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Letter to the Editor

Relationship between hallucination proneness and musical aptitude is mediated by microstructure in the corpus callosum

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Dear editor:

Poor interhemispheric communication is reported in schizophrenia patients (Endrass et al., 2002) and offers a potential explanation for the *misattribution* of internal events to external sources, which is a dominant theory for the genesis of auditory verbal hallucinations (AVH). Consistent with this, the corpus callosum (CC), the white matter (WM) tract connecting the two brain hemispheres, is reduced in volume in schizophrenia patients (Shenton et al., 2001). Furthermore, the WM integrity metric derived from diffusion tensor imaging (DTI), fractional anisotropy (FA) (Beaulieu, 2002), is reduced within the CC of schizophrenia patients (Keshavan et al., 2002). These differences are particularly prevalent in those callosal portions that interconnect frontal and temporal regions of the brain (the anterior and body sections of the CC). Moreover, FA negatively correlates with positive symptom severity, and a longitudinal study has shown there is a progressive decrease in FA which is associated with the development of psychosis (Carletti et al., 2012).

Psychometric studies show that hallucinatory experiences are not limited to schizophrenia patients, but instead are also observed to varying degrees in healthy individuals. Accordingly, AVH may be investigated in a healthy population using measures such as the Launay-Slade Hallucination Scale (Launay and Slade, 1981).

Previous studies showed striking parallels between the psychological and neural processes involved in musical aptitude and those linked to AVH. Musical experience is associated with *reduced* misattribution (de Bézenac et al., 2015), and musicians show faster interhemispheric transfer (Patston et al., 2007), increased CC volume and increased FA in the CC (Hyde et al., 2009), particularly in the anterior and body section of the CC. Taken together, these findings suggest that CC microstructure provides a neurophysiological correlate for a psychological continuum, with musicians at one end of the scale and schizophrenia patients with AVH at the other. In order to investigate this account, we examined the relationship between hallucination proneness, musical aptitude, and WM integrity of the CC in people unaffected by illness-related confounds such as medication or demoralization.

Thirty-eight healthy individuals who varied in their propensity to hallucinate (18–63 years, M = 36.5, SD = 14.3) were tested on hallucination proneness by the Launay-Slade Hallucination Scale (LSHS) and musical aptitude by the Advanced Measure of Music Audiation (AMMA) task. WM integrity in the anterior and body section of the CC was assessed by DTI and quantified by FA, a primary marker of microstructural integrity in this model. See Supplementary material S1 for method details and additional references.

We observed a significant negative (Pearson) correlation between AMMA and LSHS scores, ($r = -0.37$, $p = 0.012$): participants with higher degrees of musical aptitude showed lower degrees of hallucination proneness. Separate regressions were run to assess associations between FA in the CC and musical aptitude and hallucination proneness scores, with age as a covariate. AMMA scores significantly predicted FA ($\beta = 0.43$, $p = 0.008$), explaining approximately 16% of the variance (Fig. 1A). LSHS scores also significantly predicted FA ($\beta = -0.68$, $p < 0.001$), explaining approximately 45% of the variance (Fig. 1B). A path analysis including all three measures showed no significant direct effect of AMMA on LSHS ($\beta = -0.16$, SE = 0.191, $CI_{95\%} = -0.55$ to 0.22), but instead a significant indirect effect ($\beta = -0.34$, SE = 0.16; $CI_{95\%} = -0.69$ to -0.06) demonstrating that the relationship between AMMA and LSHS was mediated through FA (Fig. 1C).

At least two microstructural factors may contribute to FA: neurite (axonal) packing and neurite alignment (Fig. 1F). Neurite Orientation Dispersion and Density Imaging (NODDI) (Zhang et al., 2012), a multi-compartment biophysical diffusion model, separately quantifies these factors as neurite density (NDI) and neurite orientation dispersion (ODI) (see section 7 of S1). Therefore, a subset of 26 participants (20–58 years, M = 32.6, SD = 11.4) with suitable diffusion data were additionally analysed using the NODDI model. Results suggest that the critical microstructure component is the alignment (ODI), and not the packing (NDI) of neurites (e.g., axons). Only ODI measures (but not NDI measures) were negatively associated with AMMA (Fig. 1D) and positively associated with LSHS (Fig. 1E). Hence, highly aligned axons (as indicated by lower ODI) appear to be linked to better performance on musical listening tasks and a lower propensity to hallucinate.

In summary, we observed an inverse relationship between musical aptitude and hallucination proneness that is mediated by the microstructural integrity of the corpus callosum (particularly neurite orientation dispersion). This relationship could have important clinical implications: If musical experience strengthens interhemispheric transfer by enhancing the microstructural integrity of the CC, musical training could potentially counteract the callosal microstructure deficits observed in schizophrenia patients. Future research should address whether rehabilitation approaches that include musical training can benefit patients with psychosis.

Conflict of interest

None of the authors have any conflicts of interest to declare.

Contributors

All authors contributed to the design of the study and wrote the protocol. Anton Beer and Amy Spray managed the analysis. Amy Spray undertook the statistical and imaging data analysis, and wrote the first draft of the manuscript. All authors contributed to and have approved the final manuscript.

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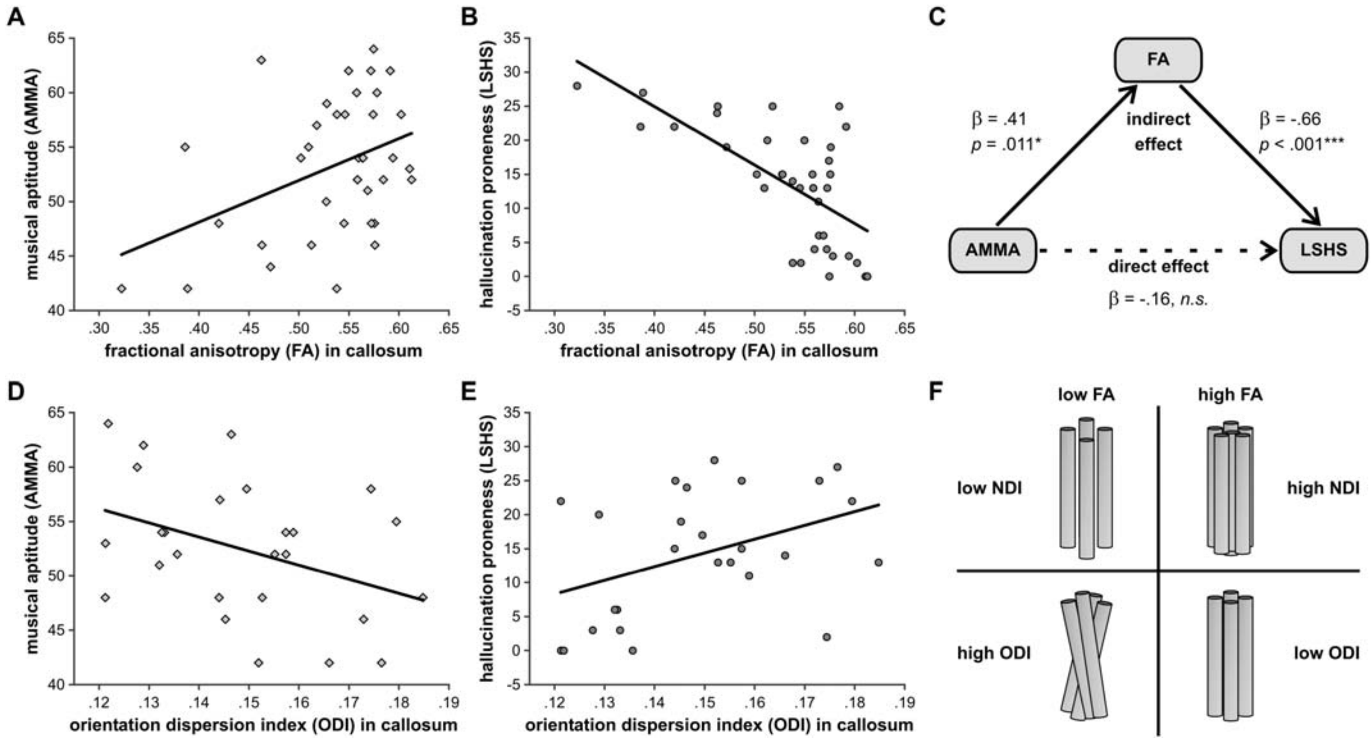

Fig. 1. Relationship between microstructure in anterior/body corpus callosum, musical aptitude (AMMA), and hallucination proneness (LSHS). Fractional anisotropy (FA) was positively correlated ($p = 0.006$) with AMMA scores (A) and negatively correlated ($p < 0.001$) with LSHS scores (B) ($n = 38$). C) A path analysis showed an indirect relationship of AMMA on LSHS mediated by FA scores, but no direct effect. D) Orientation dispersion index (ODI) was negatively correlated ($p = 0.024$) with AMMA scores (D) and positively correlated ($p = 0.018$) with LSHS scores (E) ($n = 26$). No relationship was observed with neurite dispersion index (NDI). F) Schematic of the relationship between FA, NDI and ODI measures of white matter microstructure (Zhang et al., 2012). FA scores were most closely related to neurite alignment (ODI) rather than neurite packing (NDI).

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Appendix A. Supplementary data

Details on materials and methods including the Launay-Slade Hallucination Scale (LSHS), the Advanced Measure of Music Audition (AMMA) task, and the analysis of diffusion-weighted imaging (DWI) data. Supplementary data associated with this article can be found in the online version, at doi: https://doi.org/10.1016/j.schres.2017.11.024.

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Amy Spray
University of Liverpool, Liverpool, UK
Corresponding author at: University of Liverpool, School of Psychology, Eleanor Rathbone Building, Bedford Street South, Liverpool L69 7ZA, UK.
E-mail address: ajspray@liv.ac.uk.

Anton L. Beer
University of Regensburg, Regensburg, Germany
University of Erlangen-Nürnberg, Erlangen, Germany

Richard P. Bentall
University of Sheffield, Sheffield, UK

Vanessa Sluming
Georg Meyer
University of Liverpool, Liverpool, UK

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