Reply to Dickinson and Milne

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REPLY: We are pleased to respond to the Letter to the Editor of Dickinson and Milne (2014) on our recent work (Puts et al. 2014), in which they sought to “to highlight previously published work that stands counter to the findings of Puts et al. in an attempt to ensure that the work is considered in a balanced context.” We welcome this further consideration of our work.

To summarize the points raised, Dickinson and Milne (2014) comment that: 1) While we find reduced tactile discrimination in autism spectrum disorder (ASD), other studies have shown increased discrimination; 2) The suggestion that our findings may be the result of reduced lateral inhibition runs counter to other work proposing increased lateral inhibition in ASD; and 3) Our findings are not direct evidence of altered real-life perceptual experience in autism, and that further work is required to establish this link. We will consider these points in turn.

First, Dickinson and Milne (2014) raise the issue that our findings are in direct contrast with Blakemore and colleagues (2006) who showed increased tactile detection threshold in adults with Asperger syndrome (AS). We agree that such a clear discrepancy would be noteworthy, but Dickinson and Milne rather overstate the extent to which our findings and those of Blakemore et al. (2006) are “in direct contrast.” First, it is important to state that Blakemore et al. did not test discrimination performance as Dickinson and Milne suggest, but tested detection thresholds. Furthermore, while they found significantly reduced detection thresholds in AS in the vibration range (50–250 Hz), they found a trend \((P = 0.11\) with \(n = 10\) AS and 9 controls) toward increased detection thresholds in the flutter (0–50 Hz) regime, which our experiments seek to probe. Thus, these findings, in fact, are essentially concordant with our own to the extent that the experiments overlap (flutter-range detection thresholds), given that the significant effect that we observe in a larger cohort (32 children with ASD and 67 typically developing children) would most likely only be observed as a trend in cohort sizes to match Blakemore.

Second, Dickinson and Milne (2014) state that other authors have suggested increased lateral inhibition in ASD. Our results show impaired subthreshold inhibition, and worse amplitude discrimination, as well as impaired adaptation to amplitude discrimination, three results that we believe are behavioral evidence of reduced GABAergic lateral inhibition. Although there are always counter examples to be found, our results are consistent with numerous findings of GABAergic impairments in autism: sensorimotor GABA has been shown to be altered in children with ASD (Gaetz et al. 2013); short intercortical inhibition, a metric of inhibition measured by transcranial magnetic stimulation, is impaired in ASD (Enticott et al. 2013); and numerous GABAergic genes have been shown to be linked to ASD (Abrahams and Geschwind 2008; Buxbaum et al. 2002; DeLorey 2005). Some of these metrics have also been linked to task performance: detection threshold has been linked to expression of the GABRB3 gene (Tavassoli et al. 2012); our own work has shown GABA levels predict tactile frequency discrimination (Puts et al. 2011).

We agree with Dickinson and Milne (2014) that the link between altered minicolumnar organization and altered lateral inhibition needs further clarifying investigation. Casanova and colleagues (2002) have reported minicolumnar reduction in a number of areas in the parietal cortex, primarily in the peripheral neuropil space surrounding the minicolumn structures. The peripheral neuropil space, being the area that provides the “strong vertical flow of inhibition” described by Mountcastle (1997), is the region populated by (inhibitory) double bouquet cells. The predicted decrease in inhibition at the level of the functional minicolumn is consistent with the findings of Puts et al. (2014) as well as with the hypersensitivity described by Blakemore et al. (2006).

Regarding Dickinson and Milne’s (2014) point discussion of other sensory modalities, we agree that it remains unclear how our tactile findings relate to auditory and visual function. Cross-domain investigation was not within the scope of our study and remains an important topic for future investigation. Interestingly, impaired inhibition in ASD has been suggested in auditory cortex using MEG (Rojas et al. 2008), and perisylvian GABA has been shown to be reduced (Rojas et al. 2013), but occipital GABA does not appear to be altered (Gaetz et al. 2013).

Finally, we agree with Dickinson and Milne (2014) that there is a gulf to be spanned linking laboratory psychophysics to “real world” perceptual experience. While some work [including Blakemore et al. (2006)] has sought to use complex, higher-order stimuli to this end, it is our contention that understanding altered representation of simple, low-order stimuli that probe a single sensory modality (and even a single channel within that sense) will be the best foundation from
which to develop an understanding of increasingly complex and integrated stimuli.

In conclusion, we welcome Dickinson and Milne’s further consideration of our exciting results, and obviously agree in broad terms that our results do not capture the full picture of sensory processing impairments in autism. We report a set of experiments showing differences in detection thresholds and discrimination performance and the effect of adaptation in autism, and suggest that these results are consistent with impaired cortical inhibition. We refute the specific complaint that our results are in direct contrast to those of Blakemore et al. (2006), while agreeing in general terms that ASD can be characterized by both hyper- and hyposensitivity to tactile, and other sensory, stimuli.

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REFERENCES


