Is autism a disconnection disorder?

Since Kanner and Asperger first described autism and Asperger's syndrome in the 1940s there has been an exponential increase in the number of studies examining the biological basis of these disorders. There has similarly been an exponential increase in the number of theoretical proposals to explain the cause of autistic spectrum disorder (ASD). It is widely acknowledged that ASD has a strong genetic component and there is much indirect evidence for brain abnormalities, however, these have yet to be defined precisely.

The increasing number of neuroimaging studies on autism has resulted in many new suggestions about the underlying brain abnormalities. However, diagnosis is still made from the observation of behaviour. The recent paper by Just and colleagues[1] confirms the presence of brain abnormalities, but will not provide a new diagnostic test.

Just and his colleagues scanned the brains of volunteers with ASD and those of healthy volunteers while they read simple sentences (eg, the cook thanked the father) and answered simple questions (eg, who was thanked, cook or father?). Both groups of volunteers activated the classic language areas while performing this task, but the activity was greater in Wernicke's area for those with ASD and greater in Broca's area for the controls. The authors suggested that this result showed that volunteers with ASD were concentrating on single words rather than on the sentence as a whole. This attention to details rather than to the whole (sometimes called weak central coherence) is also observed in people with ASD in many domains other than language.[2]

Apart from showing differences in the pattern of activity, Just and colleagues also showed differences in connectivity between brain regions. Connectivity is assessed in terms of the extent to which variations over time in one brain region are correlated with activity in another brain region. High correlations indicate that the two brain regions are interacting and are thus connected in terms of their function. Volunteers with ASD had substantially reduced connectivity between the classic language regions compared with healthy volunteers. My colleagues and I previously showed reduced connectivity between a different set of brain areas when we used PET to scan the brains of volunteers with ASD watching non-verbal, animated cartoons and detecting intentional behaviour[3]

How reduced connectivity is realised in brain structure is not yet clear, and there are many possibilities. Reduced interactions between brain regions need not imply that there are fewer anatomical connections. Indeed, the little evidence about abnormalities of brain structure in ASD[4] suggests that there are too many anatomical connections. Children with ASD show a greater increase in brain size, particularly of white matter, during infancy than healthy children. This could reflect a lack of pruning during the normal growth spurt, leading to excessive preservation of un-needed connections. Such an effect would certainly lead to abnormal functional connectivity between brain regions.

Also, it is not clear precisely which anatomical connections are likely to be abnormal. There is a notable distinction between feed-forward connections and feedback connections. Forward projections are driving because they trigger vigorous action potential discharge. In contrast, feedback projections have indirect effects by modulating the activity in forward projections. In cognitive terms, the main roles of feedback connections are likely to be top-down processes. One such top-down process is selective attention, in which prior knowledge and expectations modify neural and behavioural responses to stimuli. Integration and central coherence depend upon such top-down processes. There is some evidence that feed forward connections are laid down before feedback connections and that the late stages of synaptogenesis and pruning are mostly about the feedback connections. Thus there are several reasons to predict that the abnormal connectivity associated with ASD may relate to feedback connections.[4]

What is the outlook for abnormal connectivity as a plausible account of autism? A problem with explaining ASD in terms of abnormal connectivity is that the same explanation has been applied to several other disorders. Schizophrenia has been described as a disconnection syndrome,[5] as has developmental dyslexia.[6] Carl Wernicke[7] was probably the first to discuss the consequence of abnormalities in long-range corticocortical connectivity. He suggested that, whereas neurological disorders are associated with brain lesions, psychiatric disorders are associated with disruptions of connectivity, which he called sejunctions. If ASD does turn out to be a disorder of brain connectivity then much work will need to be done to delineate the abnormality that leads to this particular group of cognitive and behavioural disorders.

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Conflict of interest

I have no conflict of interest.

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