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Review article

Ripe for solution: Delayed development of multisensory processing in autism and its remediation

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ABSTRACT

Difficulty integrating inputs from different sensory sources is commonly reported in individuals with Autism Spectrum Disorder (ASD). Accumulating evidence consistently points to altered patterns of behavioral reactions and neural activity when individuals with ASD observe or act upon information arriving through multiple sensory systems. For example, impairments in the integration of seen and heard speech appear to be particularly acute, with obvious implications for interpersonal communication. Here, we explore the literature on multisensory processing in autism with a focus on developmental trajectories. While much remains to be understood, some consistent observations emerge. Broadly, sensory integration deficits are found in children with an ASD whereas these appear to be much ameliorated, or even fully recovered, in older teenagers and adults on the spectrum. This protracted delay in the development of multisensory processing raises the possibility of applying early intervention strategies focused on multisensory integration, to accelerate resolution of these functions. We also consider how dysfunctional cross-sensory oscillatory neural communication may be one key pathway to impaired multisensory processing in ASD.

1. Introduction

Humans and animals have evolved an exquisitely sensitive and highly diverse repertoire of sensory receptors to sample the multiple sources of energy available in our environment. In turn, neural plasticity during development allows the neural architecture of the infant brain to learn to combine and integrate these sources of information in ways that enhance performance and improve survival (Wallace et al., 2006). Thus, measures of task performance under multisensory conditions show that multiple species can take advantage of the often complementary or redundant sensory information available to them in their environment (Bahrick and Lickliter, 2000; Foxe and Simpson, 2002; Gibson, 1969; Hammond-Kenny et al., 2016; Stein et al., 1996), allowing them to evolve and adapt to novel ecological niches (Karageorgi et al., 2017). In the case of humans, watching lip and facial movements, hand gestures, head nods, facial configurational (Jaekl et al., 2015) and even feeling the breath of a speaker on your skin (Gick and Derrick, 2009) can all provide additional information to an observer trying to understand what a speaker is saying to them (Ma et al., 2009; Ross et al., 2011; Ross et al., 2007a; Sumby and Pollack, 1954). Even for more basic non-speech stimulus configurations, hearing a sound produced by a visual object is likely to enhance its detectability (Fiebelkorn et al., 2011; Molholm et al., 2002; Van der Burg et al., 2008). Simply put, through binding of multiple sensory inputs in the nervous system, multisensory integration (MSI) allows one to form higher fidelity representations of the environment, which in turn promote adaptive behavior (Molholm and Foxe, 2010; Stein, 1998).

Congruent multisensory inputs tend to enhance task-relevant performance when compared to circumstances under which solely unisensory input is made available (Giard and Peronnet, 2006; Molholm et al., 2002; Talsma and Woldorff, 2005; Teder-Sälejärvi et al., 2002), with performance often exceeding linear predictions based on unisensory processing. When these integrative behavioral patterns are observed, they are also generally reflected in nonlinear neural responses, i.e. multisensory integration (MSI) (Beauchamp et al., 2010; Butler et al., 2016; Foxe et al., 2000; Foxe and Schroeder, 2005; Meredith and Stein, 1983; Molholm et al., 2002). There are multiple parallel and hierarchically organized processing stages in the brain at which multisensory information may interact to affect sensory-perceptual and motor processes (Driver and Noesselt, 2008; Rohe and

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Noppeney, 2016), such as stimulus detection, localization, identification, and action planning (Fiebelkorn et al., 2013; Lucan et al., 2010; Mercier et al., 2015; Nath and Beauchamp, 2012). An important consideration pertains to the variable timing of neural transmission through the early hierarchical stages of the initially segregated sensory processing streams. Inputs arriving at the separate sensory epithelia (e.g. the skin, the hair cells in the cochlea, the retina) must be "tagged" by the central nervous system as belonging together in the face of varying transmission times from sensory receptors to subcortical regions and on into cortex. In turn, information that is represented in anatomically segregated brain regions must be communicated across significant cortical distances, perhaps involving multisynaptic cascades that propagate across several intervening functional regions, but possibly also via mono-synaptic long-range inter-regional connections (Falchier et al., 2010; Foxe and Schroeder, 2005; Keniston et al., 2010; Rockland and Ojima, 2003). Given the multiple processes that MSI must be built upon, which require long-range network integrity and functionality, it is a reasonable proposition that MSI may be particularly vulnerable to insult. Indeed, MSI has been shown to be impaired in a number of complex neurodevelopmental and neuropsychiatric disorders, such as dyslexia (Francisco et al., 2017; Hahn et al., 2014), schizophrenia (Ross et al., 2007b) and rare lysosomal storage disorders (Andrade et al., 2014), to mention just a few. As we will elaborate below, however, it is ASD in particular that has been most extensively investigated and associated with dysfunction in MSI processing.

Cardinal symptoms of autism spectrum disorder (ASD) include deficits in social interaction, and restricted interests and repetitive behaviors (APA, 2013). These are often accompanied by hypo- or hypersensitivity to sound, light, and touch (Kanner, 1943; Kern et al., 2006). It has long been proposed, based on clinical evaluations and parental observations, that dysfunction in multisensory integration may be a significant component of the sensory atypicalities and social communication deficits seen in ASD (Ayres and Tickle, 1980; Iarocci and McDonald, 2006; Martineau et al., 1992; Molholm and Foxe, 2010). In what follows, we assess the current state of knowledge regarding MSI in autism, focusing specifically on the impact of development on these processes, and on audiovisual paradigms for which there is a substantial literature. It should be pointed out that these studies all involve individuals with largely normal range IQs (this is often necessary for task performance, and also allows for comparison with a typically developing control group), and thus generalization should be limited to high functioning individuals on the autism spectrum. In turn, we consider how naturally occurring training may serve to improve MSI function in ASD, and how this can be leveraged to shift improvements in function to earlier stages of development. Finally, we forward a possible mechanistic account of altered MSI in ASD. For easy reference, Table 1 presents a list of studies that we cite here on multisensory processing in ASD, along with a brief summary of the study paradigms and major findings.

1.1. Multisensory integration in autism: a developmental perspective

The development of multisensory processing and integration has been meticulously investigated in animal models, primarily through electrophysiological recordings in the superior colliculus (SC; see (Meredith and Stein, 1983)). This midbrain structure is involved in rapid orienting responses, and contains both bisensory and trisensory neurons that receive combinations of auditory, visual, and somatosensory inputs (Meredith and Stein, 1986). From these studies, we have learned that the organism's specific experiences with the multisensory environment significantly influence the development of MSI. For example, while there are neurons present in the SC at birth that respond to more than one channel of sensory input, these cells do not initially show integrative, non-linear, responses. Rather, MSI properties develop only after experience with multisensory cues has been gained (Wallace et al., 2004; Wallace and Stein, 1997, 2001, 2007). Wallace and Stein (2007) provided a particularly powerful example of environmental influences on the development of MSI, showing how the natural spatial overlap of multisensory SC receptive fields for the different sensory modalities can be dramatically influenced through manipulations of the post-natal environment. Animals were raised in a sensory environment where the only auditory and visual stimuli they were exposed to, while temporally coupled, were spatially displaced from each other in a consistently mapped fashion. This led to massively altered functionality of the SC audiovisual neurons since they developed mismatched auditory and visual spatial fields such that only stimulation of the spatially disparate visual and auditory mappings generated integrative responses (Wallace and Stein, 2007).

Based on abundant evidence for early plasticity of the multisensory system in animal models, it is not surprising that developmental studies in humans also show that extensive experience is necessary before the nervous system can fully benefit from multisensory cues. Sensitivity to temporal coincidence of rhythmic audiovisual stimuli, and to the congruency of native audiovisual speech stimuli, appear to emerge already within the first year of an infant's life (Lewkowicz, 1996, 2003; Pons et al., 2009). Yet, multisensory influences on perception and performance are nevertheless greatly reduced in young children when compared to adolescents and young adults (Brandwein et al., 2011; Burr and Gori, 2012; Ernst, 2008; Gori et al., 2012; Ross et al., 2015, 2011; Cowie et al., 2013, 2016; Greenfield et al., 2017). Several psychophysics studies found that children younger than eight years of age do not optimally integrate haptic and visual cues, but instead that prior to that point, one sense dominates the other, depending on the specific task demands (Gori, 2015; Gori et al., 2008, 2012). This protracted plasticity of multisensory processing may enable the flexible use of multisensory information. For example, the child can learn to integrate multisensory speech cues that are specific to their native language (Lewkowicz, 2014), and individuals readily adapt to changes in body schema to effectively interact with objects in their environment (Cardinali et al., 2009).

Given the prolonged trajectory of the development of multisensory processing and the extensive influence of the environment on MSI operations, MSI deficits in ASD may be best understood in a developmental context. Here we focus on audiovisual MSI in ASD, where the bulk of the relevant studies are found. We note that it is likely that the developmental course of multisensory processing, and how it is impacted in ASD, will differ somewhat as a function of the sensory modalities and the specific processes under consideration.

1.1.1. Multisensory integration of audiovisual speech

Deficits in language and socio-emotional processing are canonical symptoms of autism (APA, 2013). Audiovisual speech is a particularly rich and natural occurring multisensory signal that conveys both linguistic and extra-linguistic (including social and emotional) information, and thus it is not surprising that many studies of MSI in ASD have focused specifically on the integrity of audiovisual speech perception (Bebko et al., 2006; Irwin and Brancazio, 2014; Kujala et al., 2005; Paul et al., 2005; Silverman et al., 2010; Smith and Bennetto, 2007). In general, these studies have demonstrated multisensory speech deficits in children with autism. For example, in a cross-sectional study performed by our group (Foxe et al., 2015), we assessed the development of multisensory speech perception in individuals with and without ASD, from 7 to 19 years of age. Spoken monosyllabic words were presented in varying degrees of background noise, making them difficult to identify, and the benefit of an accompanying video of the speaker saying the word was then assessed. In this audiovisual speech-in-noise paradigm, younger children with ASD (7–12 year olds) showed severe deficits in multisensory speech perception when compared to controls (see also (Irwin et al., 2011; Stevenson et al., 2017)). Crucially, although identification of the auditory-alone words was essentially equivalent between the ASD and TD groups (i.e. unisensory processing appeared to be largely intact), individuals with ASD simply did not