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Letter to Editor

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TO THE EDITOR

We appreciate the interest shown and the issues raised by Drs. Maurits van den Noort, Peggy Bosch, Katrien Mondt, and Sabina Lim in reference to our article (van den Noort et al, 2009).

Van den Noort et al. indicate that interscan intervals are not well-controlled for our two comparison groups (schizophrenia patients, healthy comparison subjects) and assert that the significantly different interscan intervals between the two groups are responsible for the results obtained in the study, basing their conclusions on Jernigan et al.'s data on aging. While we agree that a controlled interscan interval is desirable and had already addressed this limitation in our article (page 92), we do not believe that the data cited from Jernigan et al. showing differential rates of decline for different brain regions as a function of age somehow invalidate our results. The Jernigan conclusion was based on ages 30-80, where the data showed that hippocampal volume loss was significantly greater than in neocortex. However, Jernigan et al.'s Fig. 3 and 4 show that, between ages 40-42, roughly corresponding to subjects' age range discussed in our paper, changes in both regions are extremely small. Furthermore, the assertion that there would be a greater decline in the hippocampus is simply not borne out by our data. Our Table 3 shows that the decline is greater in temporal neocortex than in hippocampus in comparison subjects. Moreover, since age at scan was matched for two groups, both at the initial and second scan in our study, and we measured the same regions of interest in the two groups, we think that the factor of age-related volume reduction was well-controlled in the two groups.

The issue of a small sample size of subjects was raised. The number of subjects with schizophrenia was 16 and the number of normal healthy comparisons was 20. Since effect sizes comparing percent change in groups were small to medium (0.006-0.56) (Table 3 in the manuscript), we do not believe we could find a significant difference in percent volume

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Contributors

Takeshi Yoshida wrote the first draft of the manuscript. All authors contributed to and have approved the final manuscript.

Conflict of interest

There are no conflicts of interest for any authors to declare.

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change both in superior temporal gyrus (STG) and amygdala-hippocampal complex (AHC) even if the sample size were substantially increased. The only structure where significant progressive volume change might have been found with an increased sample size is right posterior AHC where Cohen's d was medium (0.56).

We note that the limitations of this study also include a short interscan interval. We believe that the reason that our study did not find progressive volume change of STG and AHC while other studies showed progressive volume change may be due to the fact that an interscan interval in this study and others showing a lack of progressive volume reduction (Takahashi et al, 2010; Yoshida et al, 2009) has been shorter than that of studies showing progressive volume change (van Haren et al, 2008; van Haren et al, 2007).

We would like to thank the letter's authors for pointing out that the Table 2 WAIS-III total scores for the two groups were inadvertently interchanged. The correct values are 88.6 (SD 11.3) for schizophrenia patients and 109.8 (SD 13.9) for healthy subjects.

We also thank the letter's writers for giving us the opportunity of commenting on the correlation between volume change and sum of positive PANSS score in our schizophrenia patients. As illustrated in our accompanying figure, the percent volume change of left total STG did not significantly correlate with sum of positive PANSS score, ($r_s = -0.04$, $p = 0.89$) (Fig. 1), as was true for other regions of interest. We emphasize that both the positive symptom association with STG volume loss and a significant degree of volume loss were found in our study in first episode patients (Kasai et al, 2003).

These first episode data illustrate well the main point of the current article: that changes over time are different in chronic and in first episode schizophrenia patients. The letter's writers unfortunately confuse reports using early schizophrenia subjects (including first episodes) with studies of more chronic patients in their citation of other regions that might be explored. We of course agree that other regions should be explored longitudinally in chronic schizophrenia, but we think that the present study represents an important start as it is the first region of interest study of the important STG region, and we appreciate the opportunity to point this out.

Finally, although the report by Takahashi et al. in this journal (Takahashi et al, 2010) provides a convincing and important replication of our finding of a lack of statistically significant STG progression in chronic schizophrenia, thereby furnishing additional validation of our study, further studies with a follow-up over a longer period of time, larger sample size, and matched groups are needed to clarify the nature of chronic course of schizophrenia.

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Fig. 1. Sum of positive PANSS score
Percent change of left total superior temporal gyrus