THE TRANSDIAGNOSTIC EXTENSION OF DELUSIONS - SCHIZOPHRENIA AND BEYOND

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Abstract

Delusion is central to the conceptualisation, definition and identification of schizophrenia. However, in current classifications the presence of delusions is neither necessary nor sufficient for the diagnosis of schizophrenia, nor is it sufficient to exclude the diagnosis of some other psychiatric conditions. Partly as a consequence of these classification rules, it is possible for delusions to exist transdiagnostically. In this paper we evaluate the extent to which this happens, and in what ways the characteristics of delusions vary according to diagnostic context. We were able to examine their presence and form in delusional disorder, affective disorder, obsessive-compulsive disorder, borderline personality disorder and dementia, in all of which they have an appreciable presence. There is some evidence that the mechanisms of delusion formation are, at least to an extent, shared across these disorders. This transdiagnostic extension of delusions is an argument for targeting them therapeutically in their own right. However there is a dearth of research to enable the rational transdiagnostic deployment of either pharmacological or psychological treatments.

Introduction

The study of psychiatric symptoms across diagnostic boundaries is complicated by two structural constraints. The first is that some symptoms are crucial to the establishment of particular psychiatric categories. Thus some of their distribution is curtailed by definition, because of their involvement in the identification of disorders. The second constraint is that disorders are arranged hierarchically, such that some diagnoses trump others. Thus the spread of delusions is partly definitional and partly empirical. Studying their distribution transdiagnostically will therefore reflect both on the real world and on the nature of our classifications. In this review we seek to establish and interpret the transdiagnostic extension of delusions, symptoms central to the diagnosis of schizophrenia.

Identifying delusions

To err is human: we all make errors of reasoning and judgement, and, more rarely, errors of sensory perception and interpretation. However, some people are identified by consensus as being in consistent, persistent and idiosyncratic error, often linked to actions perceived as incomprehensible or deeply inappropriate. The recognition that they required assistance rather than exorcism or punishment meant that the lay concept of madness gradually became the province of physicians. Specific aspects of madness were consequently codified as delusions and hallucinations. In this paper we will interpret the distribution of delusions in a whole range of people with psychiatric disorders.

The identification of psychiatric symptoms generally involves the ascription of a cut-off point to what is essentially a set of continua. Symptoms vary in intensity, persistence and the level of associated distress. Thus identifying the symptom of depressed mood, for example, requires a judgement that the lowering of mood is sufficiently severe, sufficiently persistent, and sufficiently consistent to qualify. Such sufficiency is hard to define, and precise definition is in any case rarely attempted (but see WHO 1994[1]). Equivalent judgements must be made about the symptom of anxiety. Delusions too have dimensional attributes, and grandiose and persecutory delusions in particular shade into ordinary beliefs.

While most psychiatric professionals have confidence in their ability to recognise delusions, they find it very difficult indeed to offer a definition that is conceptually watertight, and immune to counter-example. Indeed we would go so far as to assert that there is no criterion or set of criteria that is sufficient and necessary in the separation of delusions from normal beliefs. Stephens and Graham[2]

describe four criteria that serve to define beliefs in general. They characterise them as: (1) beliefs have a *content*, that is, they contain statements as to putative facts; (2) the idea of a belief implies *confidence* (a degree of conviction) about its truth; (3) beliefs form the basis for both *reasoning* and *action*; and finally (4) they are associated with an *emotional response*.

These authors assert that identification of these features cannot guarantee to distinguish delusions from normal beliefs. For instance, we have operations for evaluating the truth standing of beliefs. No such operations are watertight, though some are better than others. Those used in the procedures of science and the law have formal rigour which gives them an edge, but in other circumstances we have only consensus to fall back on. Delusions are defined as false representations of reality. If we cannot guarantee their falsehood we may still *provisionally* accept them as delusional, but if they are true beliefs we should not accept them as delusions but merely as vehement ideas.

Psychiatric symptoms and psychiatric classification

Central to the practice of medicine and hence of psychiatry is the refinement of the phenomena of ill health into agreed constructs representing *symptoms* and *disorders*. The relationship between these two types of construct is both conceptual and technical.

The concept of disorder developed hand-in-hand with the observation that individual manifestations of ill health present with distinguishable features. These features were formalised under the rubric of symptoms. The fact that symptoms tended to form natural clusters led to the formulation of *syndromes* (from the Greek for "running together"), enabling ill-health to be divided into different types (think Aretaeus and the conceptualisation of diabetes mellitus[3]). The construction of syndromes requires a leap of the imagination, but if they appear plausible summaries of reality they become accepted as consistent phenomena, and hence a suitable basis for medical investigation. They may also come to be seen as real in an objective sense[4,5] (though not by us[6]).

Classification based on syndromes is the defining feature of the medical approach to issues of health. It is based on the presumption that it will ultimately enable the rational allotment of treatments and other interventions. In particular the categories are accepted on the provisional basis that they capture intrinsic mechanisms and processes (reflected as aetiology and pathology) that should provide targets for specific interventions. This is certainly a logical way of arriving at possible treatments. Such treatments may or may not work: if they do not, they call in question the hypothesised mechanisms.

Defining disorders

An ideal medical classification incorporates classes distinguishable both from each other and from a state of good health. It thus has internal boundaries and a threshold, both of which may be hard to define. This medical approach is characteristic of psychiatry, and, at least insofar as it relies on diagnostic groupings, has been used in clinical psychology.

Symptoms of physical disorders (for example, chest pain) comprise subjective experiences that map onto physical processes. They are valuable because they suggest investigations that identify the physical basis of disorder. Psychological symptoms by analogy are held to indicate psychological disorders such as anxiety or schizophrenia. However, though there may be underlying physical processes, these have not been established to a degree that enables them to be used diagnostically. In consequence, we only have the symptoms to go on.

Psychiatric symptoms do form natural clusters, albeit rather fuzzy ones. However, they are also widely distributed in the general population. Many people have a few symptoms, a few people have many. This is most clearly the case for affective symptoms, but is also seen in relation to psychotic symptoms[7-14]. Indeed the shape of the distribution curves of affective and psychotic phenomena is remarkably similar[11,16]. Thus the differentiation of psychiatric disorders requires the imposition of categories on continuous distributions[17,18].

This has consequences, both for comorbidity and for the existence within disorder-categories of symptoms that do not contribute to the diagnostic process. Symptoms tend to display a hierarchical arrangement. Usually the most disabling symptoms are the least frequent. This drives an empirical non-reflexive relationship: more severe, rarer symptoms are more predictive of common minor symptoms than the reverse[11]. To an extent, this hierarchy is reflected in the way psychiatric disorders are constructed. Thus schizophrenia is high in the hierarchy, with delusional disorder below it.

The identification of symptoms acknowledged by consensus as key to a particular disorder forms the basis of diagnosis. However, to a variable extent, each diagnostic category will also reflect the population distribution of other symptoms. Thus, within a given category, key symptoms will be present by definition, but there may also be a variable selection of non-specific, ancillary symptoms[19]. This is seen in the widespread coexistence of affective symptoms in schizophrenia[20]. However, some symptoms ancillary to a given disorder may turn out to have a more than incidental role in its development. We would argue that this is the case with schizophrenia.

Diagnosis rarely requires the presence of all potentially defining symptoms. Thus in DSM5 the diagnosis of schizophrenia requires two of the five characteristic symptoms to be present for a month, of which one must be delusions, hallucinations or disorganised speech. This clearly implies that, even in terms only of these key symptoms, cases of schizophrenia will in practice have different symptom profiles (the five domains of diagnostic symptoms in schizophrenia are, in different combinations, capable of generating 22 distinct profiles based on two or more of the domains). Moreover, if only one of these characteristic symptoms is present, for example delusions, a diagnosis of schizophrenia will not be made. In this circumstance, the symptom profile may meet criteria for delusional disorder, or for a disorder outside the schizophrenia spectrum in which the delusions become ancillary.

Syndromes and disease entities

The definition of a syndrome implies (but does not guarantee) that the syndrome captures an underlying disease entity. This then comes to be seen as the cause of the symptoms that characterise the syndrome. In this formulation, the symptoms are taken to *reflect* the disorder, rather than constituting it[21]. Something similar happens when, rather than being a theoretical construct, the underlying entity is inferred statistically, in the form of a latent variable[22]. Covariation between symptoms is then interpreted as the effect of their common origin. Moreover, causal influences external to the disorder are taken to operate on symptoms because of their effect on the disorder. Thus in this model the external cause is seen as conditionally independent of the symptoms. The transdiagnostic study of symptoms is then key to the investigation of overlap between hypothesised disease entities.

However, major problems remain in establishing the biological basis of schizophrenia. The endophenotype project is in trouble[23], and there are serious problems with the genetics of schizophrenia: the discovery of hundreds of common gene variants minimally associated with schizophrenia in GWAS studies[24-26] means that individual disease risk scores may bear little relation to one another and makes it difficult to accept that a genetic basis underpins mechanisms in any easily determined manner. Indeed, Cohen[27] has suggested more individual genotypic patterns could be associated with schizophrenia than there are people with schizophrenia on the planet. Finally, delusions appear to be the psychotic symptom least associated with familial-genetic factors[28].

However, there is an alternative interpretation, which has had increasing support[29]. Thus it is equally conceivable that symptoms might co-vary because of direct causal interaction between them;

external causes could then operate directly on individual symptoms[21,30,31]. If so, it becomes rational to study symptoms transdiagnostically, on the ground that their causes may themselves operate across diagnostic classes. Moreover, if symptoms are linked in a causal chain, interventions targeting a given symptom may ameliorate symptoms downstream of it[32,33].

The effect of definition on the phenomenology of psychiatric categories

The transdiagnostic identification of delusions is complicated by issues arising from the definition of disorders. Thus the presence or absence of delusions in given psychiatric categories is sometimes the direct consequence of the way the disorders are defined. This may therefore change as the definition is revised, as for example in the case of bizarre delusions and delusional disorder. The recent decision in DSM5 that bizarre delusions are allowable symptoms in delusional disorder means that, where previously they were excluded by definition, they are now likely to be present in some cases. Likewise the new DSM5 category of *Obsessive-Compulsive and Related Disorders* includes a specifier related to delusional insight. Consequently, delusional disorder has an exclusion criterion specifying that symptoms cannot be better explained by OCD or similar disorder with absent/delusional insight. Thus delusional beliefs no longer automatically suggest a psychotic disorder in DSM5.

Finally, two of the 14 specifiers of Major Depressive Disorder are “with mood-congruent psychotic features” and “with mood-incongruent psychotic features”. This implies that the presence of delusions is not excluded within the definition, and indeed that they may count toward the diagnosis even if they are mood-incongruent. In consequence, a diagnosis of schizoaffective disorder will be avoided where previously it would have beenaccepted.

Classification and comorbidity

In some situations the pattern of symptoms is such that the criteria for more than one disorder are met[34,35]. The implications of such comorbidity are unclear. On the face of it, if two disorders are identified, it might be inferred that the aetiological processes characteristic of each disorder are separately involved. This seems somewhat unlikely. As Goldberg[18] points out, a good classification should have points of rarity between classes. Only then will comorbidity in the individual case be truly informative, rather than the artefact of a spurious separation. However, in psychiatry points of rarity rarely exist: hence the *boundary problem*. Disorders are recognised by core (defining) features, but ancillary symptoms are so common as to be the rule. In some cases these may be used as an exclusion clause in the definition of the disorder, in other cases they are discounted as incidental.

However, symptoms ancillary to one disorder may be defining to another, thus forming the basis of what Goldberg[17] would argue is a non-informative comorbidity. The situation is further complicated by the fact that the association between symptoms that underlie comorbidity may change as time passes[36].

Systematic review

We attempted a systematic review on Medline of research comparing the form and content of delusions in different diagnostic categories. Our search was based on the following terms (delus*) AND (Compar* OR Differen* OR Similarit* OR Contrast*). We included empirical papers contrasting directly two or more groups with delusions, where one of these groups included people with schizophrenia. It turns out that there have been very few comparisons of the features characteristic of delusions in different psychiatric conditions. We identified 782 articles, and discarded 720 on the basis of their abstracts. Of the 62 papers remaining, we read and rejected 46, leaving 16 that met our criteria. However, these articles were of such variable methodology and quality that we merely refer to some of them in the following narrative review. For the purposes of illustration, we have focussed specifically on delusions in affective disorders, delusional disorder, borderline personality disorder, obsessional disorders and dementia.

Delusions in affective disorders

A majority of delusions have persecutory themes irrespective of nosological context. However, a substantial minority are characterised by content that seems to reflect the mood disturbance. They are then described as mood-congruent, although it is not always easy to distinguish reliably between mood-congruence and mood-incongruence[37]. As this distinction feeds into the diagnostic separation of schizophrenic and affective disorders, their transdiagnostic prevalence is partly definitional.

Somewhat surprisingly there has been little attempt to establish the actual frequency of delusions in affective disorders. Delusions, both mood congruent and incongruent, may occur in around 20% of patients with major depression[38], although this will vary with severity and depend on the way the samples are drawn. Delusions are more common in bipolar disorder: Azorin and colleagues[39] reported on a study of over a thousand patients with manic episodes. Half had psychotic symptoms, of which one-third were mood-incongruent. Mood-incongruence was more often associated with having had earlier diagnoses of schizophrenia and, more surprisingly, of anxiety disorders. It was also more frequent where mood was particularly unstable. Bipolar disorder is specifically associated with grandiose delusions, although delusions with persecutory content are common. However, grandiose delusions are also common in other disorders – in half of patients diagnosed with schizophrenia, and a sizeable proportion of patients with substance abuse disorders[40].

Delusions in delusional disorder

Delusional disorder is an inconsistent category[41], the consequence of its inferior position to schizophrenia in the diagnostic hierarchy. Thus Heslin et al.[42] found only 19% of cases retained the diagnosis at 10 year follow-up, whereas 57% had acquired a diagnosis of schizophrenia. This is relevant to the interpretation of comparisons of delusional disorder and schizophrenia.

There have been a number of such comparisons, but as both disorders have the presence of delusions as an identifying characteristic, they rarely involve the specific attributes of delusions. One exception is the study by Peralta and Cuesta[43,44]. Although there was a considerable overlap, they found that people with delusional disorder had higher levels of conviction and preoccupation, while themes of persecution were more salient than in schizophrenia. They had higher levels of anxiety, dysphoria and depression than people with schizophrenia, and also had more obsessional symptoms. Their delusions affected more areas of their lives. Conversely, people with schizophrenia were more likely to have bizarre and internally inconsistent delusions.

Hui et al.[45] compared patients in first episodes of delusional disorder or schizophrenia. While the former had less in the way of premorbid schizoid and schizotypal traits, there were few substantive differences in symptom severity or neurocognitive performance. Note that this study has been criticised methodologically [46].

Delusions in borderline personality disorder (BPD)

Borderline personality disorder is identified primarily through the confluence of longstanding traits and impairments, rather than the emergence of specific symptoms. However, its diagnostic standing has been in flux, exemplified by the merging of axes I and II in DSM5. Psychotic experiences might be expected in BPD because the diagnostic criteria include features that encourage their emergence. Thus people with BPD show pathological personality traits in the domains of emotional lability, anxiety, depressed mood and interpersonal hypersensitivity (hence the suggestions it should be renamed *mood dysregulation disorder* [47]).

Nevertheless there has long been a tendency to discount psychotic symptoms in BPD in a way that allowed a clear but, we would argue, spurious separation between BPD and psychotic disorders [48,49]. Thus Links et al.[50] set out what they regarded as the possible interpretations of the association of psychotic symptoms with BPD. They argued that broadly defined psychotic symptoms were common

in BPD, but defined narrowly they were rare. Moreover, when narrowly defined symptoms occurred, they were due to concomitant (psychotic) disorders, or were factitious. They claimed their study of 88 patients with BPD confirmed these tendentious suppositions.

Oliva et al.[51] contrasted people with BPD and with schizophrenia. Members of each group experienced two types of psychotic experience: a transient, circumscribed and atypical form, and a prolonged, widespread and bizarre psychotic form. Each type of experience was very frequent, but the former were more common in BPD, and the latter in schizophrenia. Non-delusional paranoia was common to both groups, though more severe in BPD. Pearse et al.[52] found a lower prevalence of actual delusions in BPD, though it was still marked (20%).

Kingdon et al.[53] compared patients with schizophrenia, BPD, and both diagnoses. Nearly two-thirds of those with a diagnosis of schizophrenia (whether comorbid with BPD or not) were identified as having paranoid delusions, compared with a third of those diagnosed as having BPD alone.

Psychotic features in obsessional disorders

Bleuler[54] recognised that obsessive compulsive symptoms occur in schizophrenia. Fenton and McGlashan[55] reported clinically significant obsessional symptoms in 13% of 163 hospitalized schizophrenia patients, a rate well above chance. It is thus also conceivable that in situations where the diagnostic criteria for obsessive compulsive disorder are met, there may be ancillary psychotic symptoms. Eisen & Rasmussen[56] found that 14% of 475 patients with diagnosed OCD had psychotic symptoms, although in a substantial minority this was restricted to lack of insight and high conviction about the reasonableness of their obsessions. Guillem et al[57] provide evidence suggesting this association came partly from a more specific relationship between delusions and obsessions (as opposed to compulsions), and that this reflected a similarity of mechanism. Obsessions are intrusive and distressing thoughts, images, or impulses, and have been analysed in detail as a form of metacognitive belief.

Like anxiety, obsessional beliefs may have a role in the development and exacerbation of psychotic episodes. However, while anxiety disorders are characterised by an increase in the threat attention and startle responses, OCD demonstrates thought-action fusion, the belief that thinking about something makes it more likely [58].

Obsessional beliefs and anxiety both appear more prominent in the acute rather than the stabilized phase of psychosis[59]. This tallies with the finding of Fear et al.[60] that where obsessions co-existed

with delusions, they generally preceded them. Thus they seem to march *pari passu* with the development of psychotic symptoms.

Delusions in people with dementia

Dementia provides a particularly interesting context in which to study delusions, given that it is a disorder with a clear biological substrate. While the underlying causal mechanisms may differ from those in conditions where the nature of biological abnormalities is less secure and less compellingly correlated with delusional processes, the psychological mechanisms may be similar.

Psychotic symptoms are certainly a frequent feature of dementia [61-63]. In their meta-analysis, Zhao et al.[62] calculated that nearly a third of cases of Alzheimer's disease had delusions, and 16% had hallucinations, though these values disguise appreciable heterogeneity between studies. Overall, delusions seem to be more common than hallucinations in dementia. Some have warned against a 'global' approach to psychotic symptoms in these conditions, as delusions and hallucinations appear to have discrete clinical and neurobiological correlates. A recent systematic review of psychotic symptoms in dementia identified 23 cohort studies[63]. As might be expected, the prevalence of delusions varied in response to methods of selection and assessment: the cumulative prevalence during follow-up ranged from 34% to 80%. While delusional ideation fluctuated, it tended to increase with time.

As in other disorders, the predominant content of delusions in dementia is persecutory[60,61]. However another very common delusional type involves misidentification: one's home is not one's home; a family member is a duplicate or an imposter; images on the television are actually people present in the house[64]. Misidentification beliefs were initially described as perceptual abnormalities[65], but are now generally classified as delusions. It has nevertheless been argued that paranoid and misidentification symptoms represent two distinct subtypes, characterised by different pathological and cognitive trajectories[66,67]. Overall, delusions in AD are associated with increased age, and with the rate and severity of cognitive decline[68-70]. However, persecutory delusions tend to emerge earlier in the illness, while misidentification delusions are typical of increased cognitive impairment and advanced dementia[63], and also have more significant genetic correlates.

Delusions in AD were initially interpreted as a logical attempt by people with cognitive deficits to understand their environment[71]. However, they soon came to be regarded as having neurobiological underpinnings[72], with the accelerated deterioration in people with delusions being taken to indicate a biological basis shared between delusional and cognitive symptoms.

Interestingly, the combination of AD and psychotic features is familial, suggesting that it is biologically distinct from non-psychotic AD[73] (and possibly also from psychosis in the absence of dementia[28]). This is supported by the fact that the presence of psychotic symptoms in AD is associated with a relatively greater increase in impairment across neocortical regions[72]. There is also a suggestion that delusions in dementia are particularly associated with right-sided brain dysfunction[74]. However, given the fluctuation in psychotic symptoms in dementia, it seems likely that the association is with a propensity to such symptoms, rather than with the symptoms themselves. Although psychotic features in Alzheimer's disease have a familial basis, it is not associated with the apolipoprotein E gene[75,76]. The mechanisms behind the genetic contribution to psychotic symptoms in AD are unknown, but there is more evidence to support the involvement of putative risk genes for schizophrenia than those directly linked to late-onset AD. Functional imaging studies in AD may overlap with those from young adults with schizophrenia, as they have implicated regions and functional networks thought to be involved in salience attribution, belief evaluation and mentalising.

Transdiagnostic mechanisms of delusion formation

The clinical and scientific investigation of delusions should involve clarification of mechanisms. The delusional type central to schizophrenia concerns persecutory ideation. More than 70% of patients presenting with a first episode of psychosis have a persecutory delusion[77].This is also the type for which psychological treatments are best established. Thus the factors maintaining persecutory delusions are plausible targets of treatment.

Because delusions are transdiagnostic there is an argument for studying and treating them in their own right. The psychological mechanisms of delusion formation appear quite consistent across diagnoses. McLean et al [78] report a meta-analysis of cognitive biases in psychosis: *jumping to conclusions (JTC* - using less information to make quick judgements), *biases against disconfirmatory and confirmatory evidence*, and *liberal acceptance* (over-rating the plausibility of absurd interpretations). These biases were marked in people with schizophrenia if they currently had delusions; those without current delusions did not differ from healthy controls. JTC was also seen in groups experiencing delusions in the context of other psychiatric disorders, but not in non-delusional psychiatric conditions, with the possible exception of obsessional disorder[79]. The jumping to conclusions bias was of similar frequency and extent in people with schizophrenia and psychotic depression[80]. Overall, these results indicate that while the biases co-vary with delusional severity,

they are associated with delusions transdiagnostically, implying that they have an intrinsic role in the process of delusion-formation.

A range of other internal factors are also important in persecutory delusions, which appear to be driven and maintained by worry, mood disturbance and instability, disrupted sleep, anomalous experiences, reasoning biases, safety behaviours, negative self-beliefs, and a propensity towards an exaggerated experience of stimulus salience (*aberrant salience*)[32,80-87]. In patients with schizophrenia, patients with depression, and non-morbid controls, paranoia appears strongly associated with negative self-esteem and pessimistic expectations[80].

Dementia is an interesting case in relation to transdiagnostic mechanisms. Although it has an established neuropathology, this may not be the direct cause of delusion formation. The impairment of cognition is likely to lead to inconsistent misinterpretations of the social and physical environment, and this in turn will provoke anxious responses. Symptoms characteristic of affective disturbance (depression, anxiety, irritability and sleep disorder) all appear to be present in around 40% of cases of dementia[62]. Thus the psychotic symptoms may plausibly have drivers similar to those in psychotic disorders unassociated with dementia. However, there have been no studies of psychological mechanisms in the development of delusions in these conditions.

The internal factors linked to delusion formation correspond to external experiences. Disorders associated with delusional symptoms consistently occur in the context of a history of trauma: bullying, physical abuse and sexual abuse[80, 88-90]. Kingdon et al.[89] found very high levels of trauma in patients with schizophrenia and borderline personality disorder. Almost all those with BPD alone (92%) or with both diagnoses (82%) reported moderate or severe emotional abuse, while nearly as many had similar levels of emotional neglect. Two-thirds of the BPD group and 44% of the comorbid group reported severe sexual abuse. Conversely, approximately half (52%) of the BPD-alone group and 67% of the comorbid group reported moderate-to-severe physical abuse. While the levels of trauma were significantly lower in the schizophrenia-only group, they were still way above those found in the general population[88]; more than half (54%) reported being severely or moderately emotionally abused in childhood, 31% physically abused, and 20% severely sexually abused. Thus differences in abuse history between schizophrenia and BPD were quantitative, not qualitative. The social aetiology of delusions in psychosis is consistent with the finding that positive symptoms of psychosis may be the attributes least driven by familial-genetic factors[24].

Alternative approaches

We live in interesting times. In the past 15 years there has been a major advance in understanding the social and psychological causes of persecutory ideation. This has shaped the development of much more efficacious treatments for persecutory delusions occurring in schizophrenia and related diagnoses. The identification of mechanisms maintaining persecutory delusions has encouraged the development of specific treatments aimed at the reduction of worry[91`], enhancement of self-confidence[92], improving sleep[93], the modification of maladaptive thinking styles[94,95], and the avoidance of safety behaviours[96].

We know virtually nothing about how pharmaceutical treatments effect improvements in individual symptoms of psychosis, and hence we cannot at present use pharmacological treatments rationally in combination with psychological treatments. We need to know more. It is assumed that pharmacological agents treat the supposed underlying disorder directly and it is this that leads to symptomatic improvement; the effects may be sequential in a way that lends itself to synergy. How do pharmacological treatments affect maintenance factors? There is very little information about this. However, So and her colleagues[97] reviewed the way reasoning biases in people with schizophrenia respond to pharmacological treatment. The 17 available studies were small, and often uncontrolled. Few were longitudinal and the measures used were variable. Nevertheless *JTC* and *reduced belief flexibility* (sticking rigidly to conclusions) appear closely related to the severity of delusions, while *externalising attributional style* (avoiding self-blame) is related to overall psychopathology, and *impaired theory of mind* (a reduced understanding of why others behave as they do) to negative symptoms. Antipsychotic treatment leads to an improvement in belief flexibility and theory of mind. It is possible belief flexibility might be mediating the antipsychotic treatment response. On the other hand, the jumping to conclusions bias was unchanged by pharmacological treatment and may specifically require psychological treatment. Clearly, further longitudinal studies of the course of improvement in response to drug treatment would be valuable.

Conclusions

The ultimate purpose of conceptualising and diagnosing medical conditions is to narrow treatment choices in a productive and helpful way. Our disease constructs are therefore to be judged by how easy it is to distinguish them and how specific and effective our treatments are. Studying the distribution of psychiatric symptoms demonstrates the idiosyncrasies and imperfections of our classifications, and hence a useful corrective for intellectual and therapeutic complacency.

The concept of schizophrenia clearly retains significant functions. It is the major grounds for deciding to use antipsychotic medication, and this will not change despite recent reservations about the circumstances in which it is helpful[98]. It is also the basis for identifying samples for research, including psychological research. Nonetheless, it is clear that there are problems. The existence of key symptoms of schizophrenia in other disorders raises questions about the validity of the schizophrenia concept, but also about how to deal with transdiagnostic symptoms. There is an argument for offering to treat them wherever they cause problems, irrespective of diagnosis, but the effectiveness of treatments is less secure outside the the originally targetted disorders.

There are therefore strong arguments for research into transdiagnostic symptoms, to study their form, their underlyng mechanisms, and their response to pharmacological and psychological treatment. This would allow the development of treatment protocols. We know little enough about the time course of response to neuroleptic medication in schizophrenia, but it would be worth knowing how this differs in other conditions. It would also be interesting to see if the same social and psychological influences shape delusions in conditions other than schizophrenia, as current psychological treatments might be relatively easily transferrable.

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