

## **EXPLORING PREFRONTAL CORTEX OXYGENATION IN SCHIZOPHRENIA BY FUNCTIONAL NEAR-INFRARED SPECTROSCOPY**

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### **1. INTRODUCTION**

The specific nature of frontal lobe dysfunction in schizophrenia remains unclear. However, impairments in working memory have been proposed to underlie various cognitive and functional deficits in schizophrenia. So far, one of the most well-studied cognitive deficits in schizophrenia is that of impaired verbal fluency which some have argued is primarily due to dysfunction in access and/or retrieval of lexical information, while others have maintained that the primary defect is in the organization of the semantic memory. The verbal fluency task (VFT) is a neuropsychological task which permits assessment of the subject's ability to retrieve nouns based on a common criterion. The letter-fluency version is based on a phonological criterion, requiring the subject to pronounce as many words as possible beginning with a certain letter. Performances have been regarded to be mainly associated with frontal lobe function, particularly the left hemisphere. An attenuated frontal activation during a VFT has been demonstrated in patients with schizophrenia by functional magnetic resonance imaging (fMRI).<sup>1</sup>

Considering the several advantages of using functional near-infrared spectroscopy (fNIRS) over fMRI for performing cognitive studies, we aimed at assessing bilateral prefrontal cortex (PFC) oxygenation changes in response to VFT in schizophrenia patients and controls. We hypothesized that patients would have a PFC hypoactivation with respect to controls.

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## 2. METHODS

All the subjects participating in this study (approved by the Ethical Committee of the University of L'Aquila) were right-handed. The school education was  $12.3 \pm 1.1$  and  $13.5 \pm 2.7$  years for patients ( $n=9$ ) and controls ( $n=9$ ), respectively. The subjects with schizophrenia were diagnosed according to Diagnostic and Statistical Manual of Mental Disorders (fourth edition) established by a psychiatric evaluation. All patients were receiving medication; four (# 1, 5, 6 and 9) were receiving typical neuroleptic; four (# 2, 4, 7 and 8) were receiving atypical neuroleptic, and one (# 3) both typical and atypical neuroleptic. The dosage of antipsychotic drugs, calculated as equivalent to chlorpromazine, was  $709 \pm 551$  meq/die. The control subjects had no history of substance abuse or other medical, psychiatric or neurological disorder that might affect brain function.

A 2-min letter version of the VFT was adopted in this study.<sup>2</sup> Following a 2-min baseline, subjects were asked to produce aloud (overt speech) as many nouns as possible (within the allocated 120 s) beginning with the letters "S", "P", "F", "C" (acoustically presented at time 0, 30, 60, 90 s, respectively). No repetitions or proper nouns were permitted. Corrected responses were recorded for each subject. As control task, subjects were requested to listen to a 2-min story.

For fNIRS measurements the four-wavelength NIRO-300 oximeter (Hamamatsu Photonics, Japan) equipped with 2 channels was employed. Each optical probe (consisting of a source and a detector 5 cm apart) was placed and fixed (by double-sided adhesive sheet) over Fp1 (left) and Fp2 (right) of the 10-20 system for the EEG electrode placement. All measurements were performed on control subjects and patients seated in a comfortable chair in a quiet room. Concentration changes (expressed in  $\Delta\mu\text{M}\cdot\text{cm}$ ) of oxyhemoglobin ( $\text{O}_2\text{Hb}$ ) and deoxyhemoglobin (HHb) were collected (sampling frequency: 6 Hz) before, during and after VFT execution, and transferred on-line to a computer for storage and subsequent analysis.  $\Delta\text{O}_2\text{Hb}$  and  $\Delta\text{HHb}$  values, expressed in  $\mu\text{M}$ , were obtained dividing  $\Delta\text{O}_2\text{Hb}$  and  $\Delta\text{HHb}$  ( $\Delta\mu\text{M}\cdot\text{cm}$ ) by the optical pathlength corrected for age. Simultaneous measurement of heart rate was obtained by pulse oximetry (N-200; Nellcor, Puritan Bennett, St. Louis, MO, USA) with the sensor attached to the index finger of the subject's right hand.

The amplitude of  $\text{O}_2\text{Hb}$  and HHb task-related changes in PFC was calculated by the difference between the rest condition (mean value over the 1.5-2 min baseline) and the end of each letter interval of VFT (mean value over the last 5 s). The mean and standard deviation of  $\text{O}_2\text{Hb}$  and HHb values within left and right PFC were determined separately and compared. The paired  $t$  test was used to compare the  $\text{O}_2\text{Hb}$  or HHb values in both hemispheres within each group and between groups. Comparisons between the performance of controls and patients in the VFT were performed with the two-tailed  $t$  test. Statistics was performed by a SPSS software version 10.0 (SPSS, Chicago, IL, USA). The criterion for significance was  $P < 0.05$ .

## 3. RESULTS

No difference in education, age at the onset or duration of illness was found among medicated patients. During VFT, the controls achieved an average of  $35.1 \pm 0.7$  correct responses for the 4 letters, and the performance was almost constant over the 4-letter condition ( $S=8.3 \pm 1.7$ ,  $P=8.1 \pm 2.1$ ,  $F=8.9 \pm 2.8$ ,  $C=9.8 \pm 2.1$ ). The subjects with schizophrenia achieved an average of  $20.2 \pm 0.4$  correct responses for the 4 letters, with a