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Review

Autism, oxytocin and interoception

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ABSTRACT

Autism is a pervasive developmental disorder characterized by profound social and verbal communication deficits, stereotypical motor behaviors, restricted interests, and cognitive abnormalities. Autism affects approximately 1% of children in developing countries. Given this prevalence, identifying risk factors and therapeutic interventions are pressing objectives—objectives that rest on neurobiologically grounded and psychologically informed theories about the underlying pathophysiology. In this article, we review the evidence that autism could result from a dysfunctional oxytocin system early in life. As a mediator of successful procreation, not only in the reproductive system, but also in the brain, oxytocin plays a crucial role in sculpting socio-sexual behavior. Formulated within a (Bayesian) predictive coding framework, we propose that oxytocin encodes the saliency or precision of interoceptive signals and enables the neuronal plasticity necessary for acquiring a generative model of the emotional and social 'self.' An aberrant oxytocin system in infancy could therefore help explain the marked deficits in language and social communication – as well as the sensory, autonomic, motor, behavioral, and cognitive abnormalities – seen in autism.

Contents

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1. Introduction

This review presents cellular, anatomic, physiologic, pharmacologic, genetic and behavioral evidence that speaks to a failure of the oxytocin system early in development. Using recent advances in our understanding of learning and inference, we consider how this single but pervasive deficit could result in the autistic phenotype.

Although structural brain abnormalities (Greimel et al., 2013), soft neurological signs (Tani et al., 2006), seizures (Amiet et al., 2008), motor disturbances (Rogers, 2007) and autonomic dysregulation (Benevides and Lane, 2013; Kushki et al., 2013) commonly occur in autism, it remains a clinical diagnosis with an elusive neurobiological etiology. Kanner (1943) first described autism in 1943 as a relatively rare condition; yet, in 2012, nearly 1 in 50 children between the ages of 6–17 carried a diagnosis of autism (National Center for Health Statistics, 2013). Numerous theories have been proposed to explain autism. Neurobiologically based theories include: autonomic dysregulation (Hutt et al., 1964; Porges, 1995); mirror neuron system deficits (Williams et al., 2001); neuronal migration abnormalities (Bailey, 1998); an imbalance of excitatory and inhibitory neurons (Rubenstein and Merzenich, 2003); and dysfunctional connectivity with sparse long range connections but excessive local connectivity (Belmonte et al., 2004). Cognitive theories include: deficits in Theory of Mind (Baron-Cohen et al., 1985); executive function and imitation difficulties (Rogers et al., 1996); weak central coherence (Frith and Happe, 1994); complex processing deficits (Minshew et al., 1997); and attentional deficits (in orienting, disengaging, and switching) (Courchesne et al., 1994). Theories focused on the social and behavioral symptoms include: dysfunctional social and affective relations (Hobson, 1991); impaired joint social attention (Mundy et al., 1990); reduced social motivation (Dawson et al., 1998); empathizing vs. systemizing (Baron-Cohen, 2006); and, what has been characterized as the extreme male brain (Baron-Cohen, 2002).

Recently, a Bayesian model for autism has been advanced, suggesting that "people with autism see the world more accurately – as it really is – as a consequence of being less biased by prior experiences." (Pellicano and Burr, 2012). This formulation of weak predictions and excessive sensitivity to sensory stimulation can account for the nonsocial symptoms of autism; including the hypersensitivity to environmental stimuli, savant qualities, and their reduced susceptibility to visual illusions. However, it does not provide a complete explanation for the social and communication deficits characteristic of autism, nor does it explain why autistic children fail to develop precise prior beliefs or appropriate models of their social and emotional world.

In this paper, we extend the Bayesian model to incorporate neurodevelopment and its physiologic substrates by proposing that a dysfunction in the oxytocin system, early in life, could account for the development of autism. As a key mediator of birth (Dale, 1909), lactation (Hatton and Wang, 2008; Nickerson et al., 1954), the suckling response (Schaller et al., 2010; Wrobel et al., 2010), pair bonding (Insel et al., 1995), maternal care (Francis et al., 2000) and affiliative behaviors (Baumgartner et al., 2008; Kirsch et al., 2005; Kosfeld et al., 2005; Zak et al., 2007), oxytocin stands as the most likely candidate to orchestrate the emergence of the social and emotional brain (Adolphs, 2009). In light of this, a Bayesian formulation of the function of oxytocin may provide a formal framework for understanding aberrant social inference and learning in autism and potentially suggest therapeutic strategies.

In brief, we suppose that an early pathophysiology in the oxytocin system could disrupt the assimilation of interoceptive signals and exteroceptive cues within generative models of the 'self'. These primary deficits would impair the child's ability to assign salience to socially relevant signals in the environment and disrupt the sensory attenuation necessary for proper homeostatic regulation, coordinated movement, and an outward focus during social encounters—thus undermining the imitation-based observational learning that normal children enjoy. Without a predilection for social stimuli and imitative responses, the behavioral repertoires or routines that eventually progress – through hierarchical assimilation into social interactions, language, biological movement, Theory of Mind and empathic responses – would fail to develop.

We start with a brief overview of the Bayesian brain and how oxytocin might implement the neuromodulation necessary for successful (interoceptive) inference and learning. With this theoretical perspective in place, we then consider the known neuromodulatory function of oxytocin and how aberrant neuromodulation might give rise to the autistic phenotype. Finally, we review the empirical evidence supporting this theory—evidence that speaks to abnormal interoceptive processing and subsequent failures of socio-emotional learning in autism and suggest how this theory might inform our approach to therapeutic treatment.

2. The Bayesian brain, neuromodulation, and interoception

2.1. Predictive coding

Current concepts of cerebral information processing suggest the brain constructs probabilistic internal models of the world which are continually updated to efficiently explain the causes of its sensory inputs (Dayan et al., 1995; Friston, 2005; Gregory, 1968, 1980; Helmholtz, 1885). Predictive coding is generally regarded as the most neurobiologically feasible scheme for updating and refining these internal models (Mumford, 1992; Rao and Ballard, 1999; Srinivasan et al., 1982). Predictive coding forms perceptual