Behavioural Brain Research 298 (2016) 52–56

Contents lists available at ScienceDirect

Behavioural Brain Research

journal homepage: www.elsevier.com/locate/bbr

Short communication

Age-dependent modulation of the somatosensory network upon eye closure

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HIGHLIGHTS

- Eye closure improves somatosensory perception in healthy young and old adults.
- We performed effective connectivity analysis of MR-imaging with tactile stimulation.
- Young participants show an optimized somatosensory information flow.
- With age, the visual increasingly modulates the somatosensory network.
- Visual dominance is pronounced in the aging brain.

ARTICLE INFO

Article history:
Received 24 September 2015
Received in revised form 12 October 2015
Accepted 15 October 2015
Available online 4 November 2015

Keywords:
Closed eyes
Darkness
Effective connectivity
Granger causality
Somatosensory
Visual
Fmri
Aging

ABSTRACT

Eye closure even in complete darkness can improve somatosensory perception by switching the brain to a uni-sensory processing mode. This causes an increased information flow between the thalamus and the somatosensory cortex while decreasing modulation by the visual cortex. Previous work suggests that these modulations are age-dependent and that the benefit in somatosensory performance due to eye closing diminishes with age. The cause of this age-dependency and to what extent somatosensory processing is involved remains unclear.

Therefore, we intended to characterize the underlying age-dependent modifications in the interaction and connectivity of different sensory networks caused by eye closure. We performed functional MR-imaging with tactile stimulation of the right hand under the conditions of opened and closed eyes in healthy young and elderly participants. Conditional Granger causality analysis was performed to assess the somatosensory and visual networks, including the thalamus.

Independent of age, eye closure improved the information transfer from the thalamus to and within the somatosensory cortex. However, beyond that, we found an age-dependent recruitment strategy. Whereas young participants were characterized by an optimized information flow within the relays of the somatosensory network, elderly participants revealed a stronger modulatory influence of the visual network upon the somatosensory cortex.

Our results demonstrate that the modulation of the somatosensory and visual networks by eye closure diminishes with age and that the dominance of the visual system is more pronounced in the aging brain.

1. Introduction

A first indication on how eye closure affects brain function was provided by Berger in 1929 when he described the alpha-rhythm in the EEG. Until recently, this was mainly interpreted as a result of a lack of vision [1]. Previous studies, however, demonstrated a present Berger-effect even in the absence of any vision in complete darkness [2]. Functional imaging data could prove that the effect of eye closure is not limited to the visual cortex itself, but it also alters the activity in the somatosensory cortex [3]. In addition, eye closure is known to improve some aspects of somatosensory perception [4].

In a previous study, we demonstrated that although existent in the aging brain, the effect of eye closure upon the perception and processing of somatosensory stimuli is weakened (Brodoehl, 2015b). This is likely because the aging brain progressively depends on multisensory integration due to the reduced function of periph-

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http://dx.doi.org/10.1016/j.bbr.2015.10.035
0166-4328/

eral sensory organs and altered speed and processing capacity of the brain [5,6].

However, until now the age-dependent changes in the somatosensory network responsible for the less pronounced effect of eye closure on the somatosensory perception remained elusive. We hypothesized that the gating function of the thalamus that induces improved somatosensory perception [7] is altered in elderly. Regarding the more pronounced multisensory integration in the elderly [8], we further presumed a superior influence of the visual network on the somatosensory cortex.

To investigate these hypotheses, we investigated the processing of somatosensory stimuli in the somatosensory and visual networks under the conditions of opened and closed eyes in complete darkness in healthy young ($n = 18$, 10 females, age range 21–28 years) and older adults ($n = 16$, 7 females, age range 62–71 years) (Table S1 in the supplementary) using functional MR-imaging (fMRI, 3.0T MR Siemens Scanner) and effective connectivity analysis (Granger causality). Data analysis was performed on a PC using MATLAB (Mathworks, Natick, MA) and SPM8 software (Wellcome Department of Cognitive Neurology, London, UK, http://www.fil.ion.ucl.ac.uk/spm). A more detailed description of the methods is provided in the supplementary materials.

2. Stimulation induced brain activity

Fig. 1 shows brain areas activated by a tactile stimulation of the right hand (SPM activations of all 34 subjects, FWE corrected). Soft pressure stimuli to all fingers of the right hand were provided by an air driven pneumatic device (airpuff). Each stimulus lasted 100 ms and was repeated 35 times with closed eyes and 35 times with opened eyes; the interstimulus interval (ISI) was randomized between 8.7 and 15.8 s; blocks of eye closure/opening lasted 1 min and were arranged in a pseudorandomized fashion and presented 15 times each. In accordance with previous studies [9,10], we found highly significant activation patterns in the contralateral primary (SI) and bilateral secondary somatosensory (SII) cortex. Furthermore, we observed activations within the primary motor and the middle cingulate cortex. A more detailed description of the activated brain areas is provided in Table 1.

3. Effective connectivity analysis

In recent years, several methods to analyze interactions and dependencies of neuronal activity have been established. Using resting-state fMRI, Greicius et al. [11] could identify a default mode network. Since then, functional connectivity has become a widespread tool for brain network analysis. By nature, functional connectivity describes statistical dependencies by correlations, coherence, or transfer entropy. Therefore, this method does not necessarily describe a direct causal influence; for a review, see Friston [12]. Granger causality [13], on the other hand, has been introduced to fMRI data by Roebroeck et al. [14] to characterize the direction and influence among neuronal populations. As a major difference to other effective connectivity approaches, this method does not require a priori model specification. In brief, the basic idea behind Granger causality (GC) is that a time course X1 causes the time course X2 if the knowledge of X1 helps to predict the future of X2. Furthermore, the Granger autonomy of the brain area describes to what amount it is influenced (or not influenced) by other areas.

Based on our hypothesis, we defined regions of interest (ROI) for effective connectivity analysis (GC) within the somatosensory and visual cortices and the corresponding thalamus. Supported by the SPM activations as shown in Fig. 1 and Table 1, we defined three ROIs within the primary (Brodmann area 1, 2, 3b) and one within the secondary somatosensory cortex. In our SPM analysis, area 3a was not activated at the significance level utilized because 3a mainly receives input from muscle receptors and responds to higher threshold tactile stimuli [15]. Therefore, we did not involve area 3a in our analysis. For the visual areas V1–V3, we employed the same areas as described in our previous work [4], and for the thalamus, we defined one ROI each for the left-sided somatosensory and occipital zones as described by Behrens et al. [16]. MNI coordinates for all employed brain areas are provided in Table 2.

4. Effect of eye closure upon effective connectivity independent of age

At first we analyzed the effect of eye closure upon the effective connectivity within the somatosensory and visual networks independently of age. With eye closure, the connectivity within the somatosensory cortex increased, as did the information flow from the somatosensory thalamus to the somatosensory cortex (Fig. 2 upper/left and Table 2). Initially, we observed multiple connections within the whole somatosensory cortex. However, after applying an FDR-correction for multiple comparisons at $P \leq 0.01$, only the most prominent connections between BA2 and BA1, BA1 and SII (OP) and the somatosensory thalamus and SII (OP) survived the threshold analysis. Simultaneously, elements of the primary and secondary somatosensory cortex became less sensitive to external forces as indicated by the increased Granger autonomy. In our previous work, we proved that on the behavioral level, these changes are accompanied by an improved perception of basal tactile perception [4,7]. In humans, the dominant input from cutaneous neurons enter SI (mainly BA1 and BA3b) via the ventral posterior lateral nucleus of the thalamus. Whereas SI primarily encodes for timing, intensity and location, the next step of the serial processing pathway takes place in SII [9,10,17]. Here, our results indicate that the processing within SI is optimized and potentially reduces disturbing influences from the visual cortex (as indicated by the increased Granger autonomy), and the direct information flow from the thalamus towards SII [18] is also optimized. SII shows less linearity to the stimulus intensity than SI [17] but is greatly affected by attention, i.e., expecting a stimulus [19]. Here, the effect of eye closure might be comparable to an attentional modulation of somatosensory stimuli and promote a parallel signal transfer from the thalamus to SII.

With opened eyes on the other hand, the influence of the occipital/visual part of the thalamus upon the somatosensory cortex increases (Fig. 2 upper/right and Table 2). This modulation is accompanied by a decreased tactile performance [4,7].

5. Age dependent influence of eye-closure

Independent of age, eye closure led to increased intra-somatosensory connectivity and increased autonomy as discussed above. However, further results showed that the visual cortex (V1–3) directly influences the secondary somatosensory cortex (Fig. 2 upper/left). This result appears to be contradictory to our hypothesis of a diminishing visual influence with closed eyes and our previous observing [4]. Comparing participants based upon their age, we found that an increased connectivity between the visual and somatosensory cortices is a feature exclusive to elderly subjects (to do so, Granger analysis was performed for each young and old participant separately, and the results were compared by a 2-sample t-test). Moreover, the occipital zone of the thalamus directly influenced SII (Fig. 2 lower/left, Table 2). On the behavioral level, the effect of improving somatosensory performance with eye closure is preserved in elderly, but eased [7]. Here, we suggest that this poorer somatosensory performance in the elderly is linked to the increasing influence of the visual system on the somatosensory