Stimulating brain tissue with light - resting state fMRI analysis

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Introduction:

In most species light synchronizes various physiological and functional processes [1]. In many vertebrates photoreception involving circadian regulation can also occur without eyes [2]. It has been shown that mammalian brain responds to visible light [3], and brain tissue is known to have several proteins called opsins outside the visual system [4,5,6] that are potentially light-sensitive. Based on this knowledge, we hypothesized that bright light given directly to human brain tissue via ear canal would alter brain activity slowly during resting-state fMRI. Data-driven functional connectivity analysis on the full band data was performed in order to study the hypothesized slow response.

Methods:

Bright white light (peak at 465 nm) was delivered non-invasively via external ear canal to the brain during BOLD fMRI scanning using light fibers. Light intensity corresponded to about the condition when ear canal is directed to sun at bright sunny conditions. Light stimulation sessions took place during winter when it is remarkably dark in Oulu, Finland.

Final sample from normal healthy volunteers was 24 subjects with light stimulus and 26 sham controls. Imaging sessions consisted of consecutive resting-state scans and for light stimulus group a constant light stimulus was given during the second resting state scan. Functional connectivity analysis without high-pass filtering was carried out by comparing the second resting state scans between the light subjects and sham controls. Consecutive 8.5 min BOLD fMRI scans (GE 1.5 T HDx, TR 1.8 s, TE 40 ms) without breaks were performed with instruction to rest (eyes covered, subject could not see the stimulus light).

BOLD data pre-processing was carried out using FSL. Time-concatenation group ICA (FSL Melodic) for high-pass filtered data (cut-off 0.0067 Hz) with 30 components was run in order to provide the spatial *a priori* maps for FSL dual regression analysis. No de-trending or high-pass filtering was performed for data to be fed into functional connectivity analysis with dual regression in order to study the hypothesized slow response to constant light stimulus.

Results:

Significant differences were revealed between constant light stimulus subjects and sham controls using ICA dual-regression analysis on full band BOLD data; light stimulus seems to increase the activity of visual cortex in particular. Lateral visual IC differences (fig. 1) (665 voxels – 42.6 cm3) were widely distributed reaching medial visual regions, cerebellum and even opercular cortex. In addition, motor IC exhibited small increased activity (11 voxels) in light group. Also motion related ICs were greater in light group but both visual and motor IC differences were robustly detected also in the re-analysis excluding the most moved light group subjects.

Examining the temporal characteristic of the lateral visual component (fig. 2) shows slow increase in light group that is clearly more prominent than the control group curve that also exhibits slight increase in activity along the resting state scan.

Discussion and Conclusion:

Our results suggest that the brain tissue is inherently light-sensitive. Direct light stimulation to brain induces a gradual increase in functional connectivity of the lateral visual network in particular, less so in motor network. Exact mechanism for light-sensitivity is still open, but there are studies showing brain tissue to have inherent mechanisms for light reactivity [3,4].

Very low frequency BOLD drifts (0-0.01 Hz) in grey matter are shown to have neurophysiological origin [7] and for example drug administration induces such drifts [8,9]. Although full band data is prone to artefacts, slow motion artefacts were not observed to cause our findings and the scanner drifts should be equal between the groups in the study setup.

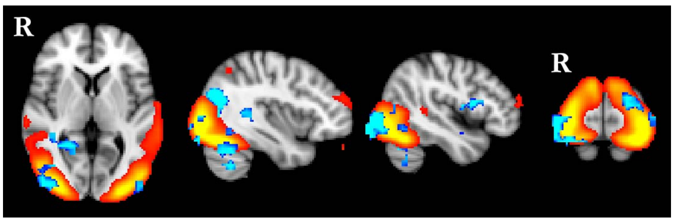

Fig. 1. ICA dual regression results between subjects with light stimulus directly to the brain and sham controls. Lateral visual IC (warm colors) show increased connectivity (TFCE-corrected $p < 0.05$, cold color) during light stimulus.

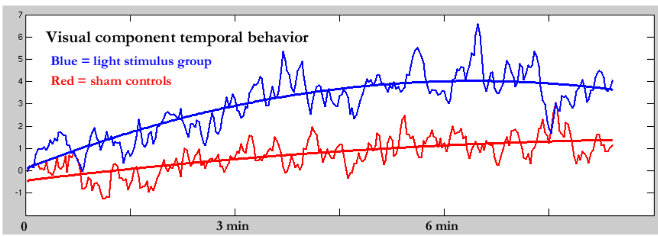

Fig. 2. Lateral visual IC group mean time-courses (and 2^{nd} order polynomial fits) from the ICA dual regression. The group of subjects with constant light stimulus to the brain (blue) and sham controls (red) demonstrate differences in activity trend.

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