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Striatal development in autism: repetitive behaviors and the reward circuitry

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Abstract

Autism spectrum disorder (ASD) is defined by two essential features – impaired social communication abilities, including deficits with social reciprocity, nonverbal communication and establishing relationships, and by the presence of restricted and repetitive behaviors and interests (RRBIs). Social deficits get the majority of attention both in science and in the popular media, but RRBIs are equally important in understanding autism. Although RRBIs are also seen in typically developing preschoolers, as well as in other psychiatric disorders such as obsessive-compulsive disorder, their impairing and persisting character is a hallmark of ASD¹.

Repetitive behaviors are among the first signs of ASD, with significant elevations by the child's first birthday². Individuals with ASD of all ages and cognitive ability levels display RRBIs to variable degrees, with males usually being more severely affected than females³. Caregivers of individuals with ASD commonly emphasize that RRBIs are among the most challenging facets of the disorder on an everyday basis¹. They negatively impact social, cognitive, family functioning and well-being, often leading to increased levels of parental stress and negative parenting styles. While the clinical description and natural history of RRBIs is becoming clear, an understanding of the biological bases of this set of features has only recently begun to emerge⁴. Better insight into the ontogenesis of RRBIs and their underlying neurobiology is needed not only to inform models of the etiology of ASD, but also to foster the development of new interventions.

In this issue of *Biological Psychiatry*, Langen et al.⁵ examine differences in the rate of basal ganglia growth in ASD relative to typically developing children (TDC). Their volumetric analyses focused on developmental trajectories of the ventral striatum (with nucleus accumbens) and dorsal striatum (with caudate nucleus and putamen). These components of the basal ganglia are the major subcortical targets within the frontostriatal behavior control loops that are recognized as likely subserving RRBIs⁴. This current study is a follow up of this same group's earlier work showing cross sectional differences in growth trajectory. While several labs have previously reported enlargement of the caudate nucleus in ASD, this current study is the first to make repeat

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morphology measurements, thus overcoming limitations associated with cross sectional analyses. This study involved 86 seven to seventeen year old cases and controls who had 2 MRI anatomical scans approximately 2 and a half years apart on average, allowing a direct test of differential striatal growth. The rate of basal ganglia growth was correlated with the severity of RRBIs as assessed by parent interview at the time of the first MRI scan, corroborating earlier work on the role of the striatum in repetitive behaviors among children with ASD.

Specifically the caudate nucleus showed a growth rate in ASD that was twice as high as the growth rate in TDC (i.e., 4.6% vs. 2.3%). This was independent of overall brain growth, use of psychotropic medications, or other major confounds. Most importantly, more severe RRBIs early in life, particularly insistence on sameness behaviors, such as avoiding trivial changes in routines and environments as well as adhering to compulsions and rituals, were related to faster striatal growth between average ages of about 9 and 12 year old, with large effect sizes (e.g., caudate nucleus: Cohen's $d = 0.86$). While Langen et al. discuss several complementary explanations for their findings, they conclude that the divergent trajectory of caudate development in relation to RRBIs most likely results from early, and possibly continuing, patterns of repetitive behaviors that shape striatal development – not the other way around.

This new set of data elegantly adds to the notion that the striatum plays a central role in core ASD phenomenology⁶. However, one question lingers: what cause RRBIs, like insistence on sameness, compulsions and rituals, to become such a force so as to impact the growth trajectory of an evolutionarily ancient brain structure like the caudate nucleus? This question ties in with a long-standing debate among clinicians and scientists concerning the potential functions that the myriad of RRBIs might serve in individuals with ASD. While several plausible ideas have been advanced⁷, convincing support for any specific one is lacking.

One hypothesis that is gaining increased research attention, however, involves the effects of alterations of the balance between social and nonsocial motivation in *reward circuitry* on RRBIs⁸. This model suggests that ASD is in part a disorder of “behavioral dependency” to RRBIs because of the rewarding effects they induce¹. Indeed, insistence on sameness and preoccupying restricted interests are reported to be quite pleasurable by affected individuals¹. The dorsal striatum with caudate nucleus, in particular, is believed to mediate reward value for purposeful actions⁵. Functional imaging studies show that the brain's reward circuitry in ASD, particularly striatum and ventral prefrontal cortices, selectively over-reacts to objects that may comprise an intense special interest, whereas it under-reacts to more typical desires such as social reward and money⁶. This may indicate that the brain in ASD cares less for conventional rewards. It is not yet known if an initial lack of social reward motivation opens the door for enhanced rewarding effects of certain circumscribed objects, topics, and routines, or whether the reverse is true – that the dominating reward effects of nonsocial objects, topic and routines diminishes the reward value of social engagement.

The rewarding effects of RRBIs are thought to be fueled by the preference of those with ASD for predictability in their environment, where they can exercise more control; social encounters are in many ways the antithesis of this, as these are often rapid, hard to control and offer much more variable reinforcement contingencies. When RRBIs are rewarding, their pursuit may be strengthened through reinforcement mechanisms that progressively turn them into rigid and strongly desired habits that are performed almost automatically with little conscious oversight.

With this heuristic model, RRBIs are self-reinforcing, and they begin to hijack the normal developmental trajectory of entire repertoires of behaviors. The dorsal (associative) striatum with caudate nucleus dominates these processes⁴. Thus, an accelerated growth rate of the caudate related to RRBIs, as reported by Langen et al.⁵, could reflect atypical brain specialization in individuals with ASD⁹. From early in life the caudate nucleus mediates habitual processes for a wide range of different stimuli and contexts. Across development, however, the caudate may become co-opted by the most rewarding aspects of the environment. This interactive and self-sustaining biobehavioral process – in concert with other mesocorticolimbic functions⁴ – may shape the growth trajectory of the caudate nucleus and strengthens the occurrence of RRBIs in ASD (Figure 1). On a day-to-day basis, RRBIs interfere with social development and functioning as they may absorb resources typically dedicated to other learning opportunities, including social ones⁶.

The observation that RRBIs in ASD involve plasticity of the caudate nucleus – one major hub within the frontostriatal circuits that control behavior – is a fascinating advance for our field. It brings us closer to the neurobiological roots of how and why affected individuals develop and maintain this set of challenging behaviors. Follow-up research will need to address several issues to improve upon the approach of the Langen et al study. One critical issue is that researchers need to use more precise behavioral measurement tools¹⁰. This could involve item rating scales with greater item density around key concepts, as it is clear to all the ADI-R is sorely lacking in this regard. Also, quantitative motion capture tools are now widely available; deploying these in natural environments seems to us to be extremely promising adjuncts to standard rating scales. Repeat behavioral measurement across time, in sync with repeat brain measurement is an important next step that will enable better characterization of the interplay between RRBIs and brain dynamics. In this regard, multimodal imaging in the same sample is called for, as structural imaging will surely only capture portions of the story. The findings by Langen et al.⁵ call attention to the importance of RRBIs in autism. Because RRBIs may be rooted in the powerful reward circuitries that motivate a great deal of behavior, strategically targeting the role of reward mechanisms promises to improve treatment practices for limiting the life interfering aspects of RRBIs among individuals with ASD and their families.

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Figure 1.

Based on data from the longitudinal study by Langen et al.⁵, we suggest a working model on the ontogenesis of higher-order restricted and repetitive behaviors and interests, such as resistance to change behaviors, among children with autism spectrum disorders. See text for details.