# Interhemispheric functional connectivity of primary motor cortex is reduced during continuous performance of an unilateral hand task

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## Introduction

In the resting state brain, low frequency BOLD oscillations are synchronized between functionally related areas [1]. Several functional connectivity MRI (fcMRI) studies have demonstrated that these correlations are modified during steady-state performance of a task that activates the respective network (e.g. [2]). In the work presented here, we investigated the variability and reproducibility both of the functional connectivity itself in two different cognitive states and of the different statistical analysis methods proposed in literature. Therefore, we repeatedly examined the same two subjects over half a year by acquiring fcMRI data sets both in resting state and during continuous performance of a unilateral motor task.

## Methods

Two healthy volunteers (both male, right handed, 39y) were scanned in ten sessions at intervals of a minimum of one week. All measurements were done on a 3.0 T head scanner (Magnetom Allegra, Siemens Medical, Erlangen, Germany). In each session, an fMRI experiment and two different fcMRI runs (resting state/continuous performance) were carried out. In all functional experiments, series of T2*w EPI (TR/TE/$\alpha$ = 2s/30ms/90°) images parallel to the inferior borders of the corpus callosum were scanned with an identical spatial resolution of 3.5x3.5x4 $mm^3$. The primary motor areas (M1) were detected by a block-design fMRI paradigm. In the active periods, the subjects were advised to move their right hand with a frequency of roughly 1 Hz; the range of motion was guided by a wooden frame. In the fcMRI experiments, 1100 volumes of three slices covering M1 were scanned (TR/TE/$\alpha$ = 0.25s/30ms/30°). In the resting state scan, subjects were instructed to close their eyes and stay still. During the performance scan the subjects also closed their eyes and moved their right hand continuously in the same matter as in the fMRI run. The order of the two fcMRI experiments was altered randomly in the ten sessions to prevent systematic effects of tiredness. Additionally, one T2w data set was acquired in each session. FMRI and fcMRI data evaluation was performed using AFNI [3]. The analysis included slice timing and motion correction, spatial smoothing, intensity normalization and realignment to a common space defined by the mid volume of the individual anatomical data sets. Individual fMRI group analysis was applied performing a t-test over all ten sessions. Based on the results of the individual fMRI analysis, the 27 most significant activated voxels in left M1 for each subject were determined. This activation defined ROI was then transferred to the fcMRI data sets. The fcMRI data sets were low-pass filtered in time (cut-off frequency 0.08 Hz) and a correlation analysis was performed to the average signal time course of left M1. In the correlation analysis, the whole brain signal time course was treated as regressor of no interest. The resulting correlation maps were then transformed to z-scores of the standard normal distribution [4]. Connectivity strength between left and right M1 was calculated by determining the mean and maximum z-score in a grey matter defined ROI in right M1. Also, the fraction of significant correlated voxels (FCV) was calculated in right M1 ($p<0.05$). To evaluate differences between resting state and continuous performance condition, paired t-tests were performed for the mean and maximum z-scores and Wilcoxon signed ranks tests for matched pairs were carried out for FCV. To address the question if mean z-scores and FCV are independent measures, we performed a linear regression of both parameters. Additionally, a voxel based multi-session statistical analysis was carried out for each subject. With the z-score maps of the 10 sessions, a paired t-test was performed to find differences between the two groups of fcMRI runs.

## Results

The difference t-maps between both states are shown in Fig. 1. Significant more correlations for the resting state were found in contralateral M1 for both subjects. Also, more correlations in resting state were found in right superior parietal and in the lateral aspects of left M1. ROI analysis revealed significant higher mean z-scores, maximum z-scores and FCV in resting state compared to continuous performance for both subjects (Tab. 1 and Tab. 2). Over all fcMRI runs, the linear regression of FCV to mean z-scores revealed high correlation of the two variables (subject 1: $r = 0.914$, $p<2*10^{-8}$, subject 2: $r = 0.856$, $p<2*10^{-6}$), indicating that changes in overall functional connectivity are mainly caused by the number of correlated voxels.

## Discussion

In our study, we were able to demonstrate a distinct loss in left-right M1 synchrony in two individuals performing continuously a unilateral motor task. This effect was reproducible over half a year with all statistical methods and all measures of connectivity under investigation. We therefore conclude that the functional connectivity of human brain is modulated by different brain activities. Despite intra- and inter-individual variability, group analysis of functional connectivity reveals stable and reliable results.

## References

[1] Biswal B et al., Magn. Reson. Med. 34: 537-541; 1995.
[2] Newton AT et al., Hum. Brain Map. 28: 663-672, 2007.
[3] Cox RW, Comput. Biomed. Res. 29:162-173; 1996.
[4] Lowe MJ et al., NeuroImage 7:119-132; 1998.

| Session | Mean Z | | Maximum Z | | Mean Z | | Maximum Z | |
|---|---|---|---|---|---|---|---|---|
| | RS | CP | RS | CP | RS | CP | RS | CP |
| 1 | 1.003 | 0.206 | 4.699 | 3.053 | 0.777 | 0.605 | 3.470 | 2.792 |
| 2 | 0.921 | 0.174 | 4.021 | 2.340 | 1.001 | 0.559 | 4.784 | 2.456 |
| 3 | 0.838 | 0.007 | 4.097 | 2.510 | 1.031 | 0.406 | 3.495 | 2.171 |
| 4 | 0.974 | 0.480 | 3.885 | 2.899 | 0.776 | 0.461 | 3.657 | 2.356 |
| 5 | 0.787 | 0.564 | 3.564 | 2.642 | 0.733 | 0.216 | 3.266 | 3.229 |
| 6 | 0.918 | 0.232 | 4.447 | 2.646 | 1.367 | 0.327 | 4.163 | 2.092 |
| 7 | 0.259 | 0.295 | 2.739 | 2.844 | 0.841 | 0.085 | 3.214 | 2.939 |
| 8 | 0.657 | 0.173 | 2.992 | 2.513 | 1.068 | 0.035 | 3.637 | 2.488 |
| 9 | 0.594 | 0.364 | 3.021 | 2.957 | 0.932 | 0.306 | 3.298 | 2.893 |
| 10 | 0.803 | 0.519 | 3.850 | 2.567 | 0.321 | -0.462 | 2.508 | 2.071 |
| | | | | | | | | |
| **mean** | **0.775** | **0.301** | **3.731** | **2.697** | **0.885** | **0.254** | **3.549** | **2.549** |
| **STD** | **0.224** | **0.178** | **0.647** | **0.230** | **0.273** | **0.313** | **0.603** | **0.397** |
| **p-Value** | **6.2E-04** | | **0.001** | | **6.2E-05** | | **0.003** | |

**Tab.1:** Mean and maximum z-scores in right M1 indicating correlation strength to left M1 during resting state (RS) and continuous performance (CP).

| | **Subject 1** | | **Subject 2** | |
|---|---|---|---|---|
| Session | RS | CP | RS | CP |
| 1 | 0.165 | 0.023 | 0.067 | 0.059 |
| 2 | 0.109 | 0.019 | 0.130 | 0.015 |
| 3 | 0.143 | 0.015 | 0.141 | 0.004 |
| 4 | 0.120 | 0.019 | 0.100 | 0.007 |
| 5 | 0.083 | 0.041 | 0.081 | 0.022 |
| 6 | 0.109 | 0.019 | 0.200 | 0.011 |
| 7 | 0.026 | 0.023 | 0.081 | 0.004 |
| 8 | 0.064 | 0.011 | 0.144 | 0.015 |
| 9 | 0.068 | 0.049 | 0.070 | 0.015 |
| 10 | 0.094 | 0.034 | 0.041 | 0.011 |
| | | | | |
| **Median** | **0.102** | **0.021** | **0.091** | **0.013** |
| **p-Value** | **1.95E-03** | | **1.95E-03** | |

**Tab.2:** Fraction of correlated voxels (FCV) in right M1.

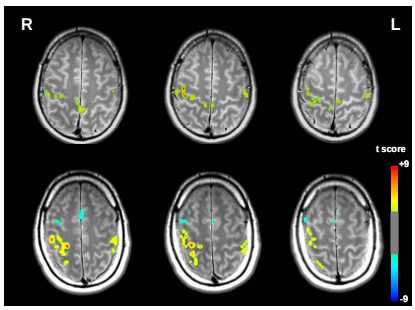


**Fig.1:** Significant differences ($p<10^{-3}$) between resting state and continuous performance. 1st row: subject 1, 2nd row: subject 2.