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Blood flow velocity changes in anterior cerebral arteries during cognitive tasks performance ☆

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ABSTRACT

Objective: Transcranial Doppler sonography (TCD) enables monitoring of blood flow velocities (BFVs) in basal cerebral arteries during different cognitive tasks performance with great temporal resolution. So far, BFVs changes during mental activity were monitored primarily in middle cerebral arteries (MCAs) and little is known about these changes in anterior cerebral arteries (ACAs).
Aim: To determine the effect of different cognitive tasks performance on BFV changes and hemispheric dominance in ACAs and to assess the most suitable activation test for monitoring of BFV changes in ACAs.
Methods: Fourteen right-handed, healthy subjects aged 20–26 were included in the study. BFVs in both ACAs were recorded simultaneously during performance of cognitive tasks designed to activate frontal lobes: phonemic verbal fluency test (pVFT), Stroop tests and Trail Making Tests (TMTs).
Results: A statistically significant BFV increase was recorded in both ACAs during performance of all cognitive tasks. Statistically significant right ACA dominance was found during performance of pVFT and TMTB. The most significant BFV increase was obtained during performance of TMTB.
Conclusion: Our result addressed cognitive tests with great activation potential for monitoring of ACAs that might be used in distinguishing of healthy individuals and patients with neurovascular or neurodegenerative diseases.

1. Introduction

Transcranial Doppler ultrasonography (TCD) noninvasively measures blood flow velocities (BFVs) and pulsatility in main intracranial arteries on a variety of anatomical levels with excellent temporal resolution (Wintermark et al., 2005). In physiological intracranial circumstances, relative cerebral blood flow (rCBF) correlates with relative BFV allowing good insight into regional metabolic demands at the microcirculatory level by measuring BFVs in cerebral arteries (Aaslid, 1987; Aaslid, Markwalder, & Nornes, 1982). TCD enables monitoring of rapid and transient changes of BFVs that cannot be recorded using PET and functional MRI (fMRI) due to their poor temporal resolution. Therefore, TCD has successfully been used in determination of the temporal pattern of BFV changes and hemispheric dominance during the performance of various cognitive tasks (Droste, Harders, & Rastogi, 1989; Duschek & Schandry, 2003; Stroobant & Vingerhoets, 2000). Low spatial resolution determined by the supply territory of each artery is the most important disadvantage of the technique (Wintermark et al., 2005). Many studies have shown an increase in cerebral BFV during the performance of different cognitive tasks (Stroobant and Vingerhoets, 2000; Stroobant & Vingerhoets, 2001). Results of these studies have substantially contributed to the field of functional neuroimaging (Deppe, Ringelstein, & Knecht, 2004; Stroobant & Vingerhoets, 2000; Stroobant & Vingerhoets, 2001).

Numerous studies have investigated BFV changes during the performance of different cognitive tasks in the middle cerebral arteries (MCAs) (Frauenfelder, Schuepbach, Baumgartner, & Hell, 2004; Schuepbach, Boeker, Duschek, & Hell, 2007; Schuepbach, Hell, & Baumgartner, 2005; Schuepbach, Weber, Kawohl, & Hell, 2007; Schuepbach et al., 2002; Schuepbach et al., 2009; Stroobant & Vingerhoets, 2000); however, less is known about BFV changes in anterior cerebral arteries (ACAs). Kelley et al. (1992) have found a significant bilateral increase in BFVs in ACAs during the performance of a mental arithmetic task without any evidence of hemispheric dominance. Varnadore, Roberts, and McKinney (1997) have investigated differences in BFV changes among posterior cerebral arteries (PCAs), MCAs and ACAs during word construction (generating new words from a nine letter word) and anagram

☆ The study was done at the Department of Neurology, University Hospital Centre Zagreb, Zagreb, Croatia.

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solving (five to eight letter anagrams) tasks depending on different answering modes (silently viewing, speaking, and writing). They concluded that "difference scores" of BFVs (BFV during task performance minus BFV during baseline interval) in MCAs were much higher than in ACAs and PCAs regardless on answering mode except during silent performance of word construction task when BFVs in MCAs and ACAs were higher in comparison to BFVs in PCAs. In both studies healthy individuals with heterogeneous handedness were included while in the latter studies only individuals with homogeneous (mostly right) handedness were included. Schuepbach et al. (2002) have investigated the effect of performing Tower of Hanoi and Wisconsin Card Sorting test (tests of prefrontal functions) on cerebral hemodynamics detecting three phases of BFV changes: an initial peak within 5 s, following decrease within 25 s and final steady state starting at 40 s. Finally, they have shown different BFVs during these three phases of each task, but during the steady state of the Tower of Hanoi task BFV was increased compared with the WCST. Frauenfelder et al. (2004) have recorded BFVs in MCAs and ACAs in healthy right-handed volunteers during performance of Stocking of Cambridge task of differing levels of complexity. They did not find significant differences between BFVs in MCAs and ACAs except for the left-sided dominance of the BFV in the ACA during the task performance. Additionally, difficulty of conditions did not influence BFVs in ACAs. Sorond, Schnyer, Serrador, Milberg, and Lipsitz (2008) were aiming to determine the effects of healthy aging on BFVs in ACAs and PCAs during performance of two cognitive tasks: word stem completion (specific executive control task for anterior circulation scanning, similar to phonemic verbal fluency test (pVFT), based on generating new words starting with given three letters) and visual search task (for posterior circulation scanning). They found a significant BFV increases in both ACAs and PCAs in both young and elderly healthy subjects; however higher BFVs in ACAs compared to PCAs during the executive control task was found only in healthy young subjects.

So far, the three cognitive tests used in our research (pVFT, Trail Making Tests (TMTs) and Stroop tests) have not been studied in ACAs. Only pVFT was studied in MCAs trials showing statistically significant increase of BFVs in MCAs with significant left lateralization (Silvestrini, Cupini, Matteis, Troisi, & Caltagirone, 1994; Stroobant, Buijs, & Vingerhoets, 2009; Szirmai, Amrein, Pálvölgyi, Debreczeni, & Kamondi, 2005; Vingerhoets & Stroobant, 1999). Those results are consistent with functional neuroimaging studies showing activation of left dorsolateral prefrontal cortex, premotor cortex, the anterior cingulated cortex and the cerebellum during performance of pVFT (Elfgren & Risberg, 1998; Gaillard et al., 2000; Ravnkilde, Videbech, Rosenberg, Gjedde, & Gade, 2002). The TMTs as tests of visuomotor tracking, divided attention and cognitive flexibility have shown greater activation in right inferior/middle frontal cortices, right precentral gyrus, left angular gyrus/left middle temporal gyrus during performance of second (more complex) part of TMT (TMTB), in comparison with first part of TMT (TMTA) (Jacobson, Blanchard, Connolly, Cannon, & Garavan, 2011; Zakzanis, Mraz, & Graham, 2005). On the other hand, the Stroop test provides information on response inhibition, interference resolution and behavioral conflict resolution (Leung, Skudlarski, Gatenby, Peterson, & Gore, 2000). The Stroop test can elicit a frontal lobe activation, particularly in the left anterior cingulate cortex and dorsolateral prefrontal cortex as well as superior and inferior parietal lobulus bilaterally, the regions implicated in the monitoring of conflict resolution (Adleman et al., 2002; Carter & van Veen, 2007).

The aim of our study was to investigate the performance of different cognitive tasks which were designed to activate frontal lobes on BFV changes and hemispheric dominance in ACAs as well as to assess suitability of cognitive activation tests for monitoring of BFV changes in ACAs.

2. Subjects and methods

2.1. Subjects

The study was conducted at the Department of Neurology, University Hospital Centre Zagreb and was approved by the local Ethics committee. Criteria for inclusion of participants to the study were: right-handedness determined by the standardized EHI (Edinburgh Handedness Inventory) questionnaire (adapted from Oldfield, 1971), age of 20–30 years, normal or adequately corrected visual acuity, no caffeine or nicotine consumption 12 h prior to testing. Left-handedness and medical history of cardiac, neurological or psychiatric disease were exclusion criteria.

2.2. Methods

General information was obtained from each subject (age, medical history, education). Additionally, handedness was determined by using EHI questionnaire. Heart rate (HR), blood pressure and visual analog anxiety scale (VAS) were assessed before and after computer paradigm was performed. Cognitive tasks included in the computer paradigm were explained verbally in detail to subjects prior to testing and instructions were displayed on computer screen before each task. During performance of cognitive tasks (presented on a computer screen), TCD monitoring of BFVs in both ACAs as well as heart rate were performed. Subjects were sitting in a semi-dark, quiet room looking at a computer screen showing the ongoing computer paradigm.

2.3. Experimental paradigm

The paradigm lasted approximately 65 min. It included 5 major tasks and their subtasks. Resting periods were two minutes between each major task and one minute between each subtask. The basal (resting) BFVs were compared to BFVs during the activation phases in order to determine the relative cerebral BFV changes. The paradigm settings had been tested preliminary and resting intervals between tasks and subtasks proved to be sufficient for BFV and heart rate to return to baseline values.

Initial resting period: during this period that lasted 180 s subjects were sitting relaxed watching presentation of conventional screen saver (Starfield, Microsoft Corp., USA). Identical screen saver was presented during all subsequent resting periods (between tasks and subtasks).

Breath Holding Test (BHT): BHT is a valuable screening test for vasomotor reactivity. Patients were asked to hold their breath for up to 30 s and then breathe normally afterwards. The breath holding index (BHI) was calculated by the following equation: $BHI = (MBFV_{end} - MBFV_{ref})/t$; $MBFV_{end}$ being the mean BFV (MBFV) at the end of breath holding, $MBFV_{ref}$ being the MBFV during the -15 to -3 s prestimulus period of the resting interval (Knecht, Deppe, Ringelstein, Wirtz, Lohmann, & Drager, et al., 1998; Knecht, Drager, Deppe, Bobe, Lohmann, & Floel, et al., 2000), and t being the duration of breath holding in seconds. Only patients with BHI between 1.03 and 1.65 were included in the study (Zavoreo & Demarin, 2004). This phase was followed by a 120 s-lasting resting period.

Phonemic verbal fluency test (pVFT): during the first cognitive task the subjects were instructed to whisper as many words as they could recollect in 25 s beginning with the given letter (proper names excluded). Five seconds later they were instructed to say out loud the number of whispered words (Szirmai et al., 2005). This task comprised a rehearsal subtask and ten subtasks, differing by the letter set. Each subtask was followed by a 1-min resting period (Fig. 1).