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Running Title: Neural correlates of temporal binding window

Neural correlates of audiovisual temporal binding window in individuals with schizotypal and autistic traits: Evidence from resting-state functional connectivity

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Lay summary

Individuals with ASD and schizophrenia are more likely to perceive asynchronous auditory and visual events as occurring simultaneously even if they are well separated in time. We investigated whether similar difficulties in audiovisual temporal processing were present in subclinical populations with high autistic and schizotypal traits. We found that the ability to detect audiovisual asynchrony was not affected by different levels of autistic and schizotypal traits. We also found that connectivity of some brain regions engaging in multisensory and timing tasks might explain an individual's tendency to bind multisensory information within a wide or narrow time window.

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Abstract

Temporal proximity is an important clue for multisensory integration. Previous evidence indicates that individuals with autism and schizophrenia are more likely to integrate multisensory inputs over a longer temporal binding window (TBW). However, whether such deficits in audiovisual temporal integration extend to subclinical populations with high schizotypal and autistic traits is unclear. Using audiovisual simultaneity judgement (SJ) tasks for non-speech and speech stimuli, our results suggested that the width of the audiovisual TBW was not significantly correlated with self-reported schizotypal and autistic traits in a group of young adults. Functional magnetic resonance imaging (fMRI) resting-state activity was also acquired to explore the neural correlates underlying inter-individual variability of TBW width. Across the entire sample, stronger resting-state functional connectivity (rsFC) between the left superior temporal cortex and the left precuneus, and weaker rsFC between the left cerebellum and the right dorsal lateral prefrontal cortex were correlated with a narrower TBW for speech stimuli. Meanwhile, stronger rsFC between the left anterior superior temporal gyrus and the right inferior temporal gyrus was correlated with a wider audiovisual TBW for non-speech stimuli. The TBW-related rsFC was not affected by levels of subclinical traits. In conclusion, this study indicates that audiovisual temporal processing may not be affected by autistic and schizotypal traits and rsFC between brain regions responding to multisensory information and timing may account for the inter-individual difference in TBW width.

Keywords: temporal binding window; audiovisual; resting-state functional connectivity; schizotypal traits; autistic traits

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Introduction

We live in a multisensory world with large amount of information from different sensory modalities. Our coherent perception of the external environment is largely dependent on the seamless integration of cross-modal information from the same sources and at the same time, the appropriate segregation of irrelevant inputs derived from separate objects. Sensory stimuli presented close in time are more likely to be integrated and perceived as a unified representation (Meredith, Nemitz, & Stein, 1987). However, our brain does not require perfect simultaneity but allows for a certain degree of temporal asynchrony to integrate multisensory stimuli. This range is defined as the temporal binding window (TBW), within which individuals find it hard to tell the time difference and have a high probability of reporting simultaneity (Wallace & Stevenson, 2014). The width of the TBW, regarded as a proxy for multisensory temporal precision (with a narrower TBW representing higher accuracy in multisensory integration), has been found to show large inter-individual variability and is associated with higher-order cognitive and social skills in the general population (Noel, De Niear, Lazzara, & Wallace, 2018; Stevenson, Zemtsov, & Wallace, 2012; Zmigrod & Zmigrod, 2016). Extending to clinical populations, abnormally enlarged TBW is a shared characteristic of several neurodevelopmental disorders, including schizophrenia and autism (Wallace & Stevenson, 2014; Zhou et al., 2018). Moreover, this stronger tendency to perceive temporally-discrete stimuli as simultaneous may cascade into unusual perceptual experiences in schizophrenia (Stevenson et al., 2017) and impaired communicative and language skills in autism (Righi et al., 2018; Stevenson et al., 2018).

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Under the hypothesis of a continuum between schizotypal/autistic traits and schizophrenia/autism (Constantino & Todd, 2003; Nelson, Seal, Pantelis, & Phillips, 2013), some researchers have tried to disentangle the relationship between subclinical traits and multisensory TBW in non-clinical individuals. Individuals with elevated autistic traits seem to have normal width of TBW compared with their low-trait counterparts (Donohue, Darling, & Mitroff, 2012; Noel, Lytle, Cascio, & Wallace, 2018; Zhou, Shi, Yang, Cheung, & Chan, 2020). This lack of significant correlation between autistic traits and audiovisual TBW may be partly due to the fact that autistic traits comprise various dimensions that are differentially and oppositely correlated with the width of audiovisual TBW (van Laarhoven, Stekelenburg, & Vroomen, 2019; Yaguchi & Hidaka, 2018). Specifically, autistic traits of social skills and attention to detail were found to be associated with a narrower TBW while autistic traits of communication and attention switching were correlated with a wider TBW (van Laarhoven et al., 2019; Yaguchi & Hidaka, 2018). As for individuals with schizotypal traits, two studies have reported that higher levels of schizotypal traits, especially in the cognitive-perceptual dimension, are correlated with reduced temporal resolution on integrating auditory-tactile (Ferri et al., 2017) and audiovisual (Ferri et al., 2018) stimuli. However, two more recent studies (Muller, Dalal, & Stevenson, 2020; Zhou, Shi, et al., 2020) did not find any significant relationship between schizotypal traits and audiovisual TBW in the general population.

Overall, although it is clear that both patients with autism and schizophrenia are less sensitive to audiovisual asynchrony as indexed by a broadened TBW (Wallace &

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Stevenson, 2014; Zhou et al., 2018), the existing findings on subclinical individuals are mixed. Furthermore, there is a lack of previous work investigating individuals with high autistic and schizotypal traits using the same multisensory paradigm. Given the significant positive correlations between autistic and schizotypal traits in non-clinical populations (Zhou et al., 2019), it would also be interesting to explore how co-occurring autistic and schizotypal traits affect multisensory temporal processing.

Notwithstanding the accumulating research on TBW, neural substrates underlying its considerable individual difference remain largely unknown. Previous task-based fMRI studies that compare audiovisual perception of asynchronous pairings with synchronous ones have indicated that a large-scale network is involved in the successful detection of temporal discrepancy (Zhou, Cheung, & Chan, 2020). Specifically, the posterior superior temporal cortex (pSTC) is a hub region for multisensory integration (Stevenson, VanDerKlok, Pisoni, & James, 2011), receiving forwarding sensory signals from primary sensory areas. The prefrontal regions may be responsible for error detection and conflict resolution of asynchronous audiovisual inputs (Lamichhane & Dhamala, 2015). The supplementary motor region, which is engaged in sensorimotor integration and the cerebellum, which tracks the onset of different sensory stimuli, also work in coordination to facilitate more accurate sensory decisions (Lee & Noppeney, 2011). Although previous task-based fMRI studies have reported some brain activation patterns associated with audiovisual temporal processing, it is not clear what interactions or connectivity

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between the above regions and other cortical areas are directly linked to the observed individual variability in TBW width. Resting-state brain activity, on the other hand, has the potential to shed light on the individual's tendency to integrate multisensory stimuli over a wide or narrow TBW (Ferri et al., 2017). Resting-state functional connectivity (rsFC) measures temporal correlation of spontaneous BOLD signals between spatially discrete brain areas and regions whose activities are highly correlated may form a functional network to fulfill specific cognitive tasks (Woodward & Cascio, 2015). Using the seed-based approach and correlating the activity of pre-defined TBW-related regions (Zhou, Cheung, et al., 2020) with the rest of the brain, it is possible to reveal specific patterns of functional connectivity that are dimensionally related to the audiovisual TBW.

This study had two aims. First, we assessed the relationship between autistic/schizotypal traits and the audiovisual TBW width for both non-speech and speech stimuli. Using audiovisual simultaneity judgment (SJ) tasks, multisensory temporal integration ability was correlated with different dimensions of autistic and schizotypal traits. Based on previous findings, we hypothesized that increased levels of these subclinical traits would be correlated with a wider TBW, and co-occurring high autistic-schizotypal traits may have additive detrimental effect on audiovisual temporal acuity. Second, resting-state functional imaging data were acquired to examine the neural correlates of the observed individual difference in audiovisual TBW width. Seed-based rsFC was correlated with the width of the audiovisual TBW. The seeds of the TBW-related network were selected based on a quantitative

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neuroimaging meta-analysis (Zhou, Cheung, et al., 2020), including some key areas activated during the perception of asynchronous audiovisual stimuli. These seeds were the pSTC bilaterally, the left cerebellum and the left inferior frontal gyrus (see Figure 1). We hypothesized that rsFC between these key regions would be correlated with the width of the audiovisual TBW and the strength of these correlations would be affected by different levels of schizotypal and autistic traits.

Methods

Participants

A total of 115 healthy young adults (18-30 years; M_{age} = 21.37 years, *SD* = 2.53; 40% males) were recruited from a large sample pool (*n* = 2241). All participants completed a series of online questionnaires to assess their self-reported subclinical symptoms. They reported no history of any developmental or psychiatric disorders, no history of severe brain injury and normal vision (or corrected-to-normal vision) and hearing. None of them had an estimated IQ below 85.

This study was approved by the Ethics Committees of the Institute of Psychology, the Chinese Academy of Sciences. Written informed consent was obtained prior to the participation of the study.

Subclinical traits

The Schizotypal Personality Questionnaire (SPQ) (Raine, 1991) was used to assess schizotypal traits. The SPQ is a 74-item yes-no dichotomous scale, consisting of three

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subscales of cognitive-perceptual, interpersonal and disorganized dimensions. Autistic traits were assessed by the 50-item Autism Spectrum Quotient (AQ) (Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001), which examines autism-like symptoms classified into five dimensions including social skills, communications, attention switching, attention to detail, and imagination. Higher SPQ and AQ scores indicate higher levels of schizotypal and autistic traits respectively. The Chinese versions of the SPQ and AQ show good psychometric properties and have been widely used in Chinese contexts (Chen, Hsiao, & Lin, 1997; Zhang et al., 2016). In this study, the SPQ and AQ have a Cronbach's α of 0.96 and 0.85. Most of the subscales of the AQ and SPQ have good and acceptable reliability (range of Cronbach's α = 0.62 - 0.93) (supplementary table 1). The attention switching and imagination subscales of the AQ show relatively low but acceptable internal consistency (Cronbach's α = 0.55 and 0.56).

Cognitive assessments

Intelligence quotient (IQ) was assessed using the brief version of the Chinese version of the Wechsler Adult Intelligence Scale (WAIS) (Gong, 1981). Four subtests of the WAIS, including the information, similarities, mathematics and digital span, were used to estimate verbal IQ of all participants.

Audiovisual temporal integration

Participants sat in a sound-attenuated, dimly lit room to complete two

audiovisual SJ tasks with different stimulus types in separate runs, with the flashbeep condition first and then the syllable utterance condition. Visual stimuli were presented in a screen about 60 cm from the participant and auditory stimuli were presented via a headphone. In the flashbeep task, a white circle centered on the screen (radius = 15 cm, thickness = 4 cm; duration =13.3 ms) was coupled with a beep (1000Hz, duration =13 ms), with various stimulus onset asynchronies (SOAs) including 0, ±13, ±27, ±53, ±80, ±106, ±147, ±200, ±253, ±306ms. Negative and positive values of SOAs corresponded to auditory-leading and visual-leading stimulus pairs. For the syllable utterance task, a short video with a female speaker uttering the single syllable "ba" was presented (25 frames per second; 400 × 400 pixels). The SOAs included 0 to ±320ms in 40ms intervals, ±400ms and 480ms. Participants were asked to report whether the auditory and visual stimuli were presented simultaneously via a button press. They completed 15 trials per SOA condition, with all trials randomly presented. It took approximately 30 minutes for the participants to complete the two SJ tasks, and they were given two chances to rest during each run (after completing one third and two thirds of all trials).

The percentage of reporting "synchrony" for each SOA was calculated to estimate the TBW for each participant and stimulus type. The Gaussian function was used to fit the distributions of "simultaneity" report across SOAs (1) (Noel, Lytle, et al., 2018):

$$\mathrm{y}(x) = amp \times \exp^{-\left(\frac{-(x-PSS)^2}{2SD^2}\right)} \qquad (1)$$

In Equation (1), the amplitude indexed an individual's general bias to perceive

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simultaneity (at their peak synchrony report); the mean was taken as the Point of Subjective Simultaneity (PSS), at which SOA the judgment of synchrony was maximum, and the standard deviation was used to represent an individual's TBW, a temporal range over which participants were highly likely to report synchrony (Noel, Lytle, et al., 2018).

We excluded participants who did not attend to the tasks and performed as outliers. Specifically, participants whose simultaneity responses at the largest auditory-leading or visual-leading SOAs were higher than the mean plus two standard deviations (SDs), or the simultaneity response at the SOA = 0 condition was lower than the mean minus 2 SDs, were excluded (Chen, Shore, Lewis, & Maurer, 2016). As a result, 10 and eight individuals were excluded in the flashbeep and the syllable utterance conditions respectively. No participant's behavioural data was excluded for both SJ tasks. For the rest of the sample, Gaussian distributions adequately represented the shape of the resulting distribution of reports of synchrony (goodness-of fit, mean adjusted R^2 = 0.78 and 0.82 for flashbeep (n = 105) and syllable (n = 107)) (Figure 2).

To investigate the effect of subclinical traits on audiovisual temporal integration, Spearman correlations between the TBW width and different dimensions of autistic and schizotypal traits were first calculated. Multiple linear regressions were then conducted in which the total scores of the AQ, the cognitive-perceptual dimension score of the SPQ and their interaction term were entered as predictors for the TBW width, apart from other demographic variables (i.e., age, gender and IQ). The trait

scores were standardized before calculating the interaction term. We chose the cognitive-perceptual dimension of the SPQ instead of the total score because there is significant overlap between the interpersonal dimension of the SPQ and autistic traits (Zhou et al., 2019). Nevertheless, we also repeated the regression analysis using the SPQ total score.

fMRI data acquisition and preprocessing

Neuroimaging data were collected on a GE 3.0 Tesla scanner. The resting-state fMRI (echo-planar imaging) entailed 300 functional volumes (time repetition (TR) = 2000ms, echo time (TE) = 30ms, 37 slices, flip angle = 90º, field of view =220mm, voxels = 3.4×3.4×3.5mm^3, and slice spacing = 0.5mm). For spatial normalization, a high-resolution T1-weighted anatomical image was also acquired using a 3-Dimensional Spoiled Gradient Recalled (SPGR) sequence (TR = 6.90ms, TE = 2.99ms; inversion time (TI) = 450ms, flip angle = 8º, voxels = 1×1×1 mm^3, 176 slices, matrix = 256×256; and field of view = 256mm). During scanning, participants were instructed to minimize their head motion, with their eyes open while a fixation was centrally projected onto a screen.

Data preprocessing was conducted using the Data Processing & Analysis for Brain Imaging (DPABI, version 4.0) toolbox (Yan, Wang, Zuo, & Zang, 2016). The preprocessing procedures included (1) removing the first 10 volumes; (2) slice time correction for interleaved acquisitions; (3) nuisance covariate regression, including motion parameters (Friston 24 model), white matter and cerebrospinal fluid signals,

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and an overall linear trend as covariates; (4) segmentation of the structural images and co-registration of the functional images; (5) normalization of all functional volumes into Montreal Neurological Institute (MNI) space with a re-sampled voxel size of 3×3×3 mm^3; (6) temporal bandpass filtering (0.01–0.10 Hz); and (7) spatial smoothing with a 8-mm full-width half-maximum Gaussian kernel. Participants whose maximum head motion exceeding 2 mm translation or 2° rotation were excluded from subsequent neuroimaging processing. Using this standard, seven participants were excluded. In addition, six participants refused to undergo fMRI scanning. As a result, full sets of behavioural and neuroimaging data were available in 102 participants. After further excluding outliers in the SJ tasks (as stated earlier under Method), 94 participants for the flashbeep SJ task and 96 for the syllable SJ task were finally included to examine the neural correlates of the TBW width.

fMRI data analysis

Six seeds are defined based on an activation likelihood estimation (ALE) meta-analysis examining the neural activities more engaged by asynchronous audiovisual processing than synchronous perception (Zhou, Cheung, et al., 2020). They included (1) the right middle temporal gyrus (the right MTG; 2120 mm^3); (2) the left superior temporal cortex (the left STC; 1936 mm^3); (3) the left cerebellum (1536 mm^3); (4) the left superior temporal cortex (the left STC; 1224 mm^3); (5) the right superior temporal cortex (the right STC; 752 mm^3); and (6) the left anterior superior temporal gyrus extending to the inferior frontal gyrus (the left aSTG/IFG; 576 mm^3).

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The exact locations of these seeds are shown in Figure 1 and supplementary Table 2. The mean time series of each seed was extracted separately and voxel-wise rsFC analysis was conducted between the activity of each seed and other voxels across the whole brain. A Fisher Z-transformation was then applied to each participant's correlation r-map to ensure normality. For all six seeds, participants' Fisher z-maps were used to conduct a linear regression analysis with audiovisual TBWs (for flashbeep and syllable) as the regressor in SPM 12. Age, gender, IQ and mean framewise displacement (FD) were added as covariates. Clusters were considered significant if they reached a threshold of voxel-level $p < .001$ and cluster-level family-wise-error (FWE) corrected $p < .05$ (Woo, Krishnan, & Wager, 2014).

Correlations between TBW-related rsFC and subclinical traits

To test whether the TBW-related rsFC was affected by different levels of subclinical traits, the rsFC values were extracted to correlate with schizotypal and autistic traits in the entire sample (Spearman correlation). Moreover, a linear regression was conducted with levels of autistic traits, scores on the cognitive-perceptual subscale of the SPQ and their interaction term predicting the strength of TBW-related rsFC. The analysis was also repeated using the total SPQ score.

In addition, we examined whether the correlation between rsFC and TBW width was moderated by autistic and schizotypal (both the total and cognitive-perceptual subscale scores of the SPQ) traits using SPSS PROCESS macro (Hayes & Matthes,

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2009). Significant interactions between trait scores and rsFC indicated that the correlations varied according to different levels of subclinical traits. The Johnson-Neyman (J-N) method further identified the values along the continuum of the moderator (i.e., subclinical traits) where the predictor (i.e., the strength of rsFC) had a significant effect on the dependent variable (i.e., the TBW width), with the regression slope of the predictor significantly different from zero.

Results

Table 1 shows the SPQ and AQ scores, and the behavioural performances on the two audiovisual SJ tasks for all the participants. The scatterplot illustrating the correlation between the AQ and SPQ total scores in the whole sample (Spearman r = 0.425, $p < .001$) is shown in the supplementary figure 1. Regarding different subscales, the social communicative difficulties as captured by the AQ showed moderate positive correlations with the interpersonal and also the disorganized dimensions of the SPQ. However, autistic traits (except the attention to detail dimension) were not significantly correlated with the cognitive-perceptual schizotypal traits (supplementary Table 3).

Behavioural results of audiovisual TBW

There were no significant correlations between the audiovisual TBW width and total and subscale scores of schizotypal and autistic traits (Table 2).

In the entire sample, linear regression analysis showed that the width of the

non-speech TBW (i.e., the flashbeep condition) was not affected by levels of autistic traits, cognitive-perceptual schizotypal traits or co-occurring autistic-schizotypal traits (Table 3). For the speech condition (i.e., syllable utterance), the TBW grew wider with increasing age (standardized β = 0.31, t = 3.08, *p* = .003), and there was a trend towards significance indicating that higher levels of cognitive-perceptual schizotypal traits were predictive of wider audiovisual TBWs (standardized β = 0.19, t = 1.89, *p* = .06) (Table 3). We further supplemented our analysis with a stepwise regression. The final model (R^2 = 0.093, F(2,104) = 5.30, *p* = .006) included age (standardized β = 0.284, t = 2.94, *p* = .004) and scores on the cognitive-perceptual subscale of the SPQ (standardized β = 0.197, t = 2.04, *p* = .04) as significant predictors, with older age and higher cognitive-perceptual schizotypal traits predicting wider speech TBWs. Other variables (e.g., autistic traits, the interaction term and IQ) were excluded in this regression model.

When the SPQ total score was used in the regression analyses, results showed that the TBW width for non-speech and speech stimuli was not correlated with levels of autistic traits or schizotypal traits (Supplementary Table 4).

Resting-state FC correlated with the width of TBW

Results of the neural correlates of TBW inter-individual variability were demonstrated in Table 4 and Figure 3. For the flashbeep condition, the rsFC between the left aSTG/IFG and the right middle and inferior temporal gyrus (Brodmann 21 and 20) was positively correlated with the TBW width for non-speech stimuli. For the

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syllable condition, rsFC between the left cerebellum and the right middle frontal gyrus (Brodmann 8 and 9; dorsal lateral prefrontal cortex, dlPFC) was positively correlated with the width of the syllable TBW. In contrast, rsFC between the left STC (Brodmann 22; 1224 mm^3) and the left precuneus was negatively correlated with the width of the syllable TBW.

Correlations between TBW-related rsFC and schizotypal and autistic traits

None of the three rsFC showing significant correlations with the audiovisual TBW were significantly correlated with the total and subscale scores of schizotypal or autistic traits in the entire sample (all *p*s > .21) (Table 5). Moreover, results from the linear regression analysis indicated that the strength of TBW-related rsFC could not be predicted by the levels of autistic traits, schizotypal traits and their interaction term (Supplementary Table 5 and Supplementary Table 6).

Moderation by autistic traits of the effects of rsFC on TBW width for non-speech stimuli

The moderation model showed that the correlation between the non-speech TBW width and the related rsFC (the left aSTG/IFG and the right middle and inferior temporal gyrus) was moderated by autistic traits. Specifically, the positive correlation between the rsFC strength and the TBW width for non-speech stimuli became weaker with increasing levels of autistic traits (effects of the interaction term: t = -2.24, $\triangle R^2$ = 0.041, p = .028). The J-N method indicated that the rsFC was a significant

predictor of TBW width for non-speech stimuli only when AQ score values were below 32. If the AQ score was greater than 32 (top 12.77%), the predictive effect of the rsFC on the TBW width became non-significant.

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Discussion

To our knowledge, this is the first study that investigates whether and how audiovisual temporal integration ability is affected by both schizotypal and autistic traits. In general, we found no significant correlation between audiovisual TBW width and levels of autistic and schizotypal traits. There was only a trend towards significance indicating that higher levels of cognitive-perceptual schizotypal traits may be predictive of a wider TBW for speech stimuli. Although accumulating evidence suggests that an enlarged TBW may be a shared feature in individuals with autism and schizophrenia (Zhou et al., 2018), relevant research in subclinical populations is only preliminary. For autistic traits, a few studies have found that abnormality in the audiovisual TBW may not extend to individuals with mild autistic-like symptoms (Donohue et al., 2012; Noel, Lytle, et al., 2018; Zhou, Shi, et al., 2020), which is consistent with our findings. Another two studies, however, did find significant correlations between increased autistic traits and altered audiovisual temporal processing. These two studies separated autistic traits into several dimensions and found that different dimensions of autistic traits were differentially correlated with the width of the TBW (van Laarhoven et al., 2019; Yaguchi & Hidaka, 2018). The above findings indicate the necessity to more carefully examine how

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multi-dimensional autistic symptoms are involved in multisensory integration. However, our correlation analysis did not find any significant correlation between any dimension of autistic traits and the TBW width. Given the small sample sizes of the previous two studies, further replication of such significant correlations is warranted. Additionally, from a developmental perspective, recent reviews have shown that multisensory integration deficits are more pronounced in younger children with autism spectrum disorders, and appear to be ameliorated or even disappear in older teenagers and adults (Beker, Foxe, & Molholm, 2018; Feldman et al., 2018). As the subclinical participants in this study were young college students, it is thus not surprising that they did not show observable deficits in audiovisual temporal binding processes.

For schizotypal traits, two studies have found that individuals with cognitive-perceptual abnormalities (i.e., positive schizotypal traits) were more likely to integrate multisensory stimuli over longer temporal intervals (Ferri et al., 2017, 2018). This is in line with our findings that higher levels of cognitive-perceptual schizotypal traits might be predictive of a wider TBW for audiovisual speech stimuli. Similar to autistic traits, schizotypal traits are also multi-dimensional and some specific dimensions may be more strongly correlated with sensory processing deficits. However, another two previous studies (Muller et al., 2020; Zhou, Shi, et al., 2020) suggest that audiovisual temporal integration is not significantly correlated with any dimension of schizotypal traits. Clearly, more research with a larger sample size is needed to divide subclinical populations into various homogenous subgroups to

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disentangle the relationship between specific schizotypal traits and audiovisual integration ability.

We also attempted to explore the neural correlates of the inter-individual variability in audiovisual TBW width by correlating it with rsFC. The strength of TBW-related rsFC for speech and non-speech stimuli was not correlated with levels of schizotypal or autistic traits. For audiovisual speech stimuli, a wider TBW was correlated with stronger rsFC between the left cerebellum and the right dlPFC. The cerebellum is a hub region for time perception, which may be responsible for stimulus-onset detection (Petter, Lusk, Hesslow, & Meck, 2016) and has been found to be robustly activated during the perception of audiovisual asynchrony (Bushara, Grafman, & Hallett, 2001; Lee & Noppeney, 2011, 2014; Petrini et al., 2011). Moreover, the asynchrony-induced activation enhancement (against the synchronous condition) in the left cerebellum could be predicted by the width of audiovisual speech TBW, with stronger cerebellar asynchrony effects correlated with narrower TBWs (Lee & Noppeney, 2011). Similarly, the right dlPFC has also been found to be involved in timing tasks, especially for cognitively controlled timing of suprasecond durations (Jones, Rosenkranz, Rothwell, & Jahanshahi, 2004; Koch, Oliveri, Carlesimo, & Caltagirone, 2002). The prefrontal cortex may serve as a top-down coordinator and send ‘conflict resolving’ signals to multisensory regions in the temporal and parietal lobes to facilitate audiovisual asynchrony detection (Adhikari, Goshorn, Lamichhane, & Dhamala, 2013; Noesselt, Bergmann, Heinze, Münte, & Spence, 2012). Based on the above findings, it seems more reasonable to speculate that stronger coupling

between the left cerebellum and the right dlPFC could contribute to higher perceptual sensitivity of audiovisual speech asynchrony and thus narrower TBWs. However, the result from our TBW-rsFC correlation does not support this hypothesis. Future task-based fMRI studies may have the potential to further disentangle the neural connections between the prefrontal and cerebellar areas in response to asynchronous stimuli.

The TBW for speech stimuli was also correlated with the rsFC between the left STC and the left precuneus. The STC has long been regarded as a multisensory region integrating cross-modal information and responding differently to synchronous versus asynchronous audiovisual signals (Marchant, Ruff, & Driver, 2012; Noesselt et al., 2007, 2012; Stevenson, Altieri, Kim, Pisoni, & James, 2010; Stevenson et al., 2011). Although the precuneus is not commonly reported to be involved in basic sensory function, it may contribute to the processing of physical characteristics (e.g., spatial locations) of sensory stimuli (Renier, Anurova, De Volder, Carlson, VanMeter, & Rauschecker, 2009). More importantly, previous fMRI studies support its role in detecting in-congruency of multisensory information (Kitada, Sasaki, Okamoto, Kochiyama, & Sadato, 2014), including the processing of audiovisual temporal asynchrony (Lavoie, 2016). The precuneus is also found to be active during long-term memory retrieval of audiovisual associations (Gonzalo, Shallice, & Dolan, 2000), and plays a key role in maintaining representations of combined multisensory inputs over time (Park & Kayser, 2019). Therefore, the precuneus may utilize the retrieved sensory memory, and compare it with the incoming stimuli to help the detection of

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conflicting multisensory representations (Kitada et al., 2014). A stronger connection between the multisensory STC and the precuneus thus could be beneficial to audiovisual matching, which in turn is related to sharpened sensitivity for speech asynchrony.

As for the non-speech TBW, the rsFC between the left aSTG and the right inferior temporal gyrus (ITG) was positively correlated with the width of the flashbeep TBW. The aSTG (a TBW-related seed region) selected from the ALE meta-analysis encompasses some areas of the temporal pole and the inferior frontal gyrus (IFG). The temporal pole is important for higher-order audiovisual processing, such as identifying individuals based on the face and voices (Perrodin, Kayser, Abel, Logothetis, & Petkov, 2015). Further, neural oscillations in the temporal pole have been found to play an important role in audiovisual temporal integration for speech stimuli (Ohki et al., 2016). The IFG has also been found to be activated in TBW-related tasks like audiovisual SJ tasks (Binder, 2015; Bushara et al., 2001) and it may be more strongly activated when integrating asynchronous cross-modal speech information into a fused representation compared to unfused perception (Miller & D'Esposito, 2005). The ITG is another associative brain region, the activation of which has been considered to serve as the neural substrate underlying the unmasking effect of visual-speech signal (mouth movement) during speech recognition in noise (Wu et al., 2017). These previous neuroimaging studies suggest that the involvement of the aSTG/IFG and the ITG could facilitate the binding of multisensory information into a unified perception, at least for more complex speech stimuli. Here, although the

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TBW-related rsFC between the aSTG/IFG and the ITG was found for arbitrary flashes and beeps rather than speech stimuli, it still supports the role played by these higher-order brain regions in tolerating larger temporal misalignment and allowing for a wider TBW to integrate audiovisual inputs. Interestingly, it should be noted that the significant correlation between non-speech TBW width and rsFC was found only in individuals with moderate and low levels of autistic traits but not in those with high levels of autistic traits (who scored above the clinical cut-off point of 32 on the AQ, Baron-Cohen et al., 2001). This suggests that the neural correlates for audiovisual TBW width may be different in individuals with extreme levels of autistic-like behaviours.

This study has several limitations. First, using seed-based connectivity with pre-defined TBW brain regions may miss some potentially important effects in other cortical areas not included in the analysis. Future studies could evaluate whole-brain connectivity to examine the relationship between large-scale network connectivity and the phenotype of interest such as the audiovisual TBW. Secondly, this study only examined functional connectivity during resting wakefulness. Spontaneous neural activity has been found to exhibit rich temporal structures characterized by long-range temporal correlations (i.e., scale-free dynamics) (He, 2014). Such resting-state temporal structure may be associated with temporal binding of multisensory events (Ferri et al., 2017). More work is needed to investigate whether and how temporal dynamics in the sensory and multisensory cortex contributes to audiovisual temporal acuity. Thirdly, our fMRI results were correlational in nature,

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and the interpretations of TBW–related rsFC were largely dependent on the functions of relevant brain regions as indicated by previous studies. Task-based neuroimaging is therefore required to complement our findings to examine the involvement and interactions of different brain regions during audiovisual temporal processing. Forthly, we did not control for the potential cognitive confounders such as attention. Considering the key role played by attention in audiovisual temporal integration (Zhou, Cheung, et al., 2020) and the impaired attention in clinical populations (Allen & Courchesne, 2001; Braff, 1993), it is important to additionally assess attention when investigating multisensory temporal acuity in subclinical samples. Fifthly, we did not conduct structured interviews to screen the participants and could not completely exclude the possibility that some participants, especially those with high levels of schizotypal and autistic traits, may meet the diagnostic criteria for psychiatric disorders. Finally, only non-clinical individuals were recruited. Future research should explore the neural substrates of multisensory impairment in clinical populations.

Notwithstanding these limitations, this study is the first that simultaneously examines the correlation between audiovisual TBW width and two types of subclinical traits (autistic and schizotypal), and demonstrates the neural mechanisms related to inter-individual differences in multisensory integration in participants with varying levels of subclinical traits. Our results suggest that the ability to use temporal cues for multisensory integration is not correlated with the level of schizotypal and autistic traits. Several brain regions responding to cross-modal sensory information

and timing (e.g., STC, cerebellum) may be involved in audiovisual asynchrony detection.

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Figure Legends

Figure 1. Significant clusters for audiovisual asynchrony detection selected as TBW-related seeds

The seeds were put in numerical order based on their cluster sizes, with the largest cluster ranking first. STC = superior temporal cortex; MTG = middle temporal gyrus; aSTG/IFG = anterior superior temporal gyrus/inferior frontal gyrus; L. = left; R. = right.

Figure 2. Gaussian fittings of reports of synchrony as a function of SOA in the non-speech (panel (a)) and speech (panel (b)) conditions

Error bars represented ±1 standard error of the mean.

Figure 3. Resting-state functional connectivity (rsFC) significantly correlated with the audiovisual TBW width

(A) The TBW width for non-speech stimuli was positively correlated with the rsFC between the left anterior superior temporal gyrus/inferior frontal gyrus (aSTG/IFG) and the right middle temporal gyrus and inferior temporal gyrus (MTG/ITG).

(B) The TBW width for speech stimuli was positively correlated with the rsFC between the left cerebellum and the right dorsal lateral prefrontal cortex (dlPFC), and was negatively correlated with the rsFC between the left superior temporal cortex (STC) and the left precuneus.

Table 1. Demographic information and behavioural performance of audiovisual temporal integration in healthy adults

	Mean	SD	Range
Estimated verbal IQ	126.19	8.51	106 - 144
SPQ	34.46	17.27	2 - 67
SPQ-cog	15.35	8.60	0 - 31
SPQ-inter	14.71	8.15	1 - 31
SPQ-dis	7.75	4.92	0 - 16
AQ	23.77	8.07	6 - 39
AQ-social	5.26	3.08	0 - 10
AQ-att.switch	5.60	1.93	1 - 9
AQ-att.detail	5.79	2.47	0 - 10
AQ-comm	3.68	2.23	0 - 10
AQ-imag.	3.50	2.08	0 - 9
Flashbeep_amp[†]	0.79	0.18	0.43 – 1.07
Flashbeep_PSS	18.53	39.84	-97.21 – 149.46
Flashbeep_TBW	198.34	63.74	76.53 – 381.72
Syllable_amp[‡]	0.92	0.16	0.40 – 1.13
Syllable_PSS	19.33	63.35	-129.95 – 230.57
Syllable_TBW	214.65	79.07	90.85 – 574.55

Notes: [†]the final sample included in the flashbeep simultaneity task: *n* = 105; [‡]the final sample included in the syllable simultaneity task: *n* = 107. SPQ = Schizotypal Personality Questionnaire; SPQ-cog = cognitive-perceptual; SPQ- inter = interpersonal; SPQ-dis = disorganization; AQ = Autism Spectrum Quotient; AQ-social = social skills; AQ-att.swith = attention switching; AQ-att.detail = attention to detail; AQ-comm. = communications; AQ-imag. = imagination; amp = the amplitude of the fitted Gaussian function; PSS = Point of Subjective Simultaneity, corresponding to the mean of the fitted Gaussian function; TBW = Temporal Binding Window, corresponding to the standard deviation of the fitted Gaussian function.

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Table 2. Spearman correlations between audiovisual TBW and schizotypal and autistic traits

	AQ	Social skills	Att. Switch	Att. Detail	Commu.	Imag.	SPQ	interpersonal	Cognitive-perceptual	disorganized
Flashbeep TBW	-0.091	-0.041	-0.091	0.015	-0.082	-0.072	0.024	-0.078	0.096	-0.018
(*n* = 105)	[-0.28, 0.10]	[-0.24, 0.16]	[-0.29, 0.12]	[-0.19, 0.21]	[-0.26, 0.11]	[-0.26, 0.14]	[-0.18, 0.22]	[-0.27, 0.12]	[-0.09, 0.28]	[-0.22, 0.17]
df = 103	*p* = .36	*p* = .68	*p* = .36	*p* = .88	*p* = .41	*p* = .47	*p* = .81	*p* = .43	*p* = .33	*p* = .85
Syllable TBW	0	0.028	0.038	0.063	-0.032	-0.012	0.118	0.034	0.145	0.006
(*n* = 107)	[-0.21, 0.20]	[-0.18, 0.23]	[-0.16, 0.23]	[-0.13, 0.27]	[-0.23, 0.15]	[-0.21, 0.20]	[-0.07, 0.31]	[-0.16, 0.24]	[-0.04, 0.33]	[-0.17, 0.20]
df = 105	*p* = 1	*p* = .78	*p* = .70	*p* = .52	*p* = .74	*p* = .90	*p* = .22	*p* = .73	*p* = .14	*p* = .95

Notes: The values presented in the brackets represented the 95% confidence intervals of the correlation estimates. AQ = Autism Spectrum Quotient; Att. Switch = attention switching; Att. Detail = attention to detail; Commu. = communications; Imag. = imagination; SPQ = Schizotypal Personality Questionnaire; TBW = temporal binding window

Table 3. Linear regression analyses of TBW width predicted by cognitive-perceptual schizotypal traits and autistic traits in the flashbeep (*n* = 105) and syllable (*n* = 107) conditions

	R^2	F value	Standardized β	*p* value
Flashbeep TBW	0.056	0.964		.45
Age			0.075	.47
Gender			0.027	.80
IQ			-0.159	.14
SPQ-cog			0.121	.25
AQ total			-0.116	.27
SPQ-cog X AQ			-0.010	.92
Syllable TBW	0.108	1.991		.07
Age			0.313	.003
Gender			-0.072	.48
IQ			-0.111	.29
SPQ-cog			0.191	.06
AQ total			0.042	.68
SPQ-cog X AQ			0.048	.64

Notes: AQ = Autism Spectrum Quotient; SPQ-cog = the cognitive-perceptual dimension of the Schizotypal Personality Questionnaire; TBW = temporal binding window; SPQ-cog X AQ = the interaction term for cognitive-perceptual schizotypal traits and AQ total scores.

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Table 4. Significant correlations between audiovisual TBW and rsFC in the entire sample

TBW-related seeds from ALE meta-analysis	Direction of the correlation between the TBW and rsFC	Brain regions	Number of Voxels (3×3×3 mm^3)	Peak MNI coordinates			Z value
				x	y	z	
Flashbeep TBW (*n* = 94)							
Left aSTG/IFG	Positive	Right MTG/ITG	98**	63	-24	-18	4.86
(cluster 6; 576		(Brodmann 21 and 20)		54	-36	-9	4.06
mm^3)				63	-12	-27	3.18
Syllable TBW (*n* = 96)							
Left cerebellum	Positive	Right MFG	62*	33	45	39	4.60
(cluster3; 1536		(Brodmann 8 and 9)		39	33	36	3.62
mm^3)				30	36	45	3.20
Left STC	Negative	Left precuneus	68*	-15	-57	39	4.81
(cluster 4; 1224		(Brodmann 31)		-24	-54	27	4.26
mm^3)							

Notes: rsFC = resting-state functional connectivity; TBW = temporal binding window; aSTG = anterior superior temporal gyrus; IFG = inferior frontal gyrus; STC = superior temporal cortex; MTG = middle temporal gyrus; ITG = inferior temporal gyrus; MFG = middle frontal gyrus cluster-level FWE corrected $^{*}p < .05$; $^{**}p < .01$

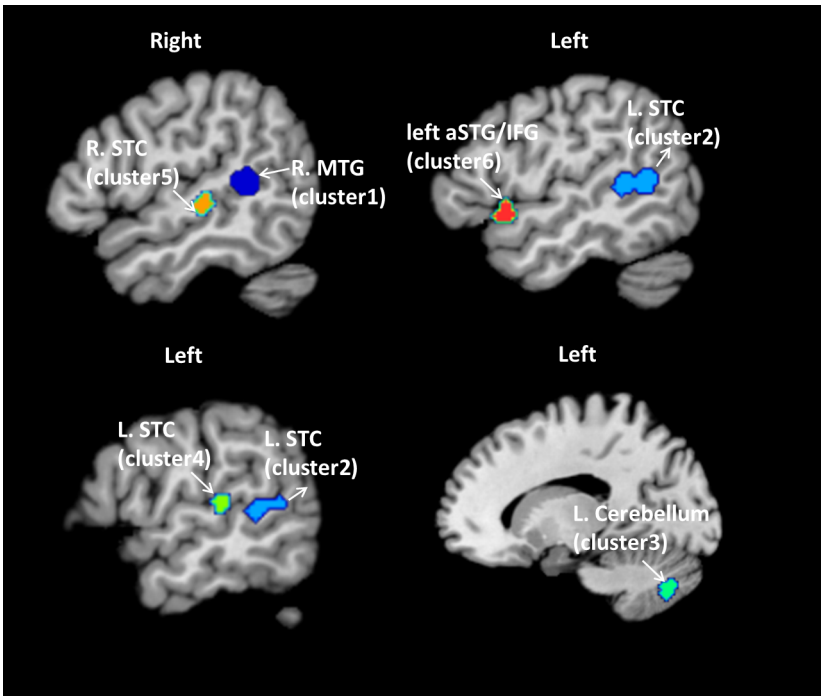
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Table 5. Spearman correlations between TBW-related rsFC and schizotypal and autistic traits

		SPQ	interpersonal	Cognitive-perceptual	disorganized	AQ	Social skills	Att. Switch	Att. Detail	Commu.	Imag.
Flashbeep TBW (*n* = 94) (*df* = 92)	rsFC between the left aSTG/IFG and the right MTG/ITG	0.060 [-0.16, 0.26] *p* = .57	0.072 [-0.14, 0.27] *p* = .49	0.018 [-0.20, 0.23] *p* = .86	0.044 [-0.17, 0.25] *p* = .68	0.007 [-0.21, 0.20] *p* = .95	0.008 [-0.21, 0.21] *p* = .94	0.009 [-0.20, 0.20] *p* = .93	-0.087 [-0.26, 0.11] *p* = .41	0.006 [-0.21, 0.20] *p* = .96	0.116 [-0.09, 0.31] *p* = .27
Syllable TBW (*n* = 96) (*df* = 94)	rsFC between the left cerebellum and the right MFG	0.042 [-0.15, 0.25] *p* = .69	0.014 [-0.18, 0.23] *p* = .89	0.051 [-0.14, 0.24] *p* = .62	0.034 [-0.18, 0.23] *p* = .74	0.008 [-0.12, 0.23] *p* = .94	0.043 [-0.16, 0.25] *p* = .68	-0.039 [-0.23, 0.16] *p* = .71	0.075 [-0.12, 0.29] *p* = .47	0.049 [-0.16, 0.27] *p* = .64	-0.031 [-0.25, 0.20] *p* = .77
	rsFC between the left STC and the left precuneus	0.030 [-0.19, 0.25] *p* = .77	0.046 [-0.17, 0.26] *p* = .66	0.011 [-0.19, 0.23] *p* = .91	0.076 [-0.15, 0.29] *p* = .47	-0.001 [-0.22, 0.20] *p* = .99	-0.130 [-0.34, 0.08] *p* = .21	-0.031 [-0.23, 0.18] *p* = .77	0.113 [-0.12, 0.32] p = .27	0.039 [-0.18, 0.26] *p* = .71	0.103 [-0.09, 0.32] *p* = .32

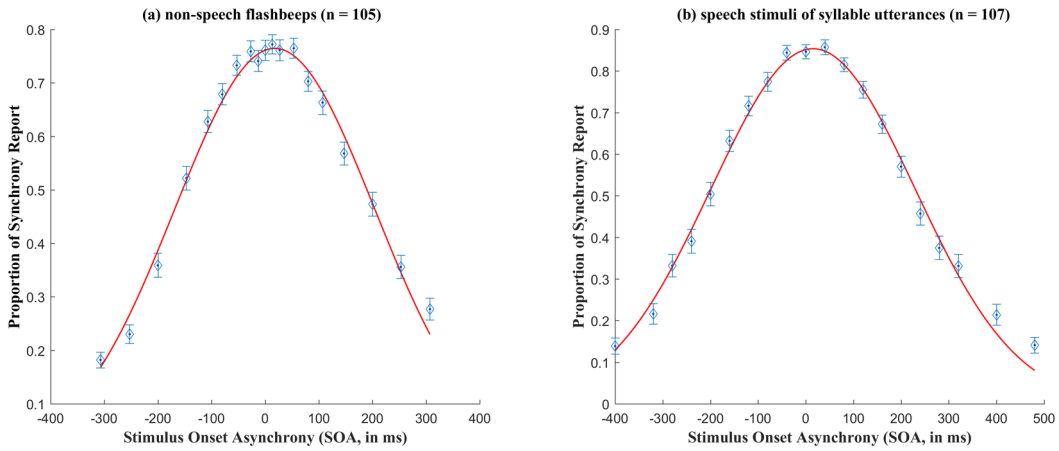
Notes: SPQ = Schizophrenia Personality Questionnaire; AQ = Autism Spectrum Quotient; rsFC = resting-state functional connectivity; TBW = temporal binding window; aSTG = anterior superior temporal gyrus; IFG = inferior frontal gyrus; MTG = middle temporal gyrus; ITG = inferior temporal gyrus; MFG = middle frontal gyrus; STC = superior temporal cortex. The values presented in the brackets represented the 95% confidence intervals of the correlation estimates.

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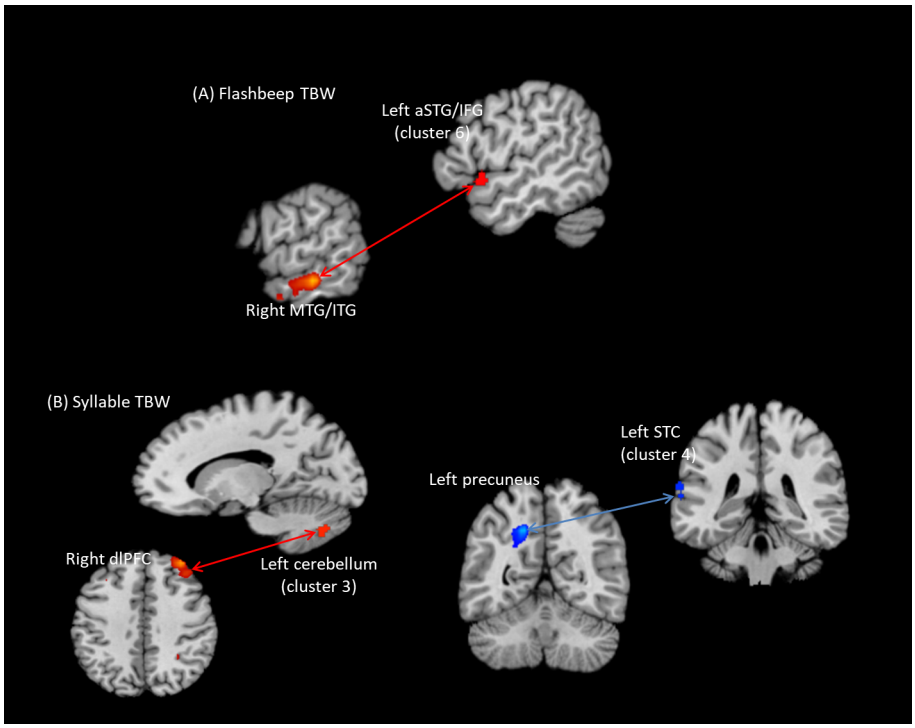
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