Differences in spontaneous functional connectivity between autism spectrum disorder (ASD) and neurotypical subjects

Abstract: In neurotypicals, there exists a sparsely connected network of brain regions associated variously with the “resting state” or “default mode” but also with self-referential reflection and social cognition. These regions generally appear to be “task-negative” in both neurotypical and ASD populations, in that they frequently exhibit a decrease in BOLD activity when engaged in an externally directed task. Functional connections between these regions are selectively attenuated in the ASD population relating to selective cognitive differences between neurotypical and autism spectrum disorder regarding social cognition. It is proposed that the pattern of long-range connectivity found in spontaneous brain activity can predict individual ability with specific cognitive functions.

Introduction: Shulman et al. (1997) have observed that while different tasks may cause increases in the neural activity of specific brain regions particular to those tasks, lending toward a theory of functional modularity in the brain, there are several regions that exhibit a decrease in neural activity in virtually all tasks when compared to rest. This led Raichle et al. (2001) to consider the possibility of a “default mode of brain function,” that is, a well-defined mode of neural activity associated with rest and that the functions associated with this resting state are interrupted by psychophysical task demands.

The various regions associated with this default mode include the medial prefrontal cortex (MPC), the posterior cingulate cortex/precuneus (PCC/PCun), and both inferior parietal lobules (IPL) among others. These regions have been found to be sparsely functionally connected (Frisoni, 1994) both during rest (Grecius et al. 2003) and while watching a movie (Golland et al. 2007). These regions have also been implicated in a variety of cognitive functions, especially self-referential thought (Blatt & Camerer, 2005), mentalizing about others (i.e. theory of mind) (Frith & Friston, 2005), and mental imagery (Fletcher et al. 1995).

It has been observed that individuals diagnosed with autism spectrum disorder (ASD) appear to suffer from a diminished capacity to develop a theory of mind or mentalize about others (Baron-Cohen et al. 1985) while possibly enjoying an enhanced capacity for mental imagery (Kanwisher et al. 2006). Since individuals with ASD appear to show the same pattern of deactivation compared to neurotypical controls (Chekkoursky et al. 2006), though for evidence to the contrary, see Kennedy et al. 2006) we hypothesized that this decrease in cognitive ability may be apparent in the functional connectivity within the default mode system, specifically with stronger connectivity between the various regions of the parietal lobe (e.g., between the PCC/PCun and IPL). An associated more with mental imagery and weaker connectivity between the anterior and posterior portions (e.g., between the MPC and the PCC/PCun) associated more with mentalizing or theory of mind. Upon analyzing the data, however, this appears not to be the case. Immiscible functional connectivity appears universally attenuated in individuals with ASD.

Data: The data used in this study come from a joint-atention experiment in which subjects (both ASD and control) had to determine at which object a face was looking. This experiment also included four control conditions: reconstituting joint attention into its various components. These control conditions included an arrow–Object condition, an Eyes: Left/Right condition, an Eyes: Open/Closed condition, and a Mouth: Open/Closed condition (Hanson et al., in submission).

In the present study, distinctions between tasks were considered secondary to the goal of distinguishing intrinsic networks which can be distinguished from the rest of the brain by virtue of the fact that they appear less active during any extrinsic task, regardless of the condition. While such a general task-negative system may seem unjustifiably idealized, previous studies have shown (Shulman et al. 1997) a remarkable uniformity in this regard. As shown below, the current findings are consistent with the “default mode” hypothesis (Raichle et al. 2001).

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Discussion: Following Chekkoursky et al. (2006) it was expected that we would find diminished functional connectivity in ASD. However, we hoped to find increased (compensating) or at least comparable connectivity strengths in a subset of connections particularly involving the precuneus and other parts of the parietal lobe. No such subset could be found. Furthermore, the connection between the MPcP and parietal regions seemed more attenuated in ASD than any other connection. This connection had been predicted to be particularly diminished.

The functional dynamics of how different regions of the brain communicate are certainly at least as important as the regions themselves. However, evaluating functional connectivity using the product moment correlation coefficient may be too coarse a measure to account for the subtleties of such a complex interconnected system like the brain. More advanced methods of evaluating effective connectivity may allow one to disentangle the influence of each region on each other leading to a more useful and nuanced diagnosis of the intrinsic system of the brain (Ramsey et al., in submission).

References: