Reviewer's report

Title: Behavioral effects of congenital ventromedial prefrontal cortex malformation

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Reviewer: Ralph Adolphs

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This is an intriguing case study of a boy with congenital malformation of the left vmPFC. The findings are valuable in linking morphometric abnormalities in this region to the impaired behavioral control and social functioning that is described.

This case study is highly valuable for several reasons. It is quite rare, it offers an important comparison to the much larger number of studies with adult-onset of developmental (but postnatal)-onset cases, and it sheds light on issues of plasticity and compensation. This latter issue is especially important. Given the congenital nature of the case, one might have expected considerable reorganization and compensation. Similarly, given the largely unilateral nature of the malformation, one might have expected the behavioral consequences to be mild, as might be expected following dorsolateral left PFC abnormalities. The fact that this is not so is very intriguing, and continues to support the idea that the vmPFC, unlike many other cortical regions, plays an indispensable role in socioemotional development whose malfunction cannot be adequately compensated. This also makes it an excellent target for other developmental disorders, including autism.

Another intriguing aspect of this case is that the behavioral symptoms, to all appearances, seem to have begun only at age 6 following otherwise largely normal development.

Overall, I think this study is timely and important to publish. I have a few suggestions for the authors:

Table 1 was not legible (just a bunch of black, red, blue colored squares). Could the authors please provide this table?

The lesion is surprisingly small. What might one expect following such a small, unilateral left lesion in an adult-onset case? The authors may have some comparisons available, which may be worth comment, since my impression is
that the behavioral impairments in the present case are substantially more severe than what would be expected following a similar lesion in an adult-onset case. Relatedly, it is very interesting that performance is so normal across most standard neuropsychological tasks. This raises the question of how context-sensitive the impairment is-- would the authors hypothesize that it materializes only, or primarily, in a real-world setting, and why?

It would seem that it would be valuable to collect data from the Psychopathy Checklist developed by Hare for comparison here. Are such data available or could they be collected and added?

It would also be highly valuable to collect functional imaging data and further establish impaired function in the left vmPFC, as well as to document possible abnormal activation in other brain regions connected with this region, since this is something the authors hypothesize. However, I realize that this is a major undertaking and therefore likely to be the topic of a future report rather than within the scope of the present one. Still, it would be nice to add near the end of the paper as one of the topics for future investigation.

Minor comments

The case is variously described as having a “malformation” or a “lesion”. It might be good to keep this consistent.

2. What was the onset of puberty, is there any information about that? This would be especially informative in light of the hypersexual behavioral that apparently emerged at age 11.