Title:
Resting-state networks of adolescents experiencing depersonalization-like illusions: Cross-sectional and longitudinal findings

Short Title:
Resting-state networks of illusion-prone adolescents

Authors:
Mélodie Derome[1,2], Eduardo Fonseca Pedrero[4], Deborah Badoud[1,2], Larisa Morosan[1,2], Dimitri Van De Ville[5], François Lazeyras[6], Stephan Eliez[1,2], Raymond C. K. Chan[7,8], David Rudrauf[9], Sophie Schwartz[10], Martin Debbané[1,2,3]

[1]*Developmental Clinical Psychology Research Unit, Faculty of Psychology and Educational Sciences, University of Geneva, Switzerland*
[2]*Developmental NeuroImaging and Psychopathology Laboratory, Department of Psychiatry, University of Geneva School of Medicine, Switzerland*
[3]*Research Department of Clinical, Educational and Health Psychology, University College London, United Kingdom*
[4]*Department of Educational Sciences, University of La Rioja, La Rioja, Spain*
[5]*Institute of Bioengineering, Ecole Polytechnique de Lausanne, Lausanne, Switzerland*
[6]*Division of Radiology and medical Informatics, Faculty of Medicine of Geneva, University of Geneva, Switzerland.*
[7]*Neuropsychology and Applied Cognitive Neuroscience Laboratory, CAS Key Laboratory of Mental Health, Institute of Psychology, Chinese Academy of Sciences, Beijing, China*
[8]*Department of Psychology, University of Chinese Academy of Sciences, Beijing, China*
[9]*CISA/FAPSE/Campus Biotech, University of Geneva, Geneva, Switzerland*
[10]*Department of neurosciences and Clinical Neurology, University of Geneva, Geneva, Switzerland*

Corresponding Author:

Mélodie Derome
Clinical Developmental Psychology Research Unit
Developmental Neuroimaging and Psychopathology Laboratory
University of Geneva
40 Boulevard du Pont d'Arve
Case Postale 50, 1211 Geneva 8
Switzerland
Telephone: +41.22.379.93.49
Fax: +41.22.379.93.59
Email: Melodie.Derome@unige.ch

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Abstract

The mirror gazing task (MGT) experimentally induces illusions, ranging from simple color changes in the specular image of oneself, to depersonalization-like anomalous self-experiences (ASE) as in experiencing the specular image as someone else than oneself. The objective was to characterize how connectivity in resting-state networks (RSNs) differed in adolescents reporting ASEs during the MGT, in a cross-sectional (T1) and in a longitudinal manner (a year after). 75 adolescents were recruited; for the cross-sectional analysis, participants were split into 2 groups: those who reported depersonalization on the MGT (ASE group), and those who did not (no ASE). For the longitudinal analysis, participants were split into 3 groups whether they experienced depersonalization: only at T1 (*Remitters*), both times (*Persisters*), or never (*Controls*). They filled in self-reports assessing schizotypal personality (SPQ), and underwent an 8-minute resting-state functional MRI procedure (rs-fMRI). A group level Independent Component Analysis (ICA) was conducted and voxel-wise inter-group differences within RSNs were examined. The rs-fMRI analysis revealed a lower co-activation of specific visual areas within the primary visual network (PVN), and a higher co-activation of regions within the Default Mode Network (DMN) in the ASE group when compared with noASE. The areas that were atypically co-activated within the PVN persisted in presenting differential pattern of co-activation in the longitudinal analysis. The aberrant co-activation of visual area within the DMN predicted higher scores on the disorganized dimension of schizotypy after a year. The present study uncovers a subtle signature in the RSNs of non-clinical adolescents who experienced task-induced ASEs.

Key words: Schizophrenia, schizotypy, psychosis, mirror task, illusions.

1. Introduction

The growing field of research focusing on early detection of psychotic disorders manifests an increasing interest toward pre-psychotic experiential anomalies that may be observable in the premorbid phases during adolescence and early adulthood. These experiential anomalies of the self have been conceptualized by some authors as anomalous self-experiences (ASE)[1], which, when meeting certain frequency and intensity criteria, may also be considered as Basic Symptoms (BS)[2]. For example, experiencing one's specular image as that of another person represents an ASE measured by the Schizophrenia Proneness interview[3], as well as by the Examination of Anomalous Self- Experiences (EASE) [4] interview. Although important conceptual differences of ASEs differentiate the two instruments, they both converge in assessing the depersonalization-like ASE, and conceive of this symptom as representing a potential risk marker for the future onset of psychosis.

An experimental approach, examining the self-face mirror illusion, was introduced by Caputo and collaborators[5]. In Caputo's first study, 66% of 50 healthy young adults participating in the MGT reported seeing a non-human identity, after 10 minutes of gazing at their own faces in a dimly lit room[6]. In another study, patients with schizophrenia reported more frequent and intense strange-face apparitions in the mirror than healthy controls[7]. Subsequently, Fonseca-Pedrero[8] and colleagues provided a validation of the MGT in a sample of 110 community adolescents, 34.6% of which presented with clear depersonalization-like phenomena. In particular, the authors found that adolescents experiencing depersonalization-like symptoms during the MGT reported higher schizotypy scores on the positive (cognitive-perceptual) and the disorganization subscales of the Schizotypal Personality Questionnaire (SPQ) [9] .

Schizotypy refers to a set of personality traits, temporally stable, that are observable in the general population[10]. Considering that the level of positive schizotypy naturally decreases during adolescence [11] but that for youths at increased risk for psychosis, schizotypal expression stays more persistent during this period, conducting research in cohorts of typically developing adolescents provides an important opportunity to identify developmental processes implicated in vulnerability to psychosis, without the limitations of medication and other risks factors, such as comorbidities with other psychopathologies and hospitalisation. Furthermore, adolescence appears to be a fairly suitable period to study the development of ASEs, as it is characterized by a profound change and consolidation of self-identity[12].

In addition, adolescence is the theatre of brain maturation and while mirror induced self-face illusions have been studied behaviourally, little is known about the potential neural correlates of these illusions. Recent neurobiological investigations have focused on examining brain changes associated with the onset of psychosis[13]. Task-based functional neuroimaging studies of self-referential processing have shown differences between adolescents and adults: adolescents activated dorsal medial prefrontal cortex (dMPFC) to a greater extent than adults[14],[15] who also activated temporal cortex[16], indicating that different neuro-cognitive strategies are at work during development. Furthermore, atypical activations during self-reflective tasks appeared to be involved when participants presented high expression of positive schizotypy [17] , as well as in first episode psychosis [18] and full blown schizophrenia[19,20,21]. These atypical activations encompassed areas such as medial PFC, and other midlines cortical structures (anterior cingulate, superior frontal gyrus and posterior cingulate gyri) independently of the sensory modality or stimuli domain[22]. However, there is no consensual knowledge about the neural signature of individuals experiencing these self-related pre-clinical symptoms. Resting state functional MRI (Rs-fMRI) studies – which

evaluate functional interaction during rest – that investigate typically developing population are rare and of great interest. In one study, Lagioia et al[17], found positive correlations between visual network low frequency fluctuations and adolescents' schizotypy scores, notably with positive and disorganized dimensions. One way to start broaching the neural correlates of ASEs is to ask whether those experiencing these illusions differ in cerebral connectivity profiles, when compared to those not experiencing these illusions. Thus, rs-fMRI will be used as it represents a powerful tool to investigate subtle differences in non-clinical population.

To the best of our knowledge, this study is the first to examine RSNs connectivity in non-clinical adolescents experiencing task-induced ASEs. Disentangling some of the early neural mechanisms sustaining depersonalisation-like illusions can contribute to uncovering the neuro-functional patterns sustaining part of the risk for psychosis. In this context, the first aim of the present study is to identify the neural signature in RSNs of adolescents experiencing task-induced ASEs. Secondly by introducing a longitudinal dimension, the aim is to investigate the link between atypical connectivity patterns and schizotypal factors after a one-year interval, and whether persisting ASEs are linked to similar atypical connectivity patterns.

2. Methods

2.1. Participants

The study included 75 (39 Males, 36 Female, mean age= 16.85, SD=2.48) native French-speaking, community adolescents and young adults with normal or corrected to normal vision. Participants were recruited by word of mouth and through advertisement at the University and schools of Geneva. Individuals were included in a longitudinal study, which comprised multiple time points. We were interested in two of these time points corresponding to the first time adolescents participated in the task (T1), and the second time they took part in the same

experiment after an interval of one year (T2). The final rs-fMRI analysis at T1 included the whole sample of 75 adolescents, but the longitudinal rs-fMRI analysis only comprised a subsample of them (N=39, 22 females and 17 males, mean age= 16.39, SD= 1.5) because 36 participants did not come back for T2. Participants received a financial compensation and written consent was obtained from each or from their parents (if they were under 18), under protocols approved by the local ethical commission (Commission Centrale d'éthique de la Recherche des Hôpitaux Universitaires de Genève). Participants included in this study consisted in a subsample of those comprised in a previously published report[8] (n=110).

2.2. Instruments: self-reported measures

At both time points, dimensions of schizotypy were measured using the Schizotypal Personality Questionnaire (SPQ)[9]. Adult Self Report (ASR[23]) and Youth Self Report (YSR[24]) questionnaires were also assessed to evaluate adaptive behaviour in our cohort and scores on externalized and internalized dimensions were used as covariates in each of the following statistical analysis. *Questionnaires are described in the supplementary material*.

2.3. Mirror-gazing task (MGT)

Set up of the MGT

Participants faced a large mirror mounted on a tripod in a parcel of a room where the light was dimed (see figure.1). Before the beginning of the task, the experimenter gave the following instructions: "*Your task is to look at yourself in the mirror. You should keep staring*

into your eyes. The task will last 10 minutes". Participants were also informed to press a button every time they experienced a variation in perception and hold it until the change disappeared, their responses were digitally recorded through COGENT software (http://cogent.psyc.bbk.ac.uk). The event-related responses to perceptions of modifications in the specular image were recorded in terms of number and duration of abnormal perceptions. After the mirror-gazing session ended, participants were administered a questionnaire assessing the abnormal perceptions experienced during the MGT. *See supplementary material.*

Cross-sectional groups

All participants were distributed into one of two groups, on the basis of depersonalisation-like phenomena they experienced, which were assessed through the questionnaire. The first group included adolescents who experienced only slight changes of colour/light and/or deformation of their own faces (participants experiencing no aberrant self-experiences during the MGT= noASE). The second group gathered participants who perceived another facial identity and/or had non-human visions (participants experiencing aberrant self-experiences during the MGT= ASE). Individuals were included into one of these groups on the basis of the most significant illusion they reported.

Longitudinal groups

To explore the longitudinal trajectories of our adolescents between T1 and T2, we constituted three groups: The Control group included participants who did not experience aberrant self-experiences on the MGT in T1, nor in T2, the Remitters consisted in adolescents who experienced ASE the first time they took the MGT but not the second time, the Persisters

comprised individuals experiencing ASE at both time points. Only two participants did not experience ASE at T1 but experienced ASE at T2: they were excluded from the analyses.

2.4. MRI Acquisition and pre-processing

Acquisition and pre-processing methods were common to both cross-sectional and longitudinal analyses.

Acquisition

Anatomical, and functional resting-state imaging data were acquired on a 3T Siemens Trio scanner. For the detailed acquisition parameters, see *supplementary material.*

fMRI Pre-processing

Functional MRI data was pre-processed using SPM12 analysis software (http://www.fil.ion.ucl.ac.uk/spm). A classic pre-processing pipeline was used, including slice timing correction, realignment, co-registration, normalization, and, smoothing. To avoid our results to be biased by motion artefacts, none of the participants had a range of movement greater than 3 mm translation or 3 degrees of rotation, and movement parameters were regressed out at the individual level. These criteria have been widely employed in non-clinical population[25,26,27]. Linear detrending and bandpass filtering (0.001-0.1 Hz) were conducted using DPARSF (http://ffmri.org/DPARSF). Ultimately, connectivity values were z-transformed. *For more details, see supplementary material.* For cross-sectional and

longitudinal analysis, and, in the correlation analysis, we co-varied for gender, demeaned age, externalized, and, internalized scores.

2.5 Cross-sectional statistical analysis of rs-fMRI data

rs-fMRI analysis

Group-level spatial ICA was conducted on the entire sample of participant (N=75) using GIFT toolbox implemented in Matlab (http://mialab.mrn.org/software/gift). ICA technique allows the separation of spatio-temporal BOLD signal into spatially statistically independent components (ICs)[28]. The Infomax ICA algorithm[29] was run 50 times in ICASSO and resulting components were clustered to estimate the reliability of the decomposition – the index I_q, ranging from 0 to 1[30], was greater than 0.9 for each component. Ten components were visually identified as RSNs (supplementary-figure.1) and confirmed using correlations computed between the components and resting-state network templates (http://findlab.stanford.edu/functional_ROIs.htlm). *See supplementary material for more details.*

Group differences within networks

To test for spatial differences among groups in each network, we fed the connectivity maps from participants into 2 independent samples t test. A full factorial analysis was completed in SPM12 for each component. We generated contrasts between ASE and noASE, from which we extracted significant clusters exhibiting peak activity (*t*-values) passing FWE-correction[31] (family wise error), $p<0.05$.

Group differences between networks

To investigate variations of inter-network connectivity, we constructed a connectivity matrix per group (Nparticipants x NICA x NICA). Functional connectivity between pairs of ICs was assessed using partial correlations, resulting in a 10 x 10 matrix in which each element represented the connectivity strength between two ICs. Statistical analysis was conducted using 2-sample t-test for each connection. Acceptance criteria of the results included a threshold of $p<0.05$, FDR[32] corrected for multiple comparisons.

2.6. Longitudinal statistical analysis of rs-fMRI data

rs-fMRI analysis

The rs-fMRI longitudinal analysis was conducted using the same method and parameters we employed for cross-sectional analysis (*see section 2.5*). The only difference concerned the whole group, as group ICA was conducted on 78 individuals because each participant (N=39) had two time points and each time point was considered as a single participant.

Analysis of the interaction groups x time points within networks

The longitudinal analysis focused on networks that presented differences in the cross-sectional analysis. We tested for spatial differences in the primary visual network (PVN) and default mode network (DMN) among groups, time points as well as the effect of their interaction. To do so we fed the connectivity maps from all participants into a mixed model ANOVA[33]. The statistical analysis was implemented in SPM12 for both components and

consisted in a 3 (groups) x 2 (time points) design. We generated F-contrasts to assess main effects and interactions and post hoc t-contrasts to precise the direction of those effects. We extracted significant clusters exhibiting peak activity (*t*-values) passing FWE-correction[31], $p<0.05$.

2.7. Correlation with clinical data

Functional connectivity intensity values were extracted using Marsbar toolbox within ROIs from each participant at MNI coordinates corresponding to peak t values at voxels clusters that had passed the FWE correction of $p<0.05$. We computed the difference of scores between T1 and T2 for each of the dimensions of the SPQ, which we correlated to the intensity values. Spearman partial correlation for non-parametric analysis was used. Results were retained at a threshold of $p<0.05$ and the Bonferroni[34] correction for multiple comparisons was applied.

3. Results

3.1. Descriptive measures

Descriptive measures are presented in Table 1 for the 75 participants. See *supplementary material* for more details.

3.2. Identification of functionally connected neural networks

After running ICA, we retained 10 networks; their spatial maps are shown in supplementary-figure.1 and coordinates of their peak activations are presented in supplementary-Table.1.

3.3. Cross-sectional results: Group differences within and between networks

Group contrasts revealed significant differences in functional connectivity between noASE and ASE groups (see figure.2). Decreased within-network connectivity in the ASE group relative to noASE (noASE > ASE) was observed in sub clusters of the primary visual network (PVN), more precisely in the right fusiform gyrus (BA 37, t=5.33, p=0.038) and the right superior parietal lobule (BA7, t=5.51, p=0.016). In contrast, individuals who experienced depersonalisation exhibited greater co-activation (ASE > noASE) in sub clusters of the dorsal default mode network (dDMN), in the left middle occipital gyrus (BA 18, t=5.90, p=0.003). Between networks analysis did not yield any statistically significant results.

3.4. Longitudinal results

Group x Time point differences within networks

Group contrasts from the mixed model ANOVA revealed a significant effect of interaction group x time points on the co-activation of two Brodmann areas within the PVN. From T1 to T2, co-activation of the right lateral occipital gyrus (BA19) was decreased in the Persisters's group whereas it was increased in the Remitters' group (*t=5.67, p=0.015 FWE-corrected*). Furthermore, co-activation of the left inferior posterior temporal gyrus (BA20) within the PVN was increased from T1 to T2 in the Persisters and decreased in the Remitters (*t=5.34, p=0.015 FWE-corrected*). See figure.3.

Correlation with clinical data

Correlations between intensity values extracted from BA 18, BA 7 and BA 37, and, SPQ dimensions (T2-T1) did not reveal significant association when analysing the whole sample or only the control group. However, in the group of adolescents who experienced ASE: mean connectivity of area 18 was positively correlated with the disorganized dimension (*Rho=0.546, p=0.006*). This result survived the Bonferroni correction for multiple comparisons. Therefore, the aberrant co-activation of the middle occipital gyrus within the dorsal DMN of the ASE group observed at T1 appears to be associated with increased scores on the disorganized dimension of schizotypy when considering an interval of one year (figure.4).

4. Discussion

In this study, we employed the Mirror Gazing Task (MGT) to characterize proneness to depersonalization-like illusions, a kind of anomalous self-experience (ASE), in a cohort of typically developing adolescents. Each participant also underwent a Resting State Functional MRI scan (rs-fMRI). Adolescents were split into two distinct groups for the cross-sectional, and three for the longitudinal analyses, based on their reports of ASEs during the MGT. Using ICA, we identified three areas presenting differences between the two groups (ASE and noASE): the right fusiform gyrus (FG, BA37) and superior parietal lobule (SPL, BA7) within the Primary Visual Network, and the left middle occipital gyrus (m-OG, BA18) within the dDMN. The longitudinal analysis yielded differences between ASEs Persisters and Remitters in the left inferior posterior temporal gyrus (ip-TG, BA20) and the left lateral OG (l-OG, BA19) within the PVN.

Before discussing our findings, we would like to address the surprising results of the rs-fMRI analysis: inter-group differences were revealed in two areas, the m-OG and the SPL which are not originally included in the theoretical definition of respectively, the DMN and the PVN. However, group-ICA performed on the whole sample of our adolescents ascertained their presence in these networks with peak values at very low threshold (*p<0.0001 FDR-corrected, see supplementary-table.1*). In addition, analyses were performed per networks and the strength of the resulting contrasts made us think that these results represented an actual intriguing effect rather than noise, thus we decided to report them.

The following discussion will firstly address the results of the cross-sectional and secondly those of the longitudinal rs-fMRI in light with existing literature on resting-state networks and self-referential processing in psychosis-prone and patients with psychosis.

Concerning the cross-sectional results, at the network level, we observed a decrease in PVN co-activations involving the right FG and the right SPL. Furthermore, we found an increased co-activation - within the DMN of adolescents experiencing ASEs - of the m-OG. Research suggests that the initial encoding of facial features and subsequent perceptual organization primarily occur in the occipital face area (BA18)[35] and fusiform face area (BA37)[36]. Therefore, areas presenting subtle connectivity alterations appear to be implicated in core steps of the face-recognition processing stream[37]. This could partly explain that adolescents carrying these subtle alterations would be more prone to experience depersonalization phenomena induced by the MGT. Early perceptual organization[38] impairments may disorganise the articulation of sensory information into coherent representations and constitute an initial step to self-experienced perceptual deficits described by patients with schizophrenia[39].

These findings may also be discussed at a conceptual level. From the standpoint of Northoff's neuroscientific model of self, three different layers of processing may be distinguished on the basis of meta-analytical analyses[22]: sensory processing related to the "bodily self"; pre-reflective self-referential processing linked to medial cortical connectivity; and higher order processing linked to the cognitive aspects of self-processing, such as autobiographical and emotional aspects of self. Our results seem to corroborate the involvement of the relationship between self-referential and sensory (visual) processing in the experienced modification of one's own face. We may hypothesize that the MGT could induce a conflict between sensory and self-referential processing, underpinned by the subtle alteration of functional connectivity within the PVN and DMN. An alternative hypothesis could propose a disconnection between the two aspects of the self that are sustained by these altered brain regions: the bodily and pre-reflective selves. A recent study[40] showed that gazing at one's self in the mirror increases the consciousness about bodily self. However, when associated with sensory deprivation; in participants experiencing ASE, the bottom-up regulation (from bodily to reflective self) could be disconnected, inducing interruption of self-face recognition, and replaced by a top-down modulation (reflective to bodily self) that creates the illusion.

In the longitudinal analysis, results did not yield a strict correspondence of Brodmann areas, as differences between groups were found in the left ip-TG and the left l-OG within the PVN. However, these areas carry functional consistency with those described with regards to the cross-sectional analyses. Additionally, they seem to have complementary but slightly different functions; for instance, the left BA20 seems to be more implicated in visual fixation[41], whereas the right FG might play a role in determining whether or not the recognized "face-like" feature is an actual face[42]. Area 18 is implicated in detection of light[43] and pattern and area 19 seem to play an important role in human object recognition[44]. Importantly, the

longitudinal results showed differential patterns of co-activation between the Persisters and the Remitters, meaning that the subtle aberrant co-activation of these areas implicated in the visual processing stream either persist or remit after a one-year interval.

Concerning the link between schizotypy and RSNs, we found a positive correlation between co-activation of the R-mOG within the DMN at T1 and scores on the disorganized dimension of schizotypy, implying that the aberrant subtle co-activation pattern observed at T1 is associated with increasing scores on this dimension within a one year interval. These results are consistent with those reported by Lagioia and colleagues on an independent sample, finding positive correlations between VN low frequency bins and adolescents' schizotypy scores, notably with positive and disorganized dimensions[17].

Finally, theoretically, it may be pertinent to evoke and build on the recently developed Bayesian modelling of positive symptoms to interpret the current results. In this model, positive symptoms of schizophrenia could be explained as a failure to represent the precision of beliefs about the world, and this failure would be underpinned by misallocation of precision to hierarchical representations in the brain[45]. Trait abnormalities are hypothesized to result from failure to balance adequately precision to prior beliefs and sensory evidence[46]. Thus, in our case, we could hypothesize that posterior beliefs about your own face direct attention to sensory features by top-down modulation of sensory precision. However, as we induced a situation of sensory deprivation, the sensory evidence here is contradictory to prior beliefs, which create illusions. Now, a failure to attenuate the consequences of inner beliefs about our own faces – meaning to attenuate the corollary discharge of self-made face-beliefs – might explain the varying degrees of depersonalization.

These results must be interpreted in light of the following limitations. Firstly, as the task was performed outside the scanner, rs-fMRI represents an indirect measure. Thus, further analysis should provide a direct measure of the emergence of ASEs, at the exact moment at which they appear, using an fMRI task. Secondly, our cohort is constituted of typical adolescents, thus, further inquiry is necessary on other risk cohorts, such as individuals experiencing BSs and/or at ultra-high risk states.

Findings of the present study suggest a subtle aberrant neural connectivity sustaining ASEs in the mirror, involving sensory and self-referential networks. Further research concerning the mechanisms at stake in the emergence of ASEs could potentially reveal phenomenological and biological markers for vulnerability to psychosis.

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Figure legends

Figure.1: Set up of the Mirror Gazing Task

Figure.2: Cross-sectional rs-fMRI: **Top**: Connectivity differences within the primary visual network (PVN) for the contrast NoASE>ASE (red) showed co-activation both within and outside the PVN. **Bottom**: Within the Default Mode Network, the contrast ASE>NoASE (blue) showed co-activation outside of the network. Results are clustered for family wise errors ($p<0.05$).

Figure.3: Longitudinal rs-fMRI: Results of contrast time point x groups within the PVN. **A**: L-lateral occipital gyrus (BA 19). **B**: L-Inferior posterior temporal gyrus (BA 20). Results are displayed for a threshold of $p<0.05$, FWE-corrected.

Figure.4: Correlation with clinical data: In the ASE group; mean connectivity values of the left middle occipital gyrus were positively correlated with scores on SPQ disorganized dimension after one year.

Supplementary material

Description of self-reported instruments

Schizotypy was measured using the Schizotypal Personality Questionnaire (SPQ)[1], which consists of a 74-item, self-report scale, modelled on DSM-III-R criteria for schizotypal personality disorder[2]. Responses are dichotomous (Yes/No) and scattered across 9 subscales collapsing into 3 schizotypy dimensions[3]. The Positive dimension includes magical thinking or odd beliefs, unusual perceptual experiences, ideas of reference and paranoid ideation. The negative dimension assembles excessive social anxiety, constricted affects and absence of close friends. And the disorganised dimension combines odd speech and odd behaviour. Validity and reliability of the SPQ have been widely assessed in non-clinical adolescents[4] and a French version, validated in adolescents[5], was used in the present study.

The Youth Self-Report (YSR)[6] is a 112-item self-report designed for adolescents (ages 11-17). It assesses behavioural problems and consists in a 3-point scale (*0= not true* to *2= very true*) based on the last 6 months. This questionnaire provides scores on several symptoms scales: anxious/depressed, withdrawn/depressed, somatic complaints, social problems, thoughts problems, rule-breaking behaviour and aggressive behaviour. The Adult Self Report (ASR) is a self-report scale, equivalent to the YSR for adults (18-59 y.o), assessing aspects of adaptive functioning and problems. Although it provides scores on the same symptoms scales, this questionnaire additionally asks about tobacco, alcohol and drug use[7]. Both ASR and YSR were validated for francophone samples[8].

Set up of the MGT

The MGT was conducted in a darkened room, a parcel of which (2 x 3 m) was dedicated to isolate the subject seated in front of a mirror, in between a white wall and a white screen. A large mirror (0.5 x 0.5 m) was disposed on the upper part of a computer desk, held on a tripod, and a keyboard was placed on the lower sliding part of the computer desk. Participants were seated at a distance of 0.4 m in front of the mirror. The room was only illuminated with a halogen light bulb (12V, 20W) mounted on a spotlight and placed 1.2 m behind the participant, with the bulb beam facing the floor. This set-up provided diffuse, indirect lighting over the room, allowing fine facial features to be distinguished in detail whereas colours were attenuated. An experimenter seated behind the screen conducted the MGT. Concerning the recording of the event-related responses, the experimenter explained the use of the keyboard: *"During the 10 minutes while you are looking at yourself in the mirror and staring at your eyes, you may or may not notice changes in your face. If you notice a change then press the button and hold it down for as long as the change lasts. If you do not notice any changes then do not press the button"*. The experimenter made sure the participant understood the instructions and further clarified any ambiguous points before the task began. Trained psychologists (M.D. and D.B.) supervised the process of answering questionnaires to ensure the understanding of the items. The following questions were retained and used in the analyses: '*During the task, have you: (1) Notice a change in light, colour or contrast? If yes, describe'; '(2) Did you see another person in the mirror? If yes, describe'; '(3) Please provide a list of all types of modifications you saw during the task'*. In addition, participants answered three five-point Likert-type scale sentences ranging from *'never'* to *'very often'*: *'(1) How often did you notice anything strange?' '(2) How often did it seem real?', '(3) How often did you see another person in the mirror?'*.

It should be noted that the subject classification we used in our study differed from the study by Fonseca-Pedrero *et al*[9] as they separated participants on 4 different groups (1= slight

changes of colour/light; 2= deformation of their own faces; 3= other facial ID; 4= non-human vision). Moreover, participants presenting negative hallucinations, such as own-face disappearance (n=10), were excluded from the no ASE group to ensure the quality of our control group.

Event related responses recorded during the MGT

Four MGT quantitative event-related responses were used in the analyses: first onset, frequency, mean duration and cumulative duration. The first onset variable corresponded to the duration from the beginning of the task until the participant pressed the button for the first time. The frequency was defined as the number of times participants pressed the button**,** averaged per minute. Mean duration translated the mean time they held the button pressed, and cumulative duration; the sum of duration of apparitions averaged per minute. Results of the behavioural analysis of the MGT are presented in table 1.

MRI acquisition and pre-processing

Acquisition

The T1-weighted sequence was collected with a 3D volumetric dimension using the following parameters: TR = 2500 ms, TE = 3 ms, flip angle = 8°, acquisition matrix = 256 x 256, field of view = 22 cm, slice thickness = 1.1 mm, 192 slices. For the rs-fMRI sequence, subjects were asked to keep their eyes open, fixate a cross on the screen, let their thoughts wander and refrain from falling asleep for the duration of the 8-minute scan. Head movement was

minimised during scanning with a comfortable vacuum cushion constraint. The 200 blood-oxygenation-level-dependent (BOLD) images were acquired as follow: TR = 2400 ms, TE =30 ms, 38 axial slices, slice thickness = 3.2 mm, flip angle = 85°, acquisition matrix = 94 x 128, field of view = 96 x 128.

fMRI pre-processing

The first 10 functional volumes were discarded to remove T1 signal equilibration effects. Images were corrected for errors in slice timing using the middle slice as reference under descending acquisition, and realigned with respect to the mean image to correct for motion. T1-weighted anatomical image of each subject was co-registered to the mean realigned functional images and segmented in six outputs (gray and white matter, CSF, bones, skin and air). The registration step employed a Diffeomorphic Anatomical Registration using Exponential Lie algebra (DARTEL)[10] to create a population-specific template. The resulting template was then spatially normalised to standard stereotaxic space (based on the Montreal Neurological Institute (MNI) coordinate system). Following normalisation, spatial smoothing was applied using an isotropic Gaussian smoothing kernel with a full width at half maximum (FWHM) of 6mm in order to decrease spatial noise prior to statistical analyses. Finally, to avoid spurious correlations due to non-neural signal, two additional steps were conducted using DPARSF toolbox (http://ffmri.org/DPARSF); the signal was linearly detrended[11] and bandpass filtered (0.01-0.1 Hz)[12] to reduce the effect of low frequency drift and high frequency physiological noise.

Important details for the Independent Component Analysis

Data were reduced through three reduction steps (two PCA and one ICA reduction) and concatenated at each of these stages. The number of independent components was fixed at 20 consistently with the minimum description length estimate[13]. Participants' spatial maps represented regional strength of functional connectivity, which is defined as statistical correspondence of each voxel to the average network time course[14]. Each set of component maps was transformed into z-scores to centre the distribution's maximum point to the normal curve at zero. ICA method has been proved to be helpful in effectively isolating artefact as distinct independent components[15], thus the 10 other components were considered as artefacts, either due to motion, or to signal from the ventricles or WM. We used ICA rather than seed-based approaches to identify networks as this data-driven method eliminates the arbitrary choice of seed regions and simultaneously take into account the relationship between all voxels (as opposed to simple pair wise correlations)[16].

Descriptive measures of participants

In our sample, 26,6% (*n=20*) reported only slight changes of light or colour, 33,3% (*n=25*) perceived deformation of their own face, 30,6% (*n=23*) saw another facial identity and 9,3% (*n=7*) had a non-human vision. The ASE group was composed of 30 participants (16 males and 14 females) and the no ASE group of 45 (23 males and 22 females).

Behavioral analysis of participants who did not come back in T2

To ensure the quality of the longitudinal results, we verified whether participants who did not come back for T2, differed from the others on the variables of interest. To do so, we classified participants in two groups: those who came at both time points and those who only

participated in the study at T1. We compared the scores, using non-parametric Mann-Whitney U tests for independent samples, on each event related measures of the MGT: mean duration (U=578, p=0.18), first-onset (U=677, p=0.79), frequency (U=632, p=0.46), cumulative duration (U=558, p=0.12) as well as their scores on the three dimensions of the SPQ: positive (U=572, p=0.08), negative (U=547, p=0.09), and, disorganized (U=517, p=0.06). None of the variables presented statistically significant differences between the two groups. They did not statistically differ in age (U=536, p=0.78) and gender (X^2=0.12, p=0.73) either.

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