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Mini Review

Mini-Review of Brain Functional Connectivity Alterations of Wernicke's Area in Individuals with Autism Spectrum Conditions in Multi-Frequency Bands: A Meta-Analysis

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ABSTRACT

One of the most enduring symptom-oriented lines of Autism Spectrum Conditions (ASC) research focuses on social communication and interaction deficits, which reflect salient ASC symptoms from the perspective of language. Grounded in promising and advancing technology (*i.e.*, resting-state functional Magnetic Resonance Imaging (rs-fMRI)) and drawing on data from a large database named Autism Brain Image Data Exchange (ABIDE), our previous work brain functional connectivity alterations of Wernicke's area in individuals with autism spectrum conditions in multi-frequency bands: A mega-analysis offered insights into the functional connectivity between Wernicke's area and the whole brain in ASC patients in the light of frequency dependence.

Keywords: Autism Spectrum Conditions (ASC); Language impairments; Wernicke's area; Functional connectivity; Frequency dependence

INTRODUCTION

Our prior work brain functional connectivity alterations of Wernicke's area in individuals with autism spectrum conditions in multi-frequency bands: A mega-analysis [1], was published on Heliyon on 14 February 2024. In the following, we will illustrate the train of thought of the paper, the literature review of the related field and discuss the practical meaning of the research by illustrating the whole research step by step. Finally, we could draw a conclusion about the creativity of the research.

Before starting to introduce the research, it would be better to elucidate Autism Spectrum Conditions (ASC) in a broad sense. ASC refer to a set of heterogeneous neurodevelopmental conditions that place individuals with ASC on a trajectory of communication impairments and language deficits, resulting in a relatively huge economic burden because of the lifelong and substantial support needed by ASC patients [2]. To fully account for external language representation in ASC, researchers tap into underlying neural mechanisms to explore internal brain abnormality of ASC utilizing promising techniques, such as resting-state functional Magnetic Resonance Imaging (rs-fMRI). Rs-fMRI has been widely used in of research of neuroscience and diagnosis of clinical disorders (e.g., stroke, ASC) and can demonstrate spontaneous brain activity in a convincing and valid way.

Functional connectivity, a commonly used metric in rs-fMRI that detects temporal correlations between distant brain regions, has been used to reflect altered connectivity patterns of ASC and Wernicke's area, a classical and traditional brain region of the language network that played a crucial role in communication comprehension and has been confirmed to be related with language deficits in ASC, has been chosen as the target brain regions in our prior research to represent the impaired language network.

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However, after sorting out the results of prior research centered on dysfunctions of Wernicke's area in ASC, our prior research found that these studies generated inconsistent results. The possible reason could be resulted from small sample sizes. Therefore, it is of great importance to utilize the large database to draw a comprehensive picture of the dysfunction of the language network in ASC using large-scale integration methods, such as mega-analysis. Also, as different frequency bands are dominant in different neural functions and are correlated with different brain regions, the property of frequency dependence should be taken into consideration.

Taken together, our previous research collected data from Autism Brain Image Data Exchange (ABIDE) and conducted a mega-analysis to examine functional connectivity of Wernicke's area in different frequency bands (conventional: 0.01-0.08 Hz; slow-4: 0.027-0.073 Hz; and slow-5: 0.01-0.027 Hz).

LITERATURE REVIEW

Labeled as one of the most salient symptoms of ASC, disabilities in social interaction and communication resulting from deviant language networks have gain currency among neurological researchers. Previous rs-fMRI studies focused on language-related dysfunctions in ASC patients could be divided into two parts according to the methods they acquired in the research: (1) functional integration analysis of ASC; and (2) functional segregation analysis of ASC. To be specific, functional integration analysis focuses on analyzing the network connections between distance brain regions, while in the analysis of functional segregation, local activities within individual brain regions is of central position.

Functional integration proposed that the achievement of certain perception or behavioral activity acquires coordinated cooperation among multiple cortical brain regions, involving Independent Component Analysis (ICA), Granger Causality Analysis (GCA), graph analysis and FC, etc. FC research that analyzed language abnormalities in ASC from the perspective of functional integration found underconnectivity between the right-hemisphere posterior Superior Temporal Sulcus (pSTS), a brain region critical for processing language prosody and the orbitofrontal cortex and amygdala, regions related to emotion-related associative learning [3]. Other brain regions that are correlated with social and language ability, such as the superior temporal cortex, have been confirmed to present atypical connection with visual and precuneus cortices in ASC toddlers [4]. Further, Xiao et al., also pointed out that the aberrant connectivity pattern found in their research has also been detected in elderly ASC patients, which explains the difficulty of achieving interventions anchoring at social and language skills. Based on this, a conclusion can be drawn that the aberrant connectivity of language-related regions could impair ASC patients' social skills development and might shed new light on language interventions in clinical conditions.

As for functional segregation analysis, commonly used metrics in rs-fMRI include Amplitude of Low Frequency Fluctuation (ALFF), the fractional Amplitude of Low Frequency Fluctuation (fALFF), Regional Homogeneity (ReHo) and Percent Amplitude of Fluctuation (PerAF). These metrics are widely known for observing and evaluating spontaneous neural activities in the brain at the voxel level, which can localize specific damaged brain regions, and provide effective biomarkers for the pathological mechanisms of different brain diseases. For example, a prior study that used fALFF to analyze alterations of local spontaneous brain activity in ASC found reduced fALFF in the right middle occipital gyrus, lingual gyrus and fusiform gyri, which may account for social and communicative abnormalities in ASC [5]. Another ReHo analysis targeting preschool boys with ASC found that increased ReHo in the right calcarine and decreased ReHo in language processing regions, including the opercular part of the left inferior frontal gyrus [6]. These findings could also enhance the understanding of clinical characteristics from the perspective of language among ASC patients.

Therefore, language regression and impairments of social interaction resulting from altered language-related regions impact ASC patient's communicative ability severely. Prior neuroimaging studies that demonstrated the necessary correlation between ASC symptoms and alterations of brain regions also suggested the inevitable exploration of language neural mechanisms in understanding pathological characteristics of ASC and proposing effective interventions. However, a classical component of language network, Wernicke's area, has not been fully investigated in ASC studies. Also, characteristics of frequency dependence have not been explored. Meanwhile, the sample sizes used in the above studies were small that may affect the statistical power and call for large datasets to promote representativeness and reliability.

DISCUSSION

The persistent influence of delayed language and heterogeneous language outcomes in ASC patients severely impact their quality of life and hinder their social interaction with other people. Therefore, to detect the underlying language processing process in ASC, our prior study took Wernicke's area as the seed region and calculated the mega-analysis of FC results.

Located at the left Superior Temporal Gyrus (STG), Wernicke's area has been defined as one of the crucial components of the language network where lesions impact both word and sentences comprehension. Specifically, Wernicke's area is responsible for transforming auditory signals into linguistic representations from the perspective of lexical and syntactical levels. Hence, the alterations of Wernicke's area may delay the conceptual-semantic processing and the cognitive progress of mapping and blending, which further hinders language comprehension. For ASC patients, their limited comprehension hinders their perception of the surrounding environment and the addressee's intentions/emotions, which affect their social interaction. Therefore, exploring the potential functions the Wernicke's area occupied in ASC is of central importance.

As for the metrics, our research chose to use FC because prior studies indicated the common occurrence of abnormal connectivity patterns in individuals with ASC. FC detects linearly correlated remote brain regions that share similar functions. Briefly, FC demonstrated functional synergy of spatially distinct regions. Therefore, the brain regions found in our prior research (*i.e.,* right thalamus, left cerebellum Crus II, right lenticular nucleus, pallidum) were all connected with Wernicke's area and related to language comprehension. The connectivity patterns demonstrated in our research might have potential in clinical intervention. Furthermore, mega-analysis is the combination of individual raw data from various cohorts into a single statistical analysis to gain a greater statistical power and effect size. Also, it can enhance the generalizability of research. Therefore, our study obtained data from ABIDE to conduct a mega-analysis.

Further, the findings that different frequency bands are prevalent in various neural functions make the frequency-dependent characteristics a meaningful aspect of studying spontaneous brain activities. In addition to the conventional frequency band (0.01-0.08 Hz), slow-4 (0.027-0.073 Hz) and slow-5(0.01-0.027 Hz) have been confirmed to present gray matter activity and might provide new avenues for the progress in clinical diagnosis and therapy in neurodevelopmental disorders. Considering the relevance between frequency bands and clinical population, the frequency-specific features in ASC might shed light on potential neurophysiological mechanisms. In our research, the slow-5 frequency band might provide additional information, as two brain regions (*i.e.,* left cerebellum Crus II, right lenticular nucleus, pallidum) have been detected in this band.

CONCLUSION

Focused on the altered connectivity pattern of Wernicke's area in different frequency bands among ASC, our previous research used mega-analysis to obtain more consistent results. The creativity of the research could be summarized as follows: (1) centering on the language-related brain regions, *i.e.,* Wernicke's area, as the target to detect and reflect the altered functional connectivity in ASC; (2) utilizing mega-analysis on ABIDE database to generate reliable results; and (3) detecting the property of frequency dependence in ASC patients.

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REFERENCES

1. Zhan L, Gao Y, Huang L, Zhang H, Huang G, Wang Y, et al. Brain functional connectivity alterations of Wernicke's area in individuals with autism spectrum conditions in multi-frequency bands: A mega-analysis. Heliyon. 2024;10(4):e26198.
2. Lai MC, Lombardo MV, Baron-Cohen S. Autism. Lancet (London, England). 2014;383(9920):896-910.
3. Abrams DA, Lynch CJ, Cheng KM, Phillips J, Supekar K, Ryali S, et al. Underconnectivity between voice-selective cortex and reward circuitry in children with autism. Proc Natl Acad Sci USA. 2013;110(29):12060–12065.
4. Xiao Y, Wen TH, Kupis L, Eyler LT, Taluja V, Troxel J, et al. Atypical functional connectivity of temporal cortex with precuneus and visual regions may be an early-age signature of ASD. Mol Autism. 2023;14(1):11.
5. Itahashi T, Yamada T, Watanabe H, Nakamura M, Ohta H, Kanai C, et al. Alterations of local spontaneous brain activity and connectivity in adults with high-functioning autism spectrum disorder. Mol Autism. 2015;6:30.
6. Lan Z, Xu S, Wu Y, Xia L, Hua K, Li M, et al. Alterations of regional homogeneity in preschool boys with autism spectrum disorders. Front Neurosci. 2021;15:644543.