Implicit Learning–related Effects Detected by Optimized ASL fMRI

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Introduction

Arterial spin labeling (ASL) fMRI provides an attractive alternative to BOLD fMRI to investigate brain activity changes during learning (1). The ASL signal is stable over long time scales (2) so learning paradigms with low task frequency can be presented to the subject. However ASL generally suffers from intrinsically low SNR compared to BOLD, thus reducing the power of the inferences at individual and group levels.We have previously reported an optimized ASL technique that yields a sensitivity improvement of 6-fold with respect to the commonly used continuous ASL (CASL) EPI at 3T (3). This sequence combines a more efficient pseudo-continuous ASL (pCASL) approach for flow driven adiabatic inversion (4), compatible with body coil transmission and array receiver, with a background suppressed (BS) single shot 3D GRASE readout. This technique has been employed in a group study to detect brain activation in a continuous motor learning task.

Materials and Methods

Studies were performed on a 3T Siemens Trio using the 8-channel head array. Fourteen healthy volunteers were scanned using the pCASL BS 3D GRASE. The scanning session consisted of: rest (3min), task (alternating finger movement, sequence 1, 6min), control (6min), task (sequence 2, 6min) and rest (3min). During the task, subjects were asked to reproduce two sequences (one per period) of six alternating finger movements with the right hand in a key pad, after visualizing the sequence on a screen, presented at a frequency of 2.5 Hz, for a total of 50 trials. The control consisted on performing 6 sequential finger movements. One perfusion image (label and control) was acquired every trial, with imaging parameters: resolution=4x4x6mm^3, FOV=250x196x96mm^3, 16 nominal partitions with 13% oversampling, 5/8 partial Fourier, measured partitions=11, matrix size=64x49, BW=2790Hz/pixel, GE spacing=0.4msec (with ramp sampling), SE spacing=26msec, read-out time=270msec, TE=52msec and TR=3.5 sec. Two inversion pulses (15.35msec duration and 220mG amplitude) were added for BS (TI_1=1800msec, selective; TI_2=500msec, non-selective). The pCASL pulse, played between the BS pulses, consisted of 1184 selective RF pulses (Hanning window, peak B_1=53mG, duration=500μsec and G=0.6G/cm, 1.2sec labeling duration). For the control, the RF phase alternated from 0 to 180°. The post-labeling delay was 600msec. Bipolar gradients (b=5sec/mm^2) were added to suppress intravascular signal. Images were realigned and co-registered to the anatomical dataset, acquired using a MPRAGE sequence, before subtraction of label and control. 200 perfusion images were obtained, normalized to the standard template and smoothed. Voxel-wise statistical analysis was performed using SPM5 for each subject, in a block design that modelled three conditions: rest, task and control. Two t-contrasts were constructed at the first level: task versus rest and task versus control, followed by a group analysis of random effects using the one-sample t-test. A second analysis was carried out with reaction time (RT) as parametric modulator for each task trial, to identify brain areas where the change in perfusion correlated with performance changes.

Results and Discussion

All subjects learned both sequences of alternating finger movements and reproduced them correctly for a total of 37±11 (mean ± standard deviation) repetitions out of 50 trials during the first period and 40±10 during the second. During both periods RT decreased with trial number.

At the group level (p<0.005, FDR-corrected, k>30), the contrast task vs. rest revealed areas involved in sensory-motor processing, visual to motor mapping, working memory and motor execution, consistent with results from previous studies (5): on the left, the hand representation area of the primary motor cortex, the dorsal premotor cortex (PM), the ventral PM cortex; medially, the suplementary motor area (SMA); and bilaterally the superior parietal lobe with maxima at the Precuneus, the anterior insulae, the inferior parietal lobes, and the primary visual cortex. The contrast task vs. control (p<0.05, FDR-corrected, k>30, Fig. 1) yielded activations in areas involved in planning of complex movements, with extended bilateral clusters at the parietal cortex with maxima at the Precuneus, the insulae extending to the rostral putamen, the ventral putamen, the dorsal PM cortex; medially pre-SMA; on the left, the ventral PM cortex; and on the right, anterior cingulate gyrus, pre-frontal cortex, Superior Temporal Gyrus and thalamus (medial dorsal nucleus).

Learning related changes in neural activity were identified at the group level. Decreases in perfusion with decreasing RT (Fig. 2) were found in areas involved in motor preprocessing: pre-SMA, SMA and ventral PM cortex; areas implicated in visuo-spatial integration: parietal cortex bilaterally with the largest cluster on the right, the right Posterior Middle Temporal Gyrus extending to the Middle Occipital Gyrus (V3) and a smaller cluster in the left V3; and areas involved in sustained attention and working memory: dorsolateral prefrontal cortex, anterior cingulate gyrus and anterior insulae. Clusters of increased perfusion with decreasing RT (Fig. 3) were found mostly on the left: posterior insula extending to the putamen, Superior Temporal Gyrus, Parahypocampal Gyrus reaching the hypocampus, a large cluster including the substantia nigra, amygdala and ventral posterior medial nucleus of the thalamus; and a single cluster on the right substancia nigra. Increased activity in the hypocampus is associated with memorization of the ordinal structure of the sequence with repetition. On the other hand, activation in the substantia nigra may be related with an improvement in the timing of the sequence reproduction that paralleled the decrease in RT in most subjects (6).

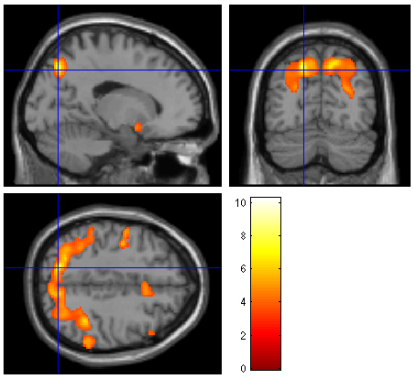

Fig. 1: Cortical areas significantly more active during task than control. Group analysis (p<0.05, FDR-corrected, k>30).

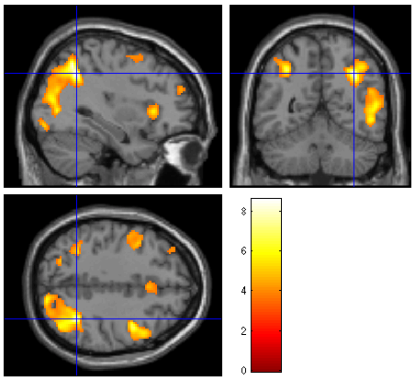

Fig. 2: Cortical areas that showed significant decrease in perfusion with decreasing RT. Group analysis (p<0.05, FDR-corrected, k>30).

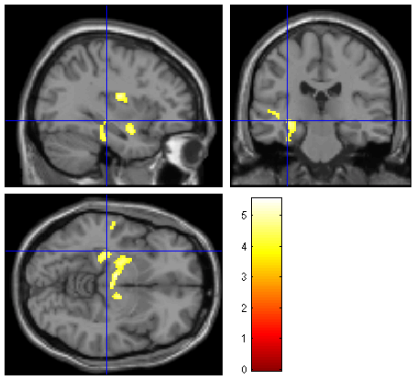

Fig. 3: Cortical areas that showed significant increase in perfusion with decreasing RT. Group analysis (p<0.001, uncorrected, k>30).

Conclusions

An optimized ASL technique was used to study changes in neural activity with motor learning. Learning effects were assessed by including the reaction time as parametric modulator at the first level analysis. This technique provided sufficient SNR to identify brain areas involved in learning at the group level using the random effects model.

Bibliography

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