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Application of Functional Near-infrared Spectroscopy in the Study of Brain Function in Children with Autism

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Abstract: ***There is a high degree of correlation between abnormal brain functional characteristics and behavioural manifestations in children with autism spectrum disorders (ASD), which are characterised by dys-synchronicity, abnormal connectivity, and functional imbalance of brain regions in neural activity. Functional near-infrared spectroscopy (fNIRS), as a non-invasive neuroimaging technique, is more suitable for brain function testing of children with ASD in natural environment with its advantages of portability, flexibility, and high temporal resolution, compared with brain function testing techniques, such as functional magnetic resonance imaging (fMRI) and positron emission tomography (PET). In recent years, fNIRS has been widely used to study the brain function of children with ASD in different cognitive tasks, especially in the areas of brain activation patterns, functional connectivity, diagnosis, and intervention therapy. fNIRS is expected to provide neural biomarkers for the diagnosis of ASD as well as individualised guidance for intervention therapy.***

Keywords: Autism spectrum disorders, Functional near-infrared spectroscopy, Brain functions**.**

1. Introduction

Autism spectrum disorder (ASD) is a group of neurodevelopmental behavioural disorders characterised by social interaction and communication, the presence of restricted interests and repetitive behaviours [1], and is one of the most disabling developmental disorders, imposing a high economic burden on families and society. According to a recent survey in 2023, the global prevalence of ASD is approximately 0.72%, with a higher prevalence in economically developed regions than in economically disadvantaged regions [2]. No specific biomarkers have been identified for the diagnosis of ASD, and the diagnosis is mainly based on behavioural observations and assessment scales [3].

Functional near-infrared spectroscopy (fNIRS) is an emerging non-invasive neuroimaging technique used to study brain function, which assesses neural activity by measuring changes in the concentrations of oxyhemoglobin (HbO2 or oxy-Hb) and deoxyhemoglobin (deoxy-Hb) in cortical regions of the brain, now widely beening used in neuroscience, cognitive psychology and other fields [4]. fNIRS, with its unique advantages and potential applications over other neuroimaging techniques, can help us to investigate the correlation between brain function and behaviour in children with ASD. In this paper, we will review fNIRS working principle, advantages and limitations compared with other common neuroimaging techniques, and applications in children with ASD.

2. A Basic Overview of fNIRS

2.1 The Basics Principles of fNIRS

fNIRS makes use of the principle of light absorption and scattering propagation in human tissues. In the near infrared band, there is a wavelength range from 700 nm to 900 nm, which is called the "optical window", in which oxyhaemoglobin and deoxyhaemoglobin have relatively small absorption coefficients of light [5-7]. Oxygen consumption increases during brain activity, and this increase in oxygen consumption is accompanied by an increase in cerebral blood flow due to neurovascular coupling [8]. This leads to changes in local HbO2 and HbR, while HbO2 and HbR in blood are the main components that absorb photons, and photons absorbed and scattered by brain tissue can be detected by highly sensitive photodetectors, and changes in HbO2 and HbR in tissues can be obtained by propagation models [5]. In practice, fNIRS uses a laser diode or light-emitting diode light source in an optical window to pass the NIR light through the skin of the skull, the skull bone, and the cerebrospinal fluid to reach the cortex, and the depth of penetration of NIR light into the tissue is approximately half the distance between the light source and the detector [9].The NIR light carried into the brain tissue by the optical fibre diffuses inside the brain tissue, and between the light source and the detector, its path profile forms a banana-shaped profile with narrow ends and a curved centre [10]. Ultimately, the absorbed and scattered near-infrared light collected and detected by the photosensitive detector in the brain tissue is used to derive changes in haemoglobin concentration using the modified Beer-Lambert law (MBLL) [11] to reflect the functional activity of the brain.

2.2 Advantages and Limitations of fNIRS

Besides fNIRS, other techniques currently used to study brain function include functional magnetic resonance imaging (fMRI), positron emission tomography (PET), event-related potential (ERP)/quantitative electroencephalography (QEEG), etc. fMRI as one of the most common functional brain imaging techniques, it is based on magnetic resonance technology and combines time-series data acquisition and analysis to indirectly reflect neural activity by measuring changes in the oxygenation level of brain blood, with high spatial resolution [12]. It is able to provide finer information

on the localisation of brain area activity and dynamic changes. However, it cannot capture rapid changes in neural activity [13]. In addition, fMRI requires large equipment and a special magnetic resonance chamber, which is expensive, requires special facilities and technicians for operation and maintenance, and requires a high degree of co-operation from the subjects. PET has a high spatial resolution, and can accurately locate the activity of the brain area. However, due to the use of radioactive tracers, the risk of radiation exposure, and the expensive equipment. It is usually used for the localisation and staging of tumours in children [14]. ERP is a time-voltage waveform measured by EEG signals of potential changes in cortical neurons following multiple repetitions of a specific event (usually sensory, cognitive, or motor) stimulus [15]. AS a neurophysiological technique used to study brain activity, ERP has the advantage of temporal accuracy in brain information processing and can accurately analyse the brain's rapid response to stimuli, but it has low spatial resolution and does not provide precise information on the location of brain activity [16].

Compared with other neuroimaging techniques, fNIRS has the advantages of being non-invasive, relatively small equipment, and relatively low cost. fNIRS is portable and can be used for real-time monitoring in natural environments, allowing subjects to be closer to real-life situations and requiring less movement and head posture, especially for specific populations such as infants and children, and helps to understand the changes in brain function of people with ASD in different social scenarios [17]. fNIRS also has limitations, as it indirectly reflects neural activity by measuring changes in cortical blood oxygen levels through near-infrared light, and therefore has relatively high temporal resolution (seconds to tens of seconds) and low spatial resolution (millimetres to centimetres). It does not provide as detailed a localisation of brain activity as functional MRI [18]. In addition due to the scattering and absorption of near-infrared light, fNIRS is limited by the depth of measurement and can only measure activity in the cerebral cortex and its near-surface structures, preventing in-depth monitoring of deeper regions of the brain. The influence of scalp tissue and hair strands can also lead to errors in the measured signal, and although these problems may be ameliorated to some extent as the technology develops, proper processing and correction of the data is still required.

3. Functional Brain Characteristics of Children with Autism Spectrum Disorders

3.1 Synchronisation Disorders

Activity between brain regions is highly coordinated in the normal population, but in people with ASD there is a synchronised dysfunction of neural activity between brain regions, which can lead to abnormalities in information processing and transmission [19]. This low level of neural synchronisation leads to abnormalities in information processing and has implications for social communication and other cognitive functions.

3.2 Connection Anomalies

There are also abnormalities in terms of brain connectivity patterns in people with ASD. Brain connectivity refers to the pattern and strength of neuronal connections between different brain regions [20] In patients with ASD, local functional connectivity in brain regions is more dense and complex, whereas inter-regional connectivity may be relatively weak, and this connectivity abnormality makes information transmission and integration difficult and is associated with the clinical manifestations associated with ASD patients [21].

3.3 Imbalance in the Functioning of Brain Regions

People with ASD have an imbalance in the functional allocation of different regions of the brain, which leads to differences in the processing of information in the brain, showing reduced activity in brain regions related to social, language and emotional understanding and increased activity in sensory processing regions [22]. It has been found that young children at risk for a diagnosis of autism are under-responsive in the left hemisphere cortex for phonological responses, and that this deficit worsens with age [23]. In another study, it was found that individuals with ASD were found to have significantly reduced activation in areas of the theory of mind network, the mirror network, and a portion of the cerebellum, and insufficient functional connectivity between anterior and posterior areas of the brain during task performance [24]. The study also found a significant reduction in activation of the mental theory network and part of the cerebellum.

It is because ASD is characterised by abnormal connections in neural networks, abnormalities in the way information is processed, and differences in the functional activity of specific brain regions that researchers need an imaging technique that can accurately capture signals of cortical activity in children with ASD without disturbing them. In this context, fNIRS is a highly sought-after tool for its non-invasiveness, portability, and high temporal resolution, which can be applied more comprehensively to probe brain function in children with ASD.

4. The Use of fNIRS in the Study of Brain Function in Children with Autism Spectrum Disorders

4.1 Brain Function Activation

4.1.1 Social interaction and emotional recognition

Children with ASD often have difficulty understanding the emotions and intentions of others during social interactions, including facial expressions and body language, and a reluctance to make eye contact during naturalistic interactions is one of the core symptoms of ASD [25]. Hirsch et al. compared "face-to-face" eye contact and video facial gaze with fNIRS data acquired during real-time eye contact between typically developing (TD) and ASD participants, and showed that during real-time eye contact, the right dorsal-parietal lobe activity was reduced and the right ventral-parietal lobe activity was reduced in participants with ASD. parietal activity was reduced, right ventral temporal parietal activity was increased, and cross-brain coherence consistent with an atypical neurological system for real-time eye contact was reduced [26]. Children with ASD have

difficulties with socially embedded movements such as imitation and interpersonal synchronisation, Su et al. compared motor characteristics and cortical activation patterns between children with ASD and children with TD when performing a rocking synchronisation task at different levels of social information in a study that found no significant increase in cortical activation in the frontal inferior frontal gyrus and superior temporal sulcus during fingertip contact (IPS) [27] Wang et al. used fNIRS to examine inter-brain communication between children with ASD and their parents in a social interaction setting. 16 pairs of children with ASD and their parents were in a co-operative situation and a single-person situation respectively, and the keys were pressed as soon as possible when the "go" signal appeared. When children with autism interacted cooperatively with their parents, interpersonal neural synchrony increased in the frontal cortex, whereas children with severe autism showed lower levels of behavioural and neural synchrony during cooperative interactions with their parents [28]. One study compared the brain activation patterns of children with autism spectrum disorders (ASD) and normal children while watching videos of robots and humans. fNIRS devices recorded neural activity in the dorsolateral prefrontal cortex (DLPFC) of 45 children with ASD and 53 children with TD aged 4-6 years while interacting with a robot or a human in a video, and the results showed that neural activity levels in the right side of the DLPFC of children with ASD were were significantly lower in the robot interaction condition than in the human interaction, and the neural activity in the right DLPFC of children with ASD was also significantly lower than that of neurologically normal children during robot interaction [29] children with ASD.

4.1.2 Multi-sensory processing and integration

Children with ASD are either overly sensitive or insensitive to sensory processing and integration, as evidenced by showing particular responses to specific sensations. A study tested changes in prefrontal HbO2 in children with ASD following 12 different types of visual music tasks. Children with ASD had lower activation of HbO in area E in the red-light and positive-music, green-light and neutral-music conditions, in area F in the blue-light and negative-music conditions, and in the HbO activation was lower in the fantasy and sketch conditions than in the TD children, but activation was lowest in the red light and positive music conditions and highest in the blue light and negative music conditions, suggesting that differences in prefrontal cortex activation in the brains of children with ASD and children with TD may be the cause of poor audio-visual integration in children with ASD and the pathogenesis of the speech and communication disorders in children with ASD [30]. Individuals with ASD are impaired not only in social skills, but also in sensory perception, especially olfaction. Xu et al. measured the brain activity elicited by odour in individuals with ASD using fNIRS, and classified these participants with ASD into a low DT group and a high DT group based on their odour detection thresholds (DTs), and their brain activity elicited by odour was measured using fNIRS, with the right side of the high DT group showing significantly weaker neural activity in the DLPFC. The neural activity of the DLPFC was significantly weaker than that of the control group, and the intensity of the activity of the right DLPFC was negatively correlated with DT, suggesting that functional differences in olfactory working memory or attention of the DLPFC are related to olfactory perceptual abnormalities in ASD, which further validates the impaired high-level functioning of olfactory processing in individuals with autism spectrum disorders (ASDs) [31].

4.1.3 Executive functions

Executive function includes processes such as inhibition, switching, working memory, planning, organisation, etc. Children with ASD often show signs of executive function impairment such as difficulty in handling complex tasks, controlling impulses, adapting to changes in the environment, etc. The portability of the fNIRS and its high tolerance for movement offer great advantages in studying executive function in children with ASD. Therefore Su et al. used the fNIRS to study the cortical activation of children with ASD in a face-to-face cortical activation in an interpersonal synchronisation task, in which 14 children with ASD and 17 normally developing (TD) children would complete three tasks of observing an adult clearing blocks (Watch), clearing them on their own (Do), and clearing them together (Together), children with ASD showed lower spatial and temporal synchronisation accuracy, with low activation in the frontal inferior gyrus and temporal supratemporal gyrus, and and hyperactivation in the inferior parietal cortex, lobules, while in the Together condition, children with ASD showed more left-sided activation than the inferior frontal gyrus and more right-sided activation than the superior temporal gyrus [32]. Kpuppa et al. used the fNIRS to test brain synchronisation in response to performing a cooperative and competitive task in which children with ASD showed lower motor synchronisation than children in the TD group [33]. Working memory is one of the core symptoms of executive function and children with ASD often show difficulties in working memory tasks (WM), therefore Han et al. used fNIRS to examine the effects of WM load on functional connectivity in ASD prefrontal cortex In their study, 22 children with high-functioning ASD aged 8-12 years old were compared to children with TD in three WM loads (0-back, 1-back and 2-back) under which a numerical task was performed, using a multichannel NIRS device to monitor haemodynamic changes in bilateral lateral and medial prefrontal cortex during task performance. The final results showed that ASD children had slower reaction times than TD children, and that the ASD and TD groups showed different load-dependent functional connectivity changes in the lateral and medial prefrontal cortex in the right hemisphere but not in the left hemisphere, suggesting that disruptions in functional neural connectivity for different cognitive processes may be responsible for the poor performance on the ASD working memory task [34].

4.1.4 Language processing tasks

Children with autism spectrum disorders (ASD) show significant difficulties in reading comprehension, and reading comprehension deficits can lead to information processing deficits with language expression problems. In a study of 21 individuals with high-functioning ASD and TD participants who underwent reading comprehension testing and verbal fluency testing, prefrontal functioning was measured using the fNIRS, and participants' information processing

efficiency was assessed; children with high-functioning ASD showed general reading comprehension, selective verbal fluency deficits, and slower processing speeds, which may be related to significantly lower functional connectivity in the prefrontal lobes of the brain [35]. Yeung et al. concluded that one of the important reasons why autism spectrum disorders (ASD) perform poorly on category fluency tests is due to the presence of word retrieval deficits, and therefore examined whether individuals with ASD showed altered frontal lobe functioning on category fluency tests using the fNIRS. adolescents with high-functioning ASD in the study, as well as adolescents with TD, underwent a category fluency test, a task in which they were asked to name animal or vehicle words, each process lasting 1 min, and it was found that adolescents with autism spectrum disorders came up with fewer animal words and that ASD's were activated to a comparable degree in extra- and medial frontal regions. This suggests that this dysfunction, which lacks a frontal extramedial-medial activation distinction, is associated with poorer word retrieval [36]. In another task distinguishing between depressed and non-depressed adolescents with autism, fNIRS was used to measure frontotemporal haemodynamic responses during a verbal fluency task in 28 ASD patients versus 14 TD participants, and it was found that patients with ASD had smaller haemodynamic responses in the left DLPFC, bilateral ventral ventral lateral tegmentum prefrontalis externa (VLPFC), and anterior temporal lobe (aTC) than the TD group. whereas the right VLPFC haemodynamic response was significantly smaller in the depressed group than in the no-depression group [37] The right VLPFC haemodynamic response was significantly smaller in the depressed group than in the group without depression.

4.2 Functional Brain Connectivity

Brain connectivity refers to the ability of information transfer and coordination between brain regions. Due to the special brain function characteristics of children with ASD, abnormal brain connectivity on the one hand manifests itself as over-connectivity, which is mainly due to over-activity of the connections between local brain regions, leading to difficulties in information processing and integration, sensory over-sensitivity, and attention deficits; and on the other hand, under-connectivity mainly manifests itself as long-distance connectivity between brain regions. On the other hand, brain under-connectivity is mainly due to long-distance connectivity between brain regions, and this limitation in information transmission and coordination is often associated with symptoms of social interaction and language communication difficulties [38-40]. This limitation in information transmission and coordination is often associated with social interaction and language communication difficulties.

4.2.1 Excessive connectivity

A prospective longitudinal study using fNIRS to examine the development of intra- and inter-hemispheric functional connectivity in the brain during the first year of life in high- and low-risk infants collected and analysed near-infrared spectroscopy data from 27 high-risk (HR) infants with autism and 37 low-risk control (LR) infants at 3, 6, 9 and 12 months of age, ultimately finding that HRA infants showed enhanced functional connectivity at 3 months of age when compared to LRC Infants demonstrated enhanced overall functional connectivity at 3 months of age compared to LRC infants, whereas no significant differences were found between HRA and LRC infants at 6 and 9 months, and by 12 months, HRA infants showed reduced connectivity relative to LRC infants [41]. Bhat et al. used fNIRS to examine functional activation and connectivity during naturalistic social interactions in nine 6- to 9-month-old HR and six LR infants; HR infants had reduced right hemisphere and left hemisphere activation compared to LR infants, and HR infants were more functionally connected than LR infants during the pre-socialisation period and the post-socialisation period, while connectivity declined during socialisation [42]. Li et al., in a task to investigate the spatial complexity of multiple dynamic functional connectivity sequences in fNIRS, found that children with ASD had deficits in information exchange in the right prefrontal cortex, that the spatial complexity of functional connectivity between the right prefrontal cortex and other brain regions was significantly enhanced, and that the spatial complexity of functional connectivity was significantly higher in patients with ASD as a whole, and in regions of the prefrontal and temporal lobes [43].

4.2.2 Inadequate connectivity

To demonstrate the relationship between short-range and homologous long-range resting state functional connectivity (RSFC) in children with ASD and TD, Wu et al. recorded resting state signals from bilateral temporal lobe recordings in 25 children with ASD and 22 age-matched children with TD using fNIRS, and found that both short-range and homologous long-range RSFC were weaker in the ASD group than the TD group, and that short-range RSFC was stronger in the ASD group than homologous The ASD group had stronger short-range RSFC than homologous remote RSFC. [44] Sun et al. found that functional near-infrared spectral signals from bilateral temporal lobes showed significantly weaker RSFC in more cortical sites in children with ASD in the 0.01-0.02 Hz band [45]. In a study by Zhu et al, fNIRS was applied to investigate the differences in prefrontal cortex activation and functional connectivity between children with ASD and children with TD. 21 children with ASD and 20 children with TD performed joint and non-joint attention tasks, and ultimately, children with ASD showed reduced activation of the prefrontal cortex and an atypical pattern of functional connectivity during joint attention, which suggests that insufficient functional connectivity in the left prefrontal cortex is one of the important causes in the social cognitive deficits of children with ASD [46].

4.3 Diagnosis and Treatment

4.3.1 diagnosis and screening

As a non-invasive and convenient brain imaging technique, fNIRS provides neurobiomarkers for early diagnosis and screening of ASD by measuring the characteristics of changes in HbO2 and HbR concentrations in the brain activity of children with ASD. In a study by Lin et al. [47] In order to differentiate between children with ASD and TD, functional near-infrared spectroscopy was used to record resting-state

haemodynamic fluctuations in the bilateral temporal lobes of 25 children with ASD and 22 children with TD, in which the coupling between low-frequency HbO2 and HbR fluctuations was assessed by correlation coefficients, and significant weak coupling was found in the right and left sides as well as the entire temporal cortex in children with ASD, suggesting that haemoglobin coupling can be used as a new cerebral haemodynamic feature for ASD screening or diagnosis. In a prospective longitudinal study of infants at familial risk for ASD, brain responses to human social videos (i.e., hide-and-seek) versus non-social images (vehicles) and human vocalisations versus non-human vocalisations were measured by fNIRS, and infants who had developed ASD at 3 years of age had reduced activation of visual social stimuli in infra-frontal and post-temporal areas of the cortex, compared with infants at low risk. These infants showed reduced activation to human voices and enhanced activation to non-human voices within the left lateral temporal region compared to low-risk and high-risk infants who did not develop ASD, amply demonstrating the correlation with later social interaction and communication difficulties in autism spectrum disorders [48] which would provide evidence for early screening for ASD.

4.3.2 Monitoring of intervention effects

fNIRS can be used to monitor the effects of ASD interventions and treatments. By comparing changes in brain activity before and after interventions, the effectiveness of intervention strategies can be assessed and guidance can be provided for the optimisation of treatment regimens. One ASD participant and one TD participant in one study received true feedback (true FB) during training, while the other two participants received false feedback (false FB). After five training sessions, the participant who received real FB showed more improvement in facial recognition performance compared to the participant who received sham FB. fNIRS-based neurofeedback can enhance therapeutic interventions for children with ASD [49]. A study in which children with ASD aged 8-12 years completed three 20-minute cycles of exercise, treadmill walking, and sedentary control on different days while being assessed using fNIRS ultimately found that circuit training was a feasible intervention to improve executive function in children with ASD [50]. In summary, fNIRS combines brain activity with clinical characteristics and behavioural manifestations of ASD patients to understand differences in brain functioning between ASD patients, thus providing guidance for individualised treatment planning.

5. Conclusions

The fNIRS technique provides a non-invasive, convenient and suitable brain imaging method for children. fNIRS reveals brain activity patterns and functional connectivity characteristics of children with ASD by monitoring different neural activities, providing evidence of the relationship between cognitive behaviours and brain function in children with ASD, and more importantly, may provide neural biomarkers for early diagnostic screening of ASD as well as individualized assessment of interventional therapy. However, fNIRS has the disadvantages of limited spatial resolution, limited depth of detection, and lack of standardised data analysis. Therefore, combining fNIRS with other brain imaging techniques (e.g., fMRI, EEG, etc.) to integrate multimodal imaging data has become a new research tool [51]. that has become a new research tool. Brain-computer interface (BCI) is an emerging artificial intelligence technology in the field of ASD treatment in recent years [52]. It has been shown that BCI can be used to intervene in the feasibility of social cognitive skills in ASD patients [53] that restoring social functioning in people with autism is the ultimate goal and driving force of future research, and the combination of fNIRS and BCI has become a new trend to provide a series of pathways for people with ASD to control external devices or communicate through brain activity, as a way to improve the social interaction and communication skills of people with ASD. These application potentials demonstrate the important role of fNIRS in the study of brain function in ASD, and offer hope for further searching for the neurobiological basis of ASD as well as the development of individualised and effective interventions.

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