ELSEVIER

Clinical Neurophysiology 116 (2005) 1041–1048

www.elsevier.com/locate/clinph

# Lateralization of cerebral hemodynamics during Wisconsin Card Sorting Test: a functional transcranial Doppler sonography study

Daniel Schuepbach[a,*], Daniel Hell[a], Ralf W. Baumgartner[b]

[a]*Psychiatric University Hospital, Zurich, P.O. Box 68, 8029 Zurich, Switzerland*
[b]*Department of Neurology, University of Zurich, Zurich, Switzerland*

Accepted 16 December 2004
Available online 1 February 2005

**Abstract**

**Objective**: Studies on lateralization of cerebral metabolism during Wisconsin Card Sorting Test (WCST), a well-known paradigm of category learning, have shown mixed results. Moreover, sorting dimension (number, color and shape) is a cofounder of laterality in WCST. Functional transcranial Doppler sonography (fTCD) has a high temporal resolution and allows the measurement of mean cerebral blood flow velocity (CBFV) in the middle (MCA) and anterior cerebral arteries (ACA), which supply lateral and medial parts of the frontal and parietal lobes, respectively. We used fTCD to investigate CBFV changes occurring in both MCA and ACA during WCST and different sorting dimensions.

**Methods**: Twenty-one subjects underwent twice two distinct phases of the WCST, namely maintaining a rule (maintaining set) and searching for a new rule (set shifting), during bilateral fTCD of the MCA and ACA.

**Results**: There was a left-sided dominance of CBFV during maintaining set and set shifting in the MCA. CBFV was not associated with test performance. The sorting dimension number caused the highest CBFV increase in both MCA and ACA during maintaining set, and the sorting dimension shape caused lowest CBFV decrease in both MCA during set shifting.

**Conclusions**: This study confirms results that cerebral blood flow (CBF) lateralizes to the left side during WCST. The 3 sorting dimensions provoked distinct processing speed during maintaining set and set shifting, but caused no effect on hemispheric lateralization.

**Significance**: Functional transcranial Doppler sonography can be used to assess CBFV during WCST and different sorting dimensions, and the latter modulate reaction time and cerebral hemodynamics.


*Keywords:* Asymmetry; Category learning; Frontal lobe; fTCD; Wisconsin Card Sorting Test

## 1. Introduction

The Wisconsin Card Sorting Test (WCST) (Grant and Berg, 1948) has been widely used to assess frontal lobe function (Retzlaff et al., 1992). Lesions of the lateral frontal cortex may lead to impaired performance during set shifting in both animals (Dias et al., 1996; Passingham, 1972) and humans (Milner, 1963, 1971; Rogers et al., 1998). Furthermore, recent brain imaging studies have demonstrated an increased activity of the lateral frontal cortex during set shifting (Barceló et al., 1997; Konishi et al., 2002; Monchi et al., 2001; Nagahama et al., 1996; Rogers et al., 2000). It has been shown that that the WCST activates parietal and fronto-temporal areas (Barceló et al., 1997; Berman et al., 1995). There has been some debate whether set shifting stimulates predominantly one hemisphere or both hemispheres equally. Using event-related functional magnetic resonance imaging (fMRI), Monchi et al. (2001) found a bilateral activation of the dorsolateral prefrontal cortex (DLPFC) during set shifting, whereas Volz et al. (1997) observed dominance of the right hemisphere. However, this latter report did not use a high temporal resolution, leaving the possibility that defined phases of WCST did or did not follow a right hemispheric dominance. In a study with event-related potentials (ERPs), Barceló et al. (1997) found left fronto-temporal asymmetry during

* Corresponding author. Tel.: +41 384 21 11; fax: +41 1 383 44 56.
*E-mail address:* daniel.schuepbach@puk.zh.ch (D. Schuepbach).

1388-2457/$30.00 
doi:10.1016/j.clinph.2004.12.014

early WCST trials, which was assumed to be due to the activation of the left DLPFC. These authors suggested that those changes reflected activation of the left DLPFC, because this structure may be more important than the right DLPFC for solving WCST (Corcoran and Upton, 1993). Nagahama et al. (1996) measured regional cerebral blood flow (rCBF) changes during WCST, and assessed subjects' performance by a task that provoked selective attention towards one of the 3 stimuli color, number or shape. Activation of the DLPFC was predominant on the left side when subjects had to sort according to color or number, and bilateral during sorting according to shape. These findings implied that selective attention to distinct sorting dimensions may activate different areas in the brain, and hence may be another relevant contribution to the multi-faceted nature of the WCST.

Our group has used functional transcranial Doppler sonography (fTCD) to assess CBF changes in the territories of the middle (MCA) and anterior (ACA) cerebral arteries during prefrontal challenge (Frauenfelder et al., 2004; Schuepbach et al., 2002a, 2004). Prefrontal stimulation was obtained by several tasks such as the WCST, the Tower of Hanoi puzzle (TOH) (Simon, 1975) and the Stockings of Cambridge (SOC) (Owen et al., 1990), a related procedure to the Tower of London paradigm (Shallice, 1982). The particular strength of fTCD consists in the high resolution in time, allowing discriminating alterations in peak mean CBF velocity (CBFV) during specific phases of tasks, such as maintaining a rule (maintaining set) and search for a new rule (set shifting) in the WCST. Since fTCD has been used to examine hemispheric differences of CBFV during a variety of physiological conditions (for review see Stroobant and Vingerhoets, 2000), we wanted to investigate lateralized CBFV patterns of MCA and ACA during maintaining set and set shifting of WCST, also with reference to sorting dimensionality. It is important to note that the MCA supplies the lateral hemisphere of the frontal and parietal lobes, whereas the territory of the ACA includes the medial part of the hemisphere including the frontal pole and also cingulated gyrus (Tatu et al., 1998).

In this study we investigated whether (1) WCST increases CBFV in the territory of the left MCA or ACA, (2) sorting dimension is a confounder of the presumed CBFV increase and affects hemispheric difference of CBFV.

## 2. Methods

### 2.1. Subjects

Twenty-one, right-handed healthy subjects (11 men, 10 women) with a mean age of $28.5 \pm 5.7$ years were included in this study. Subjects were excluded from this study, if they (1) presented a history of brain trauma, (2) showed a history of medical or neurological disease, (3) underwent neuropsychological testing within the last 3 months, and (4) slept less than 7 h in the night before of the present study. The local ethical committee approved the study, and all subjects gave written informed consent.

### 2.2. Technical procedures

Doppler measurements were performed with a Multi-Dop TCD X4 instrument (DWL Elektronische Systeme GmbH, Sipplingen, Germany). Two dual 2 MHz transducers were attached and fixed with a headband. Both MCAs were insonated at depths of 48–55 mm and both ACAs at depths of 60–70 mm through the temporal bone window (Aaslid et al., 1982; Ringelstein et al., 1990; Von Reutern et al., 2000). CBFV was assessed in all examined vessels. The sequence of insonation was predetermined, starting always with the MCAs, because anxiety may alter CBF in ACAs (Kelley et al., 1992). The distance between the participant and the test-monitor was 1 m, adjusted to the height of the subject's eyes. All measurements were conducted in a quiet room with dimmed light. Additional parameters like end-tidal $pCO_2$, heart rate and blood pressure were not registered, as they only show a negligible influence on CBFV in the basal cerebral arteries during cognitive and sensorimotor challenges (Valdueza et al., 1997). A second monitor, which showed a standard screen saver program (flying stars for Microsoft Windows—lowest speed, 30 stars) (Microsoft Corp., USA), was positioned beside the test screen (Schuepbach et al., 2002a).

### 2.3. Wisconsin Card Sorting Test

The WCST was presented through a conventional 15 in. computer display, with 4 cards at the top and a staple of cards at the bottom, always depicting symbols on the top card. The top card had to be attributed to one of the 4 cards according to one of the rules of color, shape and number, and feedback was given through a high (i.e. correct) or low (i.e. false) pitched tone. After 10 correct card sorts representing one category was achieved, the matching principle was tacitly altered. Each category was presented twice until a maximum of 6 categories were achieved or a maximum of 128 trials. The subject controlled card sorting by means of a conventional computer keyboard, using their fingers of the right hand on the numeric block (keys 1, 2, 3, 4 that indicated the 4 possible target positions on the computer screen). They were instructed to sort the cards as swiftly as possible. The following performance variables were considered: numbers of categories, percentage of perseverative errors, reaction time (RT) of 2nd and 3rd trials as means of set shift, and RT of 9th and 10th correct trials as means of maintaining set.

Motor and visual activity during WCST was controlled by a visuomotor control test (Schuepbach et al., 2002b). Briefly, subjects were asked to press the same keys (number 1–4 of the numeric block on the keyboard), with the same