·Original Article·

Low-frequency fluctuation in continuous real-time feedback of finger force: a new paradigm for sustained attention

Zhang-Ye Dong¹, Dong-Qiang Liu², Jue Wang², Zhao Qing¹, Zhen-Xiang Zang³, Chao-Gan Yan^{4,1}, Yu-Feng Zang^{2,1}

¹National Key Laboratory of Cognitive Neuroscience and Learning, Beijing Normal University, Beijing 100875, China

²Center for Cognition and Brain Disorders, Affiliated Hospital, Hangzhou Normal University, Hangzhou 310015, China

³Department of Mathematics, Beijing Jiaotong University, Beijing 100044, China

⁴The Nathan Kline Institute for Psychiatric Research, Orangeburg, NY 10962, USA

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Abstract: Objective Behavioral studies have suggested a low-frequency (0.05 Hz) fluctuation of sustained attention on the basis of the intra-individual variability of reaction-time. Conventional task designs for functional magnetic resonance imaging (fMRI) studies are not appropriate for frequency analysis. The present study aimed to propose a new paradigm, real-time finger force feedback (RT-FFF), to study the brain mechanisms of sustained attention and neurofeedback. Methods We compared the low-frequency fluctuations in both behavioral and fMRI data from 38 healthy adults (19 males; mean age, 22.3 years). Two fMRI sessions, in RT-FFF and sham finger force feedback (S-FFF) states, were acquired (TR 2 s, Siemens Trio 3-Tesla scanner, 8 min each, counter-balanced). Behavioral data of finger force were obtained simultaneously at a sampling rate of 250 Hz. Results Frequency analysis of the behavioral data showed lower amplitude in the lowfrequency band (0.004–0.104 Hz) but higher amplitude in the high-frequency band (27.02–125 Hz) in the RT-FFF than the S-FFF states. The mean finger force was not significantly different between the two states. fMRI data analysis showed higher fractional amplitude of low-frequency fluctuation (fALFF) in the S-FFF than in the RT-FFF state in the visual cortex, but higher fALFF in RT-FFF than S-FFF in the middle frontal gyrus, the superior frontal gyrus, and the default mode network. Conclusion The behavioral results suggest that the proposed paradigm may provide a new approach to studies of sustained attention. The fMRI results suggest that a distributed network including visual, motor, attentional, and default mode networks may be involved in sustained attention and/or real-time feedback. This paradigm may be helpful for future studies on deficits of attention, such as attention deficit hyperactivity disorder and mild traumatic brain injury.

Keywords: biofeedback; amplitude of low-frequency fluctuation; sustained attention; fMRI

1 Introduction

Biofeedback is a technique that, by using instruments

to measure parameters such as brain electrical activity, heart rate, and skin temperature, enables an individual to be aware of his/her physiological functions. Real-time biofeedback has been widely used in the treatment of disorders of attention, mood, and movement, among others^[1,2]. However, its brain mechanisms remain largely unknown, especially at the systemic level.

Corresponding author: Yu-Feng Zang

Tel: +86-571-88285650; Fax: +86-571-88285651

E-mail: zangyf@gmail.com

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Motor real-time feedback is commonly used and has been applied to the study and treatment of brain damage^[3], chronic stroke^[4,5], and Parkinson disease^[6-8]. The mechanism underlying motor feedback has been widely investigated using functional magnetic resonance imaging (fMRI); topics include force magnitude^[9], duration of maintained force^[10,11], accuracy and delay of feedback^[12], "power grip" versus "precision grip"^[13,14], and the maturation of hand power grip and force control^[15-18]. Previous studies have reported that the motor cortices (primary motor area, M1, and supplementary motor area, SMA)^[19,20], basal ganglia^[21,22], and several visual regions^[11,18,23] are involved in the process of motor feedback. All the above studies used a block design. Real-time feedback tasks usually last about 30 s, but are sometimes much longer in clinical practice or in daily life.

Sustained attention is the ability to consistently focus attention on a certain task and is a basic mental process. A deficit in sustained attention is a core symptom of some brain disorders, such as attention deficit hyperactivity disorder (ADHD)^[24-26] and mild traumatic brain injury (mTBI)^[27]. Sustained attention has been widely studied with stimulus-response paradigms. Castellanos and colleagues reported that the intra-individual variability of the reaction-time in ADHD patients differs significantly from control subjects, particularly at ~0.05 Hz (cycle length ~ 20 s), which indicated that ADHD patients are distracted 2-4 times/min^[24,26]. In order to acquire the low-frequency information, a prolonged continuous state (e.g., eventrelated design) and a fixed inter-stimulus interval (ISI) or inter-trial interval (ITI) (a constant ITI of 3 s in the study by Di Martino et al.^[26]) should be used in the experimental design. However, most fMRI studies have used random or pseudo-random ITIs to optimize the event-related fMRI design. In the block fMRI design, a scanning session has an intrinsic periodicity caused by the alternating blocks (e.g. task blocks and rest blocks presented every 24 s^[11]). Therefore, it is hard to investigate the low-frequency components of fMRI signals in most conventional fMRI designs.

Since the study by Biswal et al. in 1995^[28], resting-

state fMRI (RS-fMRI) has been widely applied in both basic and clinical studies to investigate the low-frequency (<0.1 Hz) fluctuation (LFF) of a long continuous state (e.g., 10 min). RS-fMRI takes the long state as a whole and then the frequency analysis is available. Inspired by the design of RS-fMRI, we here propose a new sustained attention paradigm named real-time finger force feedback (RT-FFF) to explore the underlying brain mechanisms. As a pilot study, we compared the low-frequency property of the RT-FFF state with that of the sham finger force feedback (S-FFF) state on both behavioral and fMRI data in a group of healthy adults.

2 Materials and methods

2.1 Participants Forty-three healthy right-handed adults $(22.7 \pm 1.6 \text{ years}, \text{ range } 19-25; 23 \text{ females})$ participated in the study. Each participant gave written informed consent. They were screened with a questionnaire to ensure no history of brain injury, neurological illness or psychiatric disorders. Data from 5 participants were excluded for further analysis due to technical problems or excessive head motion. Therefore, data from 38 subjects (mean age, 22.3 ± 1.6 years; 19 females) were further analyzed. All experiments were approved by the Ethics Committee of the National Key Laboratory of Cognitive Neuroscience and Learning, Beijing Normal University.

2.2 Experimental design Each participant underwent three fMRI sessions, resting state, RT-FFF state, and control state (S-FFF), each lasting for 8 min. The resting state was the first session, in which the participants were instructed to keep as motionless as possible, close their eyes and try to stay relaxed. This session was to allow the participants to adapt to the fMRI scanning environment. The order of RT-FFF and S-FFF sessions was counterbalanced across participants. In the RT-FFF state, the participants were asked to grip a pressure sensor between the right index finger and thumb. This sensor is one module of an MRI-compatible physiological multi-channel analyzer (model MP150, BIOPAC Systems, Inc., Goleta, CA). The sampling frequency was 250 Hz and the pressure sensitivity was 0.01 cmH₂O. The sensor recorded the

pressure in real time via an airtight tube. The pressure was synchronously presented to the participant on a projector. The target force was set at 20 cmH₂O, which is small enough to reduce the possibility of muscular fatigue^[29]. The participants were asked to continuously maintain the pinch force at 20 cmH₂O as far as possible (Fig. 1). In the S-FFF state, although the participants were also asked to maintain the pinch force at 20 cmH₂O as far as possible, the force was not presented to them. To match the visual input of S-FFF with that of RT-FFF, a video of another participant's performance during RT-FFF was presented during S-FFF, i.e., sham feedback. Participants were aware of this fact, and during S-FFF, they were told to watch the other's performance video but try to keep their own pinch force unaffected. It should be noted that the pinch forces of 3 participants (2 females and 1 male) were negative at some time points during S-FFF, probably due to leakage from the tube. Therefore, these data were excluded from analysis. No such technical problem occurred during RT-FFF. Before each pinch force procedure, the participants had a short training session.

2.3 Image acquisition MRI data were collected using a Siemens Trio 3-Tesla scanner in the Beijing Normal University Imaging Center for Brain Research. The participant lay supine with the head snugly fixed by straps and foam pads to minimize movement. After localization scanning, three

fMRI sessions were run using an echo-planar imaging sequence with the following parameters: 33 axial slices, TR = 2 000 ms, TE = 30 ms, flip angle = 90°, thickness/ gap = 3.5/0.7 mm, FOV = 200×200 mm², matrix = $64 \times$ 64, 8 min. Then a T1-weighted sagittal three-dimensional magnetization-prepared rapid gradient echo (MPRAGE) sequence was acquired (128 sagittal slices, thickness/gap = 1.33/0 mm, in-plane resolution = 256×192 , TR = 2530ms, TE = 3.39 ms, inversion time = 1100 ms, flip angle = 7° , FOV = 256×256 mm²).

2.4 Image preprocessing The preprocessing was carried out using Data Processing Assistant for Resting-State fMRI (DPARSF)^[30]. DPARSF is based on the Statistical Parametric Mapping (SPM8) (http://www.fil.ion.ucl. ac.uk/spm) and Resting-State fMRI Data Analysis Toolkit (REST) (REST 1.5^[31], http://www.restfmri.net). The preprocessing steps were: (1) removal of the first 10 time points for signal stabilization and participant adaptation; (2) slice timing correction for acquisition of time differences among slices; (3) head motion correction; (4) coregistration of functional images with 3D-T1 anatomical images; (5) spatial normalization to the standard Montreal Neurological Institute (MNI) template (re-sampled into $3 \times$ $3 \times 3 \text{ mm}^3$) via parameters of individual 3D image spatial normalization based on unified segmentation^[32]; (6) spatial smoothing with an 8-mm Gaussian kernel to minimize



Fig. 1. A sample period of the behavioral time-course. Upper-right insert: the finger pinch force sensor. Participants were asked to continuously maintain the pinch force at 20 cmH₂O (red curve) as accurately as possible.

individual variance and enhance the signal-to-noise ratio; and (7) removal of linear drift. The exclusion criterion for head motion was >2 mm translation or >2° rotation in any direction. Data from two female participants were excluded from further data analysis due to excessive head motion.

2.5 Fractional amplitude of low-frequency fluctuation (fALFF) calculation Previous reports have demonstrated the physiological significance of fALFF (0.01-0.08 Hz)^[33] in RS-fMRI studies^[34-38]. Thus, we applied fALFF to investigate the low-frequency properties of brain activity during the RT-FFF and S-FFF states. The individual fALFF map was calculated by REST 1.5 software^[31] (http://www.restfmri. net). The time-series for each voxel was converted to the frequency domain by fast Fourier transformation. The amplitude spectrum (square-root of power spectrum) for each voxel was obtained. The sum of amplitudes across 0.01-0.08 Hz was divided by that across the entire frequency range (0–0.25 Hz)^[33]. The individual fALFF map (0.01–0.08 Hz) was further divided by the global mean value to reduce the potential variability of global effects across participants^[39]. Paired *t*-tests were performed to compare the fALFF difference between the two states. Voxels with P < 0.01 and cluster size >1 998 mm³ (74 voxels) were considered significantly different, corresponding to a corrected P value of <0.05 as determined by AlphaSim (http://afni.nih.gov/afni/docpdf/AlphaSim.pdf).

2.6 Behavioral data analysis To detect the general behavioral differences between the RT-FFF and S-FFF states, the mean and standard deviation of individual pinch force were calculated for each state. Then paired *t*-tests on the mean and standard deviation were performed between the two states. For the behavioral data, we were also interested in the low-frequency fluctuation. However, it is unknown which specific frequency band would show an amplitude difference between the two states. Therefore, we performed an exploratory analysis. The time-courses of behavioral data were transformed to power spectra by fast Fourier transformation. The square-root of the power spectrum was calculated at each frequency to obtain an amplitude spectrum. We calculated the amplitude ratio at each frequency

point to the total amplitude of all frequencies (0-125 Hz), here called fractional amplitude of fluctuation (fAF). Then paired *t*-tests were performed on the fAF at each frequency between the two states. To reduce false-positive errors due to multiple comparisons, a frequency band containing at least 15 consecutive frequency points, each at P < 0.001, was considered to reflect a "true" difference between the states. With these criteria, the fAFs of two frequency bands showed a significant difference (Fig. 2). In the lowfrequency band (0.004-0.104 Hz), S-FFF showed a higher fAF than RT-FFF; but in the high-frequency band (27.02-125 Hz), the fAF of RT-FFF was significantly larger than that of S-FFF. Since the conventional fMRI signal lacks such high-frequency characteristics and we were more interested in the low-frequency behavioral data, this highfrequency band in the behavioral data was not analyzed further.

2.7 Correlation analysis In each of the clusters showing significant differences between the two states, a spherical region of interest (ROI) was defined (radius 6 mm, centered at the voxel that showed the largest t value within that cluster). The average fALFF was obtained for each spherical ROI. Then linear correlations were performed between the average fALFF of each ROI and the average fAF within the low-frequency band (0.004–0.104 Hz) of the behavioral data. Correlation was performed separately for the RT-FFF and S-FFF states.

3 Results

3.1 Behavioral data The paired *t*-tests showed no significant difference in the mean pinch force between the RT-FFF and S-FFF states (P = 0.788). However, the standard deviation of S-FFF was markedly higher than that of RT-FFF ($P = 1.187 \times 10^{-14}$).

Within the 0.004–0.104 Hz band, the fAF of S-FFF was higher than that of RT-FFF (P < 0.001, Fig. 2) at each frequency, while within the 27.02–125 Hz band, the fAF of S-FFF was lower than that of RT-FFF (P < 0.001, Fig. 2) at each frequency.

3.2 fMRI data Some brain regions showed significantly lower fALFF in the RT-FFF state than in the S-FFF state:



Fig. 2. Paired *t*-tests on the fAF at each frequency between the real-time finger force feedback (RT-FFF) state and the sham-FFF state on the entire frequency band (A) and the low-frequency band (0.004–0.104 Hz) (B). P = 0.001 represents the corresponding $t = \pm 3.57$ (degrees of freedom = 37).

right precentral gyrus (ipsilateral M1), right precuneus (PCu), bilateral cerebellum, and several visual regions in the occipital lobe. Regions that showed significantly higher fALFF in RT-FFF than S-FFF were: bilateral inferior temporal gyrus (ITG), bilateral middle temporal gyrus (MTG), vermis, left angular gyrus (AG), bilateral superior frontal gyrus (SFG), posterior cingulate cortex (PCC), medial cingulate cortex (MPC), and medial prefrontal cortex (MPFC) (Fig. 3 and Table 1).

3.3 Correlation analysis Pearson correlation coefficients between behavioral fAF (0.004–0.104 Hz) and fMRI fALFF (0.01–0.08 Hz) are listed in Table 2. Of the 24 coefficients, only one was significant (r = -0.388, P = 0.016, between the fALFF of the right precentral gyrus and the fAF in the RT-FFF state) (Fig. 4). It should be noted that

this correlation may be a false-positive because it did not survive the correction for multiple comparisons (1/24).

4 Discussion

4.1 Behavioral data The behavioral data are consistent with our hypothesis. We found a significantly higher amplitude of fluctuation in the low-frequency band (0.004–0.104 Hz) in the S-FFF state than in the RT-FFF state. However, the RT-FFF state showed a higher amplitude of fluctuation in the high-frequency band (27.02–125 Hz). While the reaction-time is the most common measure of behavioral performance, its mean value rather than its standard deviation has been used in most studies. However, an increased standard deviation or intra-individual variability "might represent a ubiquitous and etiologically important



Fig. 3. Results of paired *t*-tests on the fALFF between the real-time finger force feedback (RT-FFF) state and the sham-FFF (S-FFF) state. R and L: right and left in the brain. Cooler colors indicate fALFF (RT-FFF) < fALFF (S-FFF) and warmer colors indicate fALFF (RT-FFF) > fALFF (S-FFF).



Fig. 4. Pearson correlation between the fALFF (0.01–0.08 Hz) of the right precentral gyrus and the fAF (0.004–0.104 Hz) in the real-time finger force feedback (RT-FFF) state.

characteristic^{*,[40]}. Frequency analysis of the reaction-time revealed that the low-frequency band (<0.1 Hz) makes a major contribution to the intra-individual variability difference between ADHD and controls in an Eriksen Flanker

task^[24,26]. While these studies contribute substantially to our understanding of the pathophysiology of ADHD, a fixed ITI (3 s in Di Martino et al.) is seldom used in eventrelated fMRI studies. To reduce the prediction effect of the subjects and to optimize the event-related fMRI design for data analysis, the ITI is usually pseudo-randomized. But such a design is not appropriate for frequency analysis, and the condition is worse when a subject makes errors. The current study used a continuous finger-pressing task. We used two conditions to compare the differences in the amplitude of every frequency and found that the amplitude of low-frequency fluctuations was significantly larger in the non-feedback condition than in the real-time feedback condition. Interestingly, the frequency band is very similar to that showing a significant difference between ADHD and controls in the Eriksen Flanker task^[24,26]. This may

Brain region*	Brodmann area	Coordinate (x, y, z)	Volume (mm ³)	Peak t value
RT-FFF > S-FFF				
Fusiform_L	20	-21, -3, -51	2052	4.8714
Temporal Lobe	20	-60, -27, -30	2511	4.2263
Temporal_Inf_L	20	-54, -3, -27	2295	5.3693
Temporal_Inf_R	21	66, -24, -24	2376	4.4185
Vermis_3		3, -45, -18	2808	4.3880
Frontal_Sup_Orb_L	10	-15, 51, -9	6480	5.6143
Angular_L	39	-48, -63, 24	6912	4.8794
Cingulate Gyrus	31	15, -33, 30	18549	5.3202
Frontal_Sup_L	8	-12, 33, 42	3213	4.5306
Frontal_Sup_Medial_R	9	9, 42, 51	3294	4.5229
RT-FFF < S-FFF				
Lingual_L	18	-24, -57, -9	147123	-8.2750
Precentral_R	6	57, 6, 45	2754	-4.8885
Precuneus_R	7	3, -72, 57	5264	-5.6180

Table 1. Results of paired t-tests on the fALFF between the real-time finger force feedback (RT-FFF) state and the sham-FFF (S-FFF) state

*The names of brain regions are from the automated anatomical labeling (AAL) template^[46]. Inf, inferior; L, left; R, right; Sup, superior. Brain region, coordinates, volume and peak *t* value were reported by SPM8 (http://www.fil.ion.ucl.ac.uk/spm).

Table 2. Pearson	correlations between	behavioral fAF and fMI	RI fALFF in brain re	egions showing significant	fALFF differences b	etween the two
states						

Brain region*	Coordinate (x, y, z)	R	RT-FFF		S-FFF	
		r	P value	r	P value	
Fusiform_L	-21, -3, -51	0.068	0.685	-0.303	0.064	
Temporal Lobe	-60, -27, -30	-0.056	0.738	0.229	0.167	
Temporal_Inf_R	66, -24, -24	0.169	0.311	0.034	0.841	
Temporal_Inf_L	-54, -3, -27	0.08	0.632	0.05	0.765	
Vermis_3	3, -45, -18	0.131	0.432	-0.215	0.195	
Lingual_L	-24, -57, -9	-0.159	0.341	-0.073	0.665	
Frontal_Sup_Orb_L	-15, 51, -9	-0.046	0.784	-0.109	0.514	
Angular_L	-48, -63, 24	-0.218	0.188	0.202	0.224	
Cingulate Gyrus	15, -33, 30	0.104	0.534	-0.169	0.309	
Frontal_Sup_L	-12, 33, 42	-0.1	0.549	0.125	0.455	
Precentral_R	57, 6, 45	-0.388	0.016**	-0.167	0.316	
Frontal_Sup_Medial_R	9, 42, 51	0.215	0.194	-0.009	0.956	
Precuneus_R	3, -72, 57	0.151	0.364	-0.239	0.956	

r, Pearson correlation coefficient. *Names of regions from the automated anatomical labeling (AAL) template^[46]. Inf, inferior; L, left; R, right; Sup, superior. **P <0.05.



Fig. 5. Results of paired t-tests on the fALFF between the real-time finger force feedback (RT-FFF) state and the resting state. R and L: right and left.in the brain. Cooler colors indicate fALFF (RT-FFF) < fALFF (resting state) and warmer colors indicate fALFF (RT-FFF) > fALFF (resting state).

also suggest that, during a continuous performance task, the attention fluctuates at a low frequency of <0.1 Hz. In addition, the amplitude of high frequencies (>27 Hz) was significantly higher in the RT-FFF state than in the S-FFF state. This frequency band falls into the gamma frequency of electrophysiological recording. However, the relationship between the frequency of behavioral performance and the frequency of electrophysiological signals needs to be further investigated. The current study was performed in healthy adults. Future study is warranted to test whether the current paradigm is a sensitive procedure for studying attention deficits such as ADHD or mTBI.

4.2 fMRI data In RS-fMRI studies, the low frequency (<0.1 Hz) has been almost the only focus^[28]. The resting-state LFF is almost ubiquitous in the brain, with the highest

fALFF in the default mode network^[33]. This measure has been used to study various brain disorders. For example, decreased fALFF was reported in the PCC in early Alzheimer disease^[37]. In the current study, we compared the fALFF between two continuous task states: RT-FFF *versus* S-FFF. We found higher fALFF in RT-FFF than in S-FFF in the MFG and SFG [(Brodmann areas (BAs) 8, 9, 10], and the default mode network (PCC, PCu, MPFC, and left AG), but lower fALFF in the visual cortex (BAs 17, 18, 19) and ipsilateral precentral gyrus (BA 6).

One possible explanation for the higher fALFF in the visual cortex during RT-FFF is that the participants had to continuously update the visual information. Hence, the low-frequency fluctuation might have been down-regulated and high-frequency activity may be stronger, a phenom-



Fig. 6. Results of paired *t*-tests on the fALFF between the sham finger force feedback (S-FFF) state and the resting state. R and L: right and left in the brain. Cooler colors indicate fALFF (S-FFF) < fALFF (resting state) and warmer colors indicate fALFF (S-FFF) > fALFF (resting state).

enon reported in electrophysiological studies^[41]. However, the current fMRI sampling rate was too low (TR = 2 s) to reveal high-frequency fMRI signal changes.

The DMN includes the PCC, PCu, MPFC, bilateral inferior parietal lobule (IPL, including the angular and supramarginal gyri), as well as the hippocampus^[42,43]. The DMN has been consistently reported to be actively engaged in intrinsic thoughts during rest and to show task-independent or task-nonspecific deactivation during externally goaldirected tasks^[42]. A previous block-designed fMRI study found less activity during the feedback grip force condition than the non-feedback condition^[18]. An RS-fMRI study has shown reliably higher fALFF in the DMN of both children and adults^[33]. In the current study, the RT-FFF state seemed to require more sustained attention than the S-FFF state, so we expected a lower fALFF in the DMN in RT-FFF than in S-FFF. However, contrary to our expectation, RT-FFF showed significantly higher fALFF than S-FFF in the PCC, PCu, MPFC, and left AG. It should be noted that the design of the current study is quite different from the previous motor feedback fMRI study^[18]. First, the grip force in that study was 20%–75% of maximum voluntary hand contraction, but the finger force in the current study was very small (only 20 cmH₂O). Second, the task in that study was performed trial-by-trial, but the task in the current study was performed continuously. However, it is unknown to what extent these differences in design account for the discrepancies in the results between the two studies.

In the current study, we found an fALFF difference in only one area, the ipsilateral motor cortex. Conventional block-designed fMRI studies have reported differences in activation in the contralateral M1, SMA, basal ganglia, and cerebellum during various motor feedback tasks^[9-12]. The mean finger force over time in the current study was not significantly different between RT-FFF and S-FFF. This might be one reason for the reduced difference of fALFF in motor areas. The low sampling rate (TR = 2 s) of the fMRI data was not appropriate for high-frequency analysis. Future studies with fast sampling (e.g., TR = 300 ms) are warranted to investigate the higher frequency changes during real-time feedback states.

4.3 Limitations and future directions As a pilot study on the amplitude of the BOLD signal during real-time feedback, a few concerns do exist. First, the pinch force of 3 participants showed negative values at some time points during S-FFF, probably due to leakage from the tube. Technical improvements are therefore needed in future studies. Second, although in this study we tried to link the behavioral results on low-frequency fluctuation to sustained attention, whether the new paradigm can provide a sensitive measure of attention deficit (e.g., in ADHD and mTBI) is unknown. Third, despite the significant differences of fALFF in some brain areas, their physiological implications are still far from clear. In addition, some results, especially in the DMN, are contrary to our predictions. To compare the fALFF of either RT-FFF or S-FFF with that of the resting state, we further analyzed the resting state data. Paired *t*-tests showed that RT-FFF had higher fALFF than the resting state in the PCC, bilateral IPL, and MPFC (Fig. 5), while S-FFF showed almost no significant difference from the resting state in fALFF in the PCC, IPL, and MPFC (Fig. 6). The PCu is also a core node of the DMN, and its results seem to be more interesting. RT-FFF showed a more significant decrease in fALFF than S-FFF compared with the resting state (Figs. 3, 5 and 6), suggesting that the role of the PCu might be suppressed during the task, especially during real-time feedback when more attention is needed. In the visual cortex, both RT-FFF and S-FFF showed higher fALFF than the resting state. It should be noted that these results cannot exclude a possible confounding order effect. We ran the resting state

before the two task states for every participant because we did not expect to compare it with task states. Indeed, a counter-balanced order should be used in future studies to compare the real-time feedback with the resting state. Other experimental parameters could be modulated, e.g., fast versus slow real-time feedback, visual versus auditory real-time feedback, and block (every 30 s) design versus continuous performance state design (e.g., 8 min). These will help understand the brain mechanisms of real-time feedback as well as sustained attention. Fourth, the current sampling rate of fMRI scanning was low (TR, 2 s; 0.5 Hz) and was not appropriate for the analysis of high-frequency signals. Previous RS-fMRI studies have suggested that high-frequency (>0.1 Hz) fMRI signals are correlated with cardiovascular or respiratory noise^[44,45]. Few studies have paid attention to the physiological meaning of such signals. The frequency of electrophysiological signals ranges from very low (<1 Hz) to very high (>100 Hz). It is possible that the electrophysiological signal in a certain frequency band correlates with the high-frequency fMRI signal. A shorter TR (e.g., 0.3 s) is available for most 3T scanners but can cover only a few slices. The current pilot study provided preliminary information of spatial localization for future studies if a shorter TR is used. Fifth, it has been shown that head motion can drive a loss of distant connectivity and an increase of local connectivity when comparing aging and control populations^[47]. In functional connectivity analysis, the method of removing head motion time-courses is straightforward. However, removing their effect on the fALFF is complex. Therefore we did not regress out the head motion covariates in the current study. Future studies are needed to investigate which parameters of head motion have a significant effect on fALFF.

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