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Research article

Effects of long-term COVID-19 confinement and music stimulation on mental state and brain activity of young people

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ABSTRACT

The Corona Virus Disease 2019 (COVID-19) pandemic may have had a negative emotional impact on individuals. This study investigated the effect of long-term lockdown and music on young people's mood and neurophysiological responses in the prefrontal cortex (PFC). Fifteen healthy young adults were recruited and PFC activation was acquired using functional near-infrared spectroscopy during the conditions of resting, Stroop and music stimulation. The Depression Anxiety Stress Scales mental scale scores were simultaneously recorded. Mixed effect models, paired t-tests, one-way ANOVAs and Spearman analyses were adopted to analyse the experimental parameters. Stress, anxiety and depression levels increased significantly from Day 30 to Day 40. In terms of reaction time, both Stroop1 and Stroop2 were faster on Day 40 than on Day 30 ($P = 0.01$, $P = 0.003$). The relative concentration changes of oxyhemoglobin were significantly higher during premusic conditions than music stimulation and postmusic Stroop. The intensity of functional connectivity shifted from inter- to intracerebral over time. In conclusion, the reduced hemodynamic response of the PFC in healthy young adults is associated with negative emotions, especially anxiety, during lockdown. Immediate music stimulation appears to improve efficiency by altering the pattern of connections in PFC.

1. Introduction

The COVID-19 pandemic caused many restrictions to be placed on people's lives. While these measures have been critical in mitigating the spread of COVID-19, they have also had a negative impact on people's mental health and lifestyle [1–3]. An increasing number of people have a lack of physical activity, unhealthy eating behaviour, social, psychological and emotional disorders and poor sleep quality [4]. In addition, people in isolation report more severe psychological symptoms and are more likely to experience higher levels of anxiety, depression, and stress [5], some of which seem to persist long after the end of the isolation period, compared to their counterparts [6].

Music is an effective emotional inducer with the ability to evoke positive emotions [7]. Music therapy can relieve symptoms of depression, increase positive emotions [8], enhance treatment compliance, and improve quality of life [9]. According to surveys, 82% of people with depression consider listening to music to be an effective treatment [10].

The prefrontal cortex (PFC) plays an important role in emotional [11] and cognitive task processing and other executive functions. Studies have reported low activation of the PFC during cognitive tasks in patients with mood disorders or anxiety disorders [12]. Liu et al. [13] found that the change of oxyhemoglobin (ΔHbO2) concentration in PFC was correlated with the severity of depression. In addition, high levels of negative affective symptoms are associated with a variety of adverse outcomes, such as poor academic performance [14] and sleep disturbances [15]. Therefore, neuroimaging studies aimed at understanding the effects of long-term COVID-19 confinement and music stimulation on the PFC are necessary.

As one of the gold standards and the most widely used instrument in neuropsychological fields, the Stroop task is an experimental paradigm

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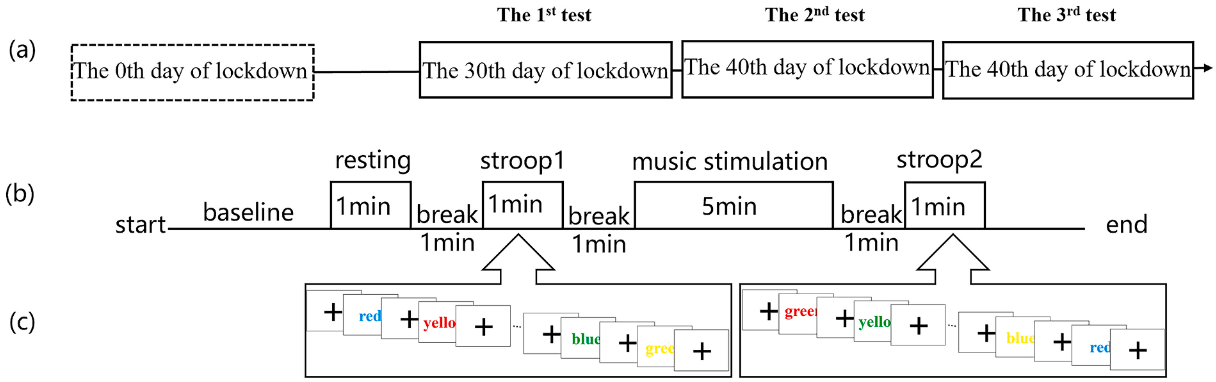

Fig. 1. (a) Experimental setup, (b)fNIRS experimental design, and (c) Stroop task paradigm.

used to measure the ability to selectively attend to task-relevant information and inhibit responses to task-irrelevant stimuli [16], reflect cognitive and attentional abilities. Hence, the analysis of Stroop performance may reveal the effect of lockdown and music on young people's cognition and attention in the PFC.

There have been few studies on the effects of prolonged dormitory confinement and music stimulation on the mental states and PFC activity of young people during the COVID-19 pandemic. According to Agnieszka et al [17], COVID-19-related lockdown may have resulted in decreased cerebral hemodynamics, which may also be associated with an increased risk of mental health disorders. Therefore, it is important to study the neurocognitive changes related to negative emotions among young people who were confined to dormitories for a long time during the COVID-19 pandemic, which can facilitate effective early prevention and intervention. Functional near-infrared spectroscopy (fNIRS) indirectly monitors brain activity by measuring changes in oxyhemoglobin (HbO2) and deoxyhemoglobin (HbR) concentrations in cerebral blood vessels [18]. Compared with other tools, fNIRS has the advantages of relatively high spatial and temporal resolution, better comfort, and less strict requirements for the experimental environment. Therefore, we will use this technique to monitor activity changes in the PFC during the music stimulation and Stroop tasks.

From April to May 2022, in Shanghai, China, lockdown management was imposed on schools due to a sudden outbreak of COVID-19, and movement was limited to the minimum necessary. Therefore, the purpose of this study was to investigate the effects of long-term dorm confinement and music stimulation on mood and cerebral hemodynamics in young adults. We hypothesized that (1) confinement would lead to negative emotions in young adults, which might inhibit the function of the PFC, and (2) immediate music stimulation might alleviate negative emotions and enhance functional brain connectivity.

2. Material and methods

2.1. Subjects

From April to May 2022, 15 healthy adults (7 males and 8 females, age: 25.1 $\pm$ 3.2 years) who were confined for 30 days were recruited from Shanghai YangZhi Rehabilitation Hospital. All participants had normal vision and hearing or normal with correction. Exclusion criteria included any clinical psychiatric history, such as anxiety and depression, and other chronic diseases. This study was approved by the ethics committee of the hospital, and all subjects signed an approved informed consent form before participating.

2.2. Experimental setup and protocol

Data were collected starting May 1, 2022, which was the 30th day of containment management in Shanghai due to the COVID-19 outbreak. A total of three tests, namely, the first, second and third test were conducted on the 30th, 40th and 50th days of containment, respectively (Fig. 1a).

Each test consisted of two parts, including the completion of the Depression Anxiety Stress Scales (DASS-21) in simplified Chinese and fNIRS data collection. Before the trials, participants were made familiar with the experimental instructions and four conditions (Fig. 1b).

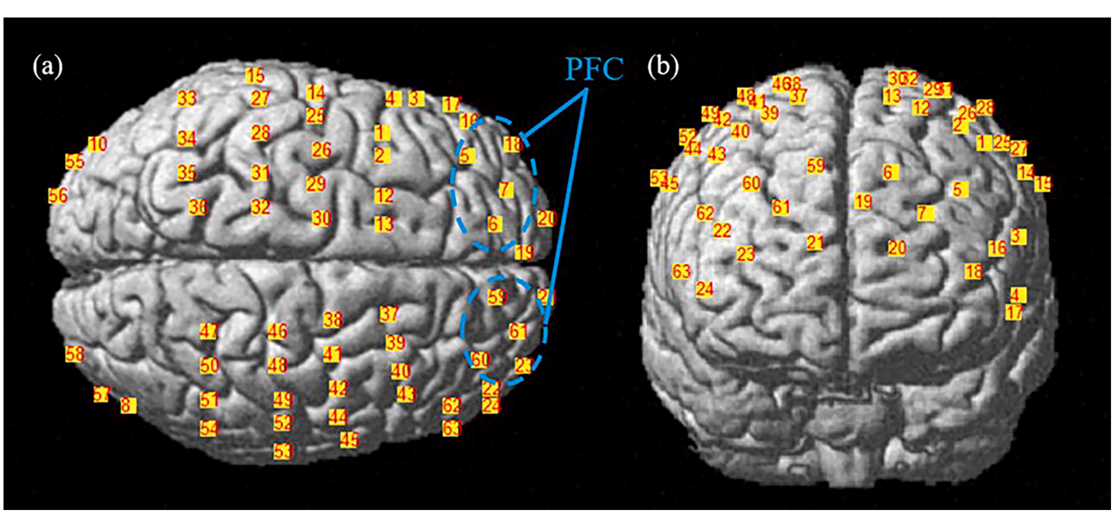

Fig. 2. Arrangement of channels (a)Top and (b)frontal views of the locations of the channels in the MNI brain.

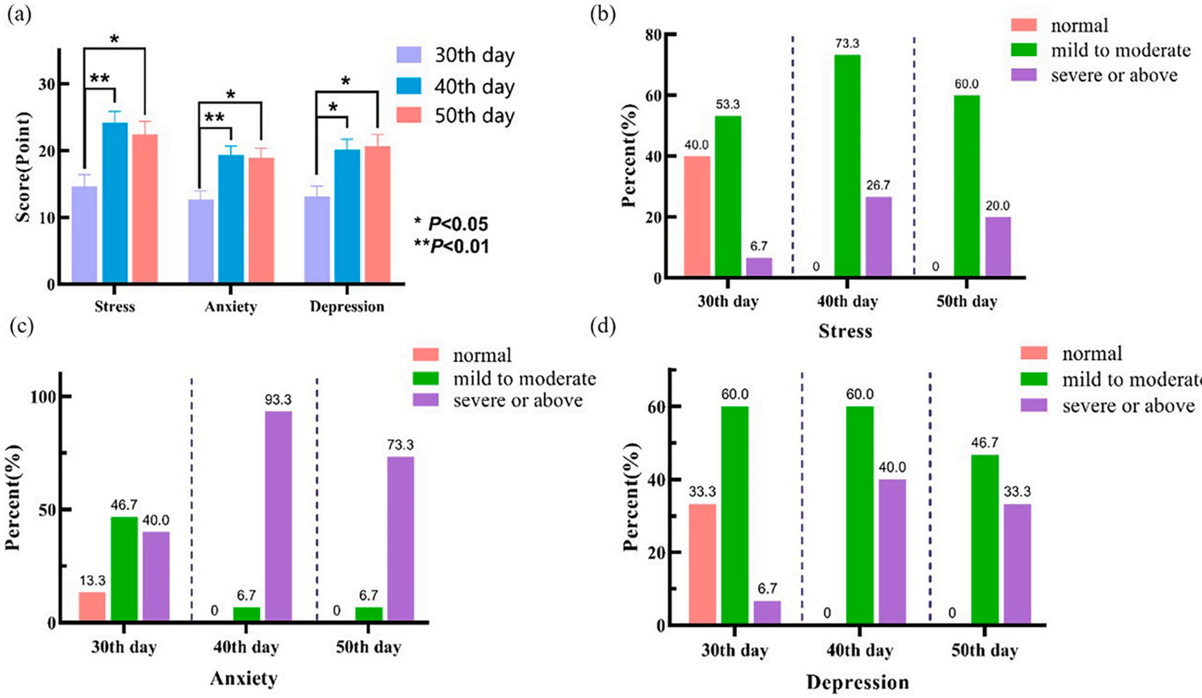

Fig. 3. Results of DASS-21 (a) total scores , (b) stress subscale scores, (c) anxiety subscale scores, and (d) depression subscale scores.

Watching the Shorebirds was selected for music stimulation and played through headphones. During rest periods, participants were asked to focus on a cross on a screen and breathe calmly while avoiding head movements and face expressions.

2.2.1. Dass-21

The DASS-21 is a mature tool for measuring anxiety, depression and stress, with good reliability and validity in psychological measurement [19] and good internal consistency in each subscale. It has also proven to be an effective tool for monitoring mental health status during the COVID-19 pandemic [20,21]. This questionnaire contains a total of 21 items comprising three intercorrelated yet distinct subscales, estimating the levels of depression, anxiety, and stress symptoms separately. Participants responded to how much the statements applied to themselves over the previous week using a four-point Likert scale ranging from 0 (“does not apply to me at all”) to 3 (“applies to me very much or most of the time”). The higher the participant’s score was, the more emotional he or she was.

2.2.2. Stroop task

The modified, computerized Stroop colour word matching task was used [22]. The Chinese characters are “red”, “yellow”, “blue” and “green” appear randomly in the center of the computer screen and the colors of the words were also randomly red, blue, yellow and green (Fig. 1c). After the stimulus demonstration, the participant was asked to name the colour of the word as quickly as possible by pressing the corresponding colour key on the keyboard. Before the experiment, participants practised the corresponding colour buttons by naming the colours of 20 words. Stroop1 and Stroop2 represent the first and second Stroop tasks (before and after the music stimulation) in each test, respectively.

2.2.3. fNIRS

A 63-channel fNIRS system (NirScan, Danyang Huichuang Medical Equipment Co., ltd., Jiangsu, China) with 2 NIR light wavelengths (740 and 850 nm) was used in this study. The sampling frequency was set at 10 Hz. The probes were arranged symmetrically on the forehead and were spaced 3 cm apart (Fig. 2). The locations of channels, which were obtained using a 3D position-measuring system (FASTRAC; Polhemus, Colchester, VT, USA), were converted into MNI coordinates [23] and further projected onto standard brain templates using the NIRS_SPM toolbox [24,25]. The spatial registration information allowed quantification of PFC activity in the left hemisphere (CH 5, 6, 7 and 18) and the right hemisphere (CH 23, 59, 60 and 61).

The fNIRS data were pre-processed using MATLAB 2014A (The MathWorks Inc., USA) and the HomER2 processing package. The raw intensity data were converted to optical density changes. To detect and correct motion artefacts caused by head movement, a spline interpolation algorithm was applied [26]. Then, a bandpass filter between 0.01 and 0.1 Hz was used to eliminate the effects of physiological noise and low-frequency system noise [27]. Finally, the optical density was transformed into the relative concentration changes of HbO2 and HbR [28]. In this study, ΔHbO2 signals were adopted as an indicator of hemodynamic response because they are more sensitive than HbR to regional cerebral blood flow [29]. For each trial, the average concentration of HbO2 was calculated 5–20 s after the start of the task, and the baseline (10 s before the task) concentration was subtracted to evaluate the mean ΔHbO2 induced by the four tasks separately [30].

The Pearson correlation coefficient was defined as the functional connectivity between channels. Fisher Z transformation and inverse Fisher transformation were used to obtain the average correlation coefficients for all channel pairs in the PFC in the four conditions. [31].

2.3. Statistical analysis

The normality of distribution (Shapiro-Wilk test) and homoscedasticity of data (Levene’s test) were verified before the application of the parametric tests. Univariate ANOVA was used for the comparison of four tasks. Paired t-tests were used for comparison of performance of pre- and postmusic between tasks. The comparison between tests of the same task was performed by means of a mixed effect model. Multiple comparisons were carried out using Bonferroni correction. Spearman’s correlation analyses (two-tailed) were used to determine the relationship between task-related PFC activation and recent negative emotions. All statistical

Table 1
Accuracy and reaction time during Stroop tasks ($\bar{x} \pm s$).

	Stroop	The 1st test	The 2nd test	The 3rd test	P
Accuracy (%)	1	0.970 ± 0.066	0.977 ± 0.037	1.000 ± 0.000	0.166
	2	0.981 ± 0.024	0.985 ± 0.184	0.989 ± 0.030	0.543
Reaction time (ms)	1	0.629 ± 0.106[a]	0.538 ± 0.079	0.597 ± 0.074	0.011*
	2	0.627 ± 0.136[a]	0.511 ± 0.058	0.585 ± 0.027	0.004**

Note: "a" indicates a statistical difference in the pairwise comparison with the data from the second test. * $P < 0.05$, ** $P < 0.01$.

analyses were performed using SPSS 26.0 (IBM Corporation, Armonk, NY, USA). The significance level was set at $P < 0.05$.

3. Results

3.1. Dass-21

Fig. 3a shows the result of DASS-21 total scores in the three tests. The average score of subjects on the 30th, 40th and 50th days of the lockdown were 40.4 ± 4.2, 63.6 ± 4.2 and 62.0 ± 4.7 (126 points in total), respectively.

After 30 days of lockdown, 8 subjects (53.3%) were considered to be under mild or moderate stress, and only 6.7% were considered to be under severe stress or above (Fig. 3b). Most people were in the mild to moderate anxiety stage (6/40%), while another 40% felt severe or very severe anxiety (Fig. 3c). 60% had mild to moderate depression and 6.7% had severe depression and above, respectively (Fig. 3d). After 40 days of lockdown, all subjects felt stress, of which most felt mild to moderate stress (73.3%), while26.7% felt severe stress or above (Fig. 3b). All subjects felt mild to moderate anxiety or above, and most people felt severe anxiety or above (93.3%) (Fig. 3c). 60% of the people had mild to moderate depression, and the remaining 40% had more serious depression (Fig. 3d).The distribution of stress, anxiety and depression scores on the 50th day was similar to that on the 40th day.

3.2. Stroop task accuracy and reaction times

Table 1 shows the improved computerized Stroop task performance. It was found that the increase in lockdown time had no significant effect on the accuracy of the Stroop task. The reaction time of the Stroop task before (after) music stimulation in the second test was significantly shorter than that in the first test ($P = 0.010$, $P = 0.003$). A paired sample *t*-test was used to find that music stimulation did not affect the reaction time or accuracy of the Stroop task.

3.3. Cortical activation and functional connectivity of PFC

Fig. 4 shows the PFC activation in four conditions across three tests. In the first test (Fig. 5a), Stroop1 had significantly higher activation than music stimulation at CH6, 7, 59 and 60 ($P = 0.011$, $P = 0.012$, $P = 0.036$, $P = 0.031$). The changes in $\Delta HbO2$ at CH 6, 7, 59 and 61 were significantly greater during Stroop2 than music stimulation ($P = 0.041$, $P = 0.022$, $P = 0.021$, $P = 0.019$). The activation of CH18 was significantly

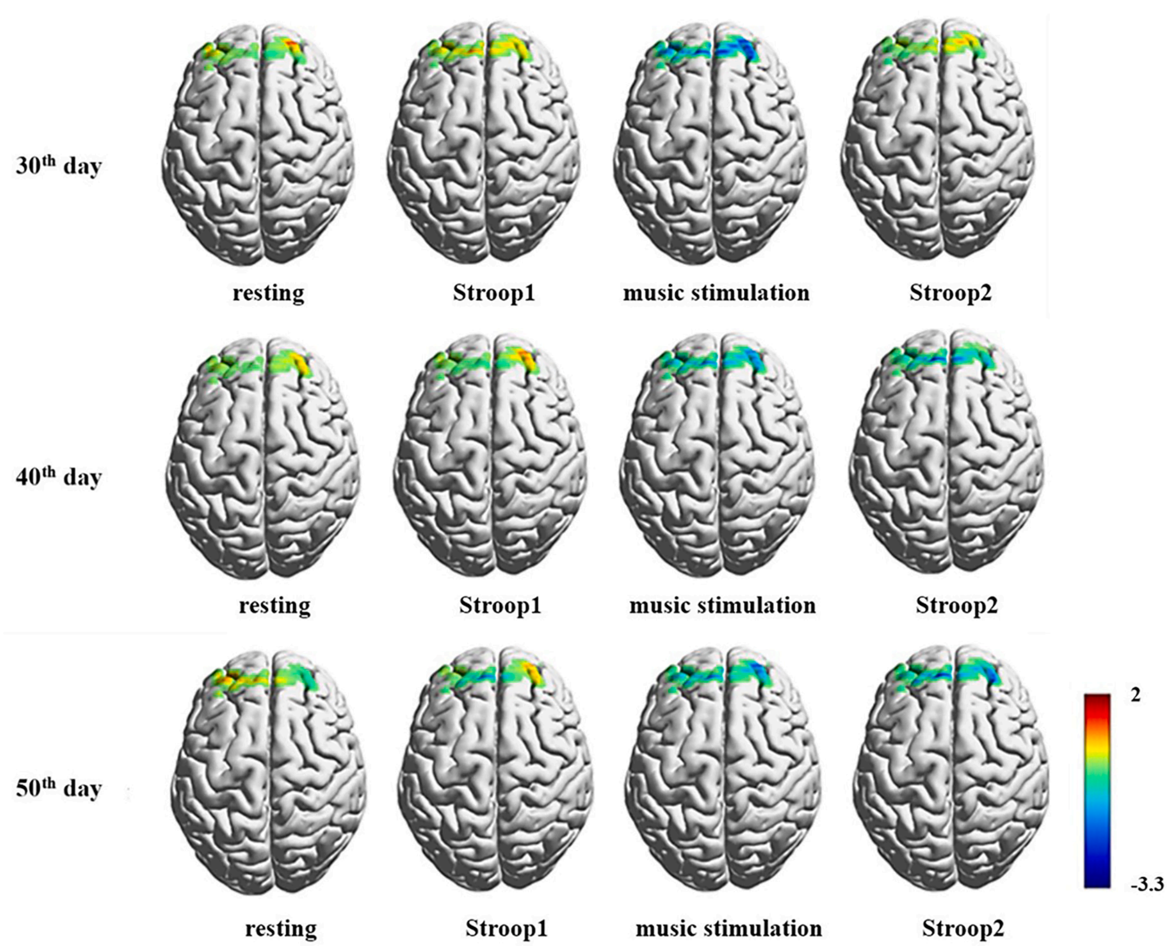

Fig. 4. PFC activation in four conditions across three tests.

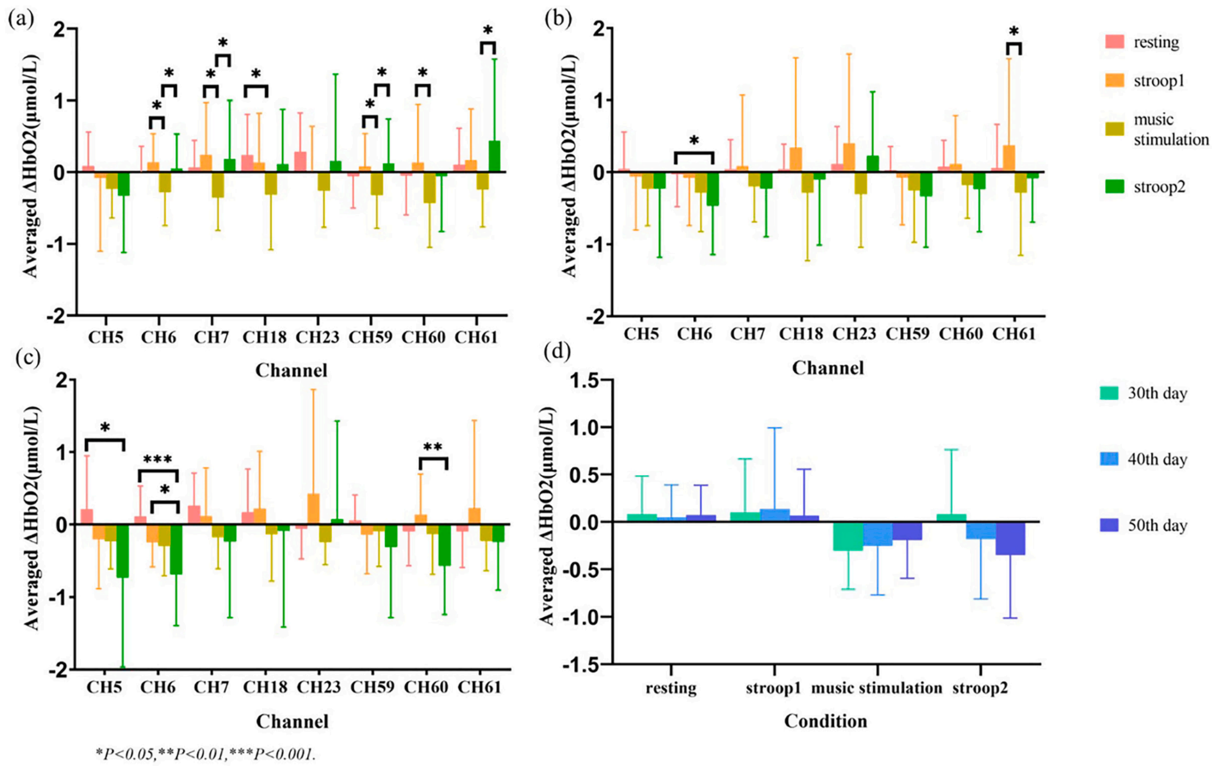

Fig. 5. Averaged ΔHbO2 concentrations of PFC between four conditions in the (a)first, (b)second and (c) third test. (d)Comparisons of PFC activation between three tests of four conditions.

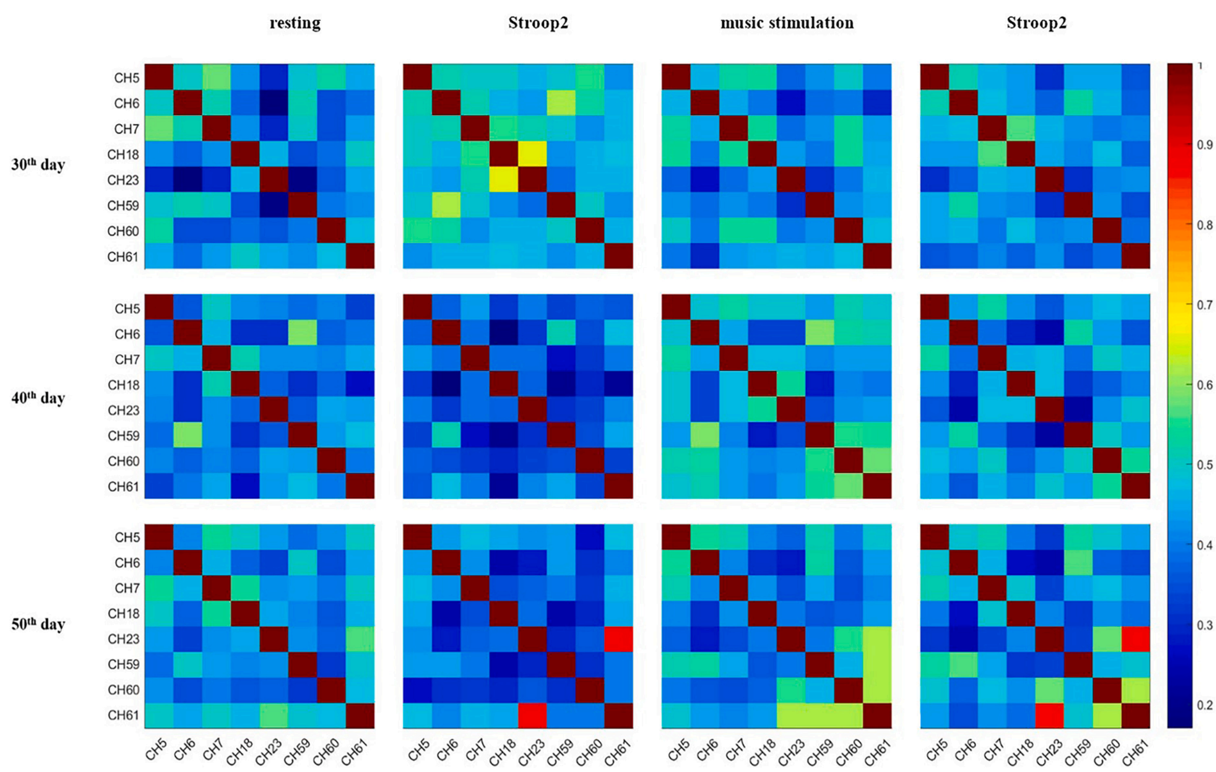

Fig. 6. Functional connection strength between channels.

greater during resting than music stimulation ($P = 0.036$). In the second test (Fig. 5b), Stroop2 had significantly greater activation than resting at CH6 ($P = 0.048$). The activation of CH61 was significantly greater during Stroop1 than music stimulation ($P = 0.04$). In the third test (Fig. 5c), the changes in ΔHbO2 at CH5 and 6 were significantly greater during resting than during Stroop2 ($P = 0.01$, $P < 0.001$). CH6 and 60 were more activated during Stroop1 than Stroop2 ($P = 0.042$, $P = 0.006$). The ΔHbO2 of other channels showed no significant difference

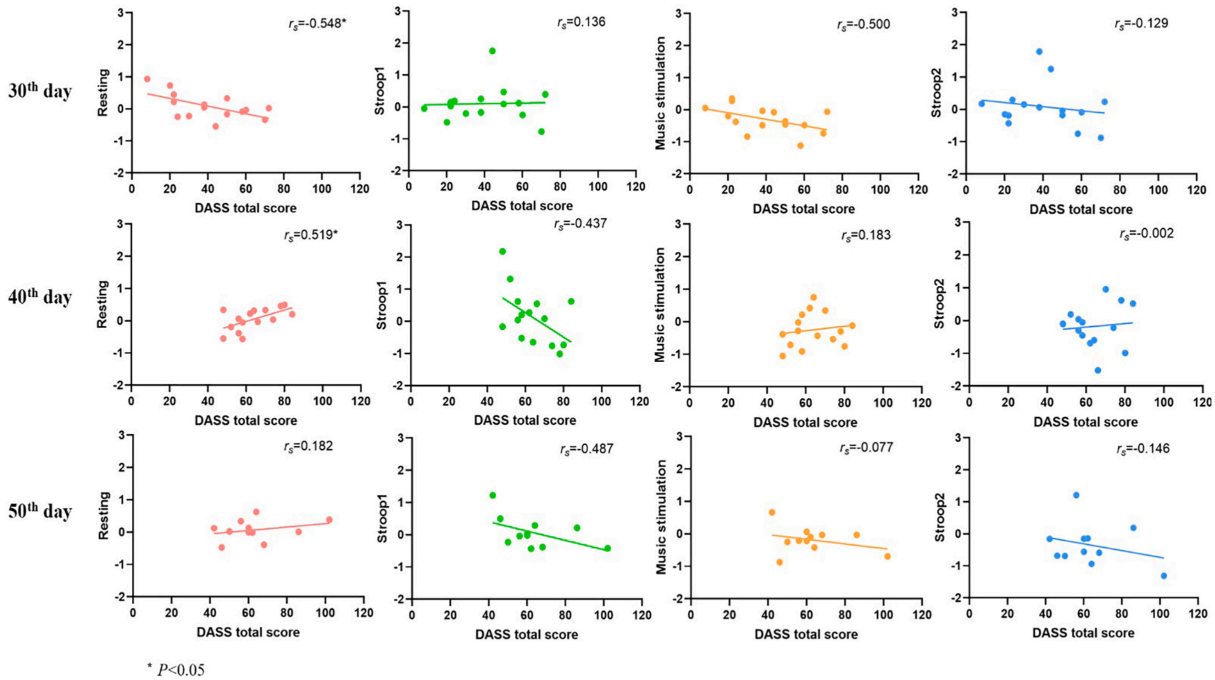

Fig. 7. Relationship between total score of DASS scale and task-related PFC activation.

between conditions. There were no significant differences in PFC activation between pairs of the 3 tests among the 4 conditions (Fig. 5d).

As shown in Fig. 6, for the Stroop1, the connection strength between the CH18 and CH6 channels was significantly stronger in the first test than in the second test ($P = 0.047$), and the connection strength between the CH18 and CH23 channels was significantly stronger in the first test than in the second and third tests ($P = 0.008$, $P = 0.020$). For the music stimulation, the channel connection strength between CH61 and CH23 in the third test was significantly stronger than that in the second test ($P = 0.036$). The channel connection strength between CH61 and CH60 in the Stroop2 task was significantly stronger than that in the first test ($P = 0.043$). There was no significant difference in connection strength between channel pairs between tasks in the same test.

3.4. Relationships between the level of recent negative mood and PFC activation

Spearman's correlation analysis was used to compare the relationship between the DASS-21 total score and the HbO2 concentration related to the four tasks in the three tests (Fig. 7). The DASS-21 total score was significantly negatively correlated with the HbO2 concentration in the resting task in the first test ($r_s = -0.548$, $P = 0.034$) and significantly positively correlated with the HbO2 concentration in the resting task in the second test ($r_s = 0.519$, $P = 0.047$). None of the other correlations were significant.

There was a significant negative correlation between depression scores and HbO2 on the Stroop1 task in the third test ($r_s = -0.645$, $P = 0.032$) (Fig. 8a). Anxiety scores were significantly negatively correlated with HbO2 of both the resting task and the musical stimulus in the first test ($r_s = -0.575$, $r_s = -0.535$, $P = 0.025$, $P = 0.040$, respectively) (Fig. 8b). In addition, stress scores were significantly negatively correlated with HbO2 of music stimulation in the first test ($r_s = -0.537$, $P = 0.039$) (Fig. 8c).

4. Discussion

This study investigated the effect of long-term containment and music stimulation on the psychological state and brain activity of young adults. The results showed that there was a negative correlation between the DASS-21 anxiety subscale score and resting-state PFC activation after 30 days of containment. Although the immediate music stimulation did not significantly affect the subjects' PFC overall, the degree of functional connectivity within the right PFC gradually increased over time during the musical stimulus and poststimulus task tests.

Groups of young adults who experienced ongoing or intermittent isolation due to the COVID-19 pandemic reported feelings of anxiety, depression and stress [20,32]. In the first evaluation on the 30th day of lockdown, this study found that anxiety was the most serious emotion reported among young people. Approximately 86.7% of young people were in a state of anxiety. Huang et al. [32] found that during an outbreak of COVID-19, young people are more likely to experience anxiety symptoms than older people, possibly because young people are more likely to be exposed to diverse online information. The amount of attention time spent on COVID-19 is also a potential risk factor for public psychological problems [32]. In addition, the scores of the DASS-21 anxiety subscale in this study were moderately negatively correlated with resting-state frontal activation. Some studies found that negative emotions led to decreased activation of the dorsolateral prefrontal cortex compared to positive emotions [33,34]. Therefore, the psychological barriers caused by lockdown, especially anxiety, may have a certain degree of prefrontal function inhibition.

PFC is not only involved in the generation and control of emotions but is also considered to be closely related to attention, cognition, and motivation [35]. According to the DASS-21 scale, there was no difference in the three emotional scores of the subjects between the 40th day and the 50th day, so there was likewise no difference in the prefrontal function activity of the resting state. The emotional scores did not fluctuate much during these 20 days. The absence of this difference may be caused by the combined effect of the inhibition of prolonged lockdown and the stimulation of instant music.

Music is an effective mood enhancer in modern medicine. In this study, there was no significant difference in activation in most channels. Studies have found that music therapy causes significant activation of PFC in healthy young people, as well as in patients with major depressive disorder, which increases parasympathetic activity, enhances positive mood, or improves cognitive function [36,37]. The main reasons

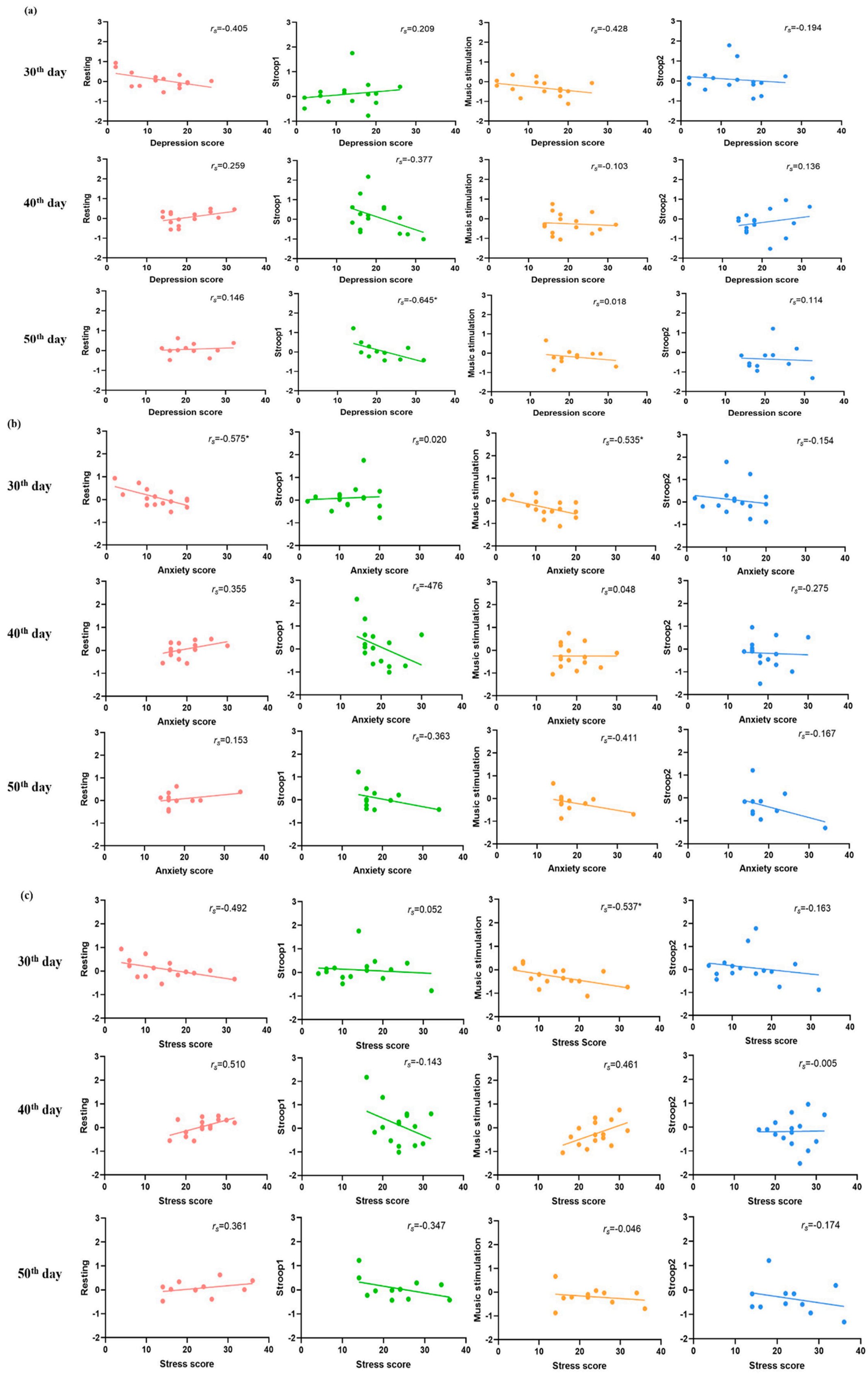

Fig. 8. Relationships between the (a) depression, (b) anxiety, and (c) stress subscale scores on the DASS-21 and PFC activation.

for this difference are the differences in music stimulation time and stimulation patterns. For example, in the study of Feng et al. [36], music stimulation was performed for 60 min per day for 10 consecutive days, while the rhythm, frequency and volume of the music changed in different segments. In addition, personal preference for music also affects the activation level of brain regions to a certain extent. Qiu et al. [37] found that the activation of PFC induced by a person's favourite music is stronger in the delta frequency band than that induced by neutral music. In this study, the music stimulus was light music, which was relatively slow and soft; however, 80% of the subjects preferred slow music with lyrics, while 20% of the subjects preferred fast music with lyrics. This inconsistency may also account for the significant negative correlation between the DASS-21 anxiety/stress scores and the degree of PFC activation in response to music stimulation in the first evaluation.

In addition, functional connectivity degree can also explain the potential mechanisms of music stimulation on the brain. There were two time-dependent trends in the brain functional connectivity patterns of the task state before and after music stimulation. First, there was a shift from the functional connectivity between bilateral PFC to the dominant functional connectivity within unilateral PFC as the evaluation time progressed. The completion time of the Stroop task was shortened between the first evaluation and the second evaluation, indicating that immediate music stimulation can promote connection efficiency between neurons in the brain. In other words, using partial neuron connections can maintain good cognitive function to reduce the cost of cooperative processing caused by the interaction between the hemispheres [37]. Second, there is a tendency to lateralize the right hemisphere, which can be explained by the inhibition theory of the corpus callosum in interhemispheric information [38]. The language mainly activates the neural network in the left hemisphere, while music and sound tend to activate the neural network in the right hemisphere [39]. Therefore, the inhibition of the corpus callosum may enhance the processing efficiency of dominant hemispheres and thus enhance hemispheric asymmetry during simple tasks [40]. In this study, the use of music without lyrics may be responsible for the increased functional connectivity between some channels in the right hemisphere.

This study also has some limitations. First, data on Day 0 of containment are missing due to the large-scale COVID-19 pandemic, the sudden release of the containment policy and the lack of rigorous experimental design. In addition, 4 participants failed to participate in the third evaluation; therefore, we applied mixed-effects models to incorporate experimental data into the analysis as much as possible. There was a potential lack of statistical power due to the small sample size; therefore, our results cannot be generalized to the entire confined population. Second, this study focused on changes in brain function in PFC associated with mood regulation, ignoring the core auditory cortex region, which may be involved in music stimulation, to analyse and encode the fundamental sonic properties of music. Therefore, this study should be considered exploratory rather than confirmatory.

5. Conclusion

After 30 days of confinement, the effects of negative emotions may suppress PFC function in the younger population. Immediate musical stimulation can improve the connection efficiency of unilateral brain regions by reducing the connection cost of bilateral brain regions and maintaining PFC function. These findings innovatively reveal changes in brain activation during lockdown, suggest a compensatory effect of short-term musical stimulation, and aim to help relevant populations detect and treat bad emotions as early as possible. It is necessary to use brain functional imaging and more physiological monitoring to further study the changes in the emotional state and brain function of different groups of people under various long-term lockdown conditions and explore the cumulative effect of different music stimulation modes on different brain regions, compared with other treatments, such as cognitive behaviour therapy (CBT) [41]. Furthermore, due to the limitations of the epidemic on offline communication, online music therapy pattern with appropriate supervision, evaluation and feedback is considered to be a valuable direction for future clinical application [42].

CRediT authorship contribution statement

Lina Luo: Methodology, Investigation, Visualization, Data curation, Formal analysis, Writing – original draft. **Mianjia Shan:** Investigation, Visualization, Formal analysis, Writing – original draft, Writing – review & editing. **Yangmin Zu:** Methodology, Visualization, Formal analysis, Writing – original draft, Writing – review & editing. **Yufang Chen:** Investigation, Visualization, Formal analysis, Writing – original draft. **Lingguo Bu:** Conceptualization, Writing – review & editing. **Lejun Wang:** Writing – review & editing. **Ming Ni:** Project administration, Writing – review & editing. **Wenxin Niu:** Conceptualization, Methodology, Resources, Writing – review & editing, Project administration, Funding acquisition, Supervision.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

Acknowledgments

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