

Table 6.7. *Results from the mixed effects model regressing frontal theta activity back on valence, provoker, age, gender, and participant improvement.*

	Wald χ^2 (29) = 32.14			*p* = 0.31
Frontal Theta	*b*	S.E.	*z*	*p*
Valence	-0.19	0.27	-0.71	0.48
Provoker	-0.12	0.27	-0.45	0.65
Valence * Provoker	0.16	0.38	0.42	0.68
Gender	-0.65	0.40	-1.63	0.10
Valence * Gender	0.02	0.42	0.05	0.96
Provoker * Gender	-0.59	0.42	-1.40	0.16
Valence * Provoker * Gender	0.81	0.60	1.35	0.18
Age	0.17	0.21	0.84	0.40
Valence * Age	-0.20	0.21	-0.94	0.35
Provoker * Age	-0.02	0.21	-0.10	0.92
Valence * Provoker * Age	0.04	0.30	0.13	0.89
Improvement	-0.46	2.02	-0.23	0.82
Valence * Improvement	-1.20	1.93	-0.62	0.53
Provoker * Improvement	-1.01	1.97	-0.51	0.61
Gender * Improvement	-1.69	2.84	-0.59	0.55
Age * Improvement	-0.91	1.65	-0.55	0.58
Valence * Provoker * Improvement	1.27	2.73	0.47	0.64
Valence * Gender * Improvement	2.44	3.02	0.81	0.42
Valence * Age * Improvement	0.06	1.70	0.04	0.97
Provoker * Gender * Improvement	3.33	3.04	1.09	0.27
Provoker * Age * Improvement	0.52	1.72	0.30	0.76
Valence * Provoker * Gender * Improvement	-4.58	4.28	-1.07	0.29
Valence * Provoker * Age * Improvement	0.85	2.40	0.36	0.72
Improvement intercept	-0.37	0.27	-1.35	0.18
Externalising	**0.38**	**0.16**	**2.41**	**0.02**
Substance Use	-0.02	0.19	-0.12	0.90
Parental Education	-0.05	0.15	-0.32	0.75
Peak Frequency	-0.10	0.05	-1.78	0.08
Peak latency	0.00	0.00	0.33	0.74
Constant	3.94	0.60	6.56	0.00
Random effects	Estimate	S.E	95% CI	
Identity	0.94	0.12	0.73	1.21
Residual	1.09	0.06	0.98	1.21

Beta activity: There was no significant main effect of improvement (*b* = 0.95, S.E. = 1.49, *z* = 0.64, *p* = 0.52; *table 6.8*), or interaction effects between valence and

improvement (b = 1.23, S.E. = 1.54, z = 0.80, p = 0.42) or provoker and improvement (b = -1.17, S.E. = 1.54, z = -0.76, p = 0.45). There were no other significant main effects.

Table 6.8 . *Results from the mixed effects model regressing frontal beta activity back on valence, provoker, age, gender, and participant improvement.*

	Wald χ^2 (29) = 50.12			p = 0.008
Frontal Beta	*b*	S.E.	*z*	*p*
Valence	-0.33	0.22	-1.53	0.13
Provoker	0.07	0.21	0.35	0.72
Valence * Provoker	-0.10	0.30	-0.33	0.75
Gender	**-0.80**	**0.30**	**-2.64**	**0.01**
Valence * Gender	-0.10	0.34	-0.28	0.78
Provoker * Gender	0.08	0.34	0.24	0.81
Valence * Provoker * Gender	0.38	0.48	0.80	0.42
Age	0.11	0.15	0.70	0.49
Valence * Age	-0.23	0.17	-1.36	0.17
Provoker * Age	-0.21	0.17	-1.28	0.20
Valence * Provoker * Age	0.31	0.24	1.30	0.19
Improvement	0.95	1.49	0.64	0.52
Valence * Improvement	1.23	1.54	0.80	0.42
Provoker * Improvement	-1.17	1.54	-0.76	0.45
Gender * Improvement	-1.57	2.12	-0.74	0.46
Age * Improvement	-0.35	1.23	-0.28	0.78
Valence * Provoker * Improvement	0.02	2.18	0.01	0.99
Valence * Gender * Improvement	1.60	2.41	0.66	0.51
Valence * Age * Improvement	0.41	1.36	0.30	0.76
Provoker * Gender * Improvement	2.73	2.41	1.13	0.26
Provoker * Age * Improvement	-0.94	1.36	-0.69	0.49
Valence * Provoker * Gender * Improvement	-0.05	3.41	-0.02	0.99
Valence * Provoker * Age * Improvement	1.50	1.92	0.78	0.44
Improvement intercept	0.04	0.19	0.22	0.83
Externalising	-0.03	0.11	-0.30	0.77
Substance Use	-0.02	0.14	-0.16	0.88
Parental Education	-0.17	0.11	-1.59	0.11
Peak Frequency	0.05	0.03	1.57	0.12
Peak latency	0.00	0.00	-1.19	0.23
Constant	-2.21	0.63	-3.54	0.00

Random effects	Estimate	S.E	95% CI	
Identity	0.64	0.09	0.48	0.84
Residual	0.87	0.05	0.78	0.97

Parietal alpha/mu activity: There was no significant main effect of participant improvement on parietal alpha (b = 4.05, S.E. = 3.51, z = 1.15, p = 0.25; *table 6.9*).

Table 6.9. *Results from the mixed effects model regressing parietal alpha/mu activity back on valence, provoker, age, gender, and participant improvement.*

	Wald χ^2 (29) = 38.35			p = 0.11
Parietal Alpha/Mu	*b*	S.E.	*z*	*p*
Valence	-0.16	0.31	-0.50	0.62
Provoker	0.05	0.31	0.16	0.88
Valence * Provoker	-0.62	0.44	-1.42	0.16
Gender	-0.40	0.67	-0.60	0.55
Valence * Gender	-0.30	0.49	-0.60	0.55
Provoker * Gender	0.05	0.50	0.09	0.93
Valence * Provoker * Gender	1.12	0.70	1.60	0.11
Age	0.21	0.35	0.60	0.55
Valence * Age	**-0.55**	**0.24**	**-2.24**	**0.03**
Provoker * Age	0.03	0.25	0.14	0.89
Valence * Provoker * Age	0.35	0.35	1.01	0.31
Improvement	4.05	3.51	1.15	0.25
Valence * Improvement	0.44	2.26	0.20	0.84
Provoker * Improvement	-2.44	2.25	-1.08	0.28
Gender * Improvement	-1.15	4.77	-0.24	0.81
Age * Improvement	-2.33	2.79	-0.84	0.40
Valence * Provoker * Improvement	1.05	3.19	0.33	0.74
Valence * Gender * Improvement	0.81	3.52	0.23	0.82
Valence * Age * Improvement	0.22	1.98	0.11	0.91
Provoker * Gender * Improvement	4.32	3.52	1.23	0.22
Provoker * Age * Improvement	-0.81	1.99	-0.41	0.69
Valence * Provoker * Gender * Improvement	-0.41	5.01	-0.08	0.94
Valence * Provoker * Age * Improvement	-2.15	2.81	-0.77	0.44
Improvement intercept	0.45	0.54	0.83	0.41
Externalising	-0.09	0.31	-0.28	0.78
Substance Use	0.02	0.38	0.05	0.96
Parental Education	-0.13	0.30	-0.46	0.65
Peak Frequency	0.05	0.05	0.99	0.32
Peak latency	0.00	0.00	-1.77	0.08
Constant	-2.94	0.97	-3.04	0.00
Random effects	Estimate	S.E	95% CI	
Identity	2.06	0.21	1.68	2.52
Residual	1.27	0.07	1.14	1.41

Moreover, there was no significant two-way interactions between valence and participant's improvement (b = 0.44, S.E. = 2.26, z = 0.20, p = 0.84) or between provoker and participant improvement (b = -2.43, S.E. = 2.25, z = -1.08, p = 0.28). No other effects were significant.

Exploratory analysis

As seen above, contrary to predictions, no significant main effects of valence in the feedback evoked theta or beta bands were found. As this may indicate a differential reward-response pattern to that predicted, I conducted exploratory permutation tests with cluster correction (at the *alpha* = 0.05 level for both the pixel and cluster level threshold) testing for differences between reward and punishment-induced activity in the -400 to 1400ms time window. This revealed only one significant cluster of time-frequency points that reached significance at the $p = 0.05$ cluster corrected level: a delta band cluster (1-4Hz) occurring 600-1000ms after feedback over frontal sites (*fig.* 6.2). Activity from this window was extracted and mixed effects models were run on them.

Task, age, and gender effects: There was a significant main effect of valence on frontal delta activity ($b = -0.66$, S.E. = 0.25, $z = -2.66$, $p = 0.008$; *table 6.10*), with larger delta activity seen in response to punishment (3.15dB) compared to reward (2.90dB). Whilst there was no main effect of provoker ($b = -0.37$, S.E. = 0.25, $z = -1.53$, $p = 0.13$), there was a significant interaction between valence and provoker ($b = 0.89$, S.E. = 0.35, $z = 2.52$, $p = 0.012$). This was due to a larger delta effects following punishment than reward under high provocation (3.40dB vs. 2.74dB, χ^2 (1) = 12.11, $p = 0.0005$), but not low provocation (2.89dB vs. 3.06dB, χ^2 (1) = 0.77, $p = 0.38$). Neither the main effect of age ($b = -0.46$, S.E. = 0.24, $z = -1.91$, $p = 0.06$) or gender reached significance ($b = -0.34$, S.E. = 0.46, $z = -0.73$, $p = 0.47$).

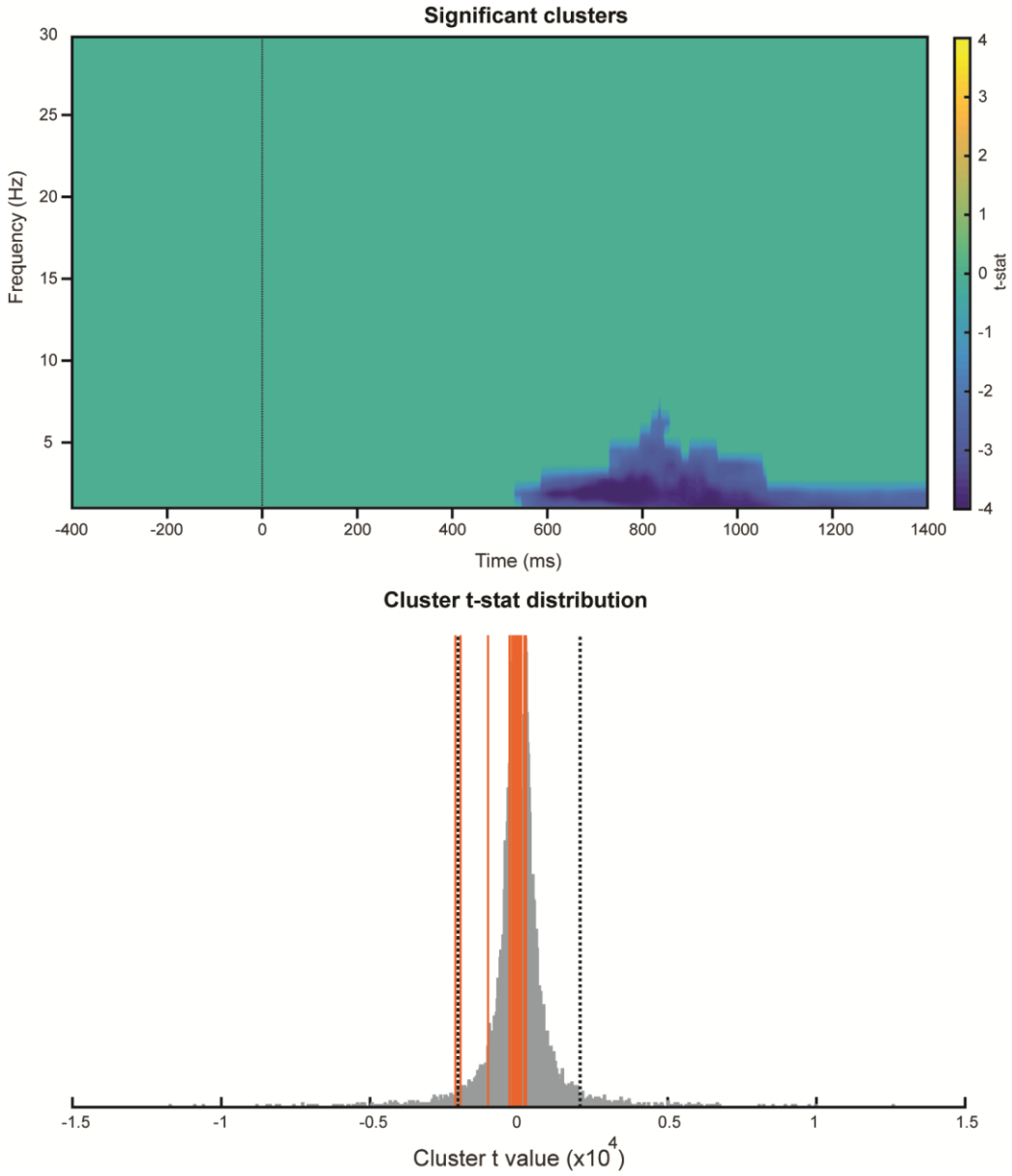

Figure 6.2. *Top: Time-frequency plot of valence differences after permutation testing with cluster correction. Bottom: Results from the permutation test demonstrating null distribution. Grey histogram results represent the null distribution. The black dashed lines indicate the two-tail significance cut-off point (equivalent to a two-tailed p = 0.05). Orange lines denoted the summed t-values for uncorrected cluster differences between valence conditions.*

Current externalising: There was a large and significant main effect of current externalising behaviour on frontal delta (b = 1.00, S.E. = 0.24, z = 4.24, $p < 0.0001$; *table 6.10*), with greater delta activity seen amongst high externalisers (3.57dB) than low externalisers (2.43dB). There were also significant interaction effects between valence and externalising (b = -0.49, S.E. = 0.21, z = -2.36, p = 0.018; *fig. 6.3*), and gender and externalising (b = -1.13, S.E. = 0.37, z = -3.06, p = 0.002). However, these were

superseded by a significant 3-way interaction valence, gender, and externalising (b = -0.77, S.E. = 0.33, z = 2.34, p = 0.019). Post-estimation tests revealed that amongst males, high externalising behaviour was associated with significantly greater delta activity to punishment compared to reward (4.47dB vs. 3.70dB; χ^2 (1) = 7.78, p = 0.005), which was not seen in the low externalising males (2.12dB vs. 2.44dB; χ^2 (1) = 1.41, p = 0.24). Neither high (2.89dB vs. 2.68dB; χ^2 (1) = 0.37, p = 0.54) nor low (2.81dB vs. 2.52dB; χ^2 (1) = 0.97, p = 0.34) externalising female groups demonstrated this difference.

There was also a significant 3-way interaction effect of provoker, gender, and externalising (b = 0.66, S.E. = 0.33, z = 2.00, p = 0.05). Amongst high externalising participants, there was a significant gender difference under high provocation, with males demonstrating larger delta activity than females (4.21dB vs. 2.88dB; χ^2 (1) = 4.00, p = 0.04). However, this difference was not significant under low provocation (3.95dB vs. 2.69dB; χ^2 (1) = 3.54, p = 0.06). By comparison, there was no gender difference in the low externalisers under either high (2.08dB vs. 2.84dB; χ^2 (1) = 1.68, p = 0.19) or low (2.49dB vs. 2.45dB; χ^2 (1) = 0.01, p = 0.95) provocation.

A significant 3-way interaction between provoker, age, and externalising (b = 0.34, S.E. = 0.15, z = 2.25, p = 0.024), was superseded by a 4-way interaction between valence, provoker, age, and externalising (b = -0.43, S.E. = 0.21, z = -2.01, p = 0.04). Post-estimation tests indicated significant differences amongst two groups – high externalising young participants under high provocation, and low externalising, older participants under low provocation. The high externalising younger participants demonstrated larger delta activity to punishment compared to reward when under high provocation (5.01dB vs. 3.64dB; χ^2 (1) = 12.96, p = 0.0003) but not low provocation (3.72dB vs. 3.68dB; χ^2 (1) = 0.01, p = 0.91). By comparison, amongst the low externalising older participants, reward elicited larger delta activity than punishment under low provocation (1.92dB vs. 2.94dB; χ^2 (1) = 5.95, p = 0.015), but not high provocation (2.09dB vs. 2.53dB; χ^2 (1) = 1.14, p = 0.29). No other groups demonstrated significant differences.

Table 6.10. *Results from the mixed effects model regressing exploratory delta activity back on valence, provoker, age, gender, and current externalising*

	Wald χ^2 (27) = 69.72			p = 0.0001
Delta	*b*	S.E.	*z*	*p*
Valence	**-0.66**	**0.25**	**-2.66**	**0.01**
Provoker	-0.38	0.25	-1.53	0.13
Valence * Provoker	**0.89**	**0.35**	**2.52**	**0.01**
Gender	-0.34	0.46	-0.73	0.47
Valence * Gender	0.08	0.42	0.20	0.84
Provoker * Gender	-0.23	0.42	-0.55	0.58
Valence * Provoker * Gender	-0.24	0.59	-0.41	0.68
Age	-0.46	0.24	-1.91	0.06
Valence * Age	0.21	0.20	1.01	0.31
Provoker * Age	0.23	0.21	1.13	0.26
Valence * Provoker * Age	-0.05	0.29	-0.16	0.87
Externalising	**1.00**	**0.24**	**4.24**	**0.00**
Valence * Externalising	**-0.49**	**0.21**	**-2.36**	**0.02**
Provoker * Externalising	-0.33	0.21	-1.60	0.11
Gender * Externalising	**-1.13**	**0.37**	**-3.06**	**0.00**
Age * Externalising	-0.30	0.17	-1.78	0.08
Valence * Provoker * Externalising	0.20	0.29	0.68	0.49
Valence * Gender * Externalising	**0.77**	**0.33**	**2.34**	**0.02**
Valence * Age * Externalising	0.20	0.15	1.31	0.19
Provoker * Gender * Externalising	**0.66**	**0.33**	**2.00**	**0.05**
Provoker * Age * Externalising	**0.34**	**0.15**	**2.25**	**0.02**
Valence * Provoker * Gender * Externalising	-0.71	0.47	-1.52	0.13
Valence * Provoker * Age * Externalising	**-0.43**	**0.21**	**-2.01**	**0.04**
Substance Use	-0.26	0.20	-1.29	0.20
Parental Education	-0.01	0.18	-0.07	0.95
Peak Frequency	**-0.32**	**0.08**	**-4.14**	**0.00**
Peak latency	0.00	0.00	-0.19	0.85
Constant	4.47	0.47	9.55	0.00
Random effects	Estimate	S.E	95% CI	
Identity	1.23	0.14	0.99	1.53
Residual	1.01	0.06	0.91	1.12

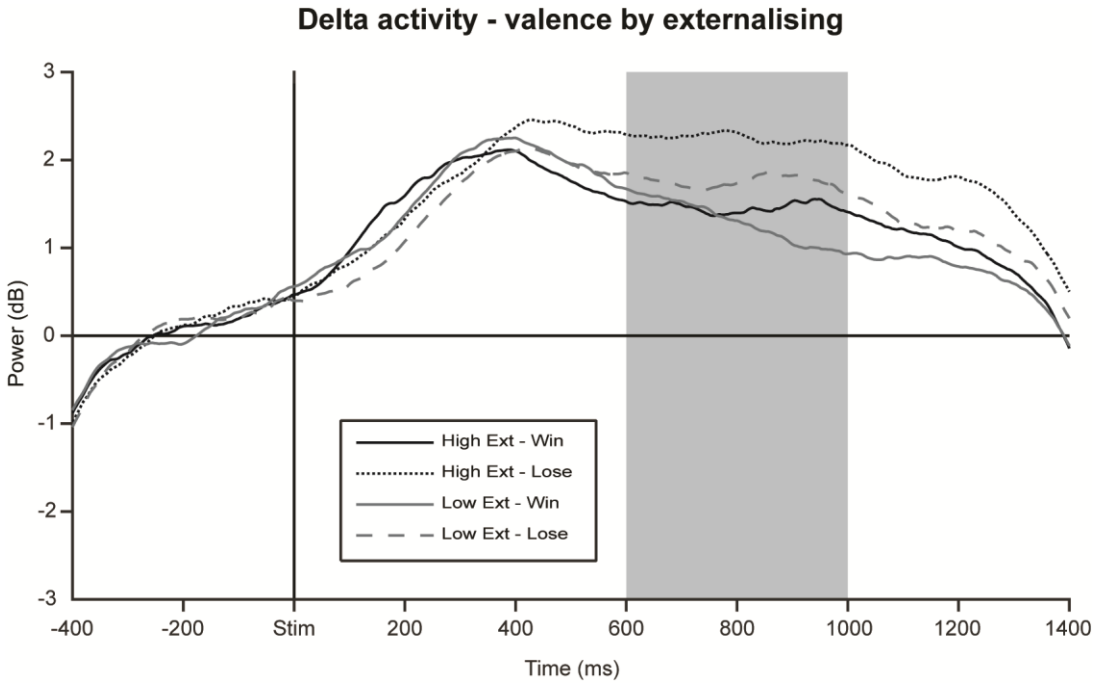

Figure 6.3. *Changes in delta activity over time, split by feedback valence and externalising group. For this plot, externalising group was based on a median split.*

Treatment effects: There were no significant effects of treatment group on delta activity (b = -0.03, S.E. = 0.60, z = -0.04, p = 0.97; *table 6.11*). Furthermore, there was no significant interaction effect between valence and externalising (b = -0.09, S.E. = 0.52, z = -0.18, p = 0.86) or provoker and externalising (b = 0.35. S.E. = 0.53, z = 0.67, p = 0.50). No other effects reached significance.

Table 6.11. *Results from the mixed effects model regressing exploratory delta activity back on valence, provoker, age, gender, and treatment group.*

	Wald χ^2 (28) = 57.79			p = 0.0008
Delta	*b*	S.E.	*z*	*p*
Valence	-0.63	0.36	-1.76	0.08
Provoker	-0.54	0.36	-1.50	0.13
Valence * Provoker	**1.12**	**0.51**	**2.19**	**0.03**
Gender	-0.11	0.61	-0.19	0.85
Valence * Gender	0.08	0.55	0.14	0.89
Provoker * Gender	0.17	0.55	0.30	0.76
Valence * Provoker * Gender	-0.55	0.79	-0.70	0.48
Age	-0.34	0.32	-1.09	0.28
Valence * Age	0.01	0.28	0.05	0.96
Provoker * Age	-0.02	0.28	-0.08	0.94
Valence * Provoker * Age	0.18	0.39	0.47	0.64
Treatment group	-0.38	0.59	-0.64	0.52
Valence * Treatment group	-0.10	0.52	-0.19	0.85
Provoker * Treatment group	0.35	0.53	0.66	0.51
Gender * Treatment group	0.10	0.90	0.11	0.91
Age * Treatment group	0.09	0.45	0.21	0.83
Valence * Provoker * Treatment group	-0.59	0.75	-0.79	0.43
Valence * Gender * Treatment group	-0.31	0.82	-0.38	0.71
Valence * Age * Treatment group	0.31	0.41	0.75	0.46
Provoker * Gender * Treatment group	-1.39	0.81	-1.71	0.09
Provoker * Age * Treatment group	0.55	0.41	1.35	0.18
Valence * Provoker * Gender * Treatment group	1.45	1.17	1.25	0.21
Valence * Provoker * Age * Treatment group	-0.51	0.58	-0.88	0.38
Substance Use	-0.30	0.21	-1.44	0.15
Parental Education	-0.05	0.18	-0.26	0.79
Externalising	**0.41**	**0.15**	**2.74**	**0.01**
Peak Frequency	**-0.33**	**0.08**	**-4.15**	**0.00**
Peak latency	0.00	0.00	0.04	0.97
Constant	4.54	0.57	8.01	0.00

Random effects	Estimate	S.E	95% CI	
Identity	1.23	0.14	0.98	1.53
Residual	1.04	0.06	0.93	1.15

Improver effects: Similar to treatment group, there was no significant effect of improvement on frontal delta activity (b = 0.24, S.E. = 2.31, z = 0.11, p = 0.92; *table 6.12*). There was no significant interaction effects between valence and externalising (b = -0.29, S.E. = 1.84, z = -0.16, p = 0.88) or provoker by externalising (b = -1.80, S.E. = 1.86, z = -0.97, p = 0.33). There were no other significant effects.***Table 6.12.*** *Results from a*

mixed effects model regressing exploratory delta activity back on valence, provoker, age, gender, and participant improver.

	Wald χ^2 (29) = 55.28			p = 0.002
Delta	*b*	S.E.	*z*	*p*
Valence	**-0.63**	**0.25**	**-2.48**	**0.01**
Provoker	-0.28	0.25	-1.12	0.26
Valence * Provoker	**0.75**	**0.36**	**2.11**	**0.04**
Gender	-0.03	0.45	-0.06	0.95
Valence * Gender	-0.09	0.40	-0.21	0.83
Provoker * Gender	-0.54	0.40	-1.34	0.18
Valence * Provoker * Gender	0.18	0.57	0.31	0.76
Age	-0.39	0.24	-1.66	0.10
Valence * Age	0.16	0.20	0.80	0.42
Provoker * Age	0.25	0.20	1.26	0.21
Valence * Provoker * Age	-0.10	0.28	-0.37	0.71
Improvement	0.24	2.31	0.11	0.92
Valence * Improvement	-0.29	1.84	-0.16	0.88
Provoker * Improvement	-1.80	1.86	-0.97	0.33
Gender * Improvement	-4.85	3.21	-1.51	0.13
Age * Improvement	-1.48	1.87	-0.79	0.43
Valence * Provoker * Improvement	2.08	2.60	0.80	0.43
Valence * Gender * Improvement	3.98	2.90	1.37	0.17
Valence * Age * Improvement	0.55	1.63	0.34	0.74
Provoker * Gender * Improvement	3.98	2.90	1.37	0.17
Provoker * Age * Improvement	0.99	1.62	0.61	0.54
Valence * Provoker * Gender * Improvement	-4.45	4.09	-1.09	0.28
Valence * Provoker * Age * Improvement	-0.22	2.30	-0.10	0.92
Improvement intercept	-0.43	0.34	-1.26	0.21
Externalising	**0.52**	**0.20**	**2.63**	**0.01**
Substance Use	-0.14	0.24	-0.58	0.56
Parental Education	-0.02	0.18	-0.08	0.93
Peak Frequency	**-0.29**	**0.08**	**-3.66**	**0.00**
Peak latency	0.00	0.00	-0.10	0.92
Constant	4.28	0.48	9.00	0.00
Random effects	Estimate	S.E	95% CI	
Identity	1.24	0.14	1.00	1.55
Residual	1.04	0.06	0.93	1.15

Discussion

This study investigated the relationship between feedback-related oscillatory activity and current externalising behaviour in a group of adolescents with a history of externalising behaviour who were part of a Multisystemic Therapy (MST) clinical trial,

and how this activity was modulated by social provocation. Furthermore, it sought to understand how different therapeutic interventions (Multisystemic Therapy or Management-As-Usual), as well as participants response to therapy, is associated with changes in the theta, beta, and alpha/mu bands. Participants EEG data collected during a competitive Go/No-Go was subjected to complex wavelet analysis. Contrary to expectation and inconsistent with the previous literature, no significant changes related to feedback valence in either frontal theta or beta band activity were found. Several studies have demonstrated larger theta response following punishment (Cavanagh, Zambrano-Vazquez, & Allen, 2012; Cohen, 2011b; Crowley et al., 2014), thought to reflect the action monitoring processes of the anterior cingulate cortex (Ishii et al., 2014), which was not seen here. Moreover, the theta band findings are inconsistent with those reported by Krämer, Kopyciok, Richter, and Münte (2009), who reported increases in theta activity following negative feedback amongst aggressive participants, but not non-aggressive participants, using a similar Taylor Aggression Paradigm. Furthermore, previous studies have found frontal beta-band sensitivity to feedback valence (Marco-Pallarés et al., 2008; Marco-Pallarés et al., 2009; van de Vijver, Ridderinkhof, & Cohen, 2011), which was not seen in this sample. This inconsistency in findings between this study and those reported previously may be attributable, in part, to differences in the task design. Unlike previous studies (including Kramer et al., 2008), feedback in this task was not associated with a single action immediately preceding the outcome cue. Instead, participants played through six rounds of competitive Go/No-Go stimuli against a fictitious opponent before being given feedback information, meaning that trial feedback is not linked directly with any one action, preventing a simple association between action and outcome monitoring processes. A similar explanation is likely to apply to frontal beta activity as well. Engel and Fries (2010) and Baker (2007) have suggested that beta activity following feedback reflects intention to maintain a set of actions. Therefore, the lack of valence effect in frontal beta activity may similarly reflect the lack of one single action resulting in received feedback. In these circumstances, the intention to maintain behaviour is more detrimental to performance than appropriate behavioural switching. This is an important distinction when considering theta and beta activity as indicators of reward processing: they may not be sensitive to the reward-related outcome per se, but to the reward-action coupling involved in adjusting behaviour in the light of feedback.

Arguably, the lack of effect in the theta band reported here despite the high sensitivity of the Feedback-Related Negativity (FRN) to valence, participant current externalising, treatment, and improvement reported in the last chapter is also noteworthy. This further supports the idea that whilst frontal midline theta and the FRN reflect highly interlinked processes, they index different neural processes (Cavanagh, Zambrano-Vazquez, & Allen, 2012) Specifically, whilst theta activity did not differ by valence here, the FRN did (in the previous chapter), which suggests that, at least in this task, FRNs magnitude was only influenced by the direction of the feedback, and not the behavioural context leading up to it, which may either been irrelevant to it or too temporally distance to influence it. This is consistent with the idea that the FRN is specifically a marker of exogenous feedback monitoring (compared to the endogenously driven ERN), whilst theta reflects general ongoing monitoring processes.

Among older participants, parietal alpha/mu activity was sensitive to feedback valence, demonstrating greater suppression following reward compared to neural stimuli. Previous work has found that parietal alpha/mu suppression is greater following facial cues with a positive valence, suggesting that it may be involved in social reward. Cooper, Simpson, Till, Simmons and Puzzo (2013) and Moore, Gorondnitsky, and Pineda (2012) found that increased alpha/mu suppression is greater when participants are presented with happy faces compared to those showing negative emotions (anger and disgust, respectively). Furthermore, social and financial rewards may have a cumulative effect. During a conditioning task, Gros, Panasiti, and Chakrabarti (2015) associated neutral faces with different magnitudes of financial reward, then exposed participants to each face smiling. They found that the face associated with higher reward elicited greater alpha/mu suppression when viewed smiling than the face associated with lower reward. Therefore, these results may suggest that parietal alpha/mu activity may be sensitive to feedback stimuli under social situations, but is not dependent on viewing social stimuli (e.g. biological movement or facial expressions). However, alpha/mu suppression has also been linked to the attention (see Klimesch, 2012, for a review), and therefore, these results may reflect increased attentional focus on reward compared to punishment.

Finally, exploratory analysis revealed changes in the delta band approximately 600-1000ms following feedback. This frontal delta activity was significantly larger in

response to punishment compared to reward, which is largely consistent with (though temporally later than) feedback-related delta activity observed by Cavanagh (2015). Using an explore-exploit learning task in which participants attempted to learn the optimal pattern of responding to maximise outcome, Cavanagh found that delta power correlated positively with reward prediction error, but did not predict switching behaviours during the task. Similarly, given that the direction of the current findings was consistent with those reported by Cavanagh (2015), the frontal delta activity observed here may reflect reward prediction error. Whilst further work looking at feedback related delta activity is limited, delta activity itself has been tied to motivational processes. In two reviews of the EEG oscillatory literature, Knyazev (2007; 2012) highlights the association between delta activity and biologically driven motivational states (such as hunger or sexual arousal), as increases in delta activities during drug cravings, which decreases when receiving the craved drug. Therefore, the change in delta activity on receipt of feedback may reflect a motivationally driven reward prediction error.

Current externalising

There were no observed valence by externalising differences in any of the predefined bands of interest (frontal theta, frontal beta, or parietal alpha/mu), nor were any main effects of externalising behaviour found in any frequency band. Potentially, this may reflect the more general neural mechanisms associated with the frequency bands that were analysed: Theta band activity is thought to reflect general outcome monitoring (Cavanagh, Zambrano-Vazquez, & Allen, 2012); Beta activity is thought to reflect motivationally driven learning and attention (Hajihosseini & Holroyd, 2015); Alpha/mu activity is sensitive to social learning and reward (Gros, Panasiti, & Chakrabarti, 2015). Comparatively, feedback-evoked ERPs are thought to reflect more singular processes, with the FRN thought to act as an RPE marker (Sambrook & Goslin, 2015), and the P3b as a marker of motivational significance (Wu & Zhou, 2009). Therefore, these results may suggest that high externalising participants demonstrate specific, rather than general, deficits in neural mechanisms related to feedback processing. Alternatively, given that no main effects of valence were found, it is possible that this reflects the task selected; the task used is poorly designed to evoke the activity in the frequency bands of interest. Certainly, visual inspection of frontal

oscillatory activity in both the theta and beta band suggest that neither were strongly induced by the task, and whilst parietal alpha/mu suppression occurred, it did not differ significant at the statistical level nor appeared to differ visually. Therefore, the lack of externalising related differences may simply be an extension of the lack of valence related findings.

In contrast to the predefined frequency bands of interest, valence by externalising differences were observed in the delta band. However, the difference in high and low externalising participants processing of valence was further modulated by other factors, suggesting a more complicated relationship between feedback valence and externalising than previously predicted. Firstly, the association between valence and externalising differed between genders. In males, high externalisers demonstrated significantly greater delta activity to punishment following punishment compared to reward, whilst low externalisers did not, suggesting that high externalising males are more sensitive to deviations from predicted reward than their low externalising counterparts. These results are somewhat consistent with chapter 5, where greater FRN differences, suggestive of greater reward responsivity, were seen amongst the high externalising males, albeit this was only under high provocation. These findings are also consistent with recent work by Gregory et al. (2015). In a study with male violent offenders, they found that BOLD response in the posterior cingulate cortex following punishment reversal errors was greater amongst participants with antisocial personality disorder with psychopathic traits than those without psychopathic traits or normative controls. Similarly, amongst adolescents, White et al. (2014) identified changes in BOLD response in the caudate amongst participants with disruptive behaviours disorder similar to the findings reported here. In their study, participants in the externalising group demonstrated significantly lower caudate activity as a function of prediction error when receiving a reward, but significantly greater caudate activity as a function of prediction error following punishment. Importantly, whilst their control sample demonstrated an even gender split, the high externalising sample was 80% male, which may have driven their differences. Therefore, these results largely fit with recent results suggesting greater reward prediction signalling in externalisers, though why this differs by gender remains unclear.

The relationship between externalising and valence differences in delta activity also varied as a function of participant age and social provocation. Specifically, young externalising participants generated a larger delta response to punishment compared to reward when under high provocation. By comparison, the older, low externalising participants generated larger delta response to reward compared to punishment under low provocation. This is an interesting finding, and given that little research has been conducted to investigate developmental changes in prediction error and externalising psychopathology, particularly under provocation, further research is warranted. Whilst it is known that early adolescence is associated with increased reward sensitivity (Ernst et al., 2005; Galvan et al., 2006), which may be further exacerbated by the social elements of the task (Chein, Albert, O'Brien, Uckert, & Steinberg, 2011), little is known about how social provocation may further alter feedback delta's response to valence.

Treatment and improver effects

Unlike findings previously reported in chapter 5, there were no significant differences between treatment groups or between improving and non-improving participants in any of the predefined frequency bands, or in the exploratory delta band. In part, this may reflect the choice of task used to elicit neural oscillations. The frontal theta and beta bands windows selected were largely insensitive to both task related factors and individual differences, suggesting that this task design may be poorly suited to induce activity in these bands. Such a conclusion is further supported by the fact that both chapter 5, and previous work investigating therapeutic effects in externalising samples (Lewis et al., 2008; Woltering et al., 2011), have found effects of improvement on theta-related ERPs.

It is noteworthy that although delta activity varied as a function of current externalising symptoms, it did not differ between the treatment groups and was not related to participant improvement. These findings, in contrast to those reported for the FRN in chapter 3, further reinforce the notion that the FRN and reward-related delta activity may index related, but distinct, aspects of reward processing. Ideally, future research should focus on investigating the source underlying feedback related delta activity as well as feedback characteristics that modulate it in order to better understand the precise function of reward-related delta and its sensitivity to externalising behaviour.

Additional findings

Frontal delta activity was also modulated by an interaction between social provocation, participant externalising, and participant gender. Primarily, this interaction was in the high externalising group where males demonstrated greater delta activity overall compared to the high externalising females, but this effect was larger under high provocation compared to low provocation. By comparison, there were no differences amongst the low externalising participants. These effects are somewhat mirrored by the FRN results reported in the previous chapter, where high externalising males demonstrated larger FRN differences under high provocation, but not low provocation, whilst the opposite was true for the high externalising females. These larger differences seen under high provocation may reflect increased attention or involvement in the game from high externalising males, either evoked from a desire to best their opponents or to prevent financial loss. Alternatively, these increased reward prediction errors amongst males under high provocation may indicate an increase in approach behaviours that manifests in greater sensitivity to deviations from expected reward. By comparison, under low provocation, this effect is difference is reduced, though whether this is due to female increases or male decreases in feedback sensitivity under low provocation remains unknown.

Limitations and future directions

This study must be considered in light of its limitations. As this study used the same design and sample as that presented in chapter 5, the limitations presented there are equally applicable to this study. In addition to those noted previously, there are further limitations unique to this study that must be considered.

Arguably, the most important limitation of this study is the exploratory statistics related to the delta findings. By conducting exploratory analysis to identify time-frequency windows for analysis, and then running subsequent mixed-effects models on these windows can bias results towards a false positive, a process known as circular inference or double-dipping (Cohen, 2014; Kriegeskorte, Simmons, Bellgowan, & Baker, 2009; Kriegeskorte, Lindquist, Nichols, Poldrack, & Vul, 2010). A better approach may have been to analyse a subset of participants using exploratory analysis to

identify potential time-frequency windows for analysis, then testing for differences amongst the remaining participants. However, given the small sample size of externalising participants tested, this may not have provided a large enough sample to detect differences. Therefore, whilst this analysis may act to indicate a potential time-frequency window to analyse in future work interested in investigating the reward processing differences associated with externalising under social conditions, the current results should be interpreted with caution, and no conclusions regarding effect size should be drawn from them (Kriegeskorte et al., 2010). Instead, the delta results reported should be viewed as exploratory with need for replication, but may highlight a window-of-interest for future analysis during a TAP task.

Secondly, without a control group, it is impossible know how the high and low externalising participants compared to typically developing adolescents, instead limiting the findings reported here to clinical participants. Future research should focus on comparison between clinical and normative samples to understand how oscillatory profiles differ between these populations.

Furthermore, the current design of the study makes comparison between this study and previous work investigating oscillatory activity under social provocation difficult. Further work should be conducted using a more simplistic design to better understand how externalising behaviour affects valence processing amongst adolescents with clinical history of externalising.

Finally, whilst not a specific limitation of this study, source localisation or concurrent EEG-fMRI work investigating the potential generators for both feedback-related beta and delta activity would allow for a clearer comparison between the existing EEG, structural MRI and fMRI literature. Consolidation of these literatures would provide a much more robust image of feedback processing changes associated with antisocial behaviour.

Conclusion

The results presented here provide some support for differences in reward sensitivity amongst externalisers, but further demonstrate the complexities surrounding

this relationship. Neither current externalising nor therapeutic intervention was associated with changes in feedback-related theta or beta activity. However, whether this is due to specific, rather than general, mechanistic changes in feedback processing associated with externalising, or flaws in the task used to elicit feedback-related oscillations is unclear. Instead, our results suggest that high externalisers with a history of antisocial behaviour may demonstrated significantly greater delta power following punishment compared to reward, possibly indicating greater sensitivity to deviations from reward amongst high externalising adolescents when compared against than their low externalising counterparts. However, this finding is exploratory and is in need of replication in an independent sample. Moreover, this relationship was further modulated by task factors, such as social provocation, and individual differences, including age and gender. Furthermore, this relationship was limited to current externalising behaviour, and did not differ based on the therapeutic intervention or participant response to treatment, suggesting that therapy does not influence processes associated with reward prediction or model updating.

Chapter 7

Final Discussion

Discussion

Motivational imbalance has been suggested by several authors to represent a potential mechanism underlying externalising behaviours (Gray, 1987; Knyazev & Slobodskaya, 2003; Newman & Wallace, 1993; Terburg, Morgan, & van Honk, 2009; Quay, 1993). In this thesis, the neural mechanisms underlying one facet of the motivational imbalance model proposed by Gray (1987), and applied to externalising individuals by Quay (1993) – reward dominance - has been investigated. Both normative and clinical samples took part in feedback tasks whilst undergoing high-density electroencephalography (EEG) and their results were analysed in both the time and time-frequency domains. Further, effects of emotion induction via social competition, and therapeutic intervention were investigated in a clinical sample of adolescents with significant externalising psychopathology, to understand changes in reward responsivity under different circumstances and in more severe presentations.

Summary of findings

In the first two empirical chapters (chapters 3 and 4), a group of typically developing adolescents were asked to complete a simple gambling task in which they selected one balloon of four, and received either a reward or a punishment (50% chance of either). In chapter 3, Event-Related Potentials (ERPs) were investigated, indicating that high levels of self-reported delinquency were associated with larger differences between reward and punishment evoked P3b response compared to low externalising adolescents. In contrast, high externalising adolescents showed smaller differences between win and loss in the FRN. Furthermore, we also noted developmental effects in the FRN, as older participants demonstrating significantly larger differences between win and loss in the FRN than younger participants (indeed, the FRN did not show a reliable difference between conditions among the younger participants).

Differences in the processing of reward-related feedback between high and low externalisers did not extend to the time-frequency domain. Instead, slow (theta) and fast (beta) wave power was equivocal between participants who reported high levels of externalising behaviour and those who reported low levels of externalising behaviour. However, similar to the ERP findings, theta power over both parietal and frontal sites

increased significantly with age, regardless of feedback valence. Moreover, parietal beta suppression was larger amongst males compared to females.

Chapters 5 and 6 investigated reward behaviours amongst adolescents with a history of clinical problems with externalising behaviour. Participants played a competitive reaction time task against two fictitious opponents, a high provoking opponent and a low provoking opponent, and ERP (chapter 5) and Event-Related Spectral Perturbations (ERSPs; chapter 6) were investigated following feedback. In contrast to results found amongst the normative population, adolescents with high levels of current externalising symptomatology demonstrated larger differences between reward and punishment in the FRN than low-scoring participants, although of course these latter participants nevertheless formed part of a clinical group in terms of their history. However, this relationship was further modulated by social provocation and gender. Most notably, high externalising males demonstrated substantially larger differences between win and loss in the FRN than other groups, but only under conditions of high provocation, not low provocation. There was also a tendency for high externalising females to the reverse - under low provocation they showed substantial FRN differences between win and loss, but not under high provocation. Sensitivity of the FRN effect to changes in social provocation appeared to be particularly characteristic of individuals with high levels of externalising symptoms. Also of note was the fact that P3b differences between win and loss were smaller among those with high levels of current symptomatology compared to those with low levels of symptoms (effectively the reverse of what was seen in the normative study, using a socially-neutral task).

Treatment effects on ERP amplitudes were more complicated. Investigating treatment group differences revealed significant valence differences in the MAU group, but not the Multisystemic Therapy (MST) group. Specifically, under low provocation, older MAU participants, showed greater FRN differences between win and loss compared to other participants, to some extent mirroring the findings for the high externalising females noted above. Surprisingly, younger participants in the MAU group demonstrated *larger* FRN amplitudes to reward compared to punishment, which is a very unusual pattern of results. Interestingly, participants who responded positively to therapy (demonstrated a decrease in externalising over the follow up period) also

showed differences in their neural responses to reward and punishment, and particularly in the extent to which these neural responses were dependent on the social context: improvers demonstrated significant valence differences in the FRN under low social provocation, whilst valence differences in FRN response amongst the non-improving participants were only seen under high provocation. Further, age influenced the effect of treatment on neural response in the P3b. In older participants, MAU was associated with larger P3b amplitudes than MST. However, no such effects were seen amongst the younger participants.

Finally, in chapter 6, there were no significant differences between externalising groups in their processing of feedback valence when analysed in the theta or beta bands. However, there was a significant main effect of externalising behaviour on theta activity, with greater theta activity seen amongst participants scoring highly on externalising measures. Furthermore, there were substantial differences between high and low externalisers' processing of feedback valence in a delta band cluster identified by exploratory analysis. Here, high externalising males demonstrated a significant difference between punishment and reward induced delta activity, with greater delta in response to punishment. Similarly, a four-way interaction revealed that high externalising, young participants demonstrated significantly greater delta activity following punishment compared to reward, whilst higher delta activity following reward compared to punishment was seen in low externalising, older participants.

Whilst there were no treatment effects on the time-frequency data, there were significant main effects of gender and age on beta and alpha activity, respectively. In contrast to chapter 4 where greater beta suppression was seen amongst females compared to males, in chapter 6, beta suppression was greater amongst males compared to females. Parietal alpha response varied as a function of age and valence, as older participants demonstrated greater suppression when receiving punishment compared to reward, but younger participants did not differentiate between the two.

These results are discussed below and potential interpretations are outlined. Following on, a theoretical model is presented to consolidate the findings, and its assumptions, merits and limitations are examined before future avenues for research are considered.

Current externalising behaviour and feedback valence

The relationship between externalising behaviour and neural signalling following feedback cues appeared to differ between typically developing and clinical samples. Amongst typically developing adolescents, high levels of externalising behaviour was associated with differential P3b and the FRN following feedback when compared to the low externalisers. Firstly, high externalising, normative participants demonstrated significant differences between reward evoked and punishment evoked P3b amplitudes, with larger amplitudes seen in response to reward. Nieuwenhuis, Aston-Jones, and Cohen (2005) have suggested that the P3b signals the motivational significance of a stimulus, and Polich (2007) indicated that this may focus attention during signal detection, inhibiting other ongoing processes. Typically, larger P3b amplitudes are seen as evoked by feedback characteristics that are thought to be motivationally engaging. In line with this, larger P3b responses are seen following reward feedback compared to punishment, and P3b amplitude parametrically increases with the magnitude of feedback (Hajcak, Holroyd, Moser, & Simons, 2005; Wu & Zhou, 2009). These results seem to suggest that higher self-reported externalising behaviour is associated with greater motivational salience attributed to reward feedback compared to punishment feedback, which supports reward dominance interpretation of feedback processing amongst high externalisers.

By comparison, high externalising participants had a smaller FRN valence differences than their low externalising counterparts. When this relationship was investigated further, it appeared to be primarily driven by differences in the punishment condition where higher externalising score was associated with smaller (less negative) FRN amplitudes. The extract interpretation of the FRN is under debate, though it is largely thought to reflect reward prediction error (RPE; Walsh & Anderson, 2012), though some evidence suggests it may encode an unsigned prediction error (e.g. Hauser et al., 2014, Talmi, Fuentemilla, Litvak, Duzel, & Dolan, 2012). In a review of the literature, Walsh and Anderson (2012) suggest that it reflects a quantitative reward prediction error, with larger differences between actual and expected outcome generating greater FRN signals. This smaller difference between reward and punishment evoked FRN response amongst high externalisers would suggest less effective reward prediction error signalling, which may be primarily due to reduced

signalling following punishment. Previous research investigating psychometric measures of approach and inhibition have found that FRN response to error and punishment feedback is greater amongst individuals scoring highly on behavioural inhibition (BIS; Balconi & Crivelli, 2010; De Pascalis, Varriale, & D'Antuono, 2010). Therefore, these results may suggest deficits in inhibition systems amongst high externalisers, which would be consistent with Quay's (1993) proposal or reward dominance. Further research directly comparing adolescents with internalising and externalising disorders, or high and low-scoring adolescents on both dimensions, would be useful in the future. Further, given the interest in the literature in differences between adolescents with conduct disorder who differ in their emotional style (e.g., low or high anxiety, callous-unemotional traits, reactive-proactive aggression), it would be valuable to examine the possibility that these would differ systematically in their FRN responses to reward and punishment.

Interestingly, these differences between high and low externalisers did not extend to the time-frequency domain, as feedback-related theta and beta band activity was largely equivalent across high and low externalising participants. Whilst links have been drawn between theta activity and the FRN (Luu, Tucker, Derryberry, Reed, & Poulsen, 2003), their response profiles to variations in feedback characteristics are not the same (Cohen, Elger, & Ranganath, 2007), and links between theta activity and other cognitive control ERPs (such as the ERN, N2, and CRN) have been established (Cavanagh, Zambrano-Vazquez, & Allen, 2012). In a recent review of the feedback theta literature, Cavanagh and Frank (2014) propose that frontal midline theta activity reflects an adaptive control mechanism evoked by uncertainty, and increased theta activity preceding task appropriate behavioural switching suggests it plays an important role in learning (Cohen, Elger, & Ranganath, 2007). In that sense, the FRN arguably indexes a more focal set of outcome monitoring processes than that captured by theta oscillations. Unlike feedback related theta activity, beta activity remains poorly understood in relation to feedback. Several researchers have expanded on work by Engel and Fries (2010) proposing that beta activation reflects intention to maintain a behavioural set. However, contrary to previous work, feedback elicited beta suppression instead of the beta activation reported in prior work. Increases in beta suppression has been linked to both working memory (e.g. Onton, Delorme, & Makeig, 2005), with greater suppression seen following higher cognitive loads, and during motor preparation

(e.g. Tzagarakis, Ince, Leuthold, & Pellizzer, 2010). However, the task design prevents us from drawing strong conclusions regarding beta's underlying function. Within these typically-developing participants at least, these results seem to suggest specific, instead of general, changes in feedback processing indicative of increased motivation attributed to reward, and decreased reward prediction error following feedback, especially punishment. However, these did not appear to reflect problems with cognitive control, or working memory/motor problems as indicated by oscillatory profiles. It is important to note that the initial hypotheses regarding the precise patterning of FRN and P3b responses among high externalizing normative adolescents were tentative because relatively little past work had examined this, and what had been reported was not consistent. Broadly speaking, extant research suggested that adolescents with externalizing problems have difficulties processing reward cues (Crowley et al., 2009), but are also highly motivated by reward (Morgan, Bowen, Moore, & van Goozen, 2014) and hence the reduced FRN response and the heightened P3b response amongst normative adolescents with relative high externalizing problems made theoretical sense.

In comparison to the typically developing sample, results amongst the clinical participants were very different, and on the face of it, harder to reconcile. Unlike the high externalising, normative participants, the FRN was highly sensitive to feedback in the adolescents with a clinical history and high current symptoms of externalising problems. However, this relationship was also moderated by other factors. For example, high externalising males and females processed feedback via the FRN differently depending on whether they received the feedback under high or low social provocation, suggesting that the level of frustration or stress externalisers are placed under dictates the sensitivity of error monitoring systems. A recent body of evidence is beginning to suggest that approach and approach-like behaviours are associated with larger valence differences in the FRN. For example, Bress and Hajcak (2013) used the signal detection task to identify individuals' reward response bias. Participants who demonstrated higher bias towards reward were more likely to present with larger differences between reward and punishment in their FRN. Consistent with this, higher scores on psychometric measures of behavioural approach (Lange, Leue, & Beauducel, 2012) and extraversion (Smillie, Cooper, & Pickering, 2011) are also associated with greater FRN valence differences. In that sense, the findings from the clinical study are not inconsistent with theorising regarding externalising psychopathology and reward sensitivity. What is

more of a challenge is to align the findings of both the normative and clinical studies. Two possibilities seem most plausible – one is that the behaviour of the high-externalising group within the clinical sample reflects something qualitatively different to that seen in the high-externalising normative adolescents. Another intriguing possibility is that when the clinical results are combined with the findings from chapter 3, they may be understood to suggest that imbalance between reward and punishment systems, and potentially the underlying approach/avoidance systems, may be modulated by both developmental (i.e. degree of externalising) and emotional states (e.g. frustration) and social contexts (e.g. provocation). I return to this point in a later section.

Along similar lines, time-frequency decomposition of outcome-related neural signals suggest that there may be activity in the delta (1-4Hz) band may be valence sensitive amongst participants scoring highly on latent externalising. Specifically, larger delta activity was seen following punishment in certain subgroups of externalisers (male externalisers and young externalisers) under high provocation. The feedback literature focusing on delta activity is relatively small when compared to feedback activity in the theta and beta bands, and is not well understood. Cavanagh's (2015) recent work found a positive correlation between delta activity following feedback and the reward prediction error in an explore/exploit task, similar to the coarse reward prediction error monitoring typically associated with the FRN. These findings need replication, they are consistent with the large body of work suggesting that delta activity contributes significantly to motivationally driven behaviours, as appetitive drug administration and pain processing, where decreases and increases in delta activity are seen, respectively (see Knyazev, 2012, for a review). Combined, the ERP and ERSP results point to greater sensitivity in deviance from expected reward outcome amongst those with clinically high externalising during a socially competitive task, especially when under provocation.

In contrast to the results found amongst the typically developing sample, amongst clinical participants, high externalising symptoms were associated with smaller P3b amplitudes to reward compared to punishment. As discussed above, the P3b is thought to reflect the motivational salience of a presented stimulus, with larger amplitudes generated by cues that are more motivationally significant. Therefore, results from the clinical population would suggest that high externalizing symptoms are

associated with reduced motivational value attached to the outcome, or reduced attention, or updating of the outcome into memory (Polich, 2007). Both the P3a (an earlier, frontally centred component) and the P3b are thought to be attentional in nature (Polich, 2007), and it has been suggested that the feedback-evoked P3b reflects downstream attentional processes (Baskin-Sommers et al., 2014). Several studies have demonstrated altered attentional processes amongst clinical externalising samples (e.g. Brazil et al., 2012; Hiatt, William, & Newman, 2004). Moreover, working memory processes may further add to attentional problems, as P3b amplitude has been shown to be negatively influenced by working memory load (Ahmed & De Fockert, 2012). Previous work has already observed problems with working memory amongst high externalising samples (Endres, Rickert, Bogg, Lucas, & Finn, 2011). The diminished attentional ability associated with high externalising behaviour combined with a relatively increased working memory load (stemming from poor working memory capacity) may decrease the P3b's ability to differentiate between valence cues amongst the high externalising clinical group.

To reiterate, discrepancies were seen between typically developing and clinical populations. In both samples, externalising behaviour was associated with some form of valence imbalance supportive of increased approach behaviours amongst high externalising groups, but the precise mechanisms driving the differences varied, and amongst the clinical population, the relationship between externalising behaviour and motivational imbalance was often complicated by other factors. Perhaps the most salient factor is the differences in the severity of externalising, as one sample was a group of typically developing adolescents recruited from the community, and the other was comprised of a sample of adolescents with a clinical history of externalising behaviour identified as being high risk. As discussed above, aside from potential differences in reward mechanisms, the severity of externalising behaviour is likely to be associated with further influential effects on participant's attentional and working memory ability. This may be especially noticeable in the P3b compared to the FRN. Furthermore, the way in which externalising was defined differed between the normative and clinical samples. In the first two empirical chapters, the externalising measure included items related to both substance use and norm violation, whereas second two empirical chapters, norm violation and substance use were measured using two separate scales. However, results in chapter 5 suggests that substance use has its own influence on FRN

and P3b amplitudes separate from other forms of externalising behaviour. The existing literature has already highlight significant decreases in both the FRN (Fein & Chang, 2008) and P3b (Kamarajan et al., 2010) amongst participants reporting high substance use. Therefore, some differences in feedback processing between samples may be attributable to differences in the definition of externalising behaviour.

Therefore, whilst the results reported here demonstrated significant differences between how neural signals encoding reward differ between high and low externalising participants, they also highlight the necessity for further work amongst clinical participants, as these individuals may be vastly different to their less impaired counterparts.

Treatment and feedback processing

In chapters 5 and 6, the effects of treatment were investigated to understand whether Multisystemic Therapy (MST) was associated with different feedback profiles compared against Management-As-Usual (MAU), and whether improving participants (those who demonstrated a general reduction in externalising behaviour over the treatment and follow up period) responded to outcome cues differently to those who did not improve. Whilst difference in effect emerged between the two therapeutic interventions, they were few, and primarily limited to difference in the ERP response and not ERSP response. Specifically, participants who received MST demonstrated smaller FRN valence effects than the MAU group when under low provocation (though neither group demonstrated differences under high provocation).

Similarly, divergent neural response patterns to feedback appeared between improving and non-improving participants. Under low social provocation, significant differences between reward- and punishment-evoked FRN response was seen in the improving participants, but not the non-improvers. However, this relationship was reversed when participants played against the high provoking opponents, with non-improving participants demonstrating significant differences in valence-related FRN response, whilst the improving participants did not. In fact, both participant improvement and therapeutic intervention findings suggest that groups demonstrating lower self-reported externalising, or reductions in externalising following treatment, are *less* likely to demonstrate valence effects on the FRN than those with increased risk of

externalising. Interestingly, these results coincide with past research investigating neural correlates of treatment amongst both internalising and externalising groups.

As noted in chapter 5, the work investigating neural correlates of therapeutic intervention has been primarily limited to internalising disorders. For example, Siegle et al. (2012) found that decreased anterior cingulate cortex (ACC) activity whilst processing emotional words was strongly associated with clinical changes in depression. Participant demonstrating lower ACC activity also demonstrated greater improvement following therapy, and ACC activity could predict remission rates with 70% accuracy. More recently, Straub et al. (2015) investigated the effects of CBT amongst a group of adolescents with depression in relation to reward elicited neural activity. They found that treatment leads to reductions in ACC signalling, with larger improvement in symptoms following therapy associated with greater ACC signal change between pre-treatment and post-treatment measurements evoked during a Monetary Incentive Delay task.. Consistently, ACC activity has been associated with treatment response to therapy, as highlighted by Pizzagalli (2011) who investigated several forms of therapy (i.e. pharmacological therapy, sleep deprivation, electroconvulsive therapy, repetitive transcranial magnetic stimulation, and cognitive behavioural therapy).

In line with this, previous work looking at therapeutic changes in neural processing amongst externalising samples has found that similar neural signatures demonstrate improvement. Similar to the FRN results in chapter 5, Woltering et al. (2011) investigated changes in two ERPs, the N2 and the P3a, following cognitive behavioural therapy in a group of pre-adolescent children. They found that child who improved following treatment demonstrated smaller N2 components, comparable to the control participants, whilst the non-improvers demonstrated larger N2s. As the N2 is thought to be generated by the ACC, and is associated with the same underlying frontal midline theta activity as the FRN (Cavanagh, Zambrano-Vazquez, & Allen, 2012), the chapter 5 results combined with those from Woltering and colleagues (2011) suggest that the ACC may be a neural site that is particularly sensitive to treatment effects.

The implication of all of these studies and the results reported here indicate that reduced neural activity in the ACC and related affective and cognitive control centres may be critical markers of treatment related change. The chapter 5 findings, combined with those particularly on internalizing disorders further suggests that these differences

may be particularly apparent when disorder-relevant affective contexts are instantiated in the experimental paradigm (e.g., emotional cues in internalizing disorders; socially-provocative [as in our study] or stress inducing [Woltering et al., 2011] contexts for externalizing disorders). This appears to make considerable clinical sense, as in many forms of treatment what the therapist and client are aiming towards is change in the typical reaction (behavioural, emotional, cognitive) to certain salient cues (e.g. Han, Kim, Lee, & Renshaw, 2012; Kendall et al., 2005; Wiers et al., 2015). This data appear to suggest that in a stressful or socially provocative context, adolescents who make clinical gains show reductions in the responsiveness of the reward system to cues signalling winning and losing in a socially-provocative context. Implicitly, what this also suggests is that reward responsiveness is not a static variable. Treatment, for example, must surely not be aiming to generally reduce reward processing, but rather moderate to its functioning to be optimally responsive to the right cues and in the right context. This in turn might provide a partial explanation for why the findings were different when using a task that was emotionally and socially much more neutral. In this case, the optimal response pattern appeared to be to show strong neural discrimination (in the FRN) between cues to reward and loss, perhaps because doing so reflects an optimal learning strategy. The optimal response to a social-provocative task is much more complex, and likely requires a balance between performance motivation and regulation in the service of social interaction – for example, considering the consequences of winning for the other person (Kramer, Büttner, Roth, & Münte, 2008).

Age and gender effects

Across all analyses, both age and gender influenced neural activity following feedback cues, though to a different extent. Age influenced FRN feedback signalling in both ERP analyses, which is unsurprising when considering the developmental changes in neuroanatomy occurring over adolescence. It is well established that decreases in grey matter and increases in white matter occur during the adolescent years (Barnea-Goraly et al., 2005; Giedd et al., 1999; Gogtay et al., 2004), which is thought to improve the efficiency of processing (Kanai & Rees, 2011). More importantly, in relation to this thesis, adolescence is associated with divergent developmental trajectories for neural circuits responsible for reward/motivational processes and cognitive control (Steinberg, 2008), with maturation of motivational circuitry occurring earlier than those responsible

for cognitive control. This is thought to be responsible for the increases in risk taking behaviours seen amongst early- to mid- adolescents (Bjork & Pardini, 2015; Byrnes, Miller, & Schafer, 1999), where the differences in development are thought to be at their largest. Several functional Magnetic Resonance Imaging (fMRI) neuroimaging studies have found increases in activity following feedback amongst adolescents not seen in adults (e.g. Cohen et al, 2010; Ernst et al., 2005; Galvan et al., 2007; van Leijenhorst et al., 2009). There is less evidence of this in the EEG literature, however Martínez-Veláquez, Ramos-Loyo, González-Garrido, and Sequeira (2015) found that, regardless of the learning rate of the task, adolescents demonstrated larger FRN amplitudes following loss than adults, suggesting an increased sensitivity to feedback.

These effects may be accentuated in chapters 5 and 6 by the inclusion of a socially-competitive dimension to the task. Whilst reviewing the literature, Blakemore (2008) highlights the increased sensitivity to social stimuli seen amongst adolescents, and that the social context surrounding decision making processes may influence adolescent choices and their associated neural computations. These findings have been reinforced by empirical studies demonstrating increases in risk taking behaviours when adolescent participants complete tasks under peer observation. Behavioural work has demonstrated that when in the presence of peers, adolescents are more likely to take risks and endorse their benefits over costs (Gardner & Steinberg, 2005), and demonstrate a preference for smaller, immediate rewards than larger, delayed rewards (O'Brien, Albert, Chein, & Steinberg, 2011) when observed by their peers compared to when they play alone, even when the participants and peer were unknown to each other (Weigard, Chein, Albert, Smith, & Steinberg, 2014). Moreover, haemodynamic response differs between adults and adolescents during risky decision-making when accompanied by peers. Chein, Albert, O'Brien, Uckert, and Steinberg (2011) found that the ventral striatum and orbitofrontal cortex were more highly activated during decision-making amongst adolescence in the presence of peers compared to when they were alone, an effect that did not occur in adult or young adult samples. Similarly, Smith, Steinberg, Strang, and Chein (2015) found bilateral increase in nucleus accumbens response following reward when accompanied by peers than when alone, an effects not seen in adults. Therefore, modulations of feedback related activity by age is to be expected, and the heightened sensitivity of neural responses to feedback cues in

social contexts is highly consistent with these findings, and may be particularly relevant to the adolescent period.

Gender differences were not as prevalent as age effects across the chapters, and aside from differences beta activity amongst the typically-developing sample, they were primarily limited to the clinical sample. In both chapters 4 and 6, differences between genders in their beta suppression was observed, though the direction of effect differed between the two studies. In chapter 4, females demonstrated significantly greater beta suppression following feedback (regardless of valence). The opposite was true for the clinical sample, where beta suppression was greater amongst males. Unfortunately, as beta suppression following feedback has not been previously reported, no firm statement regarding its interpretation can be made.

Amongst clinical participants, male and female externalisers both demonstrated larger valence related changes in FRN response. However, whilst males were more sensitive to feedback valence under high provocation, females were more sensitive to it under low provocation. Moreover, only high externalising males demonstrated a significant difference in feedback-induced delta activity. In addition to differences in reward and punishment-related neural circuitry between genders observed in the literature (Li et al., 2014; Urošević, Collins, Muetzel, Lim, and Luciana, 2014), differences in the experience of and reaction to frustration have also been reported. Females are more likely to report higher levels of sensitivity to frustration and anger when compared to males (Zajenkowska, Mylonas, Lawrence, Konopka, & Rajchert, 2014; Simon & Nath, 2004). As the ACC is known to be sensitive to frustration (Spunt, Lieberman, Cohen, & Eisenberger, 2015) and anger (Denson, Pedersen, Ronquillo, & Nandy, 2009), and even thought to potentially control negative affect (Denson, Dobson-Stone, Ronay, von Hippel, & Schira, 2014), these results may reflect differences in the level of provocation needed to maximise approach behaviours between the two genders. Specifically, reward sensitivity in high externalising males increases when under high provocation as a higher level of provocation is needed to achieve substantial changes in ACC activation. By comparison, the level of provocation is lower due amongst high externalising females due to their increased sensitivity to frustration.

It should be noted that gender appeared more influential amongst the clinical sample compared to the normative sample, in both the time and time-frequency domain.

There are a couple of potential explanations for this difference. Firstly, the samples used were different. Whilst the sample used in the first experiment were typically-developing, participants from the second were at-risk adolescents with a history of externalising behaviour. As externalising patterns differ between genders (Demmer, Hooley, Sheen, McGillivray, & Lum, 2015), differing in the typical onset period (Moffit, 2006) and expression of antisocial behaviour (Card et al., 2008), it may be that gender differences are more exaggerated amongst externalisers compared to typically developing adolescents. Given the substantial biological component associated with externalising behaviour (Cosgrove et al., 2011; Lahey et al., 2011), we may also expect differences in associated neural activation.

Secondly, the tasks used in each study differed in their nature. The task used in the first study had no social or competitive elements, whereas the second task had both. Gender differences in response to competition have been previously observed in normative populations, with men demonstrating more competitive behaviour (Van Vugt, De Cremer, & Janssem, 2009) and an increase in positive emotion during competitive circumstances (Kivikangas, Kätsyri, Järvelä, & Ravaja, 2014), which is not seen in women. On a physiological level, males demonstrate increases in testosterone and decreases in cortisol when involved in completion, whereas females do not (Kivlighan, Granger, & Booth, 2005). Moreover, in males, high levels of testosterone paired with low cortisol have been associated with increased desire to compete again after defeat, and that high cortisol was associated with defeat related decreases in testosterone (Metha & Josephs, 2010). Both testosterone (Miskovic & Schmidt, 2009; Schutter & Van Honk, 2004) and cortisol (Schutter & Van Honk, 2004; Schutter & Van Honk, 2005; van Peer, Roelofs, & Spinhoven, 2008) have been shown to alter both slow- and fast-wave EEG oscillatory activity. Given the changes in oscillatory activity associated with testosterone and cortisol levels, hormones sensitive to competition in males, it is perhaps expected that gender was more influential in the competitive task.

Potentially, these two explanations may not be separate. Reward dominance as product of testosterone-cortisol imbalance has been previously suggested (Terburg, Morgan, & Van Honk, 2009), two hormones thought to be important for approach-avoidance behaviour (Enter, Spinhoven, & Roelofs, 2014; Lombardo et al., 2012; Metha, Welker, Zilioli, & Carré, 2015), as well as playing a role in competitive

behaviours. Therefore, whilst varying impacts of gender are plausible between the two projects, it is difficult to draw firm conclusions about the underlying cause.

Optimal arousal and approach

Currently, whilst the results reported here are indicative of externalising related differences in reward sensitivity due to consistent differences between high and low externalisers across experiments, inconsistencies in the direction of effects across studies, especially in the FRN, are more difficult to reconcile with the simplistic model of motivational imbalance proposed by Quay (1993). However, it is important to note that there were consistent modulation effects of provocation on the interactions between valence and likelihood of externalising within the clinical study (e.g. current externalising, treatment group, and improvement status). Specifically, participants broadly characterised by higher levels of externalising problems (high current externalising symptoms group, the MAU group, and those demonstrating no improvement or worsening symptoms over time) showed consistently increased sensitivity to provocation relative to the low externalising subsample.

One potential explanation is that arousal, frustration or provocation mediates the relationship between externalising symptomatology and reward imbalance, instead of a simple relationship between externalising and reward hypersensitivity. In its simplest form, FRN signalling of prediction error may have an optimal range, and reduces in efficiency when arousal is too high or too low. We might speculate that high and low externalisers differ in their optimal arousal, with the level of arousal needed for high externalisers to demonstrate maximal FRN differences being higher than that of low externalisers (*fig. 7.1*). Such a model suggests a distinctively different perspective on the nature of reward processing differences associated with psychopathology, away from a static 'deficits' model, to what that is more dynamic – contextual and developmental processes may lead to the 're-setting' of the FRN-arousal response curve at different points.

Several studies have already found a relationship between the ACC, which generates the FRN, and arousal as measured by blood pressure (Critchley, Corfield, Chandler, Mathias, and Dolan, 2000), skin conductance (Milad et al., 2007), and pupillometry (Critchley, Tang, Glaser, Butterworth, and Dolan, 2005). Furthermore, neural signalling

associated with the anterior cingulate cortex demonstrates changes in activation following stress. For example, midline theta band activity, generated by the ACC (Ishii et al., 2014), demonstrates decreases in activity amongst normative participants under stress whilst completing a simple mathematics task (Gärtner, Grimm, & Bajbouj, 2015) or more complicated working memory task (Gärtner, Rohde-Liebenau, Grimm, & Bajbouj, 2014). Therefore, the evidence seems to suggest that whilst the ACC is sensitive to arousal, the functional signals sent by the ACC under high stress are diminished, and that ACC activity should be considered along a continuous response curve, similar to other arousal functions (Iffland, Sanse, Catani, and Neuner, 2014).

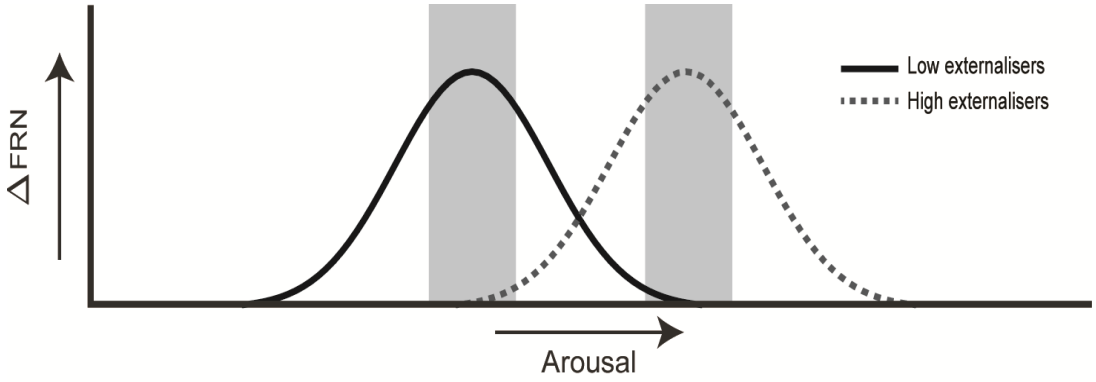

Figure 7.1. *Proposed differences in the relationship between FRN difference to reward and punishment and arousal for high and low externalising participants. The grey area highlights the optimal level of arousal for maximal difference between valence conditions.*

Findings of hypoarousal in high externalising individuals has been fairly well established, and meta-analysis of neural activity (Rudo-Hutt, 2015) and physiological arousal (Lorber, 2004) suggest that during resting activity, high externalisers demonstrate lower levels of arousal. However, Lorber (2004) also found reactive heart rate was greater amongst those with Conduct Disorder compared to typically developing samples, and more recent animal work has found that aggressive mice strains demonstrate significantly greater increases in HR response compared to baseline than non-aggressive lines (Caramaschi, de Boer, & Koolhaas, 2008). Hyperarousal following stress or frustration amongst externalisers may lead to altered processing in the ACC, influencing the FRN response to feedback. These findings provide a potential framework for understanding the findings reported in this thesis: under low arousal (chapter 3) adolescents with externalising difficulties showed under-responsiveness of

the FRN, while in a high arousal context they show heightened responsiveness of the FRN (while, presumably, their low-externalising counterparts move out of their optimal arousal zone, and showed reduced FRN responsiveness).

Within the framework of this model, treatment effects and improvement may result in a normalisation of this relationship between arousal and reward prediction errors (see *fig 7.2*), reducing the level of arousal or social provocation needed to optimise reward feedback sensitivity. As noted above, the ACC appears to be strongly associated with treatment effects, and this may in part influence the ACCs sensitivity to arousal. Furthermore, other factors that are associated with changes in reward sensitivity (e.g. age), frustration and aggressive response (e.g. gender), and approach/avoidance behaviour (e.g. externalising/internalising comorbidity) may alter arousal needed to evoked maximal difference between reward and punishment evoked FRN response.

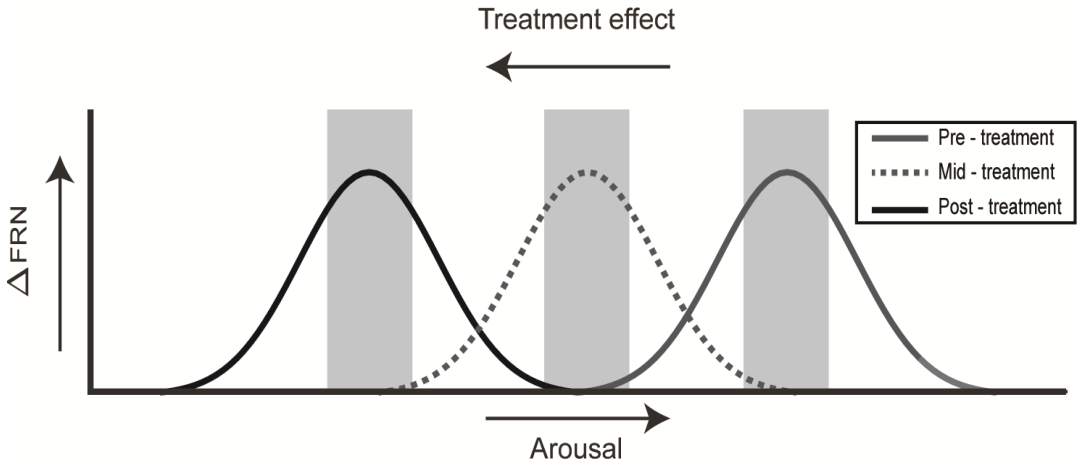

Figure 7.2. *Proposed shift in the relationship between FRN difference to reward and punishment and arousal with treatment. The grey area highlights the optimal level of arousal for maximal difference between valence conditions.*

As the larger difference between reward and punishment evoked FRN response have been associated with greater approach behaviours (Bress & Hajcak, 2013; Lange, Leue, & Beauducel, 2012), this may help to understand reactive aggression amongst externalisers. If greater approach behaviours are seen under higher levels of arousal or frustration, then these situations may lead to greater chance of aggressive response as the reward (attacking an antagonising source) may significantly outweigh the punishment (criminal charges) due to increased reward sensitivity.

However, there are problems with this interpretation based on the current data. Firstly, without parallel data on control participants under the same testing conditions (i.e., competitive task), we cannot be sure that FRN response in relation to provocation is similar between clinical participants who demonstrate low levels of externalising behaviour, and typically developing participants with no history of externalising behaviour. Ideally, future studies should include both low and high-provocative reward tasks and non-clinical controls, low-externalising clinical adolescents and high externalising clinical adolescent in the same experiment. This would allow a much more direct and complete test of the hypothesis outlined above. Secondly, whilst several source localisation studies, and more recently, concurrent fMRI-EEG studies, have located the FRN in the ACC, how stress related changes in the ACC are reflected in FRN amplitudes is relatively unknown. It is also important to note that although this hypothesis has focused on arousal as the dimension over which FRN responsiveness may vary (and over which individuals may have differing optimal response points), it is not the only dimension that could be considered. For example, regardless of arousal, social contexts may vary in their personal - or disorder - relevance or salience, which though similar to the arousal construct, may differ in the ideal variables to measure in future studies (cf. blood pressure vs. attentional capture).

Limitations

Whilst this thesis provides some potential avenues for further investigation, several limitations need to be addressed. Firstly, it is important to note that the tasks used in the first experiment (chapters 3 and 4) differed substantially from the task implemented in the second experiment (chapters 5 and 6). In the first experiment, participants were asked to complete a random gambling task, whereas, in the second, participants completed a competitive Go/No-Go flanker task. Therefore, some of the differences between normative and clinical samples discussed in this chapter may be influenced by these task differences.

Perhaps the greatest difference between the two tasks was the added social competition added to the second task. Participants in the second experiment were introduced to their (fictional) opponents via webcam, and were informed that the punishments they chose and received were going to and coming from another person. Adolescence is already established a period of social development (Blakemore, 2008;

Blakemore & Mills, 2013; Crone & Dahl, 2012), and previous work has demonstrated increase in other approach behaviours (e.g. disinhibition) during tasks where a peer is present (Gardner & Steinberg, 2005; Smith, Chein, & Steinberg, 2014), so it is plausible that reward response, as another form of approach behaviour, may also be altered in social tasks. Moreover, social competition is known to influence relative levels of testosterone and cortisol (Carre & Olmstead, 2015; Edwards & Casto, 2013; Zilioli & Watson, 2011), two hormones associated with neural changes in slow and fast wave oscillations (Miskovic & Schmidt, 2009; van Peer, Roelofs, & Spinhoven, 2008), creating further artificial differences between groups. Finally, the social element to this task could confound differences between normative and clinical samples as there is evidence to suggest that the FRN sensitive to feedback other people receive (Fukushima & Hiraki, 2006). As participants were aware of the feedback their opponents received in the second task, but there was no comparative experience in the first task, this may alter the FRNs feedback characteristic. This may be especially relevant given that samples scoring highly in aggression measures typically differ in empathy than those who score low in aggression (Carrasco, Barker, Tremblay, & Vitaro, 2006; Decety, Michalska, Akitsuki, & Lahey, 2009; Batanova & Loukis, 2011), which may influence how the FRN responds to the outcomes of others.

The tasks also differed in the number of response from participants to elicit feedback stimuli. In the first task, participants received one feedback cue per response, whilst six responses were needed before participants received feedback in the second task. Previous studies investigating the FRN (Bellebaum & Daum, 2008) and feedback-related theta activity (Cavanagh, Frank, Klein, & Allen, 2010) have found association between these ACC-generated indices of feedback processing and learning. Response-related learning may have been simpler in the first task, where the relationship between response and feedback was more direct, leading to changes in the FRN and theta response not seen in the second task.

Overall, these large differences between tasks makes it difficult to draw firm conclusions regarding differences in electrophysiological response to feedback between normative and clinical participants. Instead, a future avenue for investigation could explore differences between clinical and normative samples in how the process socially competitive vs. non-competitive feedback as this would help to understand the

relationship between externalising behaviour and reward in both social and non-social situations.

Whilst not the primary focus of this thesis, the potential for Multisystemic therapy (MST) to elicit electrophysiological change in the young people was also investigated. However, the implementation of MST is highly individualised. As each MST programme is tailored to fit the individual, it is possible that for a subsample of the participants reported here, the therapy was primarily aimed at bringing about change through tackling problems in the parent-child relationship or in the child's environment (e.g. the parents relationship), rather than the child's behaviour directly. Therefore, the lack of group differences in the electrophysiological response following intervention may be due to large variations in the therapeutic regimes instituted in the MST participant. Despite this, it is noteworthy that the results reported here are consistent with previous work investigating therapeutic effects on EEG markers in externalising children (e.g. Lewis et al., 2008), in which therapy was ineffective at changing neural responses, and instead changes in neural response was associated with participants improvement status. This suggests that participant's response to therapy is clearer indication of whether change is likely to occur at the physiological level. However, any future work investigating neural changes following MST would benefit from controlling for types of therapy implemented for each individual.

Finally, the differences between low-level visual characteristics of reward and punishment stimuli is a limitation of both empirical studies reported here, and is shared by numerous other studies designed to investigate feedback processing. Whilst visually unambiguous stimuli are necessary to allow participants to clearly differentiate between valence conditions, the distinct stimuli used may affect neural responses themselves. However, in this thesis, condition effects in the FRN remained the same when accounting for potential effects of early visual components, and feedback-related ERPs occur relatively late in the processing stream compared to visual processing ERPs, which are thought occur within 75-150ms post-stimulus (Liu, Agam, Madsen, & Kreiman, 2009; VanRullen & Thorpe, 2001). Time-frequency processing of visual characteristics are less well understood, however, low-level visual processing is thought to occur in alpha and gamma bands over occipital sites (Min & Park, 2010; Tallon-Baudry & Bertrand, 1996), neither of which were investigated for this thesis.

Future directions

This arousal-approach model of feedback sensitivity in relation to externalising behaviour outlined above presents several new directions for future research. Perhaps most important to understand is the relationship between social provocation and feedback sensitivity amongst typically developing adolescent participants compared to clinical externalisers. Specifically, by studying how these groups differ in feedback sensitivity when social provocation is parametrically modulated, we might be able to develop arousal-approach profiles. By testing both groups under 'cold', socially neutral conditions, and then high and low social provocation, we can develop a more robust image of the relationship between reward sensitivity, social provocation, and externalising psychopathology. Expanding on this, it is pertinent to ask whether this extends to the internalising domain. If so, we may expect greater reward sensitivity (or potentially decreased punishment sensitivity) when under low arousal, but for differences to diminish under higher levels of arousal, as the 'set-point' of the FRN-arousal curve would be assumed to be low amongst those with internalizing disorders.

Another important avenue of investigation in relation to this model would involve studying how optimal levels of arousal exist in different groups, and amongst different contexts (for example, socially neutral vs. unknown peer observation vs. known peer observation or social cooperation versus social competition). In chapters 5 and 6, gender and age influenced the relationships between valence, provocation, and current externalising behaviour. Similarly, treatment and improvement seemed to go some way towards normalising this effect. However, neuroendocrinologically or neuroanatomically driven studies investigating hormone levels (e.g. cortisol and testosterone) and neural structure volume, respectively, could provide a strong biological basis for understanding endophenotypes prone to increased reward sensitivity under provocation.

Furthermore, inhibition, another proposed facet of approach/avoidance imbalance, may demonstrate a similar relationship between social arousal and externalising behaviour. In a younger child sample, high frustration and low inhibition has been associated with externalising behaviour (Eisenberg et al., 2007), and experimentally induced frustration leads to increased inhibition errors (Pnevmatikos & Trikkaliotis, 2013). Studies investigating the relationship between reward processing,

inhibition and social provocation would provide a complete image of changes in motivational systems when frustrated.

Finally, advanced techniques for signal processing EEG data would allow us to answer more complicated questions regarding feedback processing. As stated in the introduction, Event-Related Spectral Perturbations (ERSPs) reflect the most fundamental interpretation of time-frequency data. Examples of more complicated methods that could be informative of differences in feedback processing are phase-amplitude coupling and inter-site coherence. Phase-amplitude coupling, a measure of how much the power a higher frequency band is modulated by the phase of a lower frequency band (for example, how gamma power is modulated by theta phase), and is thought to be a potential mechanism for synchronising the firing of several spatially distant micro clusters of neurones (Canolty & Knight, 2010; Dvorak & Fenton, 2014). Investigating changes in the interaction between frequency bands could help us to understand whether differences between externalising groups exist in local encoding or global synchrony. Alternatively, work using inter-site coherence and Granger causality could inform us of deficits in connectivity or communication between sites associated with feedback processing and behavioural response. This would further aid in understanding whether differences between high and low externalisers are widespread across all mechanisms, or is driven by changes to one mechanism in feedback processing which leads to deleterious effects on later processing stages.

Conclusions

This thesis has been primarily concerned with investigating changes in reward-related neural processes associated with externalising behaviour. The results reported here highlighted the potential value of considering reward processing among adolescents prone to externalising behaviour. They further highlight that the role of reward processing may not be as straightforward as a simple reward dominance model might suggest. Amongst typically-developing adolescents, individuals reporting higher levels of externalising behaviour demonstrated greater motivational signals in response to reward compared to punishment by one measure (the P3b), and reduced reward prediction errors as measured by another (the FRN). However, the findings looked quite different when investigating reward processing in a clinical sample using a socially-driven task. In this case, high externalisers in the clinical group showed greater reward

responsivity in the FRN, and reduced reward-related motivational or attention engagement as measured by the P3b. Moreover, the relationship between externalising behaviour and feedback valence processing was modulated by participant age and gender. Perhaps more importantly, it was also modulated by the level of social provocation that the participant was under during the task, with greater approach-related neural responses (FRN differences to reward versus punishment) among externalisers when under higher levels of social provocation. These results highlight the necessity to examine motivational imbalance amongst externalisers during frustrating, stressful or otherwise disorder-relevant contexts as this may allow us to understand how increased arousal may exaggerate approach behaviours predicating aggressive acts. Finally, changes related to therapeutic intervention in the neural signals responsible for feedback monitoring were observed. MST was associated with reduced differences between reward and punishment signalling when compared against MAU, demonstrating neural responses similar to those reporting lower rates of current externalising behaviours, potentially suggesting a response to MST at the neural level.

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Appendix 1.0 – Additional measures from the Adolescent Thoughts and Feelings Project.

The following measures were also collected in The Adolescent Thoughts and Feelings Project, but were not included in any externalising analysis.

Big Five Inventory (BFI) – The BFI (John, Donahue, & Kentle, 1991) is a 44-statement questionnaire designed to measure participants scoring on 5 personality factors: extraversion, agreeableness, conscientiousness, negative emotionality, and open mindedness. Participants' agreement with how well the scale describes them is measured using a 5-point Likert scale. A meta-analysis by Viswesvaran and Ones (2000) indicated good test-retest reliability for each of the subscales (ranging between 0.76 and 0.71) and good internal consistencies (ranging from 0.73 – 0.78).

Children's Depression Inventory (CDI) – The CDI (Kovacs, 1980) is a 3-point Likert scale, 27-item self-report questionnaire aimed at indexing depression in children and adolescents between the ages of 7 and 18 years. A recent meta-analysis found good internal reliability ($\alpha = 0.86$) across 18 studies (Stockings et al., 2015).

Early Adolescent Temperament Questionnaire (EATQ) – The EATQ (Ellis & Rothbart, 2001) aims to measure adolescent temperament across 11 subscales: activation control, activity level, affiliation, attention, fearfulness, frustration, high intensity pleasure, inhibitory control, perceptual sensitivity, pleasure sensitivity, and shyness. Participants are presented with 60 statements, and asked to rate how truthful the statement is about themselves on a 5-point scale. It has demonstrated acceptable test-retest reliability (Muris & Meesters, 2009).

The Experiences in Close Relationships Scale (ECRS) – The ECRS (Brennan, Clark, & Shaver, 1998) is a 36-item, self-report measure aimed at measuring attachment through two subscales: anxiety and avoidance. Both subscales have demonstrated good test-retest reliability and internal consistency (Wei, Russell, Mallinckrodt, & Vogel, 2007).

The Inclusion of Others in Self Scale (ISO) – The ISO (Aron, Aron, & Smollan, 1992) is a single item measure of closeness between the participant and another individual. Participants are presented with an image of seven Venn diagrams, labelled "Self" and "Other", which are increasing in their level of overlap. They are asked to indicate the circle that they feel best represents their closeness to the specified person. In this study,

the participant was asked to complete the ISO for each parent, as well as four friends. It has demonstrated good test-retest reliability (Aron, Aron, & Smollan, 1992).

The Inventory of Parent and Peer Attachment (IPPA) – The IPPA (Armsden & Greenberg, 1987) is a 53-item measure indexing parent (28 items) and peer (25 items) attachment using a 5-point scale, in which participants are required to indicate how true a statement is for them. It has demonstrated good reliability amongst adolescents (α = 0.81; Buist, Deković, Meeus, & van Aken, 2004).

NEO Personality Inventory (NEO PI) – Two facets from the NEO PI (Costa & McCrae, 1985), a personality inventory, were used in this study; the extraversion sensation seeking and the neuroticism impulsivity subscales. Participants are required to rate statements about themselves on a 5-point scale of accuracy. Both subscales have demonstrated acceptable internal reliability (Kurtz, Lee, & Sherker, 1999).

Pubertal Status – Participants were asked to give a self-report on their pubertal status by indicating the progress of developmental markers as one of four states: not started, barely started, definitely started but not finished, and definitely finished. All participants were asked to report on height changes, skin changes, and body hair changes. Female participants were asked to report on breast growth and menstruation. Male participants were asked to report on penis growth and facial hair growth.

Reflective Functioning Questionnaire – Adolescent (RFQ-A) – The RFQ-A (Sharp et al., 2009) is a 46-item questionnaire designed to assess the ability to mentalize amongst adolescent populations. It has demonstrated acceptable internal reliability (α = 0.77; Ha, Sharp, Ensink, Fonagy, & Cirino, 2013).

Rejection Sensitivity Questionnaire (RSQ) – The RSQ (Downey & Feldman, 1996) is a vignette-based questionnaire. Participants are presented with written vignettes asking something of another individual (such as a parent or friend). They are then asked to rate their expectation of rejection and the anxiety associated with it. The RSQ has demonstrate acceptable internal reliability for the expectation (α = 0.70) and anxiety subscale (α = 0.74; Zimmer-Gembeck & Nesdale, 2013)

Revised Children's Manifest Anxiety Scale (RCMAS) – The RCMAS (Reynolds & Richmond, 1978) is a 37-item self-report scale designed to measure anxiety in children and adolescents between the ages of 6-19 years. The scale is comprised of four sub-

scales (Psychological anxiety, Worry/Oversensitivity, Social concerns/concentration, and Lie) and has demonstrated good reliability and validity (Gerard & Reynolds, 2014).

Thematic Apperception Test (TAT) – The TAT (Murray, 1943) is a projective measure of personality in which participants are presented with cards showing ambiguous situations in black and white. Participants are asked to tell a story explaining the events presented in the cards. These stories are then interpreted by the experimenter on a range of themes, such as aggression or affiliation.

UPPS Impulsiveness scales (UPPS) – The UPPS is a 46-item scale designed to measure impulsiveness on four subscales: urgency, premeditation, perseverance, and sensation seeking (Whiteside & Lynam, 2001). Each subscale has demonstrated good reliability (between 0.83 - 0.89) and good construct validity (Whiteside, Lynam, Miller, & Reynolds, 2005).

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