

Neural correlates of reality monitoring during adolescence

Anna Laura Lagioia ^{a,c}, Stephan Eliez ^{a,d}, Maude Schneider ^a, Jon S. Simons ^e, Martial Van der Linden ^b, Martin Debbané ^{a,b}

^a Office Médico-Pédagogique Research Unit, Department of Psychiatry, University of Geneva School of Medicine, Switzerland

^b Adolescence Clinical Psychology Research Unit, Department of Psychology and Educational Sciences, University of Geneva, Switzerland

^c Lemanic Neuroscience Doctoral School, Department of Psychology and Educational Sciences, University of Geneva, Switzerland

^d Department of Genetic Medicine and Development, University of Geneva School of Medicine, Switzerland

^e Department of Experimental Psychology, University of Cambridge, UK

KEYWORDS: fMRI; Memory; Source monitoring; Schizotypy; Psychosis

ABSTRACT

Background: Reality monitoring processes serve the critical function of discriminating between externally derived information and self-generated information. Several reality monitoring studies with healthy adult participants have identified the anterior prefrontal cortex (PFC) as consistently engaged during the recollection of self-generated contextual cues. Furthermore, reduced activity of medial PFC has been linked with schizotypal trait expression of delusion and hallucination-like symptoms in healthy adults undergoing fMRI reality-monitoring tasks. The present study seeks to examine the cerebral underpinnings of reality monitoring during adolescence, a developmental stage where the expression of schizotypal traits may increase risk for psychosis.

Method: A group of 33 adolescents, assessed using the Schizotypal Personality Scale (SPQ), underwent fMRI while performing a reality monitoring task. After an encoding session where the subject or the experimenter read out a series of complete or incomplete word pairs, subjects were presented with the first word of studied word pairs and asked whether the corresponding word had been: (1) perceived or produced (*context monitoring*), or (2) read by the subject or by the experimenter (*origin monitoring*).

Results: Analyses revealed a common set of activated brain areas during both context and origin monitoring conditions. When compared to context monitoring, origin monitoring was associated with greater activation in anterior PFC within Brodmann area 10 (BA 10). Correlation analyses revealed that reduced signal change in BA 10 during origin monitoring was associated with greater schizotypal trait expression.

Conclusion: Much like adults performing a similar reality monitoring task, adolescents exhibit a common pattern of brain activity during origin and context monitoring, with functional specialization within the prefrontal cortex involving preferential activation of BA 10 during origin monitoring. Greater schizotypal trait expression appears to be significantly associated to reduced BA 10 activity during origin monitoring trials. Results are discussed in relation to cortical specialization within the PFC and trait expression

during adolescence.

Introduction

Reality monitoring processes allow us to discriminate between perceptually based and reflectively based mental events (Johnson and Raye, 1981). Employing the term *reality* here commonly alludes to an event's external, perceptually grounded source. When distinguishing a past perception from a past reflection, we effectively consider the available contextual information (modalities, features, etc.). This process naturally contrasts with considering information of reflective nature, such as thoughts and associated cognitive processes that more readily indicate an event's internal source (Johnson et al., 1993). Discriminating between perceptually and reflectively based information may be facilitated by self-relevant cues (Foley et al., 1983). In other words, one may more promptly identify an event's perceptual or reflective source when information on the event's origin (*who* delivered the information) is available to the individual (Johnson and Raye, 1981). Together, perceptual/reflective monitoring (hereby described as *context* monitoring) and self/other monitoring (hereby described as *origin* information) thus constitute two essential components of efficient reality monitoring.

Current neuroimaging literature supports the notion that different reality monitoring processes share neural underpinnings (Simons et al., 2006a). Evidence for this is brought by functional neuroimaging studies consistently reporting overlapping brain activity during origin and context monitoring tasks, in cerebral areas that include the lateral prefrontal cortices (PFC), the anterior cingulate, the insula, and the lateral parietal cortices (Simons et al., 2008). However these same studies also highlight subtle yet critical differences in neural activation between the two monitoring processes, showing that origin monitoring engages significantly more activity in the rostral prefrontal cortex within Brodmann area 10 (BA 10) compared to cerebral activity sustained during context monitoring (Simons et al., 2006a, 2005, 2008).

A recent conceptualization of BA 10 activity modulation argues for its implication in the coordination of stimulus-dependent and stimulus-independent mental activity (Burgess et al., 2007). Specifically, this part of the anterior prefrontal cortex is thought to act as a gateway regulating the processing of perceptually or reflectively based information. Several studies lend support to the gateway hypothesis (Gilbert et al., 2005; Simons et al., 2006b), and more specifically, to the implication of BA 10 in reality monitoring tasks that require the participant to distinguish between externally or internally derived information (Gilbert et al., 2010, 2006). Moreover, because stimulus-independent thought most likely originates from one's self, we may expect that BA 10 play a critical role in disentangling mental content originating from the self from that originating from another agent.

Interestingly, Simons et al. (2008) recently observed that schizotypal personality trait expression, which is characterized by proneness to experience delusion and hallucination-like phenomena, is associated with reduced BA 10 activity in healthy participants performing an origin monitoring task. Both context and origin monitoring are particularly relevant to schizotypal trait expression, as they usually involve a confusion between the perceptual and reflective nature of mental events (such as command hallucinations), a misattribution of self and other origin (such as experiencing alien thought control), or a combination of both (such as hearing voices outside one's head). The data reported by Simons et al. (2008) may suggest that reduced BA 10 activity during origin monitoring could, in part, reveal a faulty gateway function increasing the propensity to experience schizotypal cognitions.

Because schizotypal trait expression constitutes the single most predictive factor for the development of schizophreniform disorders during adulthood (Miller et al., 2002; Poulton et al., 2000), examining the neural underpinnings of reality monitoring during adolescence could provide critical information on the developmental pathways leading to minor or clinically relevant manifestations of schizotypy (Bentall et al., 2007). Several theorists already argue for an association between reality monitoring deficits and the expression of psychosis (Bentall et al., 1991; Frith, 1992), and numerous reports observe reality monitoring deficits in schizophrenic patients (Keefe et al., 2002; Vinogradov et al., 1997), healthy adults exhibiting schizotypal manifestations (Laroi et al., 2005, 2004), but also in diverse groups of adolescents who report increased schizotypal trait expression (Debbané et al., 2009a,b). To date however, the neural underpinnings of reality monitoring processes during adolescence remain unknown. This question entails further relevance in light of the important cortical maturation taking place during adolescence (Casey et al., 2008), most notably in the medial frontal cortices (Shaw et al., 2008). Considering that psychotic psychopathology most commonly declares itself during the early years of adulthood, it appears crucial to examine the cognitive and neural underpinnings that may mediate schizotypal trait expression early on during adolescence.

The present fMRI study examines context and origin monitoring in a sample of adolescents representative of the wide range of schizotypal trait expression. The objectives are threefold: 1) To examine the neural underpinnings of reality monitoring during adolescence; 2) To examine the potential overlapping and segregated neural activations between context and origin monitoring during adolescence; and 3) To characterize the association between schizotypal trait expression and reality monitoring processes during adolescence. On the basis of previous studies with adult participants, we first expect to find overlapping cortical activation for context and origin monitoring in our sample. Second, we hypothesize that medial anterior PFC within BA 10 will yield significantly more activation during origin monitoring trials when compared to context monitoring trials. Finally, we predict that schizotypal trait expression scores will be associated with BA 10 activation during origin monitoring trials.

Materials and methods

PARTICIPANTS

Thirty-three right handed teenagers (18 females) with a mean age of 16.61 years (s.d. = 1.9), with normal or corrected to normal vision volunteered for participation. Participants were recruited by word of mouth from secondary schools in the state of Geneva (n = 17), and also through a participant pool collected between 2006 and 2008 in the child and adolescent outpatient public service, the Office Médico-Pédagogique (n = 16) (Debbané et al., 2009a). At time of testing, none of the participants were receiving any pharmacological treatment. Two adolescents were following psychotherapeutic treatment (one male adolescent for attentional difficulties, one female adolescent for behavioural, attentional and academic difficulties). The Youth Self-Report and Adult Behavior Checklist (Achenbach and Rescorla, 2003) were employed to ensure that recruitment pools were comparable and showed no significant differences in terms of internal and external symptoms.

All participants scored within the average range of the Wechsler Intelligence Scale Cubes subtest. Schizotypy trait expression was measured using the Schizotypal Personality Questionnaire (SPQ; (Raine, 1991); French translation (Dumas et al., 2000)). This self-report questionnaire was filled out

under the supervision of a trained clinical psychologist (M.D.). It can be applied to multiple dimensional analyses in the context of a dimensional approach to schizotypy (Rossi and Daneluzzo, 2002), and its full version is appropriate for use with francophone adolescents (Badoud et al., in press). The sample's mean total SPQ score was 18.9 (s.d. = 14.5).

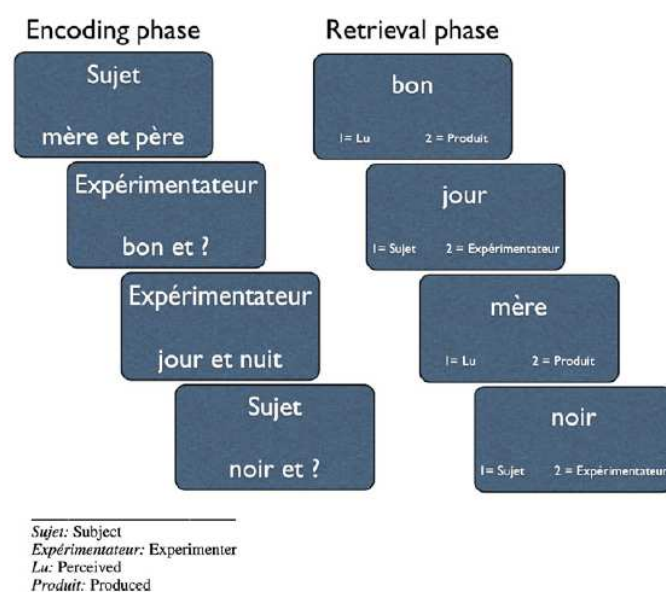
Written informed consent was obtained from participants and their parents under protocols approved by the Institutional Review Board of the Department of Psychiatry of the University of Geneva Medical School.

DESIGN AND PROCEDURES

Our fMRI block design procedure is adapted from Simons et al. (2008) to evaluate context and origin monitoring in adolescents. The task includes two phases: a study phase (encoding stage) and a test phase (retrieval phase). The target stimuli presented during the study phase were 96 French word pairs, following a 2x2 design manipulating *context* (perceived versus produced) and *origin* (subject versus experimenter). The encoding phase was characterized by the presentation of either both words of the pair (*perceived condition*), or by the presentation only of the first word of the pair followed by a question mark (see Fig. 1). Both the subject and the examiner were instructed to intentionally produce and say aloud the first free associative word coming to mind (*produced condition*). Both trials and conditions were presented in a pseudo-randomised order.

The MRI sequence started during each of the three test blocks (retrieval phase) that followed each study phase. Within the test blocks, each subject was asked to remember the condition under which the word pairs had been encoded during the study phase (context and origin monitoring). Specifically they were asked to remember whether the second word of the pair was *perceived* or *produced* (context condition), or whether the trial was performed by the *self* or the *experimenter* (origin condition). A third condition was also included to provide a baseline contrast to context and origin judgments; in this condition, new words were presented along with a question prompting subjects to make a semantic judgment by classifying words as either naturally occurring or man-made objects. Participants were asked to answer by pressing one of the two buttons of an MRI compatible button box.

Figure 1. Reality monitoring task adapted from Simons et al. (2008).



The encoding and retrieval phases were divided into 3 separate sessions to optimize memory load. Each encoding phase was constituted by 32 target trials immediately followed by the retrieval phase. An encoding session required either the subject or the examiner to read aloud the word pair appearing on the screen, with trials organized in a pseudo-randomised fashion, so that the same individual could undertake no more than 3 consecutive trials.

Each retrieval session immediately followed the encoding session and involved 12 blocks equally divided into the 3 conditions: condition A (words perceived or produced), condition B (words performed by the self or the experimenter), and condition C (baseline condition natural/man made objects). Two rest blocks (R - continuous fixation cross) started and closed the test sessions. Each retrieval phase consisted of 48 target trials (32 word pair in addition 16 naturally occurring or man made objects).

Block sequence for the first two phases was R-ACABBACAACBCB-R whereas for the last retrieval phase conditions AB were inverted. Each block was made up of 4 target words. A 4000 ms instruction display preceded trials, preceded by a fixation cross of 500 ms. The target stimuli were presented and answer given within 4500 ms, with an ITI of 100 ms separating trials. Each block lasted 24 s, totalling 6 min and 28 s for each test phase, for a total time of approximately 28 min dedicated to the task.

FMRI DATA ACQUISITION

Blood oxygenation level-dependent (BOLD) functional images [parameters: interscan repetition time (TR) = 2400ms, echo time (TE)=30ms, slice thickness = 3.20 mm, flip angle = 85°, FOV 235 mm] and high resolution three-dimensional anatomical images [TR = 2500ms, TE = 30ms, slice thickness = 1.1 mm, flip angle = 8°, 192 volumes, FOV 220 mm] were acquired using a 3 T Siemens TIM Trio system. Three scan sessions each consisting of one hundred and sixty-four volumes were acquired while subject performed the word pair task. Each volume comprised 38 slices oriented parallel to the AC-PC line and collected in a descending sequence.

FMRI DATA ANALYSIS

Data were processed and analyzed using Statistical Parametric Mapping 5, (SPM5; Wellcome Department of Neuroscience, London, UK). Functional images were first corrected for motion by realigning all images with respect to the first image acquired; re-sampling of all slices was run to match the middle slice of the entire acquisition to correct for differences in slice acquisition timing; each participant's structural image was coregistered to the mean of the realigned functional images. Grey matter separation was established by segmentation of the anatomical image. Realigned and slice timed images were then spatially normalised into the Montreal Neurological Institute template (MNI) using a 3-mm cubic voxel size and finally spatially smoothed with a 6-mm isotropic Gaussian Kernel full width half maximum (FWHM). A high pass filter of 1/128 Hz was used to remove low frequency noise, and an AR (1)+white noise model corrected for temporal autocorrelation. For each participant brain responses were estimated at each voxel using a general linear model with block regressors. The 24 sec block lengths relative to the period of appearance of the words of the context memory and baseline assignment were convolved with the canonical hemodynamic response function in the first statistical analysis. The design matrix included the realignment parameters to account for any enduring movement.

Experimental contrasts were performed to obtain subject specific estimates for each of the effects of

interest using the general linear model as implemented in SPM 5 resulting in a voxel value map of t statistics for 12 contrasts. The threshold for subject images was set at an uncorrected $p < 0.05$. These images were further smoothed (6-mm Gaussian Kernel) to conform to inter-individual brain size variability for one-sample t test group analysis.

Statistical parametric maps for each group contrast were characterized by an uncorrected height threshold of $p < 0.001$. The peak locations of local maxima cluster of contiguous voxels were localised on a mean structural scan with approximate Brodmann areas estimated from the Talairach and Tournoux (1988) atlas after having adjusted coordinates to allow for differences between the MNI and Talairach templates (www.mrc-cbu.cam.ac.uk/Imaging/Common/mninspace.shtml).

To enhance exploration differences between the controls and patients' group a region of interest (ROI) analysis was run using Marsbar (<http://marsbar.sourceforge.net/>). The ROI was obtained using an unbiased contrast-based whole-brain analysis, to insure that potential correlations between this ROI and the independently obtained schizotypy measures would not represent an artifact of ROI selection. A 6 mm radius sphere was designed around the centre of mass for each subject to extract statistical tables. A Pearson correlation was run to explore the relationship between brain activity and behavioural patterns particularly between context memory of the origin and source of the stimuli and schizotypy measures.

Results

BEHAVIOURAL RESULTS

Participants' performance for context and origin trials are reported in Table 1. Comparisons related to condition performances revealed significantly superior retrieval performances in the origin condition compared to the context condition ($t(32) = -6.12, p < 0.001$). Within the origin condition, we observed a significant difference in favour of experimenter trials ($t(32) = 6.54, p < 0.001$) in comparison to self trials. In the context condition, we observed significant difference in favour of performances on seen trials ($t(32) = 3.70, p = 0.001$) in comparison to produced trials. To investigate possible Encoding x Retrieval interactions, we performed two repeated-measure ANOVAs with post-hoc Tukey pairwise comparisons. This yielded that encoding context significantly influenced origin retrieval ($F(3,96) = 44.92, p < 0.001$; Experimenter x Context: $p = 0.009$; Self x Context: $p = 0.0001$). However, encoding origin did not significantly influence context retrieval ($F(3,96) = 10.38, p < 0.001$; Seen x Origin: $p = 0.65$; Produced x Origin: $p = 0.98$).

Origin and context condition comparisons for reaction time revealed only one significantly faster retrieval performance, suggesting faster origin retrieval compared to the context retrieval ($t(32) = -7.09, p < 0.001$). We again performed two repeated-measure ANOVAs with post-hoc Tukey pairwise comparisons to investigate possible Encoding x Retrieval interactions regarding reaction times. This yielded that encoding context significantly influenced origin reaction time but only when the origin was external ($F(3,96) = 12.57, p < 0.001$; Experimenter x Context: $p = 0.0001$; Self x Context: $p = 0.44$). Furthermore, encoding origin significantly influenced context reaction time but only for seen encoding trials ($F(3,96) = 11.93, p < 0.001$; Seen x Origin: $p = 0.0001$; Produced x Origin: $p = 0.81$).

Table 1 - Total performance accuracy on the word-pair reality monitoring task.

Conditions	Accuracy — percentage correct (s.d.)	Reaction times — milliseconds (s.d.)
Origin trials (retrieval-encoded conditions)	77.02 (9.16)	1971.2 (306.08)
Self trials	70.20 (11.79)	1938.0 (305.22)
Self-seen	57.07 (19.22)	1957.8 (327.45)
Self-produced	82.82 (9.97)	1867.9 (471.38)
Experimenter trials	83.83 (10.00)	2002.72 (343.86)
Experimenter-seen	79.29 (12.34)	2168.81 (386.3)
Experimenter-produced	88.63 (10.16)	1833.49 (367.04)
Context (retrieval-encoded conditions)	59.85 (14.40)	2279.83 (302.65)
Seen trials	69.95 (16.49)	2296.56 (332.57)
Seen-self	71.8 (14.7)	2121.40 (498.55)
Seen-experimenter	66.91 (23.6)	2401.4 (402.9)
Produced trials	49.75 (25.17)	2261.54 (345.36)
Produced-self	48.98 (28.16)	2291.48 (443.25)
Produced-experimenter	50.75 (25.54)	2237.5 (354.35)
Semantic baseline	94.25 (6.09)	1535.3 (297.49)

NEUROIMAGING RESULTS

Reality monitoring conditions versus baseline contrasts

Brain regions associated with the two types of reality monitoring task were firstly analyzed by contrasting activation maps of each condition against the semantic baseline (Table 2a). Large areas of bilateral anterior prefrontal cortex (PFC), dorsolateral PFC, middle temporal gyrus (MTG) and lateral parietal cortices were activated commonly during both conditions. Some differential areas of activation were also observed. When contrasting the Origin (Self/ Experimenter) condition against the Semantic baseline, the peak activation [$p < 0.001$ (unc.)] was registered bilaterally around the superior parietal lobe, cuneus followed by the engagement of the right middle frontal gyrus and medial frontal regions. When contrasting the activations maps for Context condition (Seen/Produced) against the semantic baseline, activity [$p < 0.001$ (unc.)] peaked around the right middle frontal gyrus and parietal areas and precuneus (Tables 2b, 2c, and 2d; Fig. 2).

Table 2a - Cerebral regions showing greater activation during retrieval of Seen/Produced stimuli than semantic baseline condition. Coordinates are in MNI atlas space (Cocosco et al., 1997), and brain regions estimated from the Talairach and Tournoux (1988) atlas after normalization.

Anatomical label	Hemi	BA	MNI (x, y, z)	t (value)
Middle frontal gyrus	L	6	-36, 3, 57	12.39
	L	46	-45,18, 27	10.05
	L	9	-51, 24, 30	9.46
	R	9	48, 27, 36	9.69
Middle frontal gyrus	L	10	-36, 54, 6	7.70
Middle temporal gyrus	L	21	57, -39, -9	6.98
	L	22	-54, -42, 0	6.04
Medial frontal gyrus	L	8	0, 21,48	9.61
	R	6	3,27,39	9.23
Anterior cingulated	R	32	12, 36, 21	5.85
Superior parietal lobule	R	7	36, -66, 54	12.36
Inferior parietal lobule	R	40	45, -54, 54	11.40
Precuneus	L	7	-6, -66, 36	10.95
Insula	R		33, 24, -6	10.79
Superior frontal gyrus	R	8	39, 6, 54	9.77

COMPARING ORIGIN AND CONTEXT MONITORING AND THEIR LINKS TO SCHIZOTYPAL TRAIT EXPRESSION

When contrasting the two reality monitoring conditions that represent origin and context monitoring, significant differences were observed around the postcentral gyrus and in medial frontal gyrus in the Self/Experimenter > Seen/Produced contrast (Fig. 3), showing increased activity in the left medial PFC (BA10 centred on -6, 69, 3; $t = 3.58$, $p < 0.001$). When Seen/Produced condition was contrasted against Self/Experimenter differences were underlined around the middle temporal gyrus and superior temporal regions.

To explore the interaction between the medial PFC activation and schizotypal trait expression, we performed a post-hoc correlation analysis between the participants' total SPQ score and signal change around the peak activation observed in the Self/Experimenter > Seen/Produced contrast. A 6 mm radius sphere was implemented around the coordinates of cluster of interest ($x = -6$, $y = 69$, $z = 3$). Signal change during recollection of origin information was extracted on a subject by subject basis. The correlation analysis between signal change in the cluster of interest and total SPQ score revealed a significant correlation ($r = 0.329$, $p < 0.001$) (Fig. 5).

Table 2b- Cerebral regions showing greater activation during retrieval of Self/Experimenter stimuli compared to semantic baseline condition. Coordinates are in MNI atlas space (Cocosco et al., 1997), and brain regions estimated from the Talairach and Tournoux (1988) atlas after normalization (Talairach and Tournoux, 1988).

Anatomical label	Hemi	BA	MNI (x, y, z)	t (value)
Superior parietal lobule	R	7	36, -63, 54	12.99
Cuneus	L	7	-6, -69, 36	10.23
Inferior parietal lobule	L	40	-36, -51, 42	9.95
Precuneus	R	7	6, -69, 39	9.42
Middle frontal gyrus	R	9	45, 27, 33	9.98
	L	46	-42, 21, 27	8.02
	L	6	-36, 6, 57	9.11
	L	6	-35, 3, 39	7.94
	L	8	-6, 18, 48	7.51
	R	10	36, 60, 3	4.94
	R	11	27, 45, -9	4.48
Precentral gyrus	R	10	21, 66, -3	3.53
	R	9	39, 12, 42	8.09
	R	8	36, 15, 54	5.71
Superior frontal gyrus	R	8	36, 15, 54	5.71
Medial frontal gyrus	L	8	-6, 18, 48	7.51
	R	8	6, 24, 48	6.29
Insula	R		33, 24, -6	7.11
Middle temporal gyrus	L	22	-54, -33, 0	5.83
	L	21	-53, -33, -9	4.92
	R	21	69, -33, -9	5.32
Fusiform gyrus	L	18	-21, -87, -18	5.51
Middle occipital gyrus	R	18	27, -84, -3	5.60

Significant correlations were found with the discrete dimensions evaluated by the SPQ, positive symptoms sub scale ($r = 0.283$, $p = 0.001$), negative symptoms subscale ($p = 0.001$, $r = 0.308$) and disorganized dimension ($r = 0.263$, $p = 0.002$).

To ensure that medial PFC activation was not a product of task performance (accuracy and reaction time) or age, we ran Pearson correlations between extracted medial PFC signal change values and both accuracy percentage and reaction times on origin trials across participants. Results did not show any

significant associations with accuracy scores ($r = 0.002$, $p = 0.798$), reaction time ($r = 0.009$, $p = 0.605$), or age at participation ($r = 0.05$, $p = 0.199$). The analyses reveal no correlation between the ROI signal change and the other two conditions (Context condition $r = -0.231$, $p = 0.246$; Control condition $r = -0.220$, $p = 0.270$). The results were not due to variability at an individual level; calculating signal change error scores for each participant (% of signal change for origin > context) and corresponding individual behavioural error score (% of origin accuracy > context accuracy) lead to a non-significant correlation between these two scores ($r = -0.002$, $p = 0.827$).

Table 2c - Cerebral regions showing greater activation during retrieval of Seen/Produced compared to Self/Experimenter condition. Coordinates are in MNI atlas space (Cocosco et al., 1997), and brain regions estimated from the Talairach and Tournoux (1988) atlas after normalization.

Anatomical label	Hemi	BA	MNI (x, y, z)	t (value)
Pyramis	L		-9, -87, -33	4.31
Middle temporal gyrus	L	21	69, -33, -1	4.20
	R	46	54, 33, 27	3.91
	R	9	51, 21, 30	3.64
Superior frontal gyrus	R	8	36, 21, 21	4.02
Cingulate	L	32	-12, 21, 33	3.37
Medial frontal gyrus	R	9	6, 36, 33	4.01

Table 2d - Cerebral regions showing greater activation during retrieval of Self/Experimenter condition compared to Seen/Produced condition. Coordinates are in MNI atlas space (Cocosco et al., 1997), and brain regions estimated from the Talairach and Tournoux (1988) atlas after normalization.

Anatomical label	Hemi	BA	MNI (x, y, z)	t (value)
Postcentral gyrus	R	3	15, -42, 72	4.61
Medial frontal gyrus	R	6	9, -30, 69	4.14
	L	6	-12, -33, 63	3.72
	L	6	-12, -24, 54	3.58
	L	10	-6, 69, 3	3.61
Insula	R	13	27, -30, 18	4.22
	L	13	-36, 15, 15	3.48
Cingulate gyrus	L	24	-9, 0, 48	3.81
Middle frontal gyrus	L	11	-33, 45, -9	3.58

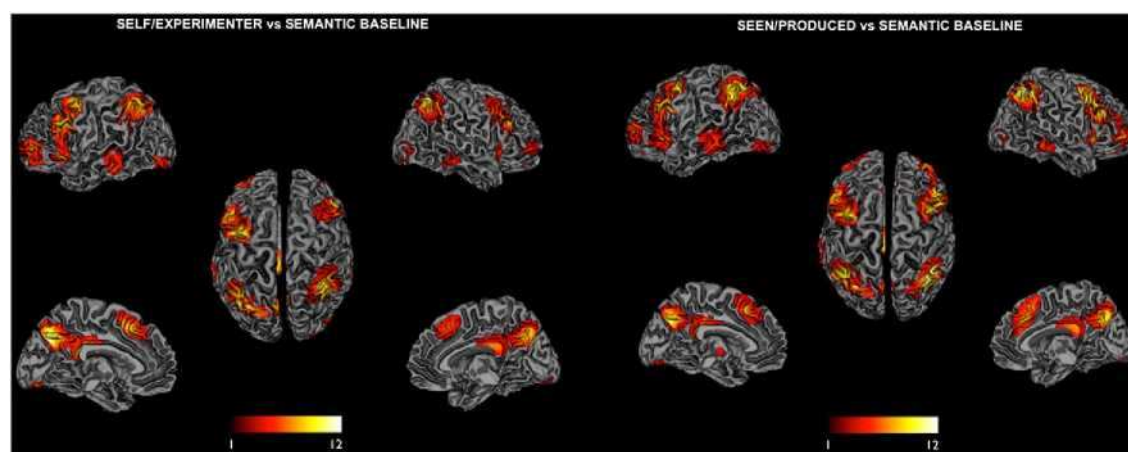
Finally, in order to ensure that our main findings concerning the specificity of BA 10 activation for origin trials and its significant relationship to adolescent schizotypal trait expression were not driven by poor behavioural performances in the context condition, we eliminated the subjects with a context ($n = 7$) or origin ($n = 0$) total accuracy score below 50%. Performing our contrast of interest on the reduced sample

($n = 26$) showed that our cluster of interest in BA 10 remained significant (BA10 centred on $-6, 69, 3$; $t = 2.61$, $p < 0.005$ unc.). Furthermore, the correlation between signal change and total SPQ score remained strongly significant ($r = 0.302$, $p = 0.004$). These additional analyses provide important support to the reliability of the present results (Fig. 4).

Discussion

Results from the fMRI reality monitoring paradigm administered to a sample of adolescents provide support to the hypotheses tested in this study. First, we observed that different reality monitoring processes, namely origin and context monitoring, largely share underlying neural activation patterns including the anterior prefrontal cortex (PFC), the dorsolateral PFC, the MTG, the posterior cingulate gyrus and both medial and lateral regions in the parietal cortex. Second, we observed that adolescents exhibit significantly more activity in left medial BA 10 during retrieval of self/experimenter information compared to retrieval of contextual information. Finally, we found that schizotypal trait expression during adolescence is negatively associated with left BA 10 engagement during self/experimenter trials. We will first briefly discuss the behavioural results and how they may inform us about reality monitoring skills during adolescence. Second, we will focus on the implications of these results for understanding the functional specialization of the PFC during adolescence with regard to previous studies performed with adults. Finally, we shall discuss the specific results relating left BA 10 activation to the expression of schizotypal traits during the adolescent developmental period.

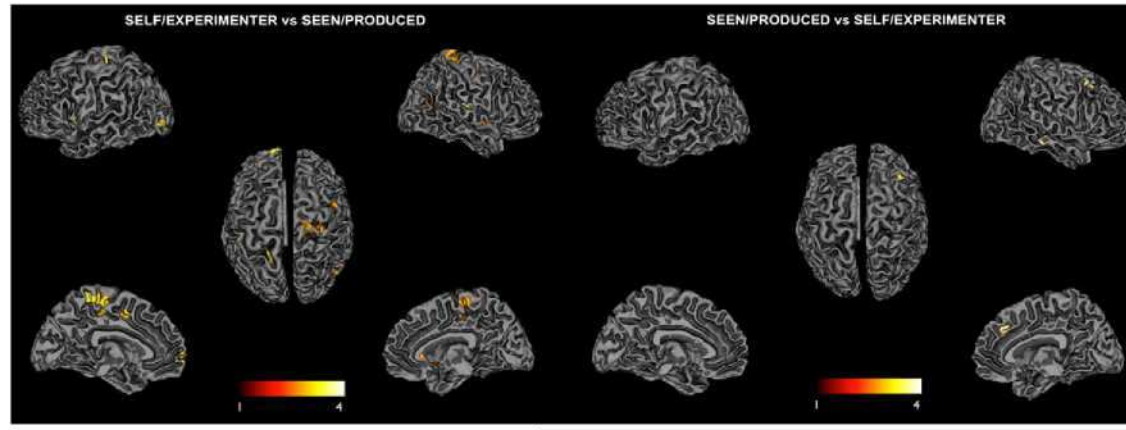
Figure 2. Activation regions during retrieval of Origin > Semantic Baseline stimuli (left); Activation regions during retrieval of Context > Semantic Baseline stimuli (right).



Performance on our reality monitoring paradigm suggested that adolescents find retrieving the origin of an event (self or experimenter) to be an easier task compared to retrieving its contextual characteristics (was the event seen or produced). This observation is consistent with [Foley et al.'s \(1983\)](#) seminal study on children's memory for speech and thought. In that study, the authors conducted a series of experiments highlighting that the ability to discriminate between one's own speech and another person's speech is developmentally mature as early as age 6, while the ability to distinguish between what one said and what one only thought undergoes further elaboration during development. Therefore, different developmental courses may underlie the monitoring of contextual cues (seen versus produced), which seem to yield a maturational advantage for distinguishing origin information

(self versus not self), as observed in our study. Consistent with this view, young adults past the stage of adolescence (aged 19-36 years) undergoing the same fMRI paradigm showed less of a discrepancy (0.87 versus 0.8) between the two reality monitoring conditions (Simons et al., 2008).

Figure 3. Activation regions during retrieval of Origin > Context stimuli (left); Activation regions during retrieval of Context > Origin stimuli (right).

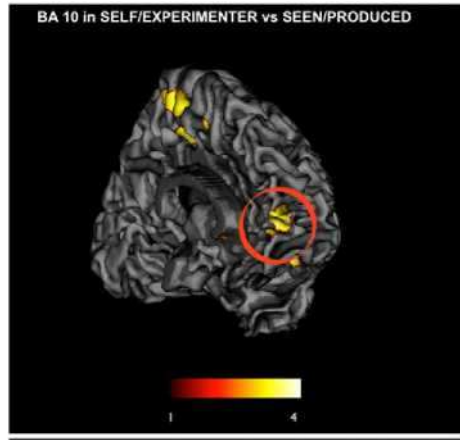


Additional studies employing a longitudinal design will help identify the progressive reinforcement of context monitoring abilities along with their potential relationships with the cortical maturation that characterizes the adolescent developmental period (Shaw et al., 2008). As an aside, it is worth noting that the differential task performance exhibited by our adolescent sample is unlikely to be a sufficient explanation for the neuroimaging results obtained, as no significant correlations were observed between anterior PFC signal and behavioural measures.

When examining the cerebral activity sustaining reality monitoring in our adolescent sample, we find strikingly similar activity patterns as those found in adult participants performing the same task (Simons et al., 2008). As with adults, we can witness a pattern of overlapping cerebral activity between origin and context monitoring. Moreover, contrasting origin with context monitoring reveals a comparable functional specialization within the anterior prefrontal cortex in adolescents, bringing confirmatory evidence that increased BA 10 activity is specifically related to origin monitoring. These observations suggest that the cerebral networks sustaining reality monitoring processes are already in place during adolescence. The lack of correlation between local specializations of BA 10 with age may appear surprising, given the important maturational processes targeting the prefrontal cortex during adolescence (Shaw et al., 2008). One possible explanation could be that while the functional components of reality monitoring already resemble those observed in adulthood, their specialization and efficiency may still be maximised through further maturation during adolescence and into adulthood, as suggested by additional regions of cerebral activation in adolescent origin monitoring, as well as poor adolescent behavioural context monitoring performances. Future analyses examining functional connectivity linking the anterior prefrontal cortex to other cortical areas may help uncover the more refined maturation of reality monitoring processes through adolescent development.

With respect to our final hypothesis, we observe a significant relationship linking reduced BA 10 signal change to the adolescents' reported schizotypal trait expression. The results can be interpreted from two main theoretical perspectives, namely the source monitoring framework (SMF; (Johnson et al., 1993)) and the gateway hypothesis (Burgess et al., 2007).

Figure 4. Medial view of signal change in left BA 10 for the Origin > Context contrast ($x = -6y = 69z = 3$).

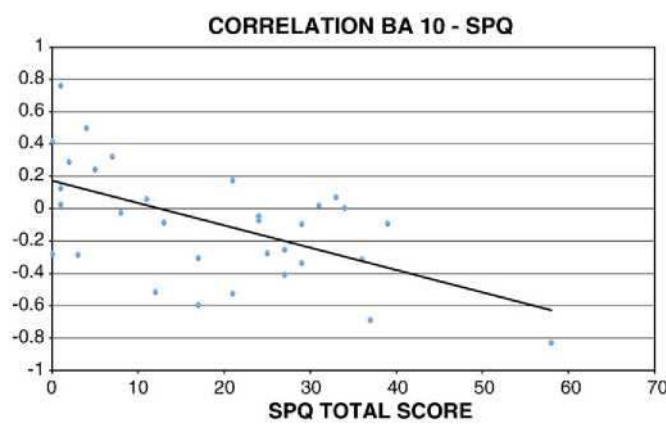


The SMF suggests that one performs source judgments of self-generated material based on the available information associated to the self-relevant mental events. This information may primarily consist in perceptually based information (contextual details associated to the event) or reflectively based information (cognitive operations performed on mental content); the first type of information will more likely lead to evaluating the mental event as coming from an external source, while the latter will more likely be perceived as originating from an internal source. In a recent update of the SMF integrating the latest neuroimaging findings relevant to source monitoring, specific activation of BA 10 is thought to be involved in the evaluation of internally-generated information, as well as the active retrieval and selection of pertinent information (Mitchell and Johnson, 2009). Our interpretation may further be informed by our behavioural results, which suggest that produced information increases the likelihood of retrieval success during self-experimenter trials. We may point out that wordpairs produced by adolescents contain both internally (private cognitive operations linked to the production of the wordpair) and externally based information (one's externally voiced response), whereas self-seen wordpairs involve the voiced response while lacking the richness of cognitive operations linked to wordpair production. Given the increased performances for self-produced in comparison to self-seen trials, we may conjecture that evaluating internal self-generated information during origin trial appears critical to successful performances. This would be consistent with the SMF account of BA 10 activity as specifically sensitive to the evaluation of internally-generated information. In turn we may suggest that adolescent failing to evaluate internally self-generated information would also tend to express more important levels of schizotypy. This interpretation would be consistent with the accumulated evidence showing impaired recalling self-generated information in psychosis-prone and schizophrenic adults (Brunelin et al., 2007; Laroï et al., 2005).

Concurrently, the gateway hypothesis may lead us to consider that a failure to evaluate internally-generated information might be further supported by inefficient modulation of attending to

perceptually versus reflectively based information.

Figure 5. Correlation between signal change extracted from the cluster of interest within the medial PFC (BA 10) during retrieval of self/experimenter trials and total SPQ score ($r = 0.329$, $p < 0.001$).



Activation of more anterior part of the medial prefrontal cortex has been associated with attending to perceptual details (Gilbert et al., 2007) and memory for task (Simons et al., 2005), nearby the BA 10 coordinates that we found discriminated the origin from the context monitoring conditions in our adolescent sample ($x = -6$, $y = 69$, $z = 3$). This suggests that the modulation of attention to externally versus internally generated information during the origin monitoring trials also recruits BA 10 activity during adolescence. Furthermore, the expression of schizotypal traits would also be promoted by inefficient regulation of the gateway managing attention between externally and internally derived information. This view is consistent with several accounts describing psychotic-like symptoms as self-generated mental events attributed to an external source (Bentall et al., 1991; Frith and Done, 1989). Characteristically, auditory hallucinations constitute internally generated mental events whose origin is experienced as greatly questionable, and whose reflective basis can be misinterpreted as perceptual. More nuanced occurrences infiltrate reflective mechanisms such as alien thought control, which again entails a confusion between mental content originating from within but experienced as under the control of an external agent. Interestingly, the cognitive processes described above may promote the expression of schizotypal trait expression through adolescent development. Future studies should examine the developmental antecedents of both reality monitoring and the attentional gateway to gain further insight into the unfolding of psychotic-like phenomena.

Together, these results point to the relevance of reality monitoring mechanisms during adolescence, and their possible implication in personality trait expression such as schizotypy. They further lend cross-sectional developmental evidence to contemporary cognitive accounts implicating self-monitoring deficits in psychotic-like experiences (Frith, 1992). They further suggest that inconsistencies in origin monitoring may constitute discrete cognitive alterations that contribute to individual differences in schizotypal trait expression. Origin monitoring processes could be further examined in high affect situations, which are known to be conducive to maintenance and exacerbation of early schizotypal cognitions (Escher, 2004; Escher et al., 2002). Finally, future investigations may examine whether origin monitoring processes could represent a primary prevention target in youths at high-risk for the unfolding of psychotic disorders.

Acknowledgments

The authors would like to thank the volunteer participants, as well as Drs Dario Balanzin and Serges Djapo-Yogwa for their collaboration. Additional thanks go to the CIBM/LAVIM neuroimaging platform, especially to François Lazeyras, Pascal Challande and Frank Henry. We would also like to acknowledge Michal Epstein and Deborah Badoud for their contributions to data collection. This work was funded by the Gertrude Von Meissner Foundation (ME 7871) grant to S. Eliez and M. Debbané, and by the Swiss National Fund (PP00B-102864) grant to S. Eliez.

References

- Achenbach, T.M., Rescorla, L.A., 2003. *Manual for the aseba adult forms and profiles*. University of Vermont, Research Center for Children, Youth, and Families, Burlington.
- Badoud D., ChanaJ., Eliez S., Van Der Linden M., and Debbané M. (in press). Validation study of the french schizotypal personality questionnaire in an sample of adolescents; a confirmatory factor analysis. *L'Encéphale*.
- Bentall, R.P., Baker, G.A., Havers, S., 1991. Reality monitoring and psychotic hallucinations. *Br.J. Clin. Psychol.* 30 (Pt 3), 213-222.
- Bentall, R.P., Fernyhough, C., Morrison, A.P., Lewis, S., Corcoran, R., 2007. Prospects for a cognitive-developmental account of psychotic experiences. *Br. J. Clin. Psychol.* 46 (Pt 2), 155-173.
- Brunelin, J., d'Amato, T., Brun, P., Bediou, B., Kallel, L., Senn, M., et al., 2007. Impaired verbal source monitoring in schizophrenia: an intermediate trait vulnerability marker? *Schizophr. Res.* 89 (1-3), 287-292.
- Burgess, P.W., Dumontheil, I., Gilbert, S.J., 2007. The gateway hypothesis of rostral prefrontal cortex (area 10) function. *Trends Cogn. Sci.* 11 (7), 290-298.
- Casey, B.J., Jones, R.M., Hare, T.A., 2008. The adolescent brain. *Ann. NY Acad. Sci.* 1124, 111-126.
- Cocosco, C.A., Kollokian, V., Kwan, R.K.S., Evans, A.C., 1997. Brainweb: online interface to a 3D mri simulated brain database. *Neuroimage* 5, 425.
- Debbané, M., Van der Linden, M., Gex-Fabry, M., Eliez, S., 2009a. Cognitive and emotional associations to positive schizotypy during adolescence. *J. Child Psychol. Psychiatry* 50 (3), 326-334.
- Debbané, M., Van der Linden, M., Glaser, B., Eliez, S., 2009b. Monitoring of self-generated speech in adolescents with 22q11.2 deletion syndrome. *Br. J. Clin. Psychol.* 49 (3), 373-386.
- Dumas, P., Bouafia, S., Gutknecht, C., Saoud, M., Dalery, J., d'Amato, T., 2000. validation of the french version of the raine schizotypal personality disorder questionnaire— categorial and dimensional approach to schizotypal personality traits in a normal student population. *Encephale* 26 (5), 23-29.
- Escher, S., 2004. Determinants of outcome in the pathways through care for children hearing voices. *Int. J. Soc. Welf.* 13 (208-222).
- Escher, S., Romme, M., Buiks, A., Delespaul, P., Van Os, J., 2002. Independent course of childhood auditory hallucinations: a sequential 3-year follow-up study. *Br. J. Psychiatry Suppl.* 43, s10-s18.
- Foley, M.A., Johnson, M.K., Raye, C.L., 1983. Age-related changes in confusion between memories for thoughts and memories for speech. *Child Dev.* 54 (1), 51-60.
- Frith, C.D., 1992. *The Cognitive Neuropsychology of Schizophrenia*. Psychology Press Ltd., Hove.
- Frith, C.D., Done, D.J., 1989. Experiences of alien control in schizophrenia reflect a disorder in the central monitoring of action. *Psychol. Med.* 19 (2), 359-363.

Gilbert, S.J., Frith, C.D., Burgess, P.W., 2005. Involvement of rostral prefrontal cortex in selection between stimulus-oriented and stimulus-independent thought. *Eur. J. Neurosci.* 21 (5), 1423-1431.

Gilbert, S.J., Spengler, S., Simons, J.S., Steele, J.D., Lawrie, S.M., Frith, C.D., et al., 2006. Functional specialization within rostral prefrontal cortex (area 10): a metaanalysis. *J. Cogn. Neurosci.* 18 (6), 932-948.

Gilbert, S.J., Williamson, I.D., Dumontheil, I., Simons, J.S., Frith, C.D., Burgess, P.W., 2007. Distinct regions of medial rostral prefrontal cortex supporting social and nonsocial functions. *Soc. Cogn. Affect. Neurosci.* 2 (3), 217-226.

Gilbert, S.J., Henson, R.N., Simons, J.S., 2010. The scale of functional specialization within human prefrontal cortex. *J. Neurosci.* 30 (4), 1233-1237.

Johnson, M.K., Raye, C.L., 1981. Reality monitoring. *Psychol. Rev.* 88, 67-85.

Johnson, M.K., Hashtroudi, S., Lindsay, D.S., 1993. Source monitoring. *Psychol. Bull.* 114 (1), 3-28.

Keefe, R.S., Arnold, M.C., Bayen, U.J., McEvoy, J.P., Wilson, W.H., 2002. Source monitoring deficits for self-generated stimuli in schizophrenia: multinomial modeling of data from three sources. *Schizophr. Res.* 57 (1), 51-67.

Laroi, F., Van der Linden, M., Marczewski, P., 2004. The effects of emotional salience, cognitive effort and meta-cognitive beliefs on a reality monitoring task in hallucination-prone subjects. *Br.J. Clin. Psychol.* 43 (Pt 3), 221-233.

Laroi, F., Collignon, O., Van der Linden, M., 2005. Source monitoring for actions in hallucination proneness. *Cogn. Neuropsychiatry* 10 (2), 105-123.

Miller, P., Byrne, M., Hodges, A., Lawrie, S.M., Owens, D.G., Johnstone, E.C., 2002. Schizotypal components in people at high risk of developing schizophrenia: Early findings from the Edinburgh high-risk study. *Br. J. Psychiatry* 180, 179-184.

Mitchell, K.J., Johnson, M.K., 2009. Source monitoring 15years later: what have we learned from fmri about the neural mechanisms of source memory? *Psychol. Bull.* 135 (4), 638-677.

Poulton, R., Caspi, A., Moffitt, T.E., Cannon, M., Murray, R., Harrington, H., 2000. Children's self-reported psychotic symptoms and adult schizophreniform disorder: a 15-year longitudinal study. *Arch. Gen. Psychiatry* 57 (11), 1053-1058.

Raine, A., 1991. The SPQ: a scale for the assessment of schizotypal personality based on DSM-III-R criteria. *Schizophr. Bull.* 17 (4), 555-564.

Rossi, A., Daneluzzo, E., 2002. Schizotypal dimensions in normals and schizophrenic patients: a comparison with other clinical samples. *Schizophr. Res.* 54 (1-2), 67-75.

Shaw, P., Kabani, N.J., Lerch, J.P., Eckstrand, K., Lenroot, R., Gogtay, N., et al., 2008. Neurodevelopmental trajectories of the human cerebral cortex. *J. Neurosci.* 28(14), 3586-3594.

Simons, J.S., Gilbert, S.J., Owen, A.M., Fletcher, P.C., Burgess, P.W., 2005. Distinct roles for lateral and medial anterior prefrontal cortex in contextual recollection. *J. Neurophysiol.* 94 (1), 813-820.

Simons, J.S., Davis, S.W., Gilbert, S.J., Frith, C.D., Burgess, P.W., 2006a. Discriminating imagined from perceived information engages brain areas implicated in schizophrenia. *Neuroimage* 32 (2), 696-703.

Simons, J.S., Scholvinck, M.L., Gilbert, S.J., Frith, C.D., Burgess, P.W., 2006b. Differential components of prospective memory? Evidence from fmri. *Neuropsychologia* 44 (8), 1388-1397.

Simons, J.S., Henson, R.N., Gilbert, S.J., Fletcher, P.C., 2008. Separable forms of reality monitoring supported by anterior prefrontal cortex. *J. Cogn. Neurosci.* 20 (3), 447-457.

Talairach, J., Tournoux, P., 1988. *Co-Planar Stereotaxic Atlas of the Human Brain*. Georg Thieme Verlag, Stuttgart, New York.

Vinogradov, S., Willis-Shore, J., Poole, J.H., Marten, E., Ober, B.A., Shenaut, G.K., 1997. Clinical and neurocognitive aspects of source monitoring errors in schizophrenia. *Am. J. Psychiatry* 154 (11), 1530-1537.