Fractional amplitude of physiological fluctuations of resting state fNIRS in Alzheimer's disease patient and healthy control

Hany Ferdinando[*a,b], Sadegh Moradi[c], Vesa Korhonen[a,d], Vesa Kiviniemi[a,d], Teemu Myllylä[a,c]
[a]Research Unit of Health Science and Technology, Faculty of Medicine, University of Oulu, Finland; [b]Department of Electrical Engineering, Petra Christian University, Indonesia;
[c]Optoeletronics and Measurement Technique Research Unit, University of Oulu, Finland;
[d]Department of Radiology, Oulu University Hospital, Finland

ABSTRACT

Functional magnetic resonance imaging (fMRI) is a common medical device to diagnose Alzheimer's disease (AD), but it is not for all subjects due to its cost and other issues. We investigated the potential of functional near-infrared spectroscopy (fNIRS) to separate AD patients from controls as a pre-screening prior to more thorough examination using fMRI. For this purpose, two-channel fNIRS device with 690 nm and 830 nm, sampled at 10 Hz, was placed on the forehead with 3 cm distance between light source and detector to provide resting state fNIRS signals from both sides of pre-frontal cortex. We applied fractional amplitude of physiological fluctuation (fAPF), modified from fractional amplitude of low frequency fluctuation (fALFF), to oxy-, deoxy-, and total-hemoglobin in very low frequency (0.008-0.1 Hz), respiratory (0.1-0.6 Hz), and cardiac (0.6-5 Hz) bands. A t-test at 0.05 significance level was used to evaluate if the fAPF score from AD patients and healthy controls is significantly different. We found that fAPF score of total hemoglobin from both side at cardiac band showed its potential to distinguish AD patients from healthy controls. This finding was in-line with the recent finding that heart failure may co-occur in AD patients with the prevalence of one third of cases.

Keywords: Alzheimer, fAPF, fNIRS, hemodynamics, fMRI, power spectral density

1. INTRODUCTION

Alzheimer's disease (AD) is one of the neurodegenerative diseases (NDDs), which brings high burden on global healthcare. It is characterized as the accumulation of amyloid-β plaques along with hyperphosphorylated tau tangles in degenerating neurons and periarteriolar structures[1]. Non-invasive evaluation of potential AD involves functional magnetic resonance imaging (fMRI)[2], nuclear imaging devices such as positron emission tomography (PET) and single photon emission computed tomography (SPECT)[3], cerebrospinal fluid analysis[4], which is relatively expensive and require highly trained persons. The solution is to have an affordable device and method to assess the potential of AD development in patients. More detail assessment can be done with fMRI or other devices when there is an indication of AD development. Thus, we investigated the potential of functional near-infrared spectroscopy (fNIRS) to separate AD patients from healthy controls as a pre-screening prior to more thorough examination using fMRI.

A method called fractional amplitude of low frequency fluctuation (fALFF) has been applied to blood oxygen level dependent (BOLD) signal recorded from resting state fMRI in post-stroke depression study[5]. fALFF was proposed as the ratio of power spectrum within 0.01-0.08 Hz band over the entire frequency range[6]. Using similar idea, we extended this method to respiratory (0.1-0.6 Hz) and cardiac band (0.6-5 Hz). For low frequency band, we chose very low frequency (VLF) band, 0.008-0.1 Hz, which is associated to vasomotor response. Hence, we called this extended version as fractional amplitude of physiological fluctuation (fAPF). We aim to evaluate if this method is also applicable to resting state fNIRS.

[*] hany.ferdinando@oulu.fi; oulu.fi

2. MATERIALS AND METHOD

This study involved 23 subjects and nine of them were AD patients (62.7 ± 1.7, 3 males), while the rest age-matched healthy control (61.9 ± 4.2, 8 males). The AD patients were verified based on the evaluation of Aβ42, tau and phospho-tau and/or functional neuroimaging by fluorodeoxyglucose positron emission tomography (FDG-PET). The control subjects were interviewed and performed mini mental state exam (MMSE) prior to the measurements. Based on the MMSE score, AD patients were in mild AD stage. Any healthy controls with psychiatric or neurological disorder were excluded from the measurement

We measured raw NIRS signal, sampled at 10 Hz, from both sides of pre-frontal cortex of the subjects using 690 nm and 830 nm light with 3 cm distance between light source and detector. The measurement was conducted inside the MRI scanner for five minutes, so the subjects were in supine position and the motion artefact was minimal.

Both oxy- and deoxy-hemoglobin, HbO and HbR respectively, concentration changes were calculated using modified Beer-Lambert law with the following extinction coefficients: 690nm: HbR: 2.1382, HbO: 0.3123; and for 830 nm: HbR: 0.7804, HbO: 1.0507[7]. We also included total hemoglobin (HbT), as a sum of HbO and HbR, in the analysis.

We calculated power spectral density (PSD) using periodogram on the selected band, VLF (0.008-0.1 Hz), respiratory (0.1-0.6 Hz), and cardiac (0.6-5 Hz) bands. Then, the fAPF score for each band was calculated by dividing PSD from particular band with that from the whole band. We applied fAPF to HbO, HbR, and HbT and evaluated if fAPF scores from AD patients and controls were different. For this purpose, we used t-test with 0.05 significant level.

3. RESULTS AND DISCUSSION

Figure 1 shows the bar charts from both groups at different bands and the whiskers represent the standard deviation. The bar charts in every band have similar shape, e.g., controls were always higher than AD patients in both VLF and respiratory bands for all concentration, while we got the opposite results from cardiac band.

Furthermore, the significant difference occurred at both sides for fAPF from HbT cardiac was another finding. It might confirm the hypothesis about a potential "head-to-heart" link in AD as a reduction in cerebral perfusion, particularly in the form of reduced systolic function[8]. Cerebral hypoperfusion may lead to formation of tau-containing neurofibrillary tangles and amyloid-β plaques. In addition, it also causes a metabolic energy crisis of the brain cells, which leads to increase neurofibrillary tangles[9]. Based on this hypothesis, the cardiac pulsation in AD patients may be altered [10] and fAPF is able to reveal it. Recent findings showed that heart failure may co-occur in AD patients with the prevalence of one third of cases[11].

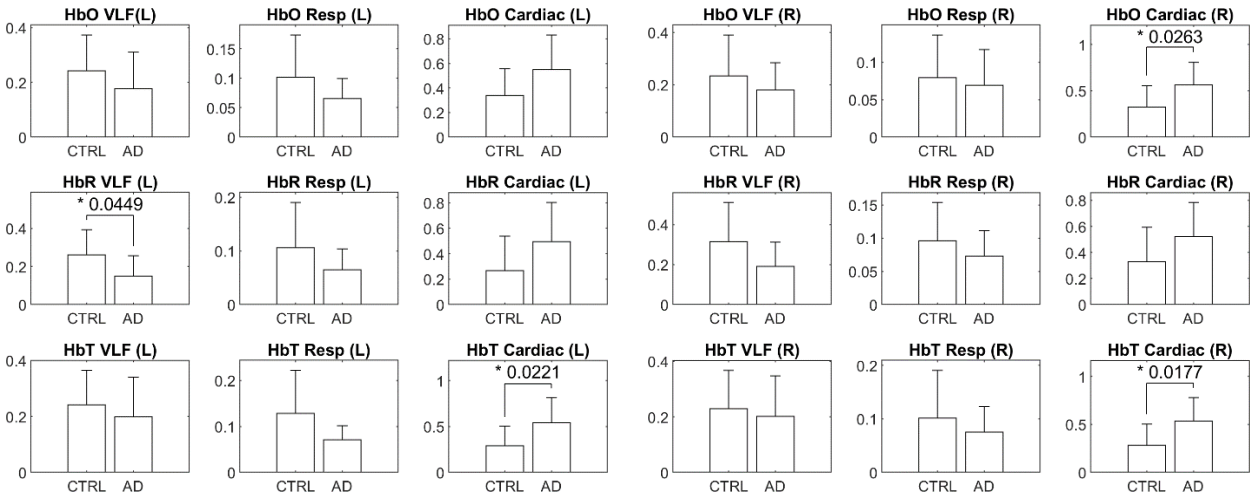

Figure 1. Bar chart with standard deviation of the fAPF score for each concentration at different bands from both sides of pre-frontal cortex.

Based on the MMSE score, all AD patients are in a mild stage and fAPF score from HbT cardiac was able to characterise these two groups differently. It demonstrated the potential of this approach for further exploration using more subjects. In addition, the significant difference from HbO cardiac was found from right hemisphere only. Looking at the detail analysis, p-value from HbO cardiac left hemisphere was slightly over 0.05. More data is needed to validate this phenomenon.

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