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Alterations in resting functional connectivity due to recent motor task

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ABSTRACT

The impact of recent experiences of task performance on resting functional connectivity MRI (fcMRI) has important implications for the design of many neuroimaging studies, because, if an effect is present, the fcMRI scan then must be performed before any evoked fMRI or after a time gap to allow it to dissipate. The present study aims to determine the effect of simple button presses, which are used in many cognitive fMRI tasks as a response recording method, on later acquired fcMRI data. Human volunteers were subject to a 23-minute button press motor task. Their resting-state brain activity before and after the task was assessed with fcMRI. It was found that, compared to the pre-task resting period, the post-task resting fcMRI revealed a significantly higher ($p = 0.002$, $N = 24$) cross correlation coefficient (CC) between left and right motor cortices. These changes were not present in sham control studies that matched the paradigm timing but had no actual task. The amplitude of fcMRI signal fluctuation (AF) also demonstrated an increase in the post-task period compared to pre-task. These changes were observed using both the right-hand-only task and the two-hand task. Study of the recovery time course of these effects revealed that the CC changes lasted for about 5 min while the AF change lasted for at least 15 min. Finally, voxelwise analysis revealed that the pre/post-task differences were also observed in several other brain regions, including the auditory cortex, visual areas, and the thalamus. Our data suggest that the recent performance of the simple button press task can result in elevated fcMRI CC and AF in relevant brain networks and that fcMRI scan should be performed either before evoked fMRI or after a sufficient time gap following fMRI.

Introduction

Resting state functional connectivity MRI (fcMRI) is now widely used in investigations of brain networks (Biswal et al., 1995; He et al., 2009; Raichle et al., 2001; Wig et al., 2011), neurological diseases such as Alzheimer's disease (Greicius et al., 2004; Wang et al., 2006, 2007), traumatic brain injury (Mayer et al., 2011; Nakamura et al., 2009; Stevens et al., 2012; Tang et al., 2011), multiple sclerosis (De Luca et al., 2005; Lowe et al., 2002), and psychiatric disorders such as schizophrenia (Bluhm et al., 2007; Liang et al., 2006; Liu et al., 2006; Salvador et al., 2007; Zhou et al., 2007), as well as in cognitive aging (Andrews-Hanna et al., 2007; Damoiseaux et al., 2008; Tomasi and Volkow, 2012). In many studies, fcMRI data are collected in the same scan session as evoked fMRI. However, it is not yet clear whether the results of fcMRI could be affected by task fMRI runs that were performed earlier in the same session.

There is some evidence in the literature that the recent experience of task performance could alter fcMRI data collected later. For example, Waites et al. provided early evidence in a sample of six subjects that performance of a five-minute language task resulted in an increased connectivity in fcMRI data acquired immediately before and after the task (5 min each), in particular in language regions such as the left middle frontal gyrus (Waites et al., 2005). Stevens and colleagues showed that resting connectivity can be affected by the context of the task performed during the preceding fMRI runs. Specifically, connectivity in face visual regions (from a 9-minute fcMRI data) following a 15-min face classification task was significantly greater than that after a scene classification task (Stevens et al., 2010). Tambini et al. showed that connectivity (from 8-minute fcMRI data) between the lateral occipital lobe and the fusiform face area was enhanced following a 21-minute object–face associative encoding task, but not after a scene–face associative encoding task of identical duration (Tambini et al., 2010). The investigators also found that the former task corresponded to a better associative memory (from a surprise memory test after the scanning session); thus it was proposed that the enhanced post-task resting activity was related to memory consolidation (Tambini et al., 2010). Modulations of fcMRI results by

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physiologic states or other cognitive tasks have also been reported (Albert et al., 2009; Barnes et al., 2009; Fukunaga et al., 2008; Lewis et al., 2009).

The influence of motor task on resting fcMRI data has also been reported. Peltier and colleagues have shown that, after a 20-minute fatiguing right handgrip motor task (120 contracts at 50% maximal grip force), interhemispheric correlation of the motor cortex in the fcMRI data (3 min and 20 s) decreased significantly (Peltier et al., 2005). Klingner et al. reported that resting connectivity (from 5-minute fcMRI data) between the primary somatosensory and the motor cortex was enhanced bilaterally following a 32-minute, right-side-only median nerve stimulation, with connectivity decreases in the thalamus and higher order somatosensory areas (Klingner et al., in press). Albert et al. noted that independent-component-analysis (ICA) based connection strength (from 11-minute fcMRI data) increased following an 11-minute left-hand joystick target tracking task, which was attributed to neural plasticity associated with motor learning (Albert et al., 2009).

However, it is not yet clear whether simpler motor tasks such as button presses could also alter an fcMRI network. We note that button presses are employed in virtually all fMRI studies as a means to obtain subject response, thus a significant effect of button presses on later fcMRI data would indicate that an fcMRI scan should ideally be performed before fMRI scans in a future study design.

In this study, we compared fcMRI data acquired before and after a 23-minute button press task (right-hand only). Sham control experiments were performed to ensure that the changes detected were not due to the subject becoming drowsy or sleepy after being inside the scanner for a while. The results were further verified by additional studies on a new cohort with a two-hand button press task. Moreover, in this cohort, three post-task fcMRI runs were performed to assess how long it takes for the fcMRI changes to dissipate. Voxelwise comparison was conducted in the entire brain to examine whether brain areas other than a priori regions-of-interest (ROI) (i.e. the motor cortex) showed these changes.

Materials and methods

General

The protocol was approved by University of Texas Southwestern Medical Center's Institutional Review Board and informed written consent was obtained from each participant. Healthy right-handed adults were recruited through flyers posted on the university campus. The subjects were divided into three substudies: a one-hand experiment, a sham experiment, and a two-hand experiment. There were no group differences in terms of age ($p = 0.35$, one-way ANOVA) or gender ($p = 0.64$). MR imaging was conducted using a 3 T system (Philips, Best, The Netherlands). FcMRI and fMRI scans used identical imaging parameters: blood-oxygenation-level-dependent (BOLD) sequence, single-shot gradient-echo EPI, TR = 1000 ms, TE = 25 ms, field-of-view (FOV) 220 × 220 mm^2, matrix size 64 × 64, slice thickness 5 mm, voxel size 3.4 × 3.4 × 5 mm^3, 21 axial slices. Ten image volumes were discarded at the beginning of every run to allow the magnetization to reach a steady state.

One-hand motor experiment

Twenty-four subjects (25 ± 14 y.o., 13 males) were recruited. The scan session lasted approximately 33 min (Figs. 1A and B) and included a five-minute pre-task fcMRI run, a 23-minute motor task, and a five-minute post-task fcMRI run. The fcMRI runs were performed while the subject fixated on a white crosshair and was instructed to think of nothing in particular. During the motor task period, the subject performed button presses using their right hand. Specifically, they fixated on a white crosshair and, when the crosshair occasionally changed color to gray for 1000 ms, they pressed a button in their right hand three times with their thumb. The response time (RT) was recorded using the E-Prime software (Version 2.0, Psychology Software Tools, Inc., Sharpsburg, PA). Only the first press (out of the three presses) of the right-hand was recorded for quantitative analysis. The color change occurred every 27–32 s with randomized intervals and there were a total of 40 trials during the motor task period.

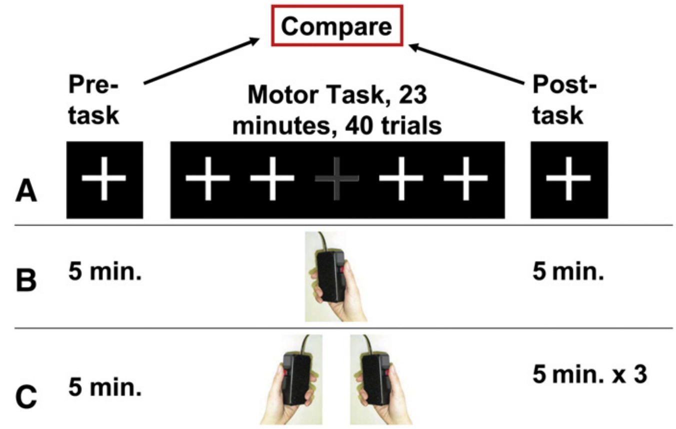

Fig. 1. Experimental design. (A) The experiment started with a pre-task fcMRI, followed by a motor task in which the subject attended to a white crosshair and pressed a button when the color of the crosshair changed to gray for 1000 ms. The session concluded with a post-task fcMRI. (B) In the one-hand motor experiment (N = 24), the post-task fcMRI was five 5 min in duration. (C) In the two-hand motor experiment (N = 24), the post-task fcMRI was 15 min in duration.

Sham experiment

Ten healthy right-handed subjects (28 ± 7 y.o., 6 males) underwent a 35-minute scan session consisting of seven fcMRI runs of 5 min each. During the scan session, the subject fixated on a white crosshair and held a button box in their right hand, thereby matching the condition of the fcMRI runs during the real experiment. No button presses took place in the sham experiment. FcMRI imaging parameters were identical to those used in the real experiment.

Two-hand motor experiment

Twenty-four healthy right-handed subjects (30 ± 10 y.o., 9 male) were recruited for the two-hand button press experiment. The experimental procedure was identical to that of the one-hand experiment with two exceptions (Fig. 1C). First, the subject held one button box in each hand and was instructed to press both button boxes simultaneously three times. Second, we performed three post-task fcMRI runs (5 min each) in these subjects, which allowed us to examine how long the changes may last.

Data preprocessing

The data were analyzed using the software AFNI (National Institutes of Health, Bethesda, MD). All image volumes were coregistered to the first volume of the first fcMRI run. Physiologic fluctuations in the signal time course were removed by regressing out time courses of the whole brain white matter, cerebral spinal fluid, and six motion vectors (Chang and Glover, 2009; He and Liu, 2012). The time series were then bandpass-filtered to 0.01–0.1 Hz using the AFNI command 3dBandpass, which is the bandwidth commonly used in fcMRI processing (Cordes et al., 2000; Damoiseaux et al., 2006). To further identify the bandwidth in which the changes are most pronounced, we further bandpass-filtered the time series to 0.01–0.05 Hz for a lower band, and from 0.05 to 0.1 Hz for a higher band (Baria et al., 2011).