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Letter to the Editor

Differential cortical thinning of auditory cortex in first episode schizophrenia: Association with auditory verbal hallucinations

Dear Editors

It has been known that auditory cortex is the main region responsible for various language processes, and postulated to be important in the underlying mechanisms of auditory verbal hallucination (AVH). Indeed, previous neuroimaging studies have reported associations between AVH and the auditory cortex, ranging from changes in brain activation to grey matter volume (Onitsuka et al., 2004; Plaze et al., 2006). These studies have provided evidence to support the crucial role of auditory cortex in the pathogenesis of perceptual abnormalities in schizophrenia. Recently, researchers have also looked into the microstructure of the cortex by investigating the cortical thickness. Cortical thickness is the average distance between the pial surface and white matter surface of the cortex, which correlates with the number of neurons within an ontogenetic column. Studies done in patients with chronic schizophrenia have found that patients with AVH (AVH+) have reduced cortical thickness in different regions of the auditory cortex when compared to those without AVH (AVH–) (Cui et al., 2018; Mørch-Johnsen et al., 2017). Since cortical thinning can progress over time, the study of cortical thickness in first-episode patients is especially important to minimize the confounding effects of chronic illness and long-term treatment on the neural substrate of AVH. The use of a finer parcellation scheme may also help to delineate the gyral and sulcal regions of auditory cortex in greater detail. Therefore, we aimed to study the cortical thickness of the auditory cortex between two groups of first-episode schizophrenia patients (AVH+ and AVH-) with matched potential confounders using a propensity score matching method.

We recruited 34 right-handed first-episode schizophrenia patients. They were divided into the AVH+ group ($n = 17$) and the AVH– group ($n = 17$) according to their clinical information and the hallucination item (P3 score of 3 or more for AVH+ group; score of 2 or less for AVH- group) of the Positive and Negative Syndrome Scale (PANSS) when they joined the study. Auditory hallucinations item of the Scale for the Assessment of Positive Symptoms (SAPS) was also used to evaluate AVH severity in the AVH+ group. Information on antipsychotic dosage and treatment duration were collected, with chlorpromazine equivalent of drugs and dosage calculated in the week of MRI scan. Gender, age, education level, duration of untreated psychosis (DUP), medication dosage and treatment duration were matched using propensity score method.

MRI scans were performed using a 3.0-Tesla Philips scanner. T1-weighted MPRAGE structural MRI scans were obtained using the following parameters: repetition time (TR) = 6.97 ms; echo time (TE) = 3.17 ms; flip angle = 8°; field of view (FOV) = 240 × 240 mm^2; reconstruction matrix = 240 × 240; slice thickness = 1 mm, gap = 0; number slices = 160. All images were inspected for motion artifacts before inclusion into subsequent analysis. Images were processed using the full stream automatic software, FreeSurfer version 5.3 (http://surfer.nmr.mgh.harvard.edu/) (Dale et al., 1999; Fischl and Dale, 2000). We used a fine-grained parcellation scheme based on anatomical sulco-gyral boundaries of the Destrieux Atlas (Destrieux et al., 2010) to parcellate the cortex of each hemisphere into 75 regions. Cortical thickness was calculated as the average of the closest distance from the white matter to the vertex and the closest distance from the vertex to the white matter. Data were analyzed using Statistical Package for Social Sciences, version 24.0 (SPSS Inc., Chicago, Illinois). Group differences in clinical demographics and cortical thickness of the left temporal lobe were tested using paired-samples *t*-tests and χ^2 tests. Spearman correlations were used to assess relationships between cortical thickness and severity of AVHs of patients.

No significant between-group differences were found in gender, age, education level, DUP, medication dosage, and treatment duration. The PANSS positive, negative, and general score were also similar between AVH+ and AVH- groups, with the only difference found in auditory hallucinations score of SAPS ($t = -14.6$, $P < 0.001$) (see Supplementary information). The AVH+ group had a significantly thinner left superior temporal sulcus than the AVH- group (see supplementary information). There was no significant difference in other regions of the auditory cortex, including superior temporal gyrus, Heschl's gyrus and transverse temporal sulcus (Table 1). There was a negative association between left superior temporal sulcus cortical thickness and auditory hallucinations score ($r = -0.463$, $P = 0.006$), but no significant association with gender, age, education level, DUP, medication dosage, and treatment duration. The mean global cortical thickness between the AVH+ group and the AVH– group were not significantly different ($t = 1.884$, $P = 0.078$).

Our results converged with previous findings of post-mortem studies, which indicated a reduced size of cortical regions, including temporal lobe structures (Vogeley et al., 1998). Contrary to a first episode schizophrenia study by Chen et al. (2015), no significant difference in the right Heschl's gyrus between the AVH+ and AVH– groups was found. This might be limited by the small sample size of this study with insufficient power to detect the difference in other regions. Another possible reason might be related to the longer duration of antipsychotic treatment of our sample as antipsychotic treatment was suggested to be associated with cortical volume reduction (Emsley et al., 2017). The study also had another limitation of lacking a healthy control group for comparison.

Despite the above limitations, this study is one of a few examining cortical thickness of AVH+ and AVH– patients with first-episode schizophrenia. We found the AVH+ group exhibited cortical thinning in the left superior temporal sulcus when compared to AVH– group, with the extent associated with severity of AVH. These provided further evidence about the involvement of auditory cortex in the pathogenesis of AVH in first episode treatment responsive schizophrenia patients. The significant association found between AVH severity and degree of

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Table 1
Cortical thickness differences in the regions of auditory cortex.

Cortical thickness	AVH+ group Mean (S.D.)	AVH− group Mean (S.D.)	*t*	*P*
Superior temporal gyrus				
Planum polare				
Left	3.317 (0.409)	3.538 (0.277)	1.931	0.071
Right	3.345 (0.293)	3.448 (0.293)	0.929	0.367
Planum temporale				
Left	2.32 (0.225)	2.449 (0.161)	1.798	0.091
Right	2.395 (0.227)	2.52 (0.245)	1.535	0.144
Lateral aspect				
Left	2.869 (0.237)	2.993 (0.199)	1.346	0.197
Right	2.997 (0.194)	3.078 (0.205)	1.209	0.244
Superior temporal sulcus				
Left	2.263 (0.158)	2.391 (0.1)	3.487	0.003*
Right	2.338 (0.132)	2.41 (0.11)	2.776	0.013
Heschl's gyrus				
Left	2.307 (0.216)	2.478 (0.269)	2.029	0.059
Right	2.417 (0.235)	2.47 (0.329)	0.551	0.589
Transverse temporal sulcus				
Left	2.357 (0.375)	2.417 (0.291)	0.462	0.65
Right	2.496 (0.333)	2.682 (0.372)	2.438	0.027

* Paired-samples *t*-test between AVH+ and AVH− was significant after correction for multiple comparisons ($P < 0.004$).

cortical thinning could further support the identification of the specific neuro-substrate of AVH as well. Future studies are warranted to explore the roles of different cortical regions in the mechanism of AVH.

Conflict of interest

E.Y.H.C. has participated on advisory boards for Otsuka; has received research funding from AstraZeneca, Janssen-Cilag, Pfizer, Eli Lilly, Sanofi-Aventis and Otsuka, and an educational grant from Janssen-Cilag. All other authors reported no conflict of interest disclosures.

CRediT authorship contribution statement

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.schres.2018.11.014.

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