Published in final edited form as:

Schizophr Res. 2016 January ; 170(1): 123–129. doi:10.1016/j.schres.2015.11.013.

Alterations of lateral temporal cortical gray matter and facial memory as vulnerability indicators for schizophrenia: an MRI study in youth at familial high-risk for schizophrenia

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Abstract

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Contributors

Dr. Brent generated the current study hypotheses, conducted the statistical analyses/literature review, and wrote the first draft of the manuscript. Dr. Rosso performed the majority of the lateral temporal cortical segmentations and carried out preliminary analyses of the structural data. Dr. Thermenos contributed to the acquisition of the structural data and worked on a draft of the paper. Dr. Holt contributed to the data interpretation and the initial manuscript draft. Dr. Makris supervised all structural MRI measurements and contributed to the conceptual model of structural brain measurement and to the writing up of the MRI structural imaging sections. Drs. Faraone, Tsuang, and Seidman designed the overarching study and protocol, received funding, and contributed to the drafts of the manuscript. Dr Seidman supervised the neuropsychological data collection.

Conflict of Interest

The authors have no conflicts of interest to declare.

Background—Structural alterations of the lateral temporal cortex (LTC) in association with memory impairments have been reported in schizophrenia. This study investigated whether alterations of LTC structure were linked with impaired facial and/or verbal memory in young first-degree relatives of people with schizophrenia and, thus, may be indicators of vulnerability to the illness.

Methods—Subjects included 27 non-psychotic, first-degree relatives of schizophrenia patients, and 48 healthy controls, between the ages of 13 and 28. Participants underwent high-resolution magnetic resonance imaging (MRI) at 1.5 Tesla. The LTC was parcellated into superior temporal gyrus, middle temporal gyrus, inferior temporal gyrus, and temporal pole. Total cerebral and LTC volumes were measured using semi-automated morphometry. The Wechsler Memory Scale – Third Edition and the Children’s Memory Scale – Third Edition assessed facial and verbal memory. General linear models tested for associations among LTC subregion volumes, familial risk and memory.

Results—Compared with controls, relatives had significantly smaller bilateral middle temporal gyri. Moreover, right middle temporal gyral volume showed a significant positive association with delayed facial memory in relatives.

Conclusion—These results support the hypothesis that smaller middle temporal gyri are related to the genetic liability to schizophrenia and may be linked with reduced facial memory in persons at genetic risk for the illness. The findings add to the growing evidence that children at risk for schizophrenia on the basis of positive family history have cortical and subcortical structural brain abnormalities well before psychotic illness occurs.

Keywords

Schizophrenia; Familial High-Risk; Lateral Temporal Cortex; Facial Memory

1. Introduction

Alterations of the structures comprising the lateral temporal cortex (LTC) are commonly reported in structural MRI (sMRI) studies of schizophrenia (Shepherd et al., 2012). This includes, most typically, gray matter (GM) abnormalities of the superior temporal gyrus (STG) (Shenton et al., 2001), but it also involves less often studied LTC structures, such as: middle temporal gyrus (MTG) (Kuroki et al., 2006; Onitsuka et al., 2004; Tang et al., 2012), inferior temporal gyrus (ITG) (Kuroki et al., 2006; Onitsuka et al., 2004), and the temporal pole (TP) (Herold et al., 2009; Kasai et al., 2003). Abnormalities of LTC structure are also found in young first-degree relatives of patients (mean age < 30), who are at familial high-risk (FHR) for schizophrenia but are without a history of psychosis and, usually, medication naïve. Findings in FHR youth include: decreased STG and ITG GM density (Job et al., 2005), as well as smaller temporal pole GM volume ((Bhojraj et al., 2011); for comprehensive reviews see: (Brent et al., 2013; Thermenos et al., 2013). FHR studies of young, non-psychotic relatives, who on average share approximately 50% of genes with their affected family member and carry a 10-fold increased risk of developing schizophrenia, allow for the identification of neural markers of schizophrenia risk associated with early development. FHR studies, therefore, can be particularly valuable in shedding light on

pathophysiological processes preceding psychosis onset (Seidman et al., 2003; Thermenos et al., 2013). In prior studies, we have shown that Harvard Adolescent FHR youth have smaller medial prefrontal cortical (Rosso et al., 2010) and medial temporal lobe (Seidman et al., 2014) GM volumes compared with controls. Here, we extend these findings to an examination of LTC structure.

Research on altered LTC structure in schizophrenia has focused most often on the STG (Shenton et al., 2001). Given its well-established role in language perception and production (Price, 2010), it is thought that STG structural abnormalities may contribute to impaired integration of language and memory processes (Stephan et al., 2009) that could underlie positive symptoms in schizophrenia (e.g., auditory hallucinations and thought disorder) – a hypothesis supported by recent meta-analyses (Palaniyappan et al., 2012a; Palaniyappan et al., 2012b). Less well studied, however, is a possible additional link between LTC structural changes and memory deficits in schizophrenia.

A variety of evidence has shown that the LTC plays a key role in memory processes (Ojemann et al., 2002). For example, electrical stimulus mapping (Fedio, 1980; Fried et al., 1982) and microelectrode recording (Lucas et al., 2003) studies have shown that the STG and MTG form part of the neural substrate mediating facial memory. Additionally, extracellular recordings of neural activity during awake neurosurgery in humans have demonstrated wide-spread LTC activation during verbal memory tasks (Haglund et al., 1994; Ojemann and Schoenfield-McNeill, 1998; Weber and Ojemann, 1995). Verbal and non-verbal memory deficits are well-documented in schizophrenia (Heinrichs and Zakzanis, 1998) and have been linked to the social dysfunction (Fett et al., 2011; Milev et al., 2005) and symptomatology (particularly negative symptoms) (Dominguez et al., 2011) associated with the disorder. Further, verbal and non-verbal memory deficits have been repeatedly found in youth at risk for schizophrenia (Agnew-Blais and Seidman, 2013). Thus, one possibility is that early LTC alterations, and associated abnormalities of non-verbal (e.g., facial) and/or verbal memory, could represent a vulnerability indicator for schizophrenia.

In schizophrenia, smaller MTG GM volumes in schizophrenia patients have been associated with poorer facial memory (Johnston et al., 2005). Additionally, reduced STG GM volume in schizophrenia has been correlated with poorer semantic retrieval (Ragland et al., 2008) and verbal memory (Nestor et al., 1993). No studies, however, have yet examined the relationship between alterations of LTC structure and memory processes in FHR youth.

Here, we tested two hypotheses in a manually-traced, regions-of-interest (ROI)-based morphometry study of LTC subregions in young FHR individuals compared with controls: 1) FHR youth would show significantly smaller GM volumes of LTC structures compared with controls; and, 2) reduced LTC GM volume in FHR youth would be associated with significantly poorer memory function. Correlations between LTC GM volumes, other cognitive domains, and symptoms were also explored.

2. Methods

2.1 Subjects

Participants included 27 FHR children of people with schizophrenia or schizoaffective disorder, depressed type and 48 healthy subjects with no family history of psychosis, ages 13 to 28. Diagnoses of affected family members were confirmed using the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID; (First et al., 2002)). FHR participants (first-degree, biological relatives of probands) were recruited as part of the Harvard Adolescent Family High Risk Study (Glatt et al., 2006; Seidman et al., 2006) and had no history of taking antipsychotic medication and no lifetime history of schizophrenia, or other Axis I psychotic disorder based on the Washington University Kiddie Schedule for Affective Disorders and Schizophrenia (Geller et al., 1996). Controls were recruited via advertisement and had no first-degree biological relatives with a history of psychotic disorders as determined by screening with the Diagnostic and Family Interviews for Genetic Studies (Maxwell, 1996; Nurnberger et al., 1994). Subjects with any lifetime history of psychotic illness, substance dependence, serious medical illness or head injury with subsequent cognitive impairment, sensory impairments, current psychotropic medication use, IQ < 70, or contraindications of MRI scanning (e.g., claustrophobia, or metal implants) were excluded. The study was approved by human research committees at the Massachusetts Mental Health Center, Massachusetts General Hospital (MGH), and Harvard University. After probands gave consent, their children (or parents for minors) (ages 13–25) were contacted to participate. Subjects 18 years and older gave written informed consent. For subjects younger than 18, legal guardians gave informed consent and the child gave assent. In prior publications, we have reported results related to prefrontal (Rosso et al., 2010) and hippocampal (Seidman et al., 2014) volumes in the same sample of subjects; FHR subjects showed smaller bilateral ventromedial prefrontal and frontal pole (Rosso et al., 2010) and left hippocampal (Seidman et al., 2014) GM volumes compared with controls. LTC volumes, however, have not been previously reported from this study.

2.2 Memory Assessments

Wechsler Memory Scale III (WMS-III)—The WMS-III (Wechsler, 1997b) is a widely used battery of tests for the assessment of memory processes. In the Faces subtest, participants initially are shown photographs of 48 faces (24 target faces and 24 distractors) and are told to remember the target faces. After a 30-minute delay, subjects are shown 48 faces one at a time, and they are asked to respond “yes” or “no” if they remember each face from the initial presentation. The Logical Memory subtest is a test of verbal memory. During the test, subjects are read brief stories (only a few sentences in duration) and are then asked to recall as many details about the stories as they can. Following a delay (approximately 30 minutes), participants are again asked to recall each story, but without any prompting or having the stories re-read to them. Here, the Faces and Logical Memory subscales were administered to participants age 17 to test facial and verbal memory.

Children's Memory Scale (CMS)—The CMS (Cohen, 1997) is a widely used test of memory for children ages 5–16 designed to be substantially comparable to the WMS-III in many respects, and was administered to participants ages 13–16 in this study. It was selected

because the tasks are similar to those in the WMS-III, but designed for younger children. In the Faces subtest, subjects are shown a series of faces one at a time. To test immediate facial recall, another series of faces is immediately presented and participants are asked to respond “yes” or “no” if they recall each face from the initial series. After 30 minutes, to test delayed facial memory, participants again view a series of faces one at a time and are asked to respond “yes” or “no” if they recall each face from the initial list. In the Stories subtest of verbal memory, subjects first hear two stories read out loud and are asked to repeat each story immediately after it has been told (immediate verbal recall). After 30 minutes, participants are then asked to retell each story from memory, without prompts (delayed verbal recall).

2.3 MRI Methods

2.3.1 MRI Data Acquisition—Whole brain high-resolution MR images were collected on a Siemens 1.5 Tesla scanner at the MGH Martinos Center. Two sagittal 3D MP-RAGE sequences were used for morphometric analyses (TR/TE/T1/flip = 2.73s/3.39ms/1.0s/7, bandwidth = 190 Hz/pixel, sampling matrix = 256×192 pixels, FOV = 256×256 mm, effective slice thickness = 1.33 mm on a 170 mm slab of 128 partitions). Images were coded for blind image analysis and transferred to the MGH Center for Morphometric Analysis (CMA) using Cardviews software.

2.3.2 Positional normalization and gray and white matter segmentation—To decrease variability owing to head position differences, all brain images were positionally normalized using a standard 3-dimensional coordinate system that uses the midpoints of the anterior commissure and posterior commissure, and the interhemispheric fissure at the level of the posterior commissure in the coronal plane (Filipek et al., 1994). The cerebrum was then segmented into gray/white matter on coronal images with Cardviews software using a semi-automated intensity contour algorithm for external border definition and signal intensity histogram distributions for delineation of gray-white borders.

2.3.3 Cortical parcellation—The neocortex was manually divided into 48 parcellation units (PUs) per hemisphere (Caviness et al., 1996; Rademacher et al., 1992). This comprehensive parcellation system approximates architectonic and functional subdivisions and is based on specific anatomical landmarks present in all brains (Rademacher et al., 1992). The second author (IMR) carried out the parcellations of 60 of the 75 subjects and achieved excellent inter-rater reliability (ICCs = .90) with a technician with extensive prior training who parcellated the remaining 15 brains (Rosso et al., 2010). Volumes were calculated for each PU by multiplying the area of each PU by slice thickness, followed by summing across all slices containing the PU. The four LTC ROIs are shown in Figure 1. All morphometric analyses were performed blind to subject and group information.

2.4 Statistical analyses

Statistical analyses used relative volumes (absolute volume/total cerebral volume *100) of LTC ROIs to control for scaling effects of brain size. Repeated measures multivariate analysis of covariance (MANCOVA) examined group differences in regional LTC volumes. LTC volumes were the dependent variables using region/ROI (STG, MTG, ITG, TP) and

hemisphere (left, right) as within-subject repeated measures. Group (FHR, controls) was the independent variable and age was an *a priori* covariate. Main effects of group, or interaction effects were followed-up with ANCOVAs only if they were statistically significant ($p \leq .05$) at the multivariate level and then collapsing across non-significant within-subject variables to control for Type I error. Partial eta-squared (η_p^2) effect sizes are also reported. Although sex and its interactions were entered in the initial MANCOVA, they were not included in the final model because their effects were non-significant. Mixed effects ANCOVAs evaluated the effect of familiarity when LTC ROIs differed significantly between groups. However, these mixed models did not alter any of the findings and, thus, are not detailed.

Correlations with memory data were limited to brain areas that showed statistically significant between group differences in GM volumes after ANCOVA. Shapiro-Wilk testing showed non-normal distributions for facial and verbal memory in both groups. Thus, associations between facial and verbal memory with LTC GM were tested using Spearman's rho. Additionally, exploratory correlations with additional cognitive domains (WISC-III (Wechsler, 1991) for subjects < age 17; WAIS-III (Wechsler, 1997a) for subjects > age 17) and symptoms (Hopkins Symptom Checklist Revised (Derogatis, 1983) and Chapman psychosis proneness scales (Chapman et al., 1976, 1978; Eckblad and Chapman, 1983)) were also performed. All p-values are two-tailed. Symptom and cognitive data for subjects included in this study have previously been published (Glatt et al., 2006; Rosso et al., 2010; Scala et al., 2013; Seidman et al., 2006).

3. Results

3.1 Demographic, Cognitive and Symptom Data

FHR participants had significantly lower mean parental socioeconomic status compared with controls, but otherwise showed no significant differences compared with controls on any other demographic variable (see Table 1 for full demographic, cognitive, and symptom data). There were no significant differences in immediate or delayed facial or verbal memory between the groups. When additional cognitive measures were examined, we found that the FHR group showed lower scores on WAIS/WISC-III symbol search. As noted in previous analyses of these data, FHR subjects showed significantly greater levels of phobic anxiety, paranoid ideation, and psychoticism on the Hopkins Symptom Checklist (HSC) compared with controls. Additionally, FHR subjects demonstrated significantly greater physical anhedonia on the Chapman psychosis proneness scales, compared with controls. There were no significant differences between the FHR and control groups on other subpsychotic symptoms (i.e., magical ideation or perceptual abnormalities).

3.2 Structural MRI Analysis

The MANCOVA analysis identified a significant main effect of group ($F = 4.50$; $df = 1, 72$; $p = .04$; $\eta_p^2 = .06$), but no significant group by brain region interaction ($F = 1.2$; $df = 4, 69$; $p = .32$; $\eta_p^2 = .02$). Group by hemisphere and brain region by hemisphere interactions were also not significant (p 's > .73). Age was a significant covariate ($F = 4.6$; $df = 1, 72$; $p = .003$; $\eta_p^2 = .12$) and showed a significant interaction with brain region ($F = 2.7$; $df = 4, 69$; $p = .$

05; $\eta_p^2 = .04$). But there was no significant interaction between age and hemisphere, or with brain region within hemisphere (p 's $> .61$).

Follow-up ANCOVAs for the significant main effect of group, controlling for age showed that the FHR group had significantly smaller GM MTG volume ($F = 5.6$; $df = 1, 72$; $p = .02$; $\eta_p^2 = .07$) compared with controls. This group difference remained significant when covarying for sociodemographic (parental socioeconomic status), cognitive (WISC/WAIS-III symbol search), and symptom variables (phobic anxiety, paranoid ideation, psychoticism, and physical anhedonia) that were significantly different between the groups ($F = 5.7$; $df = 1, 72$; $p = .02$; $\eta_p^2 = .08$). Comparisons between FHR and controls for the remaining LTC structures were not statistically significant, although their effect sizes indicated relatives had comparable decrements in ITG and TP volumes (See Table 2).

3.3 Correlations with Memory, Symptom, and Cognitive Measures

In the FHR group, delayed facial memory was positively correlated with total MTG GM volume ($r = .42$, $p = .04$) and right MTG GM volume ($r = .47$; $p = .02$) (Figure 2), but not left MTG GM volume ($r = .06$, $p = .78$). Exploratory tests showed significant negative correlations between delayed facial memory and phobic anxiety ($r = -.47$; $p = .02$) and psychoticism ($r = -.44$; $p = .03$) in the FHR group, but no correlations between delayed facial memory and any other symptom/cognitive domain, or demographic variable. In the FHR group, the correlation between delayed facial memory and right MTG GM volume (but not total MTG GM volume) remained significant when controlling for phobic anxiety and psychoticism ($r = .42$; $p = .04$). There were no significant correlations between immediate facial memory, or between immediate or delayed verbal memory, and MTG GM volumes in the FHR sample (all r 's $< .21$; all p 's $> .33$). Controls showed no significant correlations between immediate or delayed facial or verbal memory and MTG GM volumes (all r 's $< .21$; all p 's $> .18$).

4. Discussion

In this study, we found that youth at FHR for schizophrenia showed significantly smaller MTG GM volumes compared with healthy subjects. Similar trends were also observed for ITG and TP GM volumes in FHR youth compared with controls. Our findings provide support for our primary hypothesis that alterations of LTC structure are related to the genetic liability for schizophrenia and may precede psychosis onset. Further, we found a significant, positive correlation between right MTG GM volume and delayed facial memory in the FHR group. This suggests that smaller right MTG volume may be linked with poorer facial memory in youth at genetic risk for schizophrenia.

Overall, our results are consistent with a growing number of studies showing alterations of MTG structure in first-degree relatives of people with schizophrenia (Goghari et al., 2007; Hu et al., 2013; Sprooten et al., 2013). To our knowledge, however, this is the first study reporting a relationship between smaller right MTG GM volume and facial memory in FHR youth. The lack of a similar association between facial memory and left MTG GM volume is consistent with evidence for the involvement of right LTC structures (including MTG) in memory for faces (Lucas et al., 2003).

In addition to the role of the MTG in facial memory (Platek et al., 2006), studies in healthy subjects have shown that the MTG is involved in a wide range of social and emotional processes, including: theory of mind (Perner et al., 2006), empathy (Decety and Chaminade, 2003), and autobiographical memory (Svoboda et al., 2006). In adult relatives of schizophrenia patients, fMRI studies have demonstrated aberrant MTG function during social cognitive processing (e.g., reflection on self and other people (Brent et al., 2014) and emotion regulation (van Buuren et al., 2011; van der Meer et al., 2014). In conjunction with these fMRI results in older relatives, our finding of a link between smaller right MTG volume and poorer facial memory in FHR youth, therefore, suggests that one of the ways that altered MTG structure may contribute to heightened schizophrenia risk is through its disruption of social information processes. The possibility of a specific relationship between MTG structural alterations and deficits in social and emotional processing in persons at risk for schizophrenia could also help explain the absence of an association between smaller MTG GM volume in the FHR group and verbal memory. While facial memory plays an important part in social communication and social information processing (Adolphs, 1999), our verbal memory task involved verbatim prose recall of a short narrative and, thus, may not rely upon social memory, or other types of social information processing. Implicitly, therefore, smaller MTG GM volume and associated facial memory impairment in FHR individuals could contribute to greater difficulties with real world functioning and interpersonal relatedness. This possibility is suggested by our exploratory findings linking poorer facial memory with greater phobic anxiety and psychoticism in the FHR group. In schizophrenia, reduced functioning of the neural system underlying face processing has also been associated with poorer social function (Pinkham et al., 2008).

Contrary to our expectations, we did not find significant between group differences in STG volume. Although smaller STG GM volume is commonly reported in FHR youth (for reviews see: (Brent et al., 2013; Thermenos et al., 2013), several studies have also failed to show reductions of STG volume in samples of young (Sprooten et al., 2013) and older (Yang et al., 2010) relatives. Longitudinal studies linking decrements in STG volume with the emergence of prodromal symptoms (Bhojraj et al., 2011) and/or the onset of frank psychosis (Takahashi et al., 2009) suggest that STG deficits may be more closely associated with the transition to psychosis than with the genetic liability for schizophrenia *per se*. For example, Lymer and colleagues found that smaller left STG GM density was associated with greater schizotypal symptoms only among a subset of FHR individuals who went on to develop schizophrenia, but not in their total sample of FHR persons that included those who stayed well (Lymer et al., 2006). Further, one structural MRI study in adult relatives (Goghari et al., 2007) found smaller STG surface area, but not volume, suggesting that GM volume may not be the most sensitive anatomical measure of STG changes associated with schizophrenia risk. Finally, methodological differences in samples and/or MRI methodologies could account for different results.

The interpretation of our results is limited by the relatively modest sample size of young relatives in this study and the potential vulnerability of structural MRI studies to a variety of confounding factors (e.g., stress sensitivities and medication effects) (weinberger and Radulescu, 2015). However, one of the strengths of FHR studies is that probands are non-

treatment seeking and unmedicated. Thus, many of the potential confounds that may affect comparisons between structural MRI findings in patients with schizophrenia and controls are significantly reduced in a FHR designed study. Replication of our findings in larger samples is necessary to determine the generalizability of our results. Additionally, future, longitudinal studies should test if smaller MTG volume in conjunction with poorer facial memory represents a stable, trait-like feature of the genetic liability to schizophrenia, or if progressive reductions in MTG GM volume and worsening facial memory performance predict the transition to psychosis.

In summary, our results suggest that smaller MTG GM volume is related to the genetic liability to schizophrenia and to impaired facial memory among individuals at genetic risk for the disorder. Taken together with evidence for associations between aberrant MTG function and deficits of social information processing in adult relatives of people with schizophrenia, our findings support the hypothesis that alterations of MTG structure and/or function may be linked with impaired socio-emotional processing in FHR individuals. Future longitudinal studies are needed to determine if decrements in MTG volume and poorer facial memory over time index the risk for developing psychotic symptoms, or transitioning to schizophrenia.

Acknowledgements

We thank the patients with schizophrenia, their family members, and the control family members who participated in this study.

Role of funding source

None

Funding

This study was supported by funding from the Massachusetts Mental Health Institute and the Lopez Funds of the Beth Israel Deaconess Medical Center Department of Psychiatry (BKB), the Mental Illness and Neuroscience Discovery (MIND) Institute (LJS); NIMH MH 43518 and MH 65562 (MTT, LJS); MH092840 (LJS) and the Massachusetts Department of Mental Health Commonwealth Research Center — SCDMH82101008006 (LJS); National Alliance for Research on Schizophrenia and Depression (NARSAD; LJS, MTT); and, NIMH K01 MH069687 (IMR). This work was also supported in part by the K.G. Jebsen Centre for Research on Neuropsychiatric Disorders, University of Bergen, Bergen, Norway, the European Community's Seventh Framework Programme (FP7/2007–2013; SVF) under grant agreement n°602805 (SVF) and NIMH grants R13 MH 059126 (SVF) and R01 MH 094469 (SVF).

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Figure 1.

Cortical parcellation of the lateral temporal cortex (LTC) regions of interest. Parcellation units comprising the four a priori LTC regions of interest are displayed: inferior temporal gyrus (T3a + T3p; purple); middle temporal gyrus (T2a + T2p; orange) superior temporal gyrus (T1a + T1p; gray); temporal pole (TP; green).

Figure 2.

Correlation between delayed facial memory and right middle temporal gyrus (MTG) gray matter (GM) volume) in youth at familial high-risk (FHR) for schizophrenia. Scatter plot displays the positive correlation between delayed facial memory (Wechsler Memory Scale — Third Edition/Children's Memory Scale — Third Edition scaled scores) and right MTG GM volume (mm³) in the FHR youth sample ($r = .47$; $p = .02$).

Table 1

Demographic characteristics [Mean $\pm$ SD or N (%)] of youth at familial high-risk (FHR) for schizophrenia and control subjects.

	FHR <i>n</i> = 27 (9 [*])	Controls <i>n</i> = 48 (27 [*])	<i>p</i> Value	Effect size (Cohen's <i>d</i>)
Demographic Data				
Age (years)	19.0 $\pm$ 4.2	17.7 $\pm$ 3.7	.15	.32
Female	12 (44%)	28 (58%)	.25	.13
Caucasian	14 (52%)	29 (60%)	.15	.11
Right-handed	25 (93%)	42 (89%)	.64	.29
Education (years)	10.7 $\pm$ 2.7	11.1 $\pm$ 3.3	.67	-.13
Parental SES ^a	38 $\pm$ 26	47 $\pm$ 15	.01	-.42
WISC-III/WAIS-III^b				
Full-Scale IQ ^c	97.4 $\pm$ 11.3	103.2 $\pm$ 15.4	.10	-.42
Verbal IQ	98.7 $\pm$ 12.7	106.0 $\pm$ 17.0	.06	-.49
Performance IQ	96.3 $\pm$ 11.3	100.0 $\pm$ 16.0	.29	-.27
WMS-III/CMS-III^d				
Facial Memory, Immediate Recall	9.4 $\pm$ 4.1	9.6 $\pm$ 4.2	.65	-.04
Facial Memory, Delayed Recall	10.2 $\pm$ 3.7	9.4 $\pm$ 4.4	.40	.18
Verbal Memory, Immediate Recall	10.6 $\pm$ 3.8	10.1 $\pm$ 2.8	.33	.16
Verbal Memory, Delayed Recall	10.8 $\pm$ 3.3	10.3 $\pm$ 3.1	.34	.16
SCL-90-R-Scale^e				
Somatization	47.2 $\pm$ 15.1	44.8 $\pm$ 10.0	.41	.19
Obsessive-Compulsive	47.4 $\pm$ 14.8	43.5 $\pm$ 9.4	.17	.31
Interpersonal Sensitivity	46.6 $\pm$ 14.3	42.4 $\pm$ 9.4	.13	.35
Depression	48.5 $\pm$ 14.1	43.4 $\pm$ 9.6	.07	.43
Anxiety	45.8 $\pm$ 13.3	41.6 $\pm$ 8.1	.10	.38
Hostility	48.6 $\pm$ 12.9	44.7 $\pm$ 8.8	.12	.18
Phobic Anxiety	49.3 $\pm$ 11.00	44.8 $\pm$ 6.8	.03	.49
Paranoid Ideation	49.9 $\pm$ 14.0	43.6 $\pm$ 9.1	.02	.54
Psychoticism	48.1 $\pm$ 13.7	42.3 $\pm$ 8.4	.03	.51
Chapman Psychosis Proneness Scales^f				
Physical Anhedonia	17.2 $\pm$ 8.5	13.0 $\pm$ 8.1	.04	.51
Magical Ideation	6.4 $\pm$ 4.5	5.9 $\pm$ 4.8	.70	.11
Perceptual Aberrations	3.8 $\pm$ 4.3	3.2 $\pm$ 4.3	.58	.14

There were no significant differences between FHR and control participants on demographic variables, except for parental socioeconomic status, which was significantly greater among control subjects.

* Nine (31%) of the FHR and 27 (56%) of the control samples were between the ages of 13–16. There were no significant differences between 13–16 year-old participants and those 17 on any of the memory assessments in either the FHR, or the control group.

^aSES: Socioeconomic status, assessed with the Four Factor Hollingshead index.

^bWechsler Intelligence Scale for Children – Third Edition (WISC-III; for subjects 13–16 years old)/Wechsler Adult Intelligence Scale – Third Edition (WAIS-III; for subjects 17 years old) subtests; FHR and control comparisons are based on standard scores.

^cFull-scale IQ: Prorated from 8 subtests of the WISC-III, or WAIS-III.

^dWechsler Memory Scale – Third Edition (WMS-III; for subjects 17 years old)/Children’s Memory Scale – Third Edition (CMS-III; for subjects 13–16 years old) subtests (WMS-III Faces and Logical Memory; CMS Faces and Stories tests); FHR and control comparisons are based on scaled scores.

^eHopkins Symptom Checklist-90-Revised (SCL-90-R); FHR and control comparisons are based on *T* scores. Data from an overlapping sample of the subjects included here has previously been published in Scala et al., 2013.

^fHigher scores indicate greater levels of impairment. This data has previously been published in Rosso et al., 2010.

Table 2

Absolute and relative lateral temporal cortical gray matter volumes (mm^3 , mean $\pm$ SD) in familial high-risk (FHR) and control subjects.

	Absolute volumes ^a		Relative volumes ^b		Effect sizes (Cohen's <i>d</i>)
	FHR n = 27	Controls n = 48	FHR n = 27	Controls n = 48	
Total inferior temporal gyrus	144.76 $\pm$ 29.43	151.24 $\pm$ 26.07	10.59 $\pm$ 1.99	11.45 $\pm$ 1.65	-.46
Right inferior temporal gyrus	71.55 $\pm$ 13.68	74.59 $\pm$ 13.71	5.24 $\pm$ 0.10	5.65 $\pm$ 0.89	-.60
Left inferior temporal gyrus	73.21 $\pm$ 18.81	76.65 $\pm$ 15.33	5.35 $\pm$ 1.22	5.80 $\pm$ 1.10	-.38
Total middle temporal gyrus	189.02 $\pm$ 29.46	198.36 $\pm$ 31.75	13.85 $\pm$ 1.90	15.01 $\pm$ 1.82 ^d	-.60
Right middle temporal gyrus	94.40 $\pm$ 16.05	98.71 $\pm$ 17.22	6.92 $\pm$ 1.10	7.47 $\pm$ 1.09	-.48
Left middle temporal gyrus	94.62 $\pm$ 16.38	99.66 $\pm$ 16.65	6.92 $\pm$ 1.04	7.54 $\pm$ 1.09	-.56
Total superior temporal gyrus	247.04 $\pm$ 38.52	243.74 $\pm$ 31.80	18.12 $\pm$ 2.68	18.48 $\pm$ 2.06	-.16
Right superior temporal gyrus	122.08 $\pm$ 20.93	120.50 $\pm$ 16.70	8.97 $\pm$ 1.54	9.14 $\pm$ 1.08	-.12
Left superior temporal gyrus	124.95 $\pm$ 20.57	123.14 $\pm$ 17.97	9.15 $\pm$ 1.36	9.34 $\pm$ 1.23	-.14
Total temporal pole	232.85 $\pm$ 44.00	242.03 $\pm$ 39.44	16.97 $\pm$ 2.52	18.40 $\pm$ 2.81	-.52
Right temporal pole	113.95 $\pm$ 19.27	119.77 $\pm$ 21.77	8.32 $\pm$ 1.13	9.10 $\pm$ 1.59	-.54
Left temporal pole	118.90 $\pm$ 26.06	122.26 $\pm$ 19.73	8.65 $\pm$ 1.53	9.31 $\pm$ 1.39	-.44

^a Absolute volumes in cubic millimeters are given as mean $\pm$ standard deviation (SD);

^b Significant main effect of group (p .04) in the repeated measures multivariate analysis of covariance predicting left and right relative lateral temporal cortical volumes in FHR vs. control subjects, adjusting for total cerebral volume and age;

^c Absolute volumes divided by total cerebral volume;

^d Significant difference between groups in follow up analysis of covariance, p .05.