



## Reply to Hsueh YP et al.

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### To the Editor:

We thank Hsueh et al. for their interest in our article, and for their comments emphasizing the significance of anterior commissure (AC) hypoplasia/agenesis as a common feature in TBR1 deficient mice and humans. We agree that our statement about AC defects not having been previously reported in mice or humans with TBR1 alterations was mistaken, and we regret this inadvertent oversight. In fact, our main goal was to draw attention to the novel hippocampal dysgenesis that we observed in TBR1 deficient mice and humans [1], which could impact learning and memory.

Severe defects of the AC (anterior and posterior limbs) were originally reported 19 years ago in homozygous *Tbr1*<sup>-/-</sup> mice [2]. More recently, the Hsueh group made important novel contributions showing that heterozygous *Tbr1*<sup>+/-</sup> mice also had AC defects, primarily agenesis/hypoplasia of the posterior limb of the AC [3], along with subtle hypoplasia of the anterior AC [4]. Thus, AC defects are shared among heterozygous [3, 4] and homozygous [2] *Tbr1* mutant mice, as well as humans with heterozygous *TBR1* mutations/haploinsufficiency [1].

The hypothesis that abnormal connections of the amygdala, including deficient posterior AC connections, may

contribute to autism-related behavioral problems in TBR1 deficient mice and humans [3] is interesting. On the other hand, the neocortical and hippocampal dysgenesis documented in many *TBR1* patients [1] indicates that TBR1 deficiency has widespread effects on cortical as well as amygdala development. We fully agree that novel therapeutic approaches, such as treatment with D-cycloserine, should be investigated for patients with the *TBR1* neurocognitive phenotype.

### Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

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