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Differential prefrontal and frontotemporal oxygenation patterns during phonemic and semantic verbal fluency

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ABSTRACT

Movement artifacts are still considered a problematic issue for imaging research on overt language production. This motion-sensitivity can be overcome by functional near-infrared spectroscopy (fNIRS). In the present study, 50 healthy subjects performed a combined phonemic and semantic overt verbal fluency task while frontal and temporal cortex oxygenation was recorded using multi-channel fNIRS. Results showed a partial dissociation for phonemic and semantic word generation with equally increased oxygenation in frontotemporal cortices for both types of tasks whereas anterior and superior prefrontal areas were exclusively activated during phonemic fluency. Also, a general left-lateralization was found being more pronounced during semantic processing. These findings line up with earlier imaging and lesion studies emphasizing a crucial role of the temporal lobe for semantic word production, whereas phonemic processing seems to depend on intact frontal lobe function.

1. Introduction

Over the past decades, optical topography has become a valuable tool to investigate the neural correlates of language function, especially those of overt speech. Although functional magnetic resonance imaging (fMRI) studies also succeeded in this task (e.g. Birn et al., 2010), the amount of literature using functional near-infrared spectroscopy (fNIRS) is comparably immense (for recent reviews see Dieler, Tupak, & Fallgatter, in press; Quaresima, Bisconti, & Ferrari, in press). Similar to fMRI, fNIRS relies on the principle of neurovascular coupling which is accompanied by increased oxygenation of local tissue during brain activation (for the effect of genetic variation on neurovascular coupling, see e.g. Hahn et al., 2011). These ongoing changes in cortical blood oxygenation can be tracked by means of two parameters instead of just one as for fMRI, oxygenated and deoxygenated hemoglobin (O_2Hb and HHb). While local O_2Hb levels increase as a result of a greater oxygen demand during enhanced brain activation, HHb levels simultaneously decrease (Obrig & Villringer, 2003). Compared to fMRI, fNIRS offers two core advantages for the study of overt speech production: its insensitivity to movement artifacts and the relatively quiet measurement procedure.

Phonemic and semantic word processing has been extensively studied in patients with focal brain damage by means of verbal fluency tasks (VFT). During this task, subjects are asked to retrieve words with certain phonemic or semantic properties, e.g. words beginning with a given letter or words belonging to a certain semantic category. Strategies for phonemic word generation depend on phonemic cues (e.g. clustering response items according to initial syllables instead of relying on the initial letter alone) and rather correspond to lexical search criteria. During semantic verbal fluency (VF), subjects tend to group response items according to conceptual representations and subcategories (e.g. listing vegetables instead of selectively naming food products), thus referring to their meaning (Troyer, Moscovitch, & Winocur, 1997). These search strategies effectively support performance and pose the question whether the semantic and phonemic system for word generation might depend on distinct neural substrates.

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In fact, deficits in semantic VF have been associated predominantly with lesions to the temporal lobe, whereas phonemic VF depended rather on frontal brain regions though activating the temporal lobe as well (for a meta-analysis see Henry & Crawford, 2004). Also within the fNIRS literature, numerous reports exist showing both enhanced frontal and temporal activation during phonemic and semantic VF compared to e.g. an automated syllable repetition task or other comparable control tasks (e.g. Kono et al., 2007; Schecklmann, Ehlis, Plichta, & Fallgatter, 2010).

With respect to the vast amount of fNIRS literature, only few VF fNIRS studies directly contrasted both VF conditions. Two studies reported generally weaker O_2Hb changes for semantic VF in healthy control subjects (Ehlis, Herrmann, Plichta, & Fallgatter, 2007; Kubota et al., 2005) while Kubota et al. (2005) also observed a specific deficit in the semantic system in schizophrenic patients, again supporting the notion of differential neural circuits accounting for each task. Regarding effects of cortical spatiality, especially laterality, these earlier studies suffered from technical shortcomings such as limited amounts of measurement channels resulting in restricted regions of interest (ROI), rarely covering both bilateral frontal and temporal regions (e.g. only left-hemispheric ROI in the study of Ehlis et al., 2007; only 2 measurement channels in the study of Kubota et al., 2005). Despite the invention of multi-channel apparatuses allowing for bilateral large ROIs or even whole-head measurement devices, no recent study tested for left-lateralization or cortico-spatial dissociations of task-related activity as revealed by earlier imaging and lesion studies (Baldo, Schwartz, Wilkins, & Dronkers, 2006; Mummery, Patterson, Hodges, & Wise, 1996). Since there is evidence for increased left over right O_2Hb levels during phonemic VF (Herrmann, Walter, Ehlis, & Fallgatter, 2006; Schecklmann, Ehlis, Plichta, & Fallgatter, 2008), the present study investigated possible interaction effects between hemisphere, brain region, and type of VF in a sample of healthy subjects. First, we aimed to replicate earlier findings of left-lateralization and more pronounced parameter changes during phonemic compared to semantic VF, reflecting greater difficulty during lexical than conceptual word retrieval. Second, we hypothesized that dissociable cortical activation patterns can also be observed by means of fNIRS in prefrontal compared to frontotemporal regions for phonemic and semantic VF, respectively.

2. Materials and methods

2.1. Subjects

Fifty-one right-handed subjects (mean age 23.14 years, ±2.59, 17 male) gave written informed consent and were free of any psychiatric, neurological, or cardiovascular disease and medication as revealed by a brief screening questionnaire based on the Structured Clinical Interview for DSM-IV axis I disorders (First, Spitzer, Gibbon, & Williams, 2002). Subjects' verbal intelligence (mean 118.10, ±12.19) slightly exceeded the normal range as assessed with a multiple choice vocabulary test (Lehrl, 1995). One subject had to be excluded from further analyses due to technical problems during fNIRS data recording. The current study was approved by the ethics committee of the University of Wuerzburg and in agreement with the latest revision of the declaration of Helsinki from 2008.

2.2. Verbal fluency task

Two VFT versions were used in a counterbalanced block design. Subjects were asked to retrieve German nouns beginning with a certain letter (phonemic VF version 1: /A/, /F/, /S/; version 2: /G/, /P/, /E/) or items belonging to a certain category (semantic VF version 1: /animals/, /fruits/, /flowers/; version 2: /clothes/, /sports/, /occupations/). For the control condition subjects consecutively repeated the days of the week and were eventually instructed to slow down by the experimenter to approximately match the number of items named in the experimental conditions. Conditions were sequentially ordered starting with a phonemic VF block, followed by a control block, and ended with a semantic VF block. Each block lasted 30 s and was followed by 30 s of rest. This sequence was repeated three times, totaling 9 blocks interleaved with 9 periods of rest. The first experimental block was additionally preceded by a 10 s baseline measurement. Short task instructions were provided verbally by the experimenter during the last three seconds of the previous block (i.e. baseline or resting block) and a stop signal was given at the end of each VF block.

2.3. Functional near-infrared spectroscopy

Changes in frontal oxygenation parameters O_2Hb and HHb were measured with a 52-channel continuous wave system (ETG-4000, Hitachi Medical Corporation, Tokyo, Japan) at a sampling rate of 10 Hz. A 3×11 probeset including 17 semiconductive laser diodes (wavelengths: 695 ± 20 and 830 ± 20 nm) and 16 photo detectors was adjusted with elastic straps over the subjects' forehead centering the middle probe of the most inferior row over Fpz according to the international 10–20 system for electroencephalographic electrode placement (Jasper, 1958). Measurement channels covered large areas of the PFC, motor and premotor regions, and superior temporal cortex (Fig. 1).

2.4. Data analyses

2.4.1. Task performance

The number of correct words named for each condition was averaged and compared by repeated measures analysis of variance (ANOVA).

2.4.2. Functional near-infrared spectroscopy

Online changes in O_2Hb and HHb were transformed into relative changes using a modified version of the Beer–Lambert law (Obrig & Villringer, 2003). A cosine and moving average filter with a time window of 5 s were applied to remove slow drifts and the high frequency portion of the data. Since overt speech may be accompanied by considerable movement artifacts, a recently proposed correlation based signal improvement (CBSI) method was applied (Cui, Bray, & Reiss, 2010). The recommended algorithm is based on the assumption that in an ideal experimental situation O_2Hb and HHb signals should be strongly negatively correlated, whereas motion results in less negative and more positive correlation. The algorithm calculates a new signal by maximizing the negative correlation between observed O_2Hb and HHb data, thereby eliminating noise from the data and improving signal quality (for detailed information see Cui et al., 2010). This method has also been applied in a recent fNIRS study by our group (Dresler et al., 2012).

During first-level single-subject analyses mean activation per subject, channel and condition was calculated by averaging the signal time course over each block starting 3 s after the instruction given by the experimenter (i.e. from sec 3 until the end of each block). Values were baseline-corrected by subtracting the mean value of the first 0.5 s of the selected segment.

During second-level group analyses all conditions were contrasted against each other in a channel-wise manner by means of paired-samples *t*-tests. To control for multiple testing, Bonferroni corrections were applied. More detailed analyses, investigating effects of brain region, laterality, and task, were performed by using repeated measures ANOVA. ROIs included left and right prefrontal cortex on the one hand and inferior frontal, middle and superior temporal cortex on the other hand (http://brain.job.affrc.go.jp/wordpress/, accessed 07.09.11; for a detailed setup see Fig. 1). Oxygenation parameters during both conditions were corrected for activation changes due to speech-induced muscle activity by subtracting respective signal changes of the control condition. The alpha level of significance was set to 0.05 and trends were reported at a level of 0.10. Again, for post hoc tests, Bonferroni corrections were applied if necessary.

3. Results

3.1. Task performance

The average amount of produced words significantly differed between conditions ($F_{(2,98)} = 142.40$, $p < .0001$, $\eta_p^2 = .74$; Huynh–Feldt corrected). Subjects produced less words during phonemic ($\bar{x} = 8.03$) than semantic VF ($\bar{x} = 13.98$; $p < .0001$) or the control task ($\bar{x} = 14.10$; $p < .0001$). No significant difference was found between semantic VF and the control condition.

3.2. Functional near-infrared spectroscopy

3.2.1. Overall contrasts

Contrasting experimental VF conditions against the control task resulted in increased levels in 49 channels for phonemic and 27 channels for semantic VF. Phonemic compared to semantic VF revealed increased levels in 33 channels (all $p < .001$, Bonferroni corrected). While during phonemic VF the entire frontal cortex was activated, semantic VF required less anterior and superior prefrontal areas (see Fig. 1).