General Psychiatry

Reduced temporal activation during a verbal fluency test in clinical high risk of psychosis: a functional near-infrared spectroscopy-based study

Yanyan Wei ,[1] Xiaochen Tang,[1] Tingyu Zhang,[2] Wenjun Su,[1] Lihua Xu ,[1] Huiru Cui,[1] Zhenying Qian,[1] Tianhong Zhang ,[1,3] Jijun Wang [1,3,4,5]

ABSTRACT

Background Clinical high risk (CHR) of psychosis is a state in which positive symptoms cause the subjects distress but do not approach a severity level that fulfils the criteria for a psychotic episode. CHR exhibits cognitive deficits; however, the underlying neurobiological mechanisms remain unclear. This study aimed to investigate whether brain activation measured by the levels of oxygenated hemoglobin (oxy-Hb) in CHR subjects could be correlated with cognitive deficits.

Methods Fifty-eight CHR individuals who fulfilled the criteria for attenuated positive syndrome as specified in the Structured Interview for Prodromal Syndrome (SIPS) and the Scale of Prodromal Syndrome (SOPS) and 58 age- and sex-matched healthy participants were included in the study. All subjects completed the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) Consensus Cognitive Battery (MCCB) that includes tests measuring attention, verbal memory, verbal fluency, executive function, and general intelligence. Functional near-infrared spectroscopy (fNIRS) was used to measure the level of oxy-Hb in the dorsolateral prefrontal and frontotemporal cortices.

Results We observed significantly decreased oxy-Hb levels in channel 32 (located in the right superior temporal gyrus, rSTG)) within the CHR individuals compared with that in the healthy controls (HCs) (t=−3.44, Bonferroni-corrected p=0.002), indicating lower brain activity. A significant positive correlation was observed between task-related β values and working memory in the CHR group (r=0.35, p=0.008).

Conclusions The brain activation of rSTG is abnormal among subjects at cliniclal high risk for psychosis. This abnormality is probably associated with the neural mechanisms of deficits in the working memory during the early stage of psychosis.

INTRODUCTION

Clinical high risk (CHR) of psychosis is defined as a state in which subthreshold positive psychotic symptoms, such as perceptual abnormalities or overvalued ideas, occur, but their severity or duration fails to fulfil the criteria for a diagnosis of psychosis.[1 2] Cognitive deficits are a key feature of CHR

Key messages

What is already known on this topic
► Cognitive deficits are a key feature of the early stages of psychosis. Findings to date strongly indicate that memory impairments are present during the premorbid phase of psychosis and, in particular, are predictive of future conversion to psychosis.

What this study adds
► The current study investigated brain activation that was measured with functional near-infrared spectroscopy (fNIRS) in individuals with clinical high risk (CHR) and healthy controls(HCs). Compared with HCs, the CHR group showed reduced brain activation in the right superior temporal gyrus (rSTG) during the verbal fluency test (VFT). This reduced brain activation had a significant positive correlation with working memory.

How this study might affect research, practice or policy
► The current study provides evidence that abnormal brain activation in the rSTG is probably associated with the neural mechanisms of working memory deficits in CHR.

individuals and are associated with functional outcomes.[3] A meta-analysis comparing CHR individuals with healthy controls (HCs) found extensive cognitive impairments in executive function, verbal and visual memory, verbal fluency, attention, working memory, and social cognition in the at-risk group.[4] Findings to date strongly indicate that memory impairments are present during the premorbid phase of psychosis, and working memory impairments, in particular, are predictive of future conversion to psychosis.[5] However, the underlying neurobiological mechanisms are not well understood.

Functional magnetic resonance imaging (fMRI) has been widely used to investigate neurobiological deficits in CHR. However,

fMRI studies have reported inconsistent findings, with some studies reporting hyperactivation and others showing hypoactivation in the dorsal lateral prefrontal cortex (DLPFC) during working memory tasks.[6] [7] However, fMRI is inconvenient for many CHR subjects.
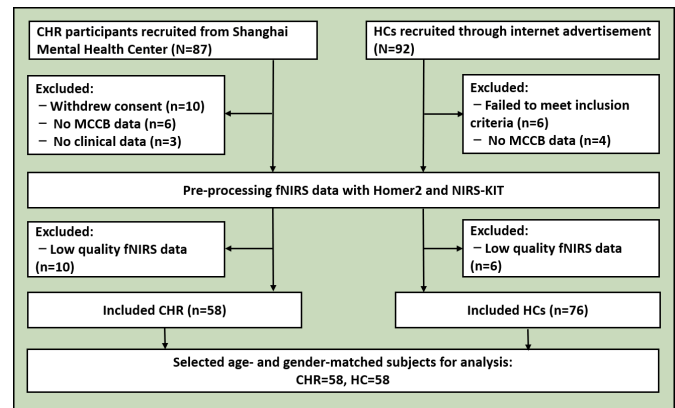
Functional near-infrared spectroscopy (fNIRS) is a recently developed, convenient, and non-invasive optical neuroimaging technology that uses changes in measured infrared light to make inferences regarding changes in the concentrations of cortical haemoglobin.[8] Cortical tissue is interrogated using emitted light from either a light-emitting diode (LED) or a laser source and is measured using a light detector. The distance between each emitter and detector was fixed at 3 cm. Compared with fMRI, fNIRS is restricted to the measurement of shallow cortical activity and offers a low-cost, well-tolerated, convenient set-up and acquisition with reduced sensitivity to motion artefacts.[8] More importantly, fNIRS provides a measurement of oxy-haemoglobin (oxy-Hb) and deoxy-haemoglobin (deoxy-Hb) concentrations, which are strongly correlated with fMRI signals.[9] Previous research has shown that fNIRS is sensitive to differences in clinical diagnoses. Studies using fNIRS have indicated that during the verbal fluency test (VFT), patients with stable chronic schizophrenia show reduced activity and characteristic waveform patterns in the prefrontal cortex.[10] A cross-sectional fNIRS study that focused on four different clinical stages of psychosis (healthy, CHR, first-episode, and chronic schizophrenia) indicated there are varying activity patterns among different prefrontal cortex (PFC) subregions.[11] Brain activity in the superior temporal gyrus(STG), inferior frontal gyrus (IFG), and middle frontal gyrus (MFG) decreased with advancing clinical stages of psychosis,[12] which was similar to the results of previous fMRI studies of the different clinical stages.[13]

In the present study, we measured brain activity in the prefrontal and temporal cortices using multichannel fNIRS measurements and assessed clinical symptoms and cognition. Our main hypotheses were that (1) CHR showed reduced brain activation compared with healthy individuals, and (2) reduced brain activity could be associated with cognitive function.

MATERIALS AND METHODS
Study participants
Eighty-seven CHR participants were recruited from the Shanghai Mental Health Center from January 2019 to November 2020. Inclusion criteria included no prior visits to mental health services and drug naivety for antipsychotic medication. The CHR evaluation was performed by a senior psychiatrist using the Structured Interview for Prodromal Symptoms (SIPS) and Scale of Prodromal Syndrome (SOPS)[14] to exclude any other psychotic symptoms or mental disorders. Nineteen CHR participants were excluded during the screening process: 10 refused to sign the informed consent, 6 failed to finish

Figure 1 Flowchart of enrolment of the subjects. CHR, clinical high risk of psychosis; fNIRS, functional near-infrared spectroscopy; HC, healthy control; MCCB, Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) Consensus Cognitive Battery; NIRS, near-infrared spectroscopy.

the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) Consensus Cognitive Battery (MCCB) test, and 3 did not complete the clinical evaluation. Ninety-two healthy controls (HCs) were recruited from a local school and the community through an internet advertisement. Exclusion criteria included prodromal psychotic symptoms, other mental disorders, or a family history of mental disorders. The Mini-International Neuropsychiatric Interview (MINI)[15] was administered by a senior psychiatrist for the HCs evaluation. Ten HCs were excluded during the screening process: 6 failed to meet the inclusion criteria, and 4 did not complete the MCCB test. An additional 10 CHRs and 6 HCs were excluded during the fNIRS data preprocessing step due to the low quality of fNIRS signals. Finally, 58 CHRs and 76 HCs were enrolled. To exclude the effects of demographic characteristics on the fNIRS results, we matched the groups according to age and sex[16] and analysed outcomes for 58 CHRs and 58 HCs (figure 1). All subjects were right-handed, as assessed using the Edinburgh Handedness Inventory.[17] All participants were provided with a detailed explanation of the study. In accordance with the Declaration of Helsinki, written informed consent was obtained from all participants prior to their participation in the study. The participants younger than 18 years submitted written informed consent forms signed by their parents. The study was approved by the Ethics Committee of the Shanghai Mental Health Center.

Clinical and cognitive assessment
The SIPS/SOPS was used for clinical assessment of CHR participants on the day of the fNIRS measurements. The SIPS/SOPS comprises 19 items: positive symptoms (scales P1–P5), negative symptoms (scale N1–N6), disorganised symptoms (scale D1–D4) and general symptoms (scale G1–G4). The assessments were conducted by a senior psychiatrist. With the permission of Yale university, a Chinese version of the SIPS/SOPS was translated by our

team and tested for reliability and validity in a Chinese population.[18 19]

The MCCB[20 21] is a standardised method to measure the cognitive function of patients with schizophrenia. The MCCB has been translated into Chinese, and both co-norming and standardisation have been performed in China. It demonstrated sufficient clinical validity and reliability in controls and patients with schizophrenia, with the test–retest reliability of the subtests ranging from 0.73 to 0.94.[22] Consistent with the original version of the MCCB, the Chinese version comprises nine tests covering seven cognitive domains: speed of processing, attention/vigilance, working memory, verbal learning, visual learning, reasoning and problem-solving, and social cognition.[23] The social cognition test is not applicable to participants aged less than 18 years; therefore, we did not apply social cognition in this study. The raw data of the MCCB test were input twice (double data entry) into the MCCB computer program and converted to T-scores as well as a composite T-score.
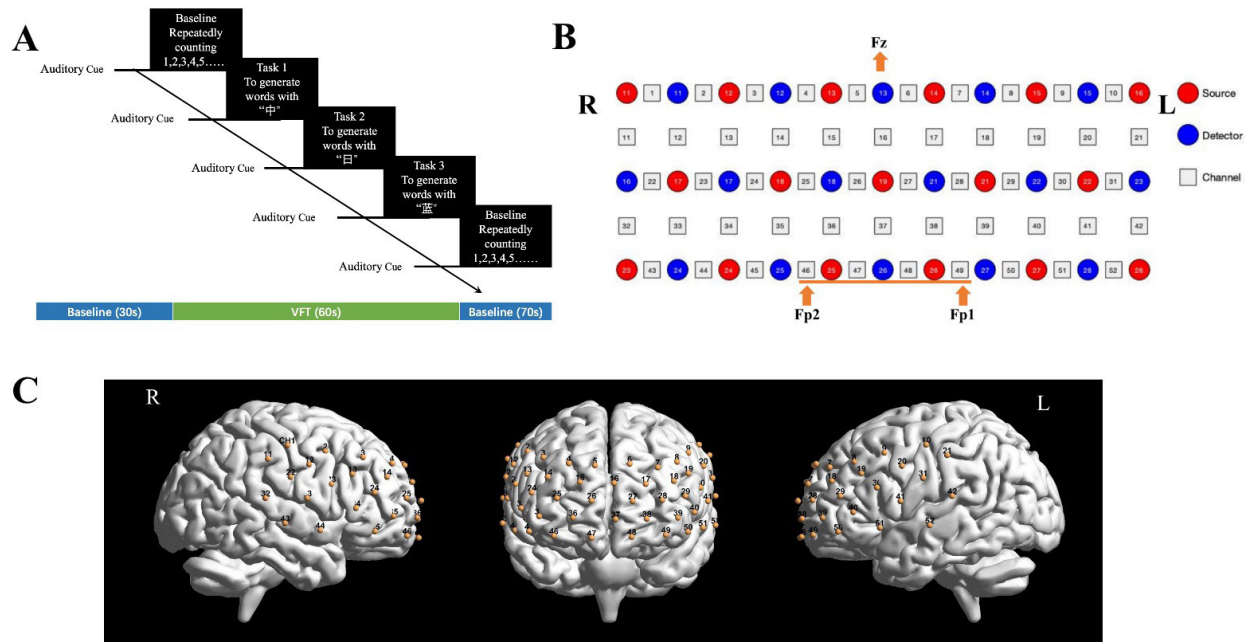
Verbal fluency test

Participants completed a 160 s block-design letter version of the VFT. The VFT has been widely used in previous fNIRS studies.[24] A 160 s block comprises three different time periods: a 30 s pretask period, a 60 s task period, and a 70 s post-task period. In the pretask and post-task periods, the participants were instructed to count numbers from one to five repeatedly. The 60 s task period comprised three 20 s subperiods. During each 20 s period, one of three Chinese syllables ('中', '日' and '蓝', which indicate middle, sun and blue) was audibly presented to the

subjects; the subjects were then instructed to generate as many words as possible that began with the same syllable (figure 2A). The experiment was conducted in a quiet environment and the participants were asked to sit in a comfortable wooden chair with their eyes open. To reduce possible distractions, a screen was placed approximately 1 meter in front of each participant and the participants were asked to look at the red asterisk at the centre of the screen to minimise head movements. Before the experiment, each subject was provided with instructions on how to answer correctly and a practice trial was conducted to ensure that they understood the instructions. Task performance was evaluated by the total number of correct words generated during the 60 s task period.

fNIRS instrument

We used a 52-channel fNIRS instrument (ETG-4000; Hitachi Medical, Tokyo, Japan) to measure changes in haemoglobin concentration. The fNIRS instrument uses two wavelengths of near-infrared light (695 nm and 830 nm) and calculates the amount of absorbed near-infrared light based on the modified Beer-Lambert law.[25] Seventeen emitters and 16 detector probes were thermoplastically set in a 3 row × 11 column matrix within the 52 channels on the participant's forehead. The lowest probe line was set along the Fp1–Fp2 line (figure 2B), as defined by the international 10–20 system. The distance between pairs of sources and detectors was set to 3.0 cm. The area between each probe set was defined as one 'channel', which was sufficient to obtain data from depths of 20–30 mm under the scalp. This arrangement allows imaging of the surface of both the bilateral prefrontal cortices as

Figure 2 (A) The verbal fluency test (VFT). It consists of a 30 s pretask resting-state period and three 20 s word-generating tasks, followed by a 70 s post-task resting-state period. (B) 3*11 optode montage. Red circles represent light sources (emitter), blue circles indicate light detectors, and numbers 1–52 indicate the location of each optode pair (channel). When we positioned the patch according to the International 10–20 system, detector 13 was located at Fz, and channels 49 and 46 were placed in Fp1 and Fp2, respectively. (C) The optode was placed on the bilateral frontal and temporal cortex. L, left; R, right.

well as the bilateral temporal cortical areas (figure 2C). The fNIRS imaging data were collected at a constant sampling frequency of 10 Hz. Relative changes in haemoglobin concentration assessed using fNIRS were provided in units of mM.mm.

The spatial information for each channel was estimated using data from the Functional Brain Science Laboratory at the Jichi Medical University in Japan.[26] As in previous studies,[27] fNIRS channels were anatomically labelled only after the Laboratory of Neuro Imaging (LONI) Probabilistic Brain Atlas (LPBA) region when the highest probability was determined. As oxy-Hb has stronger correlations with blood oxygen level-dependent signals compared with deoxy-Hb when measured using fMRI,[9] mean changes in oxy-Hb measured during the VFT were used as indices of brain cortical activity.

Statistical analysis

To test for group differences in terms of years of education, VFT performance, and neuropsychological scores, we analysed the data using paired t-test.

The two toolboxes Homer2[28] and NIRS-KIT[29] were used in the quantitative analysis of fNIRS signals and to calculate the activation of oxy-Hb levels. The fNIRS signals contain two types of noise that contaminate underlying cerebral haemodynamics. To initially remove these confounding factors from the fNIRS signal and recover the underlying brain activation patterns, the noisy channels were identified and pruned from the measurement list using the Homer2 function *hmrPruneChannels* (dRange=10^{-3}–10^{-7} and SNRthres=5). Next, the optical density (OD) was transferred from the optical intensity using the *hmrintensity2OD* function. OD is defined as the logarithmic intensity ratio of the light falling on the material to the light transmitted through the material.[30] The HOMER2 function *hmrMotionArtifactByChannel* was used to detect channel-wise motion artefacts. Channels with too many artefacts were rejected. Subsequently, OD was converted into concentration changes of oxy-Hb using the modified Beer-Lambert law.[31] Lastly, a haemodynamic response function filter was adopted for temporal smoothing and to swamp the intrinsic temporal correlations and attenuate the high-frequency components.[32] All of these steps were used to assess the quality of the raw data. Subjects whose channels had artefacts above 10% were rejected.

Before statistical analysis, fNIRS data underwent a series of preprocessing steps aimed at removing artefacts using the NIRS-KIT toolbox. The main goal was to minimise the influence of data acquisition errors and physiological artefacts. First, we used a polynomial regression model to estimate a linear trend and then subtracted it from the raw haemoglobin concentration signals. Second, the temporal derivative distribution repair method was used to correct the motion.[33] Third, an infinite impulse response filter was used to remove irrelevant low-frequency and high-frequency components with a bandpass of 0.001–0.1 Hz. A general linear model was used to analyse the fNIRS time series. Task-related β

values were defined as word-generating β values minus (pre-task+post-task β values)/2.

Paired t-test with Bonferroni correction (corrected p<0.05) was conducted on task-related β values at each channel. Images were created using the results visualisation function, in which channel-wise statistical values were mapped onto the standard brain space using the *nfri_mni_plot* function in the NFRI toolbox.[34] Finally, Pearson's correlation coefficients were used to examine the relationship between clinical variables (Positive and Negative Symptom Scale (PANSS), VFT performance and cognition), and task-related β values.

RESULTS

Demographic characteristics

The demographic characteristics of the participants are presented in table 1. They were matched in age and sex, but the HC group had more years of education than the CHR group. Moreover, the HC group showed significantly better VFT performance than the CHR group. Compared with the HC group, the CHR group showed cognitive deficits in the broad cognitive domain, including speed of processing, attention/vigilance, working memory, verbal learning, reasoning and problem-solving, and social cognition.

Brain activation during the VFT

The changes in oxy-Hb levels during the VFT task significantly decreased in channel 32 in the CHR group (the right superior temporal gyrus, rSTG) compared with the HC group. Paired t-test showed that the task-related β values in the CHR group were lower than those in the HC group (Bonferroni correction, p=0.002) (figure 3). The activation map for oxy-Hb level changes during the VFT task is shown in figure 4.

Correlation between cortical activation and clinical symptoms

Pearson's correlation analysis showed that task-related β values in channel 32 were positively correlated with working memory scores in the CHR group (r=0.35, p=0.008). The verbal learning scores were marginally significant (r=0.22, p=0.095; figure 5). However, there was no significant correlation in either working memory or verbal learning scores in the HC group.

DISCUSSION

Main findings

The present study investigated brain activation changes during the VFT in CHR, as well as whether these brain activation changes were associated with clinical symptoms and cognition. The main findings were that the CHR group showed reduced brain activation in channel 32, located in the right STG. Moreover, task-related brain activation in channel 32 was positively correlated with working memory; however, there was no significant correlation between brain activation and VFT

Table 1 Demographic data of the participants

Characteristics	CHR	HC	Paired t	P value
n	58	58	NA	NA
Education, mean (SD)	12.93 (3.14)	14.36 (2.88)	2.56	<0.001
VFT performance, mean (SD)	6.72 (3.00)	8.59 (3.36)	3.14	0.003
SIPS/SOPS				
P1	2.79 (1.91)	NA	NA	NA
P2	2.21 (1.85)	NA	NA	NA
P3	0.54 (1.07)	NA	NA	NA
P4	1.24 (1.57)	NA	NA	NA
P5	0.55 (1.03)	NA	NA	NA
P_total	7.33 (3.66)	NA	NA	NA
N_total	9.50 (5.66)	NA	NA	NA
D_total	3.78 (2.99)	NA	NA	NA
G_total	6.48 (3.74)	NA	NA	NA
GAF_current	59.75 (8.06)	NA	NA	NA
GAF_past	75.62 (6.55)	NA	NA	NA
MCCB (T-score)				
Speed of processing, mean (SD)	47.05 (10.67)	55.48 (9.41)	4.51	<0.001
Attention/vigilance, mean (SD)	48.56 (8.23)	53.91 (7.68)	3.61	<0.001
Working memory, mean (SD)	40.10 (11.65)	47.79 (9.43)	3.91	<0.001
Verbal learning, mean (SD)	43.07 (10.17)	50.29 (8.07)	4.22	<0.001
Visual learning, mean (SD)	49.88 (7.89)	53.24 (7.31)	2.38	0.028
Reasoning and problem-solving, mean (SD)	50.22 (9.21)	54.19 (8.03)	2.47	0.022
Social cognition, mean (SD)	35.60 (7.41)	38.63 (7.14)	2.09	0.039

CHR, clinical high risk; D, disorganised symptoms; G, general symptoms; GAF, global assessment of function; HC, healthy control; MCCB, Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) Consensus Cognitive Battery; N, negative symptoms; NA, not applicable; P1, unusual thought content/delusion ideas; P3, grandiosity; P, positive symptoms; P2, suspiciousness/persecutory ideas; P4, perceptual abnormalities/hallucinations; P5, disorganised communication; SD, standard deviation; SIPS/SOPS, Structured Interview for Prodromal Symptoms/Scale of Prodromal Syndrome; VFT, verbal fluency test.

performance or clinical symptoms. There was no significant correlation between brain activation and cognition in the HC group. Generally, in the CHR group, a higher task-related β value indicated better working memory.
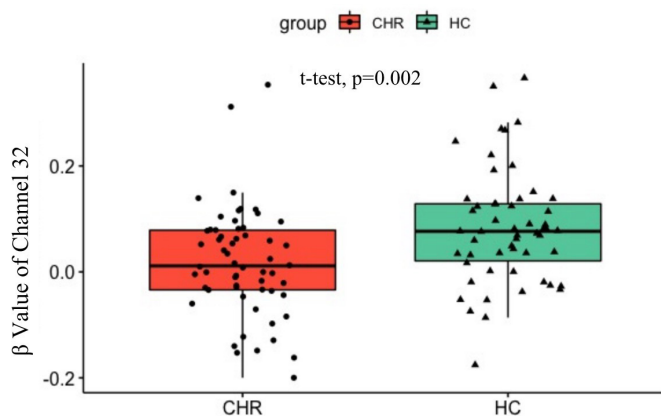
Figure 3 Task-related β value of channel 32 in the CHR and HC group. CHR, clinical high risk; HC, healthy control.
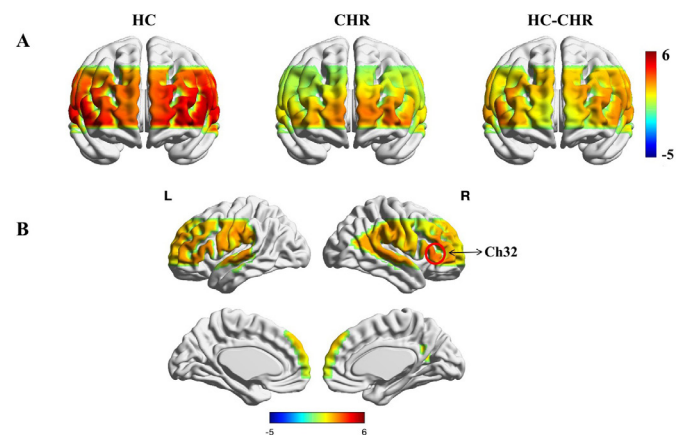
Figure 4 Cortical activation map of oxy-Hb level during the VFT in different groups. (A) Compared with the HC group, the CHR group showed significantly decreased activation in Ch32; (B) Ch32 was located in the right superior temporal gyrus. Ch, channel; CHR, clinical high risk; HC, healthy control; oxy-Hb, oxy-haemoglobin; VFT, verbal fluency test.
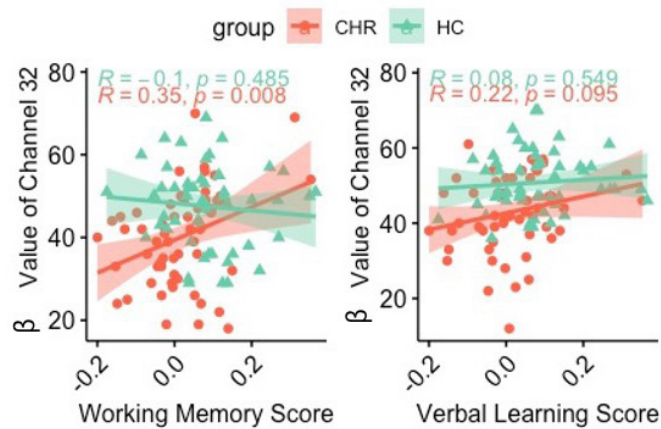
Figure 5 Correlation analysis between task-related β values of channel 32 and cognition (working memory and verbal learning). The results showed that the β value had a significant positive correlation with working memory and showed a marginally significant level with the score of verbal learning in the CHR group, while there was no significant correlation found in the HC group. CHR, clinical high risk; HC, healthy control.

Our study is in line with previous studies that have provided evidence of decreased brain activity prior to the onset of psychosis. The VFT is a commonly applied cognitive task in fNIRS research,[35] and we used the letter fluency task, which requires the generation of words based on phonemic cues. The performance of the VFT not only requires retrieval of items from long-term memory storage but also the working memory capacity to hold already-generated words.[36] These task characteristics demand a wide variety of functions from the bilateral frontotemporal regions. The main decrease in activity was observed in the right STG. One of the functions of the STG is acoustic perception and comprehension for integrating meaningful verbal information in the dominant hemisphere.[37] Moreover, task-related β values showed a marginal correlation with verbal learning. A previous study demonstrated that verbal fluency deficits are often present during the early stages of CHR and are a possible predictor of the transition to psychosis.[38]

Frontotemporal lobe dysfunction is a core feature of patients with schizophrenia.[39 40] Many studies on fNIRS have used clinical variables to investigate symptom changes and their association with brain activity. They found a significant correlation between brain activation and PANSS total scores, as well as positive and negative scores.[10 41] Chou *et al*[42 43] found that in first-episode schizophrenia, there was a significant negative association between brain activity and PANSS negative scores in the bilateral inferior frontal gyrus and bilateral temporal regions. In another study conducted by Koike *et al*,[12] the brain activity of the bilateral ventrolateral prefrontal cortex and the frontopolar and anterior parts of the temporal cortical regions in the CHR group was lower than those in the HCs.

Limitations

All findings must be interpreted with caution as this study has several limitations. First, in the current study, the CHR group only included 58 individuals and further studies with larger sample size are needed. Second, we only observed the cross-sectional outcome between the groups; the longitudinal outcomes of CHR and whether fNIRS can predict conversion to psychosis remain unclear. Future research will include a follow-up study investigating the various mechanisms of CHR progression in relation to cognition and brain activity. Finally, we divided the CHR patients into severe and mild groups but did not find any significant results. Most CHR cases were mild. Therefore, these results should be considered preliminary.

Implications

In conclusion, the brain activation of rSTG is abnormal among subjects at clinical high risk of psychosis when they perform VFT. This abnormality probably plays a key role in the neural mechanisms of deficits in working memory in the early stage of psychosis.

Author affiliations
[1]EEG and Neuroimaging Department, Shanghai Mental Health Center, Shanghai Jiao Tong University School of Medicine, Shanghai, China
[2]The Seventh Affiliated Hospital Sun Yat-sen University, Shenzhen, China
[3]Shanghai Key Laboratory of Psychotic Disorders, Shanghai Mental Health Center, Shanghai Jiao Tong University School of Medicine, Shanghai, China
[4]CAS Center for Excellence in Brain Science and Intelligence Technology (CEBSIT), Chinese Academy of Science, Shanghai, China
[5]Institute of Psychology and Behavioral Science, Shanghai Jiao Tong University, Shanghai, China

ORCID iDs
Yanyan Wei http://orcid.org/0000-0002-8218-1954
Lihua Xu http://orcid.org/0000-0002-2237-9336
Tianhong Zhang http://orcid.org/0000-0002-5379-7119
Jijun Wang http://orcid.org/0000-0001-5427-7425

REFERENCES

1 McGorry PD, Yung AR, Phillips LJ. The "close-in" or ultra high-risk model: a safe and effective strategy for research and clinical intervention in prepsychotic mental disorder. *Schizophr Bull* 2003;29:771–90.
2 Yung AR, McGorry PD. The prodromal phase of first-episode psychosis: past and current conceptualizations. *Schizophr Bull* 1996;22:353–70.
3 Lam M, Lee J, Rapisarda A, *et al*. Longitudinal cognitive changes in young individuals at ultrahigh risk for psychosis. *JAMA Psychiatry* 2018;75:929–39.
4 Fusar-Poli P, Deste G, Smieskova R, *et al*. Cognitive functioning in prodromal psychosis: a meta-analysis. *Arch Gen Psychiatry* 2012;69:562–71.
5 Seabury RD, Cannon TD. Memory impairments and psychosis prediction: a scoping review and theoretical overview. *Neuropsychol Rev* 2020;30:521–45.
6 Manoach DS, Gollub RL, Benson ES, *et al*. Schizophrenic subjects show aberrant fMRI activation of dorsolateral prefrontal cortex and basal ganglia during working memory performance. *Biol Psychiatry* 2000;48:99–109.
7 Callicott JH, Ramsey NF, Tallent K, *et al*. Functional magnetic resonance imaging brain mapping in psychiatry: methodological issues illustrated in a study of working memory in schizophrenia. *Neuropsychopharmacology* 1998;18:186–96.
8 Ferrari M, Quaresima V. A brief review on the history of human functional near-infrared spectroscopy (fNIRS) development and fields of application. *Neuroimage* 2012;63:921–35.
9 Sato H, Yahata N, Funane T, *et al*. A NIRS-fMRI investigation of prefrontal cortex activity during a working memory task. *Neuroimage* 2013;83:158–73.
10 Chou P-H, Koike S, Nishimura Y, *et al*. Similar age-related decline in cortical activity over frontotemporal regions in schizophrenia: a multichannel near-infrared spectroscopy study. *Schizophr Bull* 2015;41:268–79.
11 Koike S, Nishimura Y, Takizawa R, *et al*. Near-Infrared spectroscopy in schizophrenia: a possible biomarker for predicting clinical outcome and treatment response. *Front Psychiatry* 2013;4:145.
12 Koike S, Takizawa R, Nishimura Y, *et al*. Different hemodynamic response patterns in the prefrontal cortical sub-regions according to the clinical stages of psychosis. *Schizophr Res* 2011;132:54–61.
13 Dietsche B, Kircher T, Falkenberg I. Structural brain changes in schizophrenia at different stages of the illness: a selective review of longitudinal magnetic resonance imaging studies. *Aust N Z J Psychiatry* 2017;51:500–8.
14 McGlashan TH, Walsh BC, Woods SW. *The psychosis-risk syndrome. Handbook for diagnosis and follow-up*. Oxford/New York: Oxford University Press, 2010.
15 Sheehan DV, Lecrubier Y, Sheehan KH, *et al*. The Mini-International neuropsychiatric interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *J Clin Psychiatry* 1998;59 Suppl 20:22–33.
16 Zhang T, Cui H, Wei Y, *et al*. Neurocognitive assessments are more important among adolescents than adults for predicting psychosis in clinical high risk. *Biol Psychiatry Cogn Neurosci Neuroimaging* 2022;7:56–65.
17 Oldfield RC. The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia* 1971;9:97–113.
18 Zhang T, Li H, Woodberry KA, *et al*. Prodromal psychosis detection in a counseling center population in China: an epidemiological and clinical study. *Schizophr Res* 2014;152:391–9.
19 Zheng LN, Wang JJ, Zhang TH. Reliability and validity of the Chinese version of scale of Psychosis-risk symptoms. *Chinese Mental Health Journal* 2012;26:571–6.
20 Nuechterlein KH, Green MF, Kern RS, *et al*. The MATRICS consensus cognitive battery, part 1: test selection, reliability, and validity. *Am J Psychiatry* 2008;165:203–13.
21 Kern RS, Nuechterlein KH, Green MF, *et al*. The MATRICS consensus cognitive battery, part 2: co-norming and standardization. *Am J Psychiatry* 2008;165:214–20.
22 Shi C, Kang L, Yao S, *et al*. The MATRICS consensus cognitive battery (MCCB): Co-norming and standardization in China. *Schizophr Res* 2015;169:109–15.
23 Nuechterlein KH, Barch DM, Gold JM, *et al*. Identification of separable cognitive factors in schizophrenia. *Schizophr Res* 2004;72:29–39.
24 Huang C-J, Chou P-H, Wei H-L, *et al*. Functional connectivity during Phonemic and semantic verbal fluency test: a multichannel near infrared spectroscopy study. *IEEE J. Select. Topics Quantum Electron.* 2016;22:43–8.
25 Delpy DT, Cope M, van der Zee P, *et al*. Estimation of optical pathlength through tissue from direct time of flight measurement. *Phys Med Biol* 1988;33:1433–42.
26 Tsuzuki D, Jurcak V, Singh AK, *et al*. Virtual spatial registration of stand-alone fNIRS data to MNI space. *Neuroimage* 2007;34:1506–18.
27 Chou P-H, Koike S, Nishimura Y, *et al*. Distinct effects of duration of untreated psychosis on brain cortical activities in different treatment phases of schizophrenia: a multi-channel near-infrared spectroscopy study. *Prog Neuropsychopharmacol Biol Psychiatry* 2014;49:63–9.
28 Huppert TJ, Diamond SG, Franceschini MA, *et al*. Homer: a review of time-series analysis methods for near-infrared spectroscopy of the brain. *Appl Opt* 2009;48:D280–98.
29 Hou X, Zhang Z, Zhao C, *et al*. NIRS-KIT: a Matlab toolbox for both resting-state and task fNIRS data analysis. *Neurophotonics* 2021;8:010802.
30 Steinegger A, Wolfbeis OS, Borisov SM. Optical sensing and imaging of pH values: spectroscopies, materials, and applications. *Chem Rev* 2020;120:12357–489.
31 Cope M, Delpy DT. System for long-term measurement of cerebral blood and tissue oxygenation on newborn infants by near infra-red transillumination. *Med Biol Eng Comput* 1988;26:289–94.
32 Worsley KJ, Friston KJ. Analysis of fMRI time-series revisited--again. *Neuroimage* 1995;2:173–81.
33 Fishburn FA, Ludlum RS, Vaidya CJ, *et al*. Temporal derivative distribution repair (TDDR): a motion correction method for fNIRS. *Neuroimage* 2019;184:171–9.
34 Singh AK, Okamoto M, Dan H, *et al*. Spatial registration of multichannel multi-subject fNIRS data to MNI space without MRI. *Neuroimage* 2005;27:842–51.
35 Kumar V, Shivakumar V, Chhabra H, *et al*. Functional near infra-red spectroscopy (fNIRS) in schizophrenia: a review. *Asian J Psychiatr* 2017;27:18–31.
36 Henry JD, Crawford JR. A meta-analytic review of verbal fluency performance following focal cortical lesions. *Neuropsychology* 2004;18:284–95.
37 Warren JE, Crinion JT, Lambon Ralph MA, *et al*. Anterior temporal lobe connectivity correlates with functional outcome after aphasic stroke. *Brain* 2009;132:3428–42.
38 Addington J, Liu L, Perkins DO, *et al*. The role of cognition and social functioning as predictors in the transition to psychosis for youth with attenuated psychotic symptoms. *Schizophr Bull* 2017;43:57–63.
39 Lawrie SM, Buechel C, Whalley HC, *et al*. Reduced frontotemporal functional connectivity in schizophrenia associated with auditory hallucinations. *Biol Psychiatry* 2002;51:1008–11.
40 Mahurin RK, Velligan DI, Miller AL. Executive-frontal lobe cognitive dysfunction in schizophrenia: a symptom subtype analysis. *Psychiatry Res* 1998;79:139–49.
41 Noda T, Nakagome K, Setoyama S, *et al*. Working memory and prefrontal/temporal hemodynamic responses during post-task period in patients with schizophrenia: A multi-channel near-infrared spectroscopy study. *J Psychiatr Res* 2017;95:288–98.
42 Chou P-H, Lin W-H, Li W-R, *et al*. Reduced language lateralization in first episode schizophrenia: a near infrared spectroscopy study. *Prog Neuropsychopharmacol Biol Psychiatry* 2017;78:96–104.
43 Chou P-H, Lin W-H, Lin C-C, *et al*. Duration of untreated psychosis and brain function during verbal fluency testing in first-episode schizophrenia: a near-infrared spectroscopy study. *Sci Rep* 2015;5:18069.

Wei Yanyan obtained a master degree in Medical Psychology from the Second Military Medical University in Shanghai, China in 2016. After graduation, she became a member of Shanghai Mental Health Center, Shanghai Jiao Tong University School of Medicine in China. At present, she is working towards a doctorate in psychiatry and mental health at the Shanghai Jiao Tong University School of Medicine. In addition, she is also an associate researcher in the EEG and neuroimaging department. Her main research interest includes early identification and intervention for mental disorders. She is also interested in the use of infrared functional brain imaging technology to explore brain activity in the cognitive process of patients with psychosis and towards the prediction of clinical intervention efficacy.