Stimulating brain tissue with bright light - resting state fMRI analysis

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Introduction: Light stimulation studies of rat brain have demonstrated increased GABA release [1], increased NMDA-receptor mediated currents [2] and increased GABA-induced currents [3]. In human brain several potentially light-sensitive opsin proteins are expressed at least on the mRNA level: melanopsin [4], panopsin [5] and neuropsin [6].

We hypothesized that non-ocular brigh light stimulation to human brain via ear canal would alter brain activity during the stimulation. Bright light was given during resting-state BOLD fMRI and functional connectivity was studied in a data-driven manner on the full frequency band.

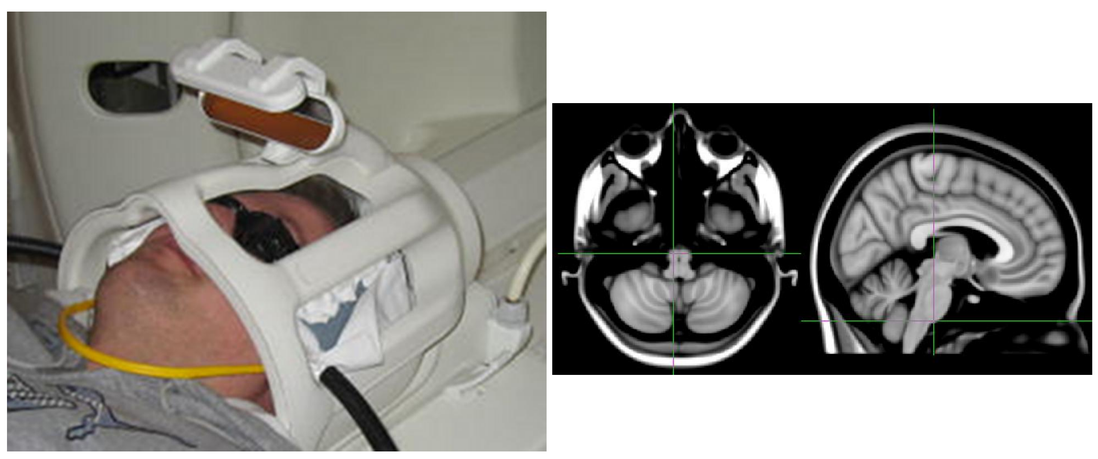

Fig 1. Stimulus set-up (left). Ear-canal position (right).

Methods: Bright white light (peaks at 465 and 550 nm) was delivered via external ear canal to the brain during BOLD fMRI scanning using light fibers (Fig. 1). Light intensity corresponded to about the condition when ear canal would be directed to the sun at the brightest sunny conditions. Light stimulation sessions took place during winter when it is remarkably dark in 65° northern latitude.

Final sample from normal healthy volunteers was 23 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 scan. The first scans were used for warming up the scanner to diminish the instrumental drifts, thus within-subject comparison could not be carried out on the full band. Consecutive 8.5 min BOLD fMRI scans (GE 1.5 T HDx, TR 1.8 s, TE 40 ms, 4 mm voxel) without breaks were performed with instruction to rest (eyes covered, subject could not see the stimulus light).

Analysis was carried out using FSL Melodic ICA and dual regression. Group ICA decomposition to 30 ICs with high-pass filtering (0.0067 Hz) was run in order to provide the spatial *a priori* maps for dual regression analysis. However, no de-trending or high-pass filtering was performed for data to be fed into dual regression. Resulting individual maps were tested between light group and controls in a non-parametric 2-sample t-test and multiple comparison corrected (TCFE).

References:

[1] Wade (1988), *PNAS*, vol. 85, pp. 9322-9326.
[2] Leszkiewicz (2000), *J Physiol,* vol. 524, pp. 365-374.
[3] Leszkiewicz (2003), *Eur J Neurosci,* vol. 17, pp. 2077-2083.
[4] Allen Institute for Brain Science. (http://human.brain-map.org)
[5] Blackshaw (1999), *Journal of Neuroscience*, vol. 19, pp. 3681-3690.
[6] Mitsui (1999), *Eur J Biochem*, vol. 260, pp. 627-634.

Results: Light stimulus group demonstrated increased activity (corr. $p < 0.05$, blue voxels in Fig. 2) in lateral visual network. In addition, sensorimotor component exhibited small increased activity in light group. Also motion artefact components were greater in light group but both visual and motor component differences remained after exclusion of light group subjects with greatest motion component contribution.

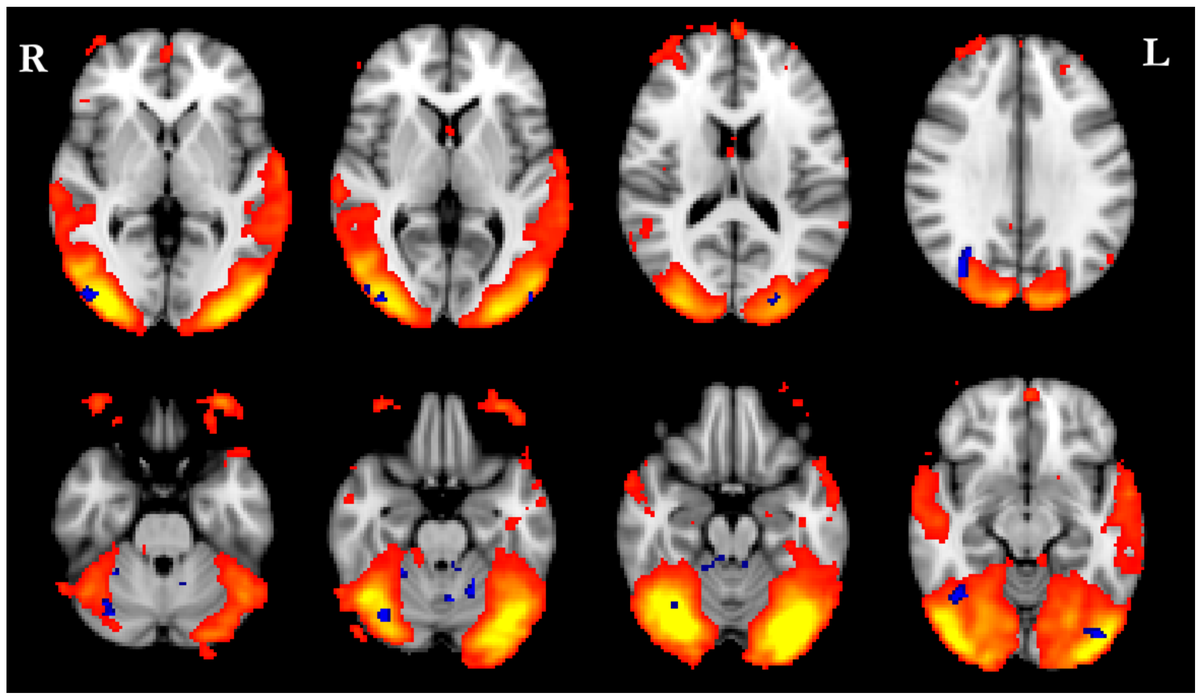

Fig 2. Lateral visual network (warm colors) and greater functional connectivity in light stimulus group (blue)

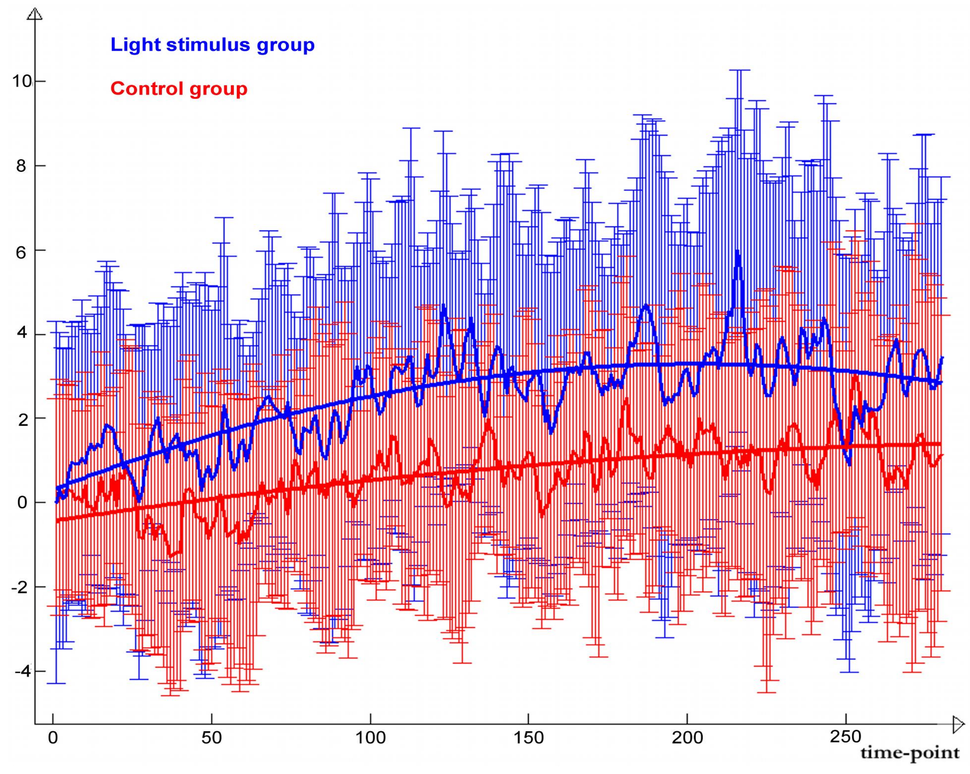

Fig 3. Lateral visual time-courses (blue=light group, red=control). Slow increase in light group is clearly more prominent than the control group curve. Corresponding curves in the first scans without stimulus showed no trend differences.

Discussion and conclusion: Results suggest that the brain is inherently photosensitive. Non-ocular bright light stimulation to brain seems to induce a gradual increase in functional connectivity of the lateral visual network that could be a projection originating from actual phototransduction site. Extrastriate visual areas are involved in brain function like visual awareness. Peculiarly this coincides with a few spontaneous comments describing clearer sight and widened view of sight some time after the light stimulus.

Brain regions encountering most of the light are probably anterior cerebellum, brainstem and inferior temporal cortex, also posterior diencephalon and anterior occipital lobe can be within the range of light photons. Hypothetical site for phototransduction could be cerebellar Purkinje cells that are rich of panopsin in rats [5]. Also, brainstem nuclei related to neurotransmitters like dopamine, serotonin or noradrenaline may be directly or indirectly involved in the photoreception.