Functional connectivity in the motor and auditory systems: a reproducibility study at 3 T

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Introduction: In functionally related regions of the brain, synchronised fluctuations of cerebral blood flow have been observed with BOLD MRI as well as with other techniques. Experimental studies suggest that these fluctuations are likely to reflect oscillations of neuronal activity [1]. As BOLD MRI is thought to represent neuronal activity by neurovascular coupling it has been accepted, that reproducibility of fMRI studies within subjects and between subjects is limited due to numerous variables involved in the underlying physiology. We attempted to investigate the reproducibility of typical resting state fcMRI studies comparing auditory and motor fcMRI maps obtained in two normal controls at five time points in resting state or continuous activation conditions.

Materials and Methods: Timeseries BOLD-weighted data were acquired on a 3.0T system (Siemens Allegra) using a EPI-FID sequence; TE = 30 ms, slice thickness = 6mm, matrix size = 64x64, field-of-view = 240x240 mm^2. For the symmetric block design fMR study (alternating 32 s of rest and stimulation), 15 slices were collected using TR = 2000 ms and a flip angle = 90°; for the resting state and continouosly activated state fcMR study, 3 slices were acquired using TR = 250 ms and a flip angle = 30°. Two different paradigms were chosen: A) simultaneously bilateral finger tapping (opposing fingers 1,3,5,2,4) and prescribing slices containing the primary motor cortex, basal ganglia and cerebellar regions; B) auditory stimulation (backward speech), prescribing slices containing the primary motor cortex, the Heschl gyrus and the medial geniculate. Corresponding T1-weighted slices and high resolution anatomical 3D T1-weighted were acquired for anatomic reference.

In 2 subjects, repeated scans were done five times within 48 hours. Careful positioning using orthogonal localizers and midsagittal alignment at the inferior borders of the corpus callosum assured reproducible slice positioning which was monitored on T1w before and after each scan.
For data evaluation, T2*w images were Hamming filtered [2]; furthermore, images from resting and continouosly activated state were digitally low-pass filtered (frequency 0.08 Hz) to remove temporal fluctuations arising from cardiac and respiratory-related physiological noise [3].

Block design fMRI identified activated areas in right and left precentral gyrus (primary motor cortex PMC), supplementary motor areas (SMA), basal ganglia areas and cerebellar regions with paradigm A, and insular gyri (Heschl gyri) and the medial geniculate with paradigm B. For cross-correlation estimation in resting and continouosly activated state timeseries, reference ROIs (3x3 pixels) were drawn in right PMC (slice #1, paradigm A) and in right Heschl gyrus (slice #2, paradigm B). Connectivity maps were calculated showing the corrected cross-correlation between each single pixel and the reference ROI [4].

Results: Both motor and auditory stimulation showed robust and reproducible results in regard to the anatomic localisation and number of activated pixels in both primary motor cortices, the cerebellar hemispheres, the supplementary motor area, resp. the auditory cortex bilaterally. Correlation analysis of LFBF showed at 5 time points each with four different conditions (2 resting states, 2 continuous performance experiments motor and auditory) in a total of 20 maps matching spatial distributions of synchronous LFBF in the presumed motor network located in both primary motor cortices extending up to midline cortex.

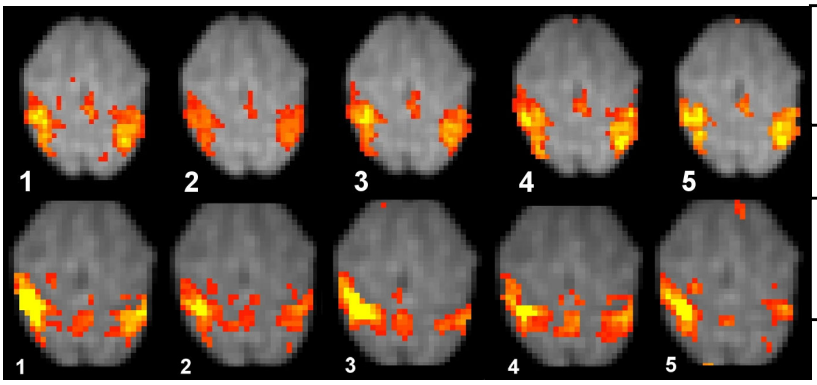

Fig. 1: fMRI block design (finger tapping); series of five studies of the same volunteer. Activation maps are scaled according to 10 < t < 25.

Fig. 2: fcMRI activation pattern of a resting state timeseries, following a block designed auditory stimulation; series of five studies of the same volunteer. Activation maps are scaled with varying threshold of t-test value.

fMRI block design (finger tapping)	1	2	3	4	5
left PMC	58	46	49	56	49
right PMC	53	59	60	76	47
SMA	14	9	13	14	10

Number of activated pixels with values of student's t-test >10.

fcMRI resting state (after audiotory block design)	1	2	3	4	5
left PMC	38	32	23	42	19
right PMC	56	52	57	53	50
SMA	19	19	22	25	6

Reference ROI for connectivity analysis within right PMC. No. of activated pixels; threshold of student's t-test was adjusted (t = 17-40) to achieve a similar pattern.

Discussion and Conclusion: In an attempt to evaluate reproducibility of LFBF correlations it was demonstrated that by adjusting the statisitical criteria used a similar anatomical pattern was identified in the motor and auditory network regardless of the continuous activation or resting state. As LFBF may be influenced by the underlying basal neuronal activity, one would assume that different brain states might influence the reproducibility of fcMRI. Further work will have to identify the potential influence of physiological and technical variables i.e. motion artifact. Given those limitations of fcMRI, this study may provide a starting point for conservative interpretation of normal control and clinical studies.

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