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Very-low-frequency oscillations of cerebral hemodynamics and blood pressure are affected by aging and cognitive load

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ABSTRACT

Spontaneous slow oscillations occur in cerebral hemodynamics and blood pressure (BP), and may reflect neurogenic, metabolic or myogenic control of the cerebral vasculature. Aging is accompanied by a degeneration of the vascular system, which may have consequences for regional cerebral blood flow and cognitive performance. This degeneration may be reflected in a reduction of spontaneous slow oscillations of cerebral hemodynamics and BP. Therefore, we aimed to establish the dependency of slow oscillations of cerebral hemodynamics and BP on the factors age and cognitive load, by using functional near-infrared spectroscopy (fNIRS). Fourteen healthy young (23–32 years) and 14 healthy older adults (64–78 years) performed a verbal n-back working-memory task. Oxygenated and deoxygenated hemoglobin concentration changes were registered by two fNIRS channels located over left and right prefrontal cortex. BP was measured in the finger by photoplethysmography. We found that very-low-frequency oscillations (0.02–0.07 Hz) and low-frequency oscillations (0.07–0.2 Hz) of cerebral hemodynamics and BP were reduced in the older adults compared to the young during task performance. In young adults, very-low-frequency oscillations of cerebral hemodynamics and BP reduced with increased cognitive load. Cognitive load did not affect low-frequency oscillations of the cerebral hemodynamics and BP. Transfer function analysis indicated that the relationship between BP and cerebral hemodynamic oscillations does not change under influence of age and cognitive load. Our results suggest aging-related changes in the microvasculature such as declined spontaneous activity in microvascular smooth muscle cells and vessel stiffness. Moreover, our results indicate that in addition to local vasoregulatory processes, systemic processes also influence cerebral hemodynamic signals. It is therefore crucial to take the factors age and BP into consideration for the analysis and interpretation of hemodynamic neuroimaging data.

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Introduction

Neuroimaging with fNIRS and fMRI has registered the occurrence of spontaneous slow oscillations of cerebral hemodynamics (Elwell et al., 1999). The driving force for these oscillations may vary between neurogenic, metabolic and myogenic control of the cerebral vasculature (Fukunaga et al., 2008; Hudetz et al., 1998; Katura et al., 2006; Mayhew et al., 1996). Different physiological origins for slow oscillations of cerebral hemodynamics are suggested in the literature and may be summarized as follows: 1) spontaneous slow changes in cerebrovascular tone (vasomotion), 2) changes in systemic hemodynamics (blood pressure (BP)) reflected in cerebral hemodynamics and 3) slow oscillations in neuronal activation, related to functional network connectivity. Slow oscillations are further characterized by their frequencies. Very-low-frequency oscillations (VLFOs) occur at approximately 0.04 Hz and low-frequency oscillations (LFOs) are centered around 0.1 Hz (Obrig et al., 2000). These slow oscillations can thus be differentiated from high-frequency oscillations (HFOs) that are known to be of respiratory origin, around 0.2–0.3 Hz, and the heartbeat cycles that occur at approximately 1 Hz (Elwell et al., 1996).

Slow oscillations of cerebral hemodynamics are modulated by functional stimulation. Obrig et al. (2000) established using fNIRS that functional activation affects slow oscillations of cerebral hemodynamics in the visual cortex in young adults. In comparison to rest, visual checkerboard stimulation reduced VLFOs of oxygenated hemoglobin ([O_2Hb]), centered around 0.04 Hz. No significant effects of functional activation were found for VLFOs of [HHb] or for LFOs centered around 0.10 Hz. For functional activation research it is relevant to know how slow oscillations are affected not only by functional stimulation versus rest, but also by cognitive load. To date, however, it is unclear if and how cognitive load influences these oscillations. Furthermore, because systemic

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(BP) oscillations have been investigated together with cerebral hemodynamics only in a relatively small number of studies, it remains insufficiently known to what extent the effects of cognitive load on cerebral oscillations may be mediated by effects on these systemic oscillations.

In addition to functional activation, slow oscillations may be affected by aging. Schroeter et al. (2004) showed with fNIRS that LFOs (0.07 to 0.11 Hz) of [O_2Hb] and [HHb] in the cerebral microvasculature strongly declined with aging during both rest and visual checkerboard stimulation. VLFOs (0.01 to 0.05 Hz) were not affected by age, but functional stimulation increased VLFOs of [O_2Hb] and [HHb] in young adults and increased VLFOs of [HHb] in older adults. These results might indicate a decline in spontaneous activity in microvascular smooth muscle cells in conjunction with an increase in vessel stiffness in the elderly. Aging is further accompanied by a degradation of the cerebrovascular system encompassing changes in resting cerebral blood flow, vascular reactivity and vascular ultrastructure (Farkas and Luiten, 2001). For example, changes in the ultrastructural integrity of the cerebral vasculature result in a decrease in the elasticity and compliancy of affected vessels, including capillaries, larger arterioles and cerebral arteries (Kalaria, 1996). Accordingly, the diversity of aging-related vascular pathological changes may have a large influence on the cerebral hemodynamic oscillations, and hence on the interpretation of hemodynamic neuroimaging data (D'Esposito et al., 2003).

Recently, spontaneous slow oscillations of the fMRI BOLD-signal have gained much interest. Specifically, it has been suggested that these oscillations reflect spontaneous neuronal activity and that they may play a role in functional connectivity between different brain regions. Accordingly, several studies have focused on inter-regional correlations in slow BOLD oscillations during resting-state and task performance (Fox and Raichle, 2007). Sambataro et al. (2010) investigated slow oscillations (0.03–0.08 Hz) of the fMRI BOLD-signal during performance of the n-back working-memory task. In older adults oscillations were reduced in power in posterior regions of the default mode network in comparison to young adults. With increasing cognitive load (1-back and 2-back versus 0-back), power decreased in both groups, but the power attenuation was smaller in older adults. The authors concluded that older adults show decreased functional connectivity and a decreased ability to suppress slow oscillations of the default mode network. Systemic oscillations were not measured in that study however.

It is relevant to know how the amplitude of the hemodynamic oscillations is affected by different cognitive loads, since aging-related changes in these oscillations are likely to reflect aging-related changes in neurogenic, metabolic or myogenic regulation of microvascular blood flow. This knowledge will contribute to improved analysis and interpretation of hemodynamic neuroimaging data. Therefore, the first aim of this study was to examine interaction effects of age and cognitive load on oscillations of cerebral hemodynamics by using functional near-infrared spectroscopy (fNIRS), a noninvasive neuroimaging technique which is particularly sensitive to the microvasculature.

When analyzing task-related changes in the regional cerebrovascular response, the systemic response is often neglected or assumed to be unchanged. However, Tachtsidis et al. (2008) found significant task-related changes in both regional cerebral hemodynamic and systemic signals during functional activation of the frontal cortex. In some participants, these changes were highly correlated. These results suggest a centrally mediated mechanism influencing both the cerebrovascular and cardiovascular systems. Therefore, the second aim of our study was to examine the impact of age and cognitive activation on BP oscillations. We performed transfer function analysis to gain more insight into the relationship between the task-induced BP oscillations and cerebral hemodynamic oscillations.

Taken together, we hypothesized that not only aging, but also cognitive load may affect slow oscillations of cerebral hemodynamics. To enhance our understanding of the origins of these oscillations, we recorded both cerebral and systemic (BP) oscillations and investigated their possible relationship using transfer function analysis.

Materials and methods

Participants

Fourteen healthy young adults (8 female, mean age = 26.4 ± 3.0 years, range 23–32) and 14 healthy older adults (10 female, mean age = 70.3 ± 4.7 years, range 64–78) participated in this study. Educational level slightly differed between the young (M = 16.7 ± 2.8 years, range 10.5 − 18.0) and older adults (M = 12.6 ± 3.2 years, range 9.0–18.0) (Mann–Whitney U = 33.00, p = .002). All participants completed secondary school or higher. None of the older adults experienced subjective memory problems, all were living independently, and all had unimpaired overall cognitive function as assessed with the Mini Mental State Examination (Folstein et al., 1975; mean score = 29.1 ± 0.9, range 27–30). All participants were right-handed and had normal or corrected-to-normal vision. None of the participants had a history of neurological or psychiatric disease, or used psychopharmacological drugs. Four older adults used antihypertensive medication. All participants refrained from alcohol, caffeine, and nicotine from at least 3 h before the experimental session. The study was approved by the local medical ethics committee and all participants gave written informed consent.

Experimental procedure

The experimental procedure utilized in the present study and the accompanying behavioral results have previously been described in detail by Vermeij et al. (2012). Participants performed two versions of a verbal n-back task; after the 0-back task (control condition) the 2-back task (high working-memory load condition) was realized. This paradigm has reliably and validly been employed in establishing cerebral activity patterns in the prefrontal cortex in relation to increasing working-memory load in fMRI research (Jansma et al., 2000; Owen et al., 2005). The 2-back task places a large demand on a number of key processes within working memory. The 0-back task has regularly been used as control condition to measure attention and alertness without working-memory load. Since the aim of our study was to specifically investigate the effects of working-memory load, and cognitive processes are uncontrolled during resting periods, we decided to use 0-back as control situation instead of rest.

Prior to both conditions, participants practiced the task for 1 min and received feedback about their performance. Both conditions were preceded by a baseline period of 1 min, during which a black fixation cross was displayed at the center of the 15 inch screen. Both conditions consisted of 60 trials, 17 of which were target trials. In each trial, a letter that was randomly selected from a set of 20 consonants was presented in black on a light gray background with a presentation time of 500 ms. Interstimulus interval was 3000 ms. During each trial, participants indicated whether the stimulus was a target by pressing the button under the right index finger, or a non-target by pressing the button under the right middle finger (PST Serial Response Box, Psychology Software Tools Inc., PA, USA). In the 0-back condition, the letter "X" was defined as target. In the 2-back condition, the target was any letter that was identical to the letter presented two trials before, while the letter "X" was no longer shown.

Data acquisition

We used a continuous-wave NIRS device (Oxymon Mk III, Artinis Medical System, The Netherlands), using light of three wavelengths (765, 857, 859 nm), to monitor concentration changes in cortical oxygenated hemoglobin ([O_2Hb]) and deoxygenated hemoglobin ([HHb]) with high temporal resolution. The principle behind fNIRS is that near-infrared light penetrates the skull and brain and is absorbed by the chromophores O_2Hb and HHb, which have different absorption spectra. Assuming constant scattering (Sakatani et al., 2006) and by

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