287.16 Functional MRI in alert behaving monkeys during goal-directed saccades

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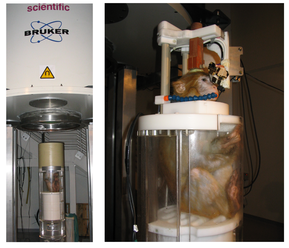
introduction

Functional MRI in alert behaving monkeys is a new powerful approach for studying multiple brain areas and elucidating the neural basis of the BOLD signal. We used this technique to study brain activity during visually- and memory-guided saccades, tasks extensively applied in primate electrophysiology. The delayed memory-guided saccade task allows for separating sensory, motor, and preparatory processes, and introduces cognitive demands such as inhibition of reflexive responses and working memory.

The goals of the current work were:

1) To develop methods for imaging behaving monkeys in high-field vertical scanner
2) To characterize the time-courses of BOLD correlates of sensory, motor and cognitive signals during eye movement tasks using event-related analysis

methods



Imaging

Bruker Biospec 4.7T/60cm vertical bore
dedicated primate scanner, ParaVision 3.0.2.
Linear birdcage transmitter-receiver RF coil.
Functional: GE-EPI, single-shot, TR 1s,
128x128 12.8 cm FoV, 1x1x2 mm voxel,
10 oblique slices.
Structural: T1-weighted IR-RARE
in-plane during same session;
high-resolution (0.5/1 mm voxel) T1-weighted
3D-MDEFT or MDEFT-RAGE in separate session.

Stimuli, behavioral control and data acquisition

Visual stimuli were presented on 800x600@60Hz LCD goggles (Resonance Technology) subtending 30x24 of visual angle using OpenGL. Eye position was monitored at 60Hz with mini-IR camera (Resonance Technology /Arrington Research) and recorded as an analog signal together with stimulus and timing information and TTL triggers from the scanner. Online behavioral control and feedback were achieved using LabVIEW RealTime platform. Incorrect trials were aborted; successful trials were rewarded with water.

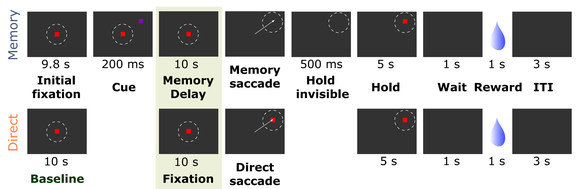
Custom plastic (PEEK) headpost embedded in Palacos bone cement headcap was attached to the MRI-compatible chair via headholder. Monkeys were habituated to the acoustic noise and confined space during training sessions. A video motion detection sensor was used to train monkeys to minimize their body and limb motion.

Data analysis

Data were analyzed in BrainVoyager QX and MATLAB. All trial events - visual cues, fixation and delay periods, instructed saccades, reward delivery - were extracted and used as predictors for GLM after convolution with HRF. For event-related averages (ERA), only successful trials were combined. In monkeys, the epochs of the run affected by motion were automatically detected and eliminated from ERA analysis. Fixational saccades and blinks were detected, but not used for GLM predictors.

Paradigm: randomized memory vs. direct saccades

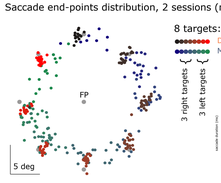
Trial sequence

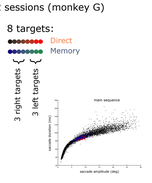


results

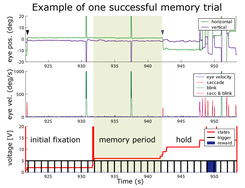
Behavior

Saccade end-points distribution, 2 sessions (monkey G)

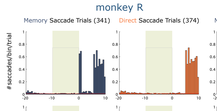




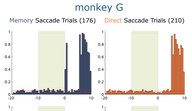
Example of one successful memory trial



monkey R



monkey G

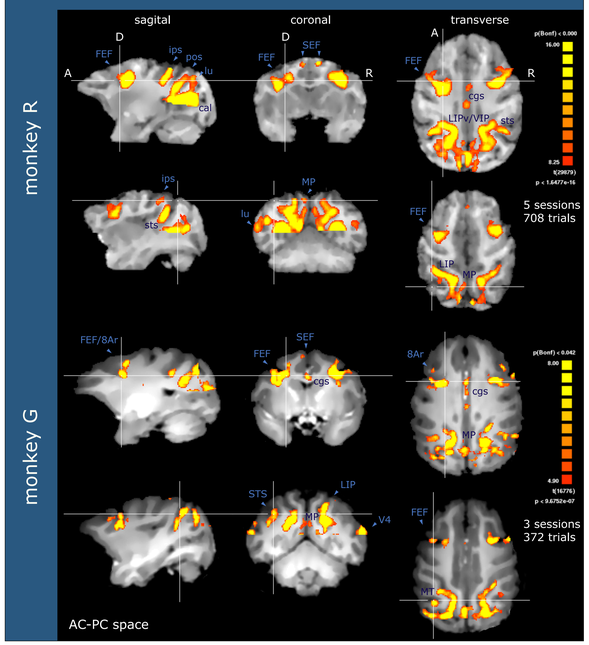


Time relative to saccade onset (s)

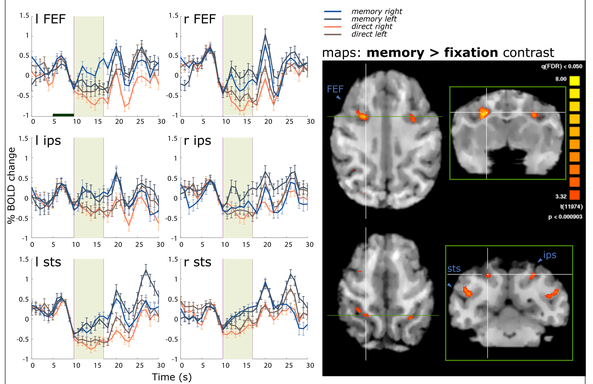
No difference in eye movement patterns in the delay period (shaded) between memory and direct saccade trials.

Most memory saccades were followed by smaller corrective saccade after target re-appearance.

Saccade activation: cross-sections

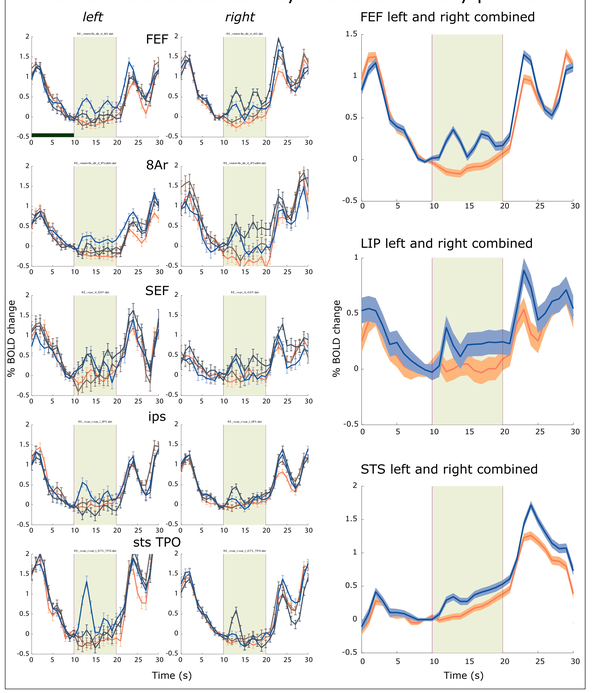


Time-course of BOLD activity with 7s memory period



maps: **memory > fixation** contrast

Time-course of BOLD activity with 10s memory period



FEF left and right combined

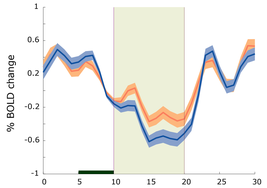
LIP left and right combined

STS left and right combined

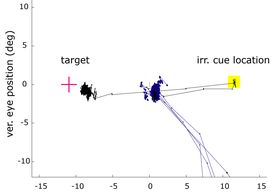
Irrelevant cue - an attempt to rule out sensory and/or attentional confounds

As of yet, the monkeys still seem to remember the irrelevant cue location.
In up to 1/3 of direct trials, they were first saccading to the remembered irrelevant cue location before acquiring the visual target:

FEF left and right combined



Error trial example



summary

Our experimental system was sensitive enough to detect weak (~0.5% BOLD change) "cognitive" signals: spatial working memory and/or movement preparation, even with a modest amount of data. This is prerequisite for future studies of action planning and decision making.

This memory/preparation signal was seen as a separate peak or elevated activity in the late memory period. Frontal and, to a lesser degree, parietal and STS areas showed contralaterality for the cue and late memory responses.

We confirm involvement of medial parietal area (MP) in the control of goal-directed eye movements.

Future work

Control experiments: cue-only response, memory saccades without target confirmation (no corrective saccades).

Use multiple targets sequence to increase memory load.

Explore spatial specificity - topographical organization? (higher resolution may be needed)

FMRI-guided neurophysiological recordings (spikes and LFPs) in the same monkeys using identical paradigms, to study underlying neuronal correlates of the BOLD signal.

Decision-making studies using effector-specific (eye and joystick movements) responses.

Acknowledgements

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