

Running Title: Social Attention, Autism and the RDoC

Research on Social Attention in Autism and the Challenges of the Research Diagnostic Criteria (RDoC) Framework

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Lay Summary: Some researchers have suggested the study of categories of psychopathology, such as Autism Spectrum Disorder, may be less useful than examining how a common set of important mental processes contribute to all forms of psychopathology. However, the study of categories of psychopathology can sometimes reveal the important dimensions of human mental development that we need to study. This commentary argues that that this is the case for research on the nature and development of social attention in autistic people.

Abstract: The fuzzy nature of categories of psychopathology, such as Autism Spectrum Disorders, leads to significant research challenges. Alternatively, the study of a common set of important and well-defined mental processes across psychiatric conditions may make the fundamental etiological processes of psychopathology easier to discern and treat (Cuthbert, 2022). However, a categorical approach to psychopathology can serve to identify important constructs for such a “dimensional” approach to psychiatry because knowledge gleaned from the study of both normative and atypical development are mutually informative. This commentary describes a case in point provided by evidence of the pivotal nature of social attention as a major construct in the study of ASD (Mundy & Bullen, 2022), as well as in the study of psychopathology more generally (Tso et al. 2020).

Key Words: Social Orienting, Joint Attention, Eye Contact Effect, Face Processing, Autism, Research Diagnostic Criteria, Psychopathology

Introduction

There are significant neurobehavioral and genetic commonalities between Autism Spectrum Disorders (ASD) and other psychiatric conditions (Antshel & Russo, 2019; Baribeau et al. 2019; Hyman, 2019; Stergiakouli et al. 2017), as well as significant heterogeneity of the expression of ASD (Goergiadis et al. 2013; Warrier et al. 2022). These observations, among others, challenge a categorical definition of autism. Instead, adopting a dimensional approach to ASD, as well as psychopathology more broadly may be beneficial (Kim et al. 2019; Hollander et al. 1998; Sanislow et al. 2010). Such an approach is exemplified by the experimental Research Diagnostic Criteria (RDoC) framework of the National Institute of Mental Health in the USA (Cuthbert, 2022; Insel et al. 2010). The RDoC encourages research that would identify a common set of biobehavioral process that contribute to symptoms across diagnostics groupings. The goal is to make the fundamental etiological processes of psychopathology easier to discern and treat (Cuthbert, 2022). To this end, the RDoC framers identified six biobehavioral dimensions for study, 1) cognitive systems, 2) behavioral approach systems, 3) behavioral avoidance systems, 4) arousal modulation systems, 5) sensory motor systems and 6) social process systems¹. Operationally defined constructs are also identified within each dimension.

The creation of the current RDoC was a challenging task that was based largely on the knowledge acquired up through the first decade of the millennium (Insel et al. 2010). It has been successful in many ways, but has also created new research challenges along the way (Cuthbert, 2022). For example, the framework would benefit from revisions as new knowledge emerges. However, an explicit goal or mechanism to encourage such revisions was not clearly emphasized in the framework (Cuthbert, 2022). Revision of the social process systems dimension of the RDoC may be especially important because research on the emotional, social cognitive, and social neuroscience was only early in its development by 2010 and had been rapidly evolving (Carver & Johnson, et al. 2018; Kliemann & Adolphs, 2018; Pan et al. 2022; Redcay & Schilbach, 2018). In this regard it is useful to recognize that a categorical approach to psychopathology can serve to identify important constructs for a dimensional approach to psychiatry research (Franklin et al. 2015) and that knowledge gleaned from the study of both normative and atypical development are mutually informative (Cicchetti & Toth, 2006). A case in point is provided by evidence of the pivotal nature of social attention as a major construct in the study of ASD (Mundy & Bullen, 2022) and psychopathology more generally (Tso et al. 2020).

Social Attention as a Construct in Autism Research

Social attention refers to the behaviors, mental processes and underlying biobehavioral mechanisms involved in: 1) social orienting or the prioritization of attention to social stimuli such as faces, eyes, biological motion, social sounds and speech, 2) the eye contact effect or the impact of being the object of attention of another person, and 3) joint attention or the social coordination of attention between two or more people (Birmingham & Kingstone, 2009; Braithwaite et al. 2020; Mundy & Bullen, 2022; Nummenmaa & Clader, 2009; Salley & Columbo, 2016). Atypical early social attention is a characteristic symptom of the emergence of autism in infants between 6- to 12-months of age (e.g. Bussu et al. Chawarska et al. 2013; Franchini et al. 2019; Jones & Klin, 2015; Stallworthy et al. 2022). After three years of age these differences are associated with large group difference effect sizes and substantial diagnostic sensitivity and specificity, ranging from .82 and .81 (Dawson et al. 2004) to .92 and .92 respectively (Mundy et al. 1986). Large diagnostic group effect sizes, and diagnostic sensitivity and specificity, are essential characteristics of a valid dimension or construct in categorical research in psychopathology.

¹ See <https://www.nimh.nih.gov/research/research-funded-by-nimh/rdoc/constructs/rdoc-matrix>

Items that assess social attention are included in many evidence-based diagnostic and screening instruments for autism (Gotham et al. 2007; Mosconi et al. 2009; Robins et al. 2014; Stone et al. 2004). For example, joint attention items comprise five of the ten items of the Social Affect (SA) scales of Revised Autism Diagnostic and Observation Schedule used to assess social communication symptoms in young children (ADOS-2, Modules 1 and 2, Gotham et al. 2007). Hence, measures of social attention are a significant part of the reliable operational diagnostic definition of the preschool phenotype of autism (Mundy & Bullen, 2022).

Social attention can also be validly measured in children, adolescents and adults with typical development and autism (e.g., Bayliss et al. 2013; Gregory & Kessler et al. 2022; Freeth & Bugmenbe, 2019; Freeth et al. 2020; Grynszpan et al. 2019; Mundy et al. 2016; Nowell et al. 2018; Oberwelland et al. 2016), as well as among individuals who exhibit the broad autism phenotype (Elsabbagh et al. 2009; Morgan et al. 2021; Nayar et al. 2022; Swanson et al. 2013; Swanson & Siller, 2014; Zhou et al. 2015).

Social attention may be sensitive to sex differences in ASD (Charwaska et al. 2016; Harrop et al. 2018) and it can be assessed with multivariate measures (Nayar et al. 2022), parent report measures (Mundy et al. 2017), measures of temporal dynamics (Del Blanco et al. 2021) and response to eye contact measures (Akechi et al. 2014; Grynszpan et al. 2017; Mundy et al. 2016). Social attention can be assessed measured with visual measures directly in social interactions (Freeth & Bugmembe, 2019), and auditory measures in brain imaging studies in children with autism (Henandez et al. 2020). Latency measures can also be used to assess the effort associated with social attention/joint attention (Gredebeck et al. 2010; Oberwelland et al. 2016; Vaughn Van Hecke et al. 2012). Moreover, research suggests that social-attention remains less efficient or more effortful in older autistic individuals and those who exhibit the broad autism phenotype (Birmingham et al. 2017; Freeth et al. 2020), as well as in social interactions involving higher perceptual or cognitive load (Haskins et al. in press; Hernandez et al. 2020). Thus, children and adults with autism may be able to engage in social attention, but this may require greater effort which taxes the adaptive and effective use of social attention in social communication or didactic learning interactions (Mundy & Bullen, 2022). Finally, as alluded to above the neurodevelopment of social attention may be examined with EEG, fMRI, diffusion tensor imaging or optical imaging methods (see Mundy 2018, Tso et al. 2020 for reviews).

Social Attention and the Current RDoC Matrix

Although social attention is an important construct in the study of human development (Itier & Batty 2009; Mundy & Newell, 2007) and autism (Dawson et al. 2012; Klin et al. 2015; Mundy & Bullen, 2022) the construct of social attention does not appear in the current RDoC framework. Instead, social attention behaviors such as joint attention, reciprocal eye contact, and eye gaze detection, as well as face scanning or animacy perception measures of social orienting, are included as measures of other constructs, such as the *Reception of Facial Communication*, *Production of Facial Communication*, *Reception of Non-Facial Communication*. This designation is debatable for at least four reasons.

First, social attention is not limited to the visual modality and, therefore, does not always occur in conjunction with looking at faces (Adamson et al. 2021; Bigelow, 2003; Henandez et al. 2020). Indeed, the first observations of social orienting symptoms in autism came from research on orienting to social sounds, not faces (Dawson et al. 1998; Klin, 1991;).

Second, social attention often involves the “eye contact effect” (Becchio et al. 2008; Niedzwiecka, 2020; Senju & Johnson, 2009a). This refers to the effects that gaze directed to one’s self has on arousal, cognition, attention engagement, stimulus salience, motivation and affiliative behavior in infants, children and adults (Conty et al. 2016; Heitanen, 2018; Jarick et al. 2016; Rogers et al. 2014). Hypothetically, the eye contact effect is a function of a “fast track” neural network that is engaged approximately 150-170 msec after perception of eye-gaze directed either toward or away from an individual (Conty et al. 2010). Eye gaze direction is first processed via the superior colliculus, pulvinar,

and amygdala (Senju & Johnson, 2009a) and relayed for cortical processing. Both the time scale and cortical systems involved in this effect are distinct from those more specific to face processing (George et al. 2001; Hoffman & Haby, 2000, Hooker et al. 2003; Senju & Johnson, 2009a), such that gaze and face processing involve interactive but unique subcortical and cortical systems (Hadders-Algar, 2022; Yang & Friewald, 2021). Hypothetically, the mechanisms specific to the eye contact effect play a distinct role in the early development of joint attention and the social symptoms of ASD (Aketchi et al., 2014; Mundy, 2018; Mundy & Bullen 2022; Rayson et al. 2019; Senju & Johnson, 2009b).

Third, the communicative functions of face processing and social attention are distinctly different. The former often involves the conveyance of information about emotions through the expression and perception of facial affect (Mehu & Scherer, 2015). This plays a role in the social regulation of behaviors, such as when negative affect of parent inhibits approach behaviors in a preschool child (Sigman, et al. 1992), as well as other forms of social-emotional reciprocity in ASD (Zamplella et al. 2020). Alternatively, the function of social attention, or at least joint attention, involves referential and declarative communication (Bates, 2014). It involves adopting a common point of view about a common spatial or mental referent (Butterworth & Jarrett, 1991; Mundy, 2018; O'Madagain & Tomasello, 2021) with or without the mediation of facial or vocal affect.

The capacity to attend to a common referent is fundamental to both the phylogenetic (Gong & Shuai, 2012; Kwisthout et al. 2008) and ontogenetic development of human language (Baldwin, 1995; Rudd et al. 2008; Mundy et al. 2007; Tomasello et al. 2005), *as well as individual differences in the development of language in ASD* (Bottema-Beutel, 2016; Kasari et al. 2008; Kelty-Stephen et al. 2020; Loveland & Landry, 1986). These observations have motivated research on the role of mutual gaze and joint attention in early intervention for autism (Kasari et al. 2008; Murza et al. 2016; Rollins et al. 2021). There is far less evidence that directly links face processing, or facial communication and language development (but see, Bigelow et al. 2022; Glauser et al. 2021; Pascalis, et al. 2014). Of course, facial affect *may* impact joint attention in typical development and autism (Kasari et al. 1990), but joint attention symptoms in autism can be observed in the context of neutral facial affect (Gangi et al. 2014).

Fourth, evidence also links joint attention with intellectual development in autism (Harrison et al. 2016; Mundy et al. 1990; Sano et al. 2021). Didactic instruction requires that a “learner” coordinate their attention with a “teacher”, and visa-versa, in order to share information about a common point of reference (Striano et al. 2006; Madagain & Tomasello, 2021; Mundy, 2018). Hence, the development of social attention/joint attention plays a fundamental role in human learning (Baldwin, 1995). Autism, in turn, is associated with a syndrome specific distribution of intellectual development wherein 35% of children are comorbid for intellectual disability and another 23% are affected by intellectual disturbance or borderline intellectual difficulties (IQ = 71-85), but 42% function in the average or above average range (IQ > 85%, Maenner et al 2021). An early onset and chronic disturbance of social attention/joint attention may contribute to the syndrome specific distribution of IQ through its link to learning and cognitive development (Dawson, 2008; Klin et al. 2015; Mundy & Crowson, 1997; Vivanti et al. 2013). Such a link between face processing and intelligence is far less clear (Karle et al. 2018).

Notably, the RDoC also classifies joint attention as a measure of the *Perception and Understanding of Others* but under the subconstructs of *Animacy Perception and Action Perception*, rather than the subconstruct of *Understanding of Mental States*. Paradoxically, though, theory and developmental research have long made the case for the formative role of social attention in the development of the human capacity to understand the mental states of others (e.g., Baron-Cohen, 1997; Charman et al. 2000; Frieschen et al. 2007; Itier & Batty, 2009; Mundy, 2018; Stephenson et al. 2021; Tomasello et al. 2005). Accordingly, the early development of joint attention allows infants to repeatedly adopt and experience shared perspectives with other people between 6- to 18-months of age. This provides a necessary but not sufficient social information processing that stimulates the development of our human capacity to mentally adopt the perspective of another person (see Mundy et

al. 2009 for details). In other words, understanding mental states involves the cognitive developmental internalization of joint attention or the the action of sharing perceptual states with other people (Mundy, 2018). The current classifications of the social attention construct in the RDoC is not well aligned with these literatures.

Social Attention and a Revised RDoC Framework

If the construct of social attention is not well classified in the current RDoC frame work, what is the alternative? Social attention could be delineated in detail and designated as construct in *Understanding Mental States* within the dimension of the *Perception and Understanding of Others*. However, a revision of the RDoC framework would likely require evidence that social attention is a construct with applications not just for research on autism, but for a variety of other psychiatric conditions as well. Indeed, research on social attention/joint attention has contributed to understanding the common and distinct phenotypic feature of autism, specific language delay, fragile X syndrome, Down syndrome, Williams Syndrome, and sex chromosome trisomies (Bouw, 2022; Brewe et al. 2018; Franchini et al. 2019; Hahn et al. 2018; Thurman & Dimachkie Nunnally, 2022; Vivanti et al. 2017; Wolff et al. 2012). Moreover, Tso et al. (2020) have argued that disruptions of eye gaze perception mechanisms of social attention is a fundamental component of several other mental health conditions.

Schizophrenia is characterized by a tendency to over interpret ambiguous gaze direction information as indicative of self-referenced gaze or the perception of being the object of attention of another person (Caruana et al 2019; Chan et al. 2021; Hooker & Park, 2005; Tso et al. 2014; 2021a). This “self-referential bias” in the perception of gaze plays also appears to play a role in bipolar disorder and social anxiety (Berchio et al. 2017; Gamer et al. 2011; Schmitz et al. 2012; Schulze et al. 2013, Yao et al. 2018), and possibly ADHD (Mauriello et al. 2022). Alternatively, Hypo-responsiveness to self-referential gaze or the eye contact effect has been observed in research on ASD (Akechi et al. 2014; Grynszpan et al. 2017, Mundy & Bullen 2022). Interestingly, different patterns on unconscious processing of eye contact have been reported for autism (Akechi et al. 2014) and schizophrenia (Seymore et al. 2016) and the perception or response to gaze direction may distinguish social attention symptoms in autism from those in social anxiety (Hessels et al. 2018). Evidence also indicates that atypical social attention correlates with differences in social cognition in schizophrenia (Tso et al. 2014) and bipolar disorder (Tso et al. 2021b; Yao et al. 2018), just as it does in ASD (Oberwelland et al. 2017; von dem Hagen et al. 2014). This literature recently led Tso et al. (2020) to propose that social attention, or at least the altered eye-gaze perception, represents a common pathway to social dysfunction across psychiatric conditions regardless of diagnosis.

Of course, in the study of social-attention it is necessary to employ methods to distinguish whether what appear to be *social* attention mechanisms can be more parsimoniously explained in terms of general attention mechanisms (Lasagna et al. 2020). Tso et al. (2014; 2021a) have reported that self-referential or eye contact effects of gaze may be regulated by different neural networks and contribute to different symptoms and functions in individuals with psychopathology than do non-social mechanisms of attention regulation. Similarly, domain-general visual attention disengagement and domain specific social attention have been observed to provide unique and additive predictive information about the development of ASD in infant siblings (Bedford et al. 2014). Thus, rather than one dimension being primary or explanatory, social and non-social attention measures may provide additive and complimentary information about the development of ASD (Capozzi & Ristic, 2020; Bedford et al. 2014; Ramsay & Ward, 2020) and psychopathology more generally (Tso et al. 2022).

One reason to expect a complimentary rather the mediational relation between social attention and general attention is that the former taps into specific neural systems (e.g. Yang & Freiwald, 2021; Klein et al. 2009) and interpersonal mental processes that are not involved in the latter (Mundy & Bullen, 2022). Social attention is often bi-directional in that it involves both seeing *and being seen*

(Myllneva & Heitenen, 2016). As previously noted, social neuroscience has begun to document numerous significant effects of the perception of being seen or being the object of attention of other people (Heitenen et al. 2008; Mundy & Bullen, 2022; Rayson et al. 2019; Redcay & Schilbach, 2019; Reddy, 2003; Senju & Johnson, 2009a; Stephenson et al. 2021). These phenomena and their underlying neural mechanisms are not general or asocial attention paradigms, but current research raises the hypothesis that processes associated with self-referenced attention may play important roles in various forms of psychopathology (Mundy & Bullen, 2022; Shulze et al. 2013; Schmitz et al. 2012; Tso et al. 2020).

Summary and Implications

We are still in the age of initial discovery about the nature and mechanisms of human development (Miller, 2003; Ochsner & Libberman 2001), and psychiatric conditions, especially with respect to social process systems (Pan et al. 2022). Thus, there is a need to systematically update dimensional frameworks, such as the RDoC, that are designed to guide the development of more refined taxonomies of mental disorders. Observations of dimensions or constructs associated with large or consistent diagnostic groups differences can inform this process and this appears to be the case with the construct of social attention. Assuming that the social attention becomes a more precisely designated in the RDoC framework, here are few examples of how that could support new and valuable programs of study.

ASD and Attention Deficit Hyperactivity Disorder may be related childhood neurodevelopmental disorders of attention, rather than distinct conditions (Antshel & Russo, 2019; Baribeaur et al. 2019; Grzadzinski et al. 2011; Stergiakouli et al. 2017). However, few studies have compared these diagnostic groups on measures of social attention (Braithwaite et al. 2020). Nevertheless, Groom et al. (2017) observed that ASD and ADHD children differ in electrophysiological response to gaze cues (Groom et al. 2017) and ASD children differ for children with ADHD symptoms in response to having their own gaze followed in the context of joint attention (Mundy et al. 2016). It is reasonable to expect more comparative research on social attention in preschool and school aged children would provide new insights into the common or unique attention mechanisms involved in in ASD and ADHD (Braithwaite et al. 2020).

A significant neuroimaging literature has emerged that provides a foundation for understanding the neurodevelopment of social attention development in autism (Greene et al. 2011; Mundy, 2018; Nummenmaa & Calder, 2009; Senju & Johnson, 2009b; Stephenson et al. 2020). However, surprisingly little research has been conducted to examine the cortical correlates of social attention development in autism (Mundy, 2018) or comparatively across psychiatric conditions (Tso et al. 2020). There are, however, examples of intriguing sets of findings. For one example, Shen et al. (2022) observed altered growth in the amygdala among infants who went on to receive the diagnosis of autism. Previously, the rate of growth of the amygdala by two years of age was observed to be associated with joint attention at 4 years of age in ASD (Mosconi, et al. 2009). Finally, a third study indicates that connectivity of amygdala with the ventral-medial prefrontal cortex, via the arcuate fasciculus, at six months of age predicts joint attention in the 9th month of typical development (Elison et al. 2013). This illustrates how patterns of data from research on the neurodevelopment of social attention in autism, and other forms of developmental psychopathology may be of value.

There is a much smaller literature available on the genetics of social attention, but a foundation for future research has emerged (Mundy & Bullen, 2022). Behavioral genetics studies provide evidence of significant heritability of attention to eyes in 18-month-olds (Constantino et al. 2017), as well as gaze direction perception in adolescents (Wang et al. (2018, 2020). Several studies indicate that the dopamine, oxytocin and vasopressin transported genes are related to individual difference in joint attention and social orienting in primates, typical development and autism (Gangi et al. 2016; Hopkins et

al. 2014; Tops et al. 2011; Sjaarda et al. 2019; Wade et al. 2014). Moreover, genome wide DNA methylation is associated with attention to face stimuli with direct gaze in infant siblings of children with ASD (Gui et al. 2020) and methylation of the oxytocin receptor gene correlates with individual differences in social attention in typical adults (Puglia et al. 2018). If the construct of social attention is as central to autism, as is suggested here, then an increase in the recognition of the value of the construct for research on the genetics of social attention could advance autism science and developmental psychopathology more generally.

Finally, there is relatively little data on the development of social attention across childhood and adults in ASD or other conditions. Paradigms used for preschool social attention research may not be sensitive to significant differences in social attention in older individuals (Mundy & Bullen, 2022). Instead, measures of the effort or efficiency of social attention may be more useful. Moreover, the need to consider the ecological validity in research on social processes argues that we likely need to employ new methods of second person or interpersonal neuroscience in psychiatric research on social attention (e.g., Canigual et al. 2022; Hoehl & Markova, 2018; Pan et al. 2022; Redcay & Schibach, 2019).

In conclusion, over the past two decades science has begun to reveal the fundamental role of social attention in typical and atypical human social development. However, there is much more to be learned about the unique nature and role of social attention in autism and developmental psychopathology in general, and that is perhaps the most important point to be made in this commentary.

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