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Fast cerebral functional signals in the 100 ms range detected by frequency-domain near-infrared spectroscopy

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Introduction
Using non-invasive near-infrared spectroscopy (NIRS) fast changes in the range of milliseconds in the optical properties of cerebral tissue have been described, which are associated with brain activity [1]. This signal is small and related to changes in light scattering due to alteration in the refractive index at neuronal membranes [2]. We obtained functional maps of this fast signal in the visual cortex during visual stimulation with a new type of sensor, the τ-sensor.

Material and methods
We used a frequency-domain tissue oximeter (modified model no: 96208 Omnia ISS Champaign IL USA). The light intensity of the laser diodes was modulated at 110MHz and the amplitude (AC) and the phase of the modulated optical signal was measured.

The τ-sensor is called τ-sensor because it involves the product (τ) of the signals collected by two crossed source-detector pairs (distance 2.8cm). These two signals are discriminated using laser diodes at two different wavelengths (670nm and 830nm) and light filters at the detectors. This sensor strongly reduces the sensitivity to fluctuations near the surface and is more sensitive to signals referring to deeper regions of tissue [3]. The data was recorded at a sample rate of 80Hz.

Measurement protocol
The subject was lying in front of a checkerboard in a dark environment. The τ-sensor was sequentially positioned at 8 different locations (4 on each hemisphere) on the head above the visual cortex. For each location 20 cycles, each including the following sequence were carried out: (1) 10s checkerboard on, (2) 20s checkerboard reversing at 5Hz and (3) 30s checkerboard turned off.

Control-data were obtained from a solid medium of approximately the same optical properties as the human head.

Data analysis
The normalized product of the two source-detector pairs was taken. All reversing periods were averaged together in order to better detect the fast signal. The same averaging was performed for the periods without stimulation (checkerboard turned off). The control-data from the solid medium were analyzed in the same way.

There were 16 samples per reversing period. The first 3 samples were used as a reference for a paired t-test. It was tested whether the subsequent samples differed significantly from the reference samples.

Subject
The volunteer was a 35 years old female. Written informed consent was obtained.

Results
In the eight locations measured, we have neither observed a significant increase in the AC nor a decrease in the phase in response to the stimulus. In four locations (3 on the right, 1 on the left hemisphere) significant decreases in the AC-signal were found starting at 50ms, 50ms, 125ms and 100ms after the onset of the stimulation.

In two locations (both on the left hemisphere) significant increases in the phase were detected. They appeared 75ms and 150ms after the onset of the stimulation. One location showed a significant change in the AC as well as in the phase. For the periods without stimulation 6 samples in 2 locations with significant changes were detected in the AC as opposed to 20 samples in 4 locations during stimulation. In the phase we found 3 significant samples in one location during the period without stimulation, as opposed to 6 significant samples in two locations during stimulation.

The measurement on a solid medium showed, that the instrumental noise was at least 100 times smaller than the signal detected in vivo.

Discussion
We believe that the detected fast signal is not an artifact because the measurement on the solid block did not show such signals. The clear difference between the periods without and with stimulation indicates that the fast signal can be measured. This is further confirmed by the fact that the detected changes always had the same direction.

The significant changes in AC and phase did not always occur at the same locations. This can be explained by taking into consideration that the phase signal originates from deeper tissue layers than the AC signal.

The different locations on each hemisphere were only 5 mm apart. The fast signal was clearly detected in one location, but not in an adjacent one. This shows that the fast signal is highly localized and that the τ-sensor approach of NIRS provides a high spatial resolution.

Separate analysis of the signal of each source-detector pair (without the product of the signals) gives a much lower signal-to-noise ratio and the fast signal is difficult to discern.

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