LETTER

Reply to Joel and Tarrasch: On misreading and shooting the messenger

We would like to thank Joel and Tarrasch (1) for their comments on our paper (2), although we regret that the critique seems intended to misrepresent our scientific findings. The caption of figure 2*A* of ref. 2 (upon which they are commenting) clearly states that these are statistically significant connectivity differences between men and women seen over the entire population. These differences are not in a single "representative" male or female, as the Joel and Tarrasch (1) seem to indicate. Rather, they are differences in connectivity observed in the population and represent "averages." Comprehension of basic statistics shows that such an analysis does not preclude overlap between populations, or imply that one group is completely devoid of a particular connectivity or that individual differences cannot exist. It is the overwhelming predominance of the within-hemispheric connections (blue lines) in the male brain and the equally predominant cross-hemispheric connections (orange lines) in the female brain that produces the dramatic difference in appearances of the male and female brain. On looking closely, one will find some blue lines dominant in the female connectivity and some orange lines dominant in the male connectivity.

In our dataset, 949 participants met the inclusion criterion and were part of this study, which is an unusually large sample. Disliking the findings of a study that does not agree with one's beliefs is understandable.

We accrued and studied this sample to understand progression of neuropsychiatric disorders (3), and examined sex differences because of their prominence in the development and course of these disorders. However, we also studied the commonality and encourage Joel and Tarrasch to do so on the data that has been released.

In ref. 2, we report the differences that we observed in the population through valid scientific means and interpreted them as showing complementarity between genders. We neither state nor imply that men and women are from different planets or galaxies, as Joel and Tarrasch misrepresent (1).

The critique by Joel and Tarrasch (1) mentions a study indicating that the causal relationship between structure and function is difficult to explain. We agree, and nowhere in the paper (2) do we claim otherwise. The functional behavioral aspects presented were based on known functionality of different brain regions, as a means of stimulating further study. Notably, there are several structural and functional studies (4–6; see also references 1–9, 14–16, 21, 22, and 24–27 in ref. 2) using alternate modalities that have shown differences between men and women based on brain tissue volume and functionality.

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1 Joel D, Tarrasch R (2014) On the mis-presentation and misinterpretation of gender-related data: The case of Ingalhalikar's human connectome study. *Proc Natl Acad Sci USA* 111:E637.
2 Ingalhalikar M, et al. (2014) Sex differences in the structural connectome of the human brain. *Proc Natl Acad Sci USA* 111(2): 823–828.
3 Cahill L (2006) Why sex matters for neuroscience. *Nat Rev Neurosci* 7(6):477–484.
4 Gur RC, et al. (2012) Age group and sex differences in performance on a computerized neurocognitive battery in children age 8–21. *Neuropsychology* 26(2):251–265.
5 Gur RC, et al. (2000) An fMRI study of sex differences in regional activation to a verbal and a spatial task. *Brain Lang* 74(2):157–170.
6 Davatzikos C, Resnick SM (1998) Sex differences in anatomic measures of interhemispheric connectivity: Correlations with cognition in women but not men. *Cereb Cortex* 8(7):635–640.

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