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Multisensory temporal binding window in autism spectrum disorders and schizophrenia spectrum disorders: A systematic review and meta-analysis

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ABSTRACT

Multisensory temporal integration could be compromised in both autism spectrum disorders (ASD) and schizophrenia spectrum disorders (SSD) and may play an important role in perceptual and cognitive impairment in these two disorders. This review aimed to quantitatively compare the sensory temporal acuity between healthy controls and the two clinical groups (ASD and SSD). Impairment of sensory temporal integration was robust and comparable in both patients with SSD (Hedges' g = 0.91, 95%CI[0.62–1.19]; Z = 6.21, $p < .001$) and ASD (Hedges' g = 0.85, (95%CI[0.54–1.15]; Z = 5.39, $p < .001$). By further separating studies into unisensory and multisensory (bimodal: audiovisual) ones, subgroup analysis indicated heterogeneous and unstable effects for unisensory temporal binding in the ASD group, but a more consistent and severe impairment in multisensory temporal integration represented by an enlarged temporal binding window in both clinical groups. Such multisensory dysfunction is associated with symptoms like hallucinations and impaired social communications. Future studies focusing on improving multisensory temporal functions may have important implications for the amelioration of schizophrenia and autistic symptoms.

1. Introduction

After the establishment of autism as a separate category from early-onset schizophrenia in DSM-III(American Psychiatric Association, 1987), autism spectrum disorders (ASD) and schizophrenia spectrum disorders (SSD) have been considered distinct disease entities with different aetiologies, clinical manifestations and diagnostic classification. However, substantial findings have shown that these two "distinct" clinical entities may in fact be closely related and may even lie on the same continuum of neurodevelopmental disorders (King and Lord, 2011). The two disorders share significant overlap in genetics (Carroll and Owen, 2009), connectivity deficits (Friston et al., 2016; Just et al., 2004) and impaired social cognition (Pinkham et al., 2008). There is also a high rate of co-morbidity between schizophrenia and autism/pervasive developmental disorders in both children (Rapoport et al., 2009) and adults (Chisholm et al., 2015). On the other hand, results from comparative studies have suggested that different underlying mechanisms may account for these apparent similarities (Crespi and Badcock, 2008; Crespi et al., 2010; Russell-Smith et al., 2010). Examining this overlap using a trans-diagnostic approach may help to advance our understanding of these two disorders.

One of the hallmark features of both disorders is sensory and multisensory dysfunctions (Baum et al., 2015; Tseng et al., 2015). Sensory abnormalities are prominently prevalent in ASD (Baranek et al., 2006) and are now included as a core symptom of this disorder in the DSM-5 (American Psychiatric Association, 2013). Considering early sensory stages and local processing, a subgroup of autistic children has been shown to possess improved sensory acuity (e.g., recognizing perfect pitch, superior ability to discriminate visual appearance with minor changes) (Happé and Frith, 2006; Mottron et al., 2006; Mottron et al., 2009). However, when it comes to high-level global function and multisensory interactions, robust and consistent impairment has been demonstrated in ASD (see reviews, Baum et al., 2015; Wallace and Stevenson, 2014), with neuroimaging evidence showing failure to

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activate large-scale cortical networks (Damarla et al., 2010) and reduced long range connectivity (Damarla et al., 2010; Glazebrook and Wallace, 2015). Thus, it is important to extend beyond unisensory function to further investigate multisensory integration in ASD. As for SSD, basic unisensory deficits including impaired auditory gating and fragmented visual perception may underlie abnormal perceptual experience (e.g., hallucinations) and difficulties in interpersonal and social interactions (Javitt and Freedman, 2015). Beyond unisensory function, a recent review has demonstrated the presence of deficits in integrating cross-modal information, especially audiovisual linguistic stimuli in patients with schizophrenia (Tseng et al., 2015). Neuroimaging studies have reported that multisensory deficits in schizophrenia are associated with alterations in brain networks responsible for sensory and language functioning, including the superior and inferior frontal cortices, and the superior and middle temporal cortices (Sass et al., 2014; Straube et al., 2014; Szycik et al., 2013). Other subcortical regions like the thalamus, which is consistently found to be dysfunctional in schizophrenia (Cobia et al., 2017; Giraldo-Chica and Woodward, 2016), may also affect multisensory performance in this clinical group. Multisensory processing may therefore serve as a “gateway” to investigate the underlying pathology of ASD and SSD.

In this study, we specifically focused on the temporal factor of multisensory integration as accumulating evidence supports its relevance in neurodevelopmental disorders (Wallace and Stevenson, 2014) since Brock et al. (2002) first put forward the temporal binding hypothesis to explain sensory abnormalities in ASD. “Temporal Binding Window” (TBW), an epoch of time within which paired stimuli are highly likely to be bound, is a concept commonly used to reflect multisensory temporal function or acuity. Two of the most common paradigms to measure the width of TBW are the Simultaneity Judgement (SJ) and the Temporal Order Judgement (TOJ) task. In these tasks, participants are asked to judge the relative timing of an auditory and visual stimulus with different stimulus onset asynchronies (SOA) (i.e., “Were the auditory and visual stimuli presented at the same time?” for SJ and “Which stimulus came first?” for TOJ). Rates of perceived simultaneity or accuracy for judging temporal order across different SOAs are used to calculate the width of the TBW. Typically, the time interval between 75% threshold of the audio-first presentations and visual-first presentations is defined as the individual’s TBW (Stevenson et al., 2017a). Within this “window”, participants have a high probability of reporting simultaneity and find it hard to discriminate the temporal order of the paired sensory stimuli. An extended TBW reflects imprecise temporal processing of sensory stimuli. Combining sensory information which could be distinguished by individuals with a narrower TBW may result in sensory overload, ambiguous perceptual identity and perception of an improperly filtered confusing world (Sartorato et al., 2017). It may also undermine speech comprehension (Stevenson et al., 2012), contribute to reading difficulties (Hairston et al., 2005), and result in hallucinations (Stevenson et al., 2017a) and a disturbed sense of “self” (Postmes et al., 2014).

Developmentally, multisensory TBW tends to be longer in late adolescence, progressively shortens in adulthood (Hillock-Dunn and Wallace, 2012), and gradually lengthens again with ageing (Diederich et al., 2008; Setti et al., 2011). In clinical populations, previous findings have demonstrated multisensory temporal dysfunction indexed by a prolonged sensory TBW in both ASD and SSD (Wallace and Stevenson, 2014). However, little is known about the differences and similarities of the underlying mechanisms underlying the prolonged TBW in these two clinical groups. The aim of this study was to quantitatively review the literature on sensory temporal integration impairment in ASD and SSD. In addition, we examined the unsolved issues of multisensory impairments in these two clinical groups and discussed the future directions for multisensory integration.

2. Methods

2.1. Literature search

Four authors (HYZ, PB, XLC, MW) independently conducted literature search in PubMed, PsychoInfo, Web of Knowledge and Academic Search Complete for peer-reviewed, original studies published up to May 12, 2017. We included papers in all languages. The following terms were used: ("temporal binding window" OR "temporal binding" OR "binding window" OR "temporal processing" OR "temporal integration" OR "binding problem") AND (schizo* OR autis*). In addition, the reference lists of all included studies and three relevant systematic reviews (Baum et al., 2015; Tseng et al., 2015; Wallace and Stevenson, 2014) were also manually searched for further relevant studies. Studies were included if they met the following criteria: 1) used an appropriate paradigm for (multi-)sensory temporal processing. Two of the most common paradigms are the SJ Task and the TOJ Task mentioned earlier. Other possible paradigms include the Sound-induced-Flash Illusion Task and the McGurk task with different audiovisual SOAs. In the Sound-induced Flash Illusion Task, one flash is accompanied by two sound stimuli to induce double flash illusion. The first sound coincides with the onset of the flash, while the second sound is presented with a delay after the first flash-sound pair. The intensity of audiovisual integration is indicated by the amount of perceived illusions, which depends on the influence of auditory stimuli on vision. As defined by Foss-Feig et al. (2010), the multisensory TBW is the span of illusory SOAs where the mean percentage of reported double flashes is significantly greater than the mean percentage of reported double flashes in the control condition (i.e., one flash one sound). In the McGurk task, the percentage of perceived “da” for mismatched audiovisual stimuli (visual “ga” and auditory “ba”) is the proxy for the intensity of multisensory integration. The mean rates of McGurk fusion across different SOAs are normalized to an individual’s maximum fusion rate, and then used to calculate the width of the TBW within which fusion is reported for at least 75% of the trials (Woynaroski et al., 2013). It is important to note that one study (Grimsen et al., 2013) we included in our meta-analysis used a seemingly irrelevant paradigm. However, a further examination suggested that the temporal figure-and-ground segmentation task used in this study measured an individual’s visual asynchrony detection ability (Grimsen et al., 2013). In other words, this paradigm was a variant of the SJ task and thus was also included in our meta-analysis. 2) included a clinical sample (either schizophrenia or autism spectrum disorders) and a healthy control group; and 3) provided sufficient data for calculating effect size. Specifically for Criterion 3, we extracted the reported means, standard deviations and sample sizes for patient and control groups. If the means and standard deviations were not reported, effect sizes were calculated based on the t or F values and the sample sizes. If one study met the first two criteria but failed to fulfill the third, they were excluded from the meta-analysis but retained in the systematic review (see in Table 1). We excluded the studies if they met any of the following exclusion criteria: 1) the study was a review, meta-analysis, comment or a dissertation paper; 2) the study did not have an appropriate paradigm which was specific to (multi-)sensory temporal binding; and 3) the study only involved non-clinical samples or clinical groups (e.g. ADHD) other than schizophrenia and ASD.

2.2. Data extraction

First, all the included studies were separated into four subgroups randomly. Then, demographic and clinical characteristics (sample size, age, gender, clinical symptoms, medication, illness duration and comorbidities), study design (paradigm, sensory modality and stimulus type), mean differences in the widths of TBWs or raw data were extracted independently by four authors (HYZ, PB, XLC, MW) for each subgroup. Finally, the first author (HYZ) thoroughly went through all