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A novel GLM-based method for the Automatic IDentification of functional Events (AIDE) in fNIRS data recorded in naturalistic environments

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ABSTRACT

Recent technological advances have allowed the development of portable functional Near-Infrared Spectroscopy (fNIRS) devices that can be used to perform neuroimaging in the real-world. However, as real-world experiments are designed to mimic everyday life situations, the identification of event onsets can be extremely challenging and time-consuming. Here, we present a novel analysis method based on the general linear model (GLM) least square fit analysis for the Automatic IDentification of functional Events (or AIDE) directly from real-world fNIRS neuroimaging data. In order to investigate the accuracy and feasibility of this method, as a proof-of-principle we applied the algorithm to (i) synthetic fNIRS data simulating both block-, event-related and mixed-design experiments and (ii) experimental fNIRS data recorded during a conventional lab-based task (involving maths). AIDE was able to recover functional events from simulated fNIRS data with an accuracy of 89%, 97% and 91% for the simulated block-, event-related and mixed-design experiments respectively. For the lab-based experiment, AIDE recovered more than the 66.7% of the functional events from the fNIRS experimental measured data. To illustrate the strength of this method, we then applied AIDE to fNIRS data recorded by a wearable system on one participant during a complex real-world prospective memory experiment conducted outside the lab. As part of the experiment, there were four and six events (actions where participants had to interact with a target) for the two different conditions respectively (condition 1: social-interact with a person; condition 2: non-social-interact with an object). AIDE managed to recover 3/4 events and 3/6 events for conditions 1 and 2 respectively. The identified functional events were then corresponded to behavioural data from the video recordings of the movements and actions of the participant. Our results suggest that "brain-first" rather than "behaviour-first" analysis is possible and that the present method can provide a novel solution to analyse real-world fNIRS data, filling the gap between real-life testing and functional neuroimaging.

Introduction

Functional Near Infrared Spectroscopy (fNIRS) is a neuroimaging technique able to measure concentration changes in oxygenated (HbO_2) and deoxygenated (HHb) haemoglobin secondary to neuronal activation. Like functional Magnetic Resonance Imaging (fMRI), fNIRS is a neurovascular coupling-based neuroimaging technique that recovers the hemodynamic response related to functional brain activity. While fMRI relies on the paramagnetic nature of HHb to measure the blood oxygen level-dependent (BOLD) response, fNIRS optically detects changes in HbO_2 and HHb taking advantage of the low absorption of the biological tissue in the near-infrared range (700–1000 nm) (see Scholkmann et al. (2014a) for a review). Whilst fNIRS is a relatively new neuroimaging method, over the last 20 years it has become a popular tool for clinical and psychological applications (Boas et al., 2014), being extensively used to monitor brain activity in response to a wide variety of cognitive tasks. The fast spreading of this technology is also related to the advantages that the technique offers. For example, thanks to its being non-invasive, portable and robust to motion artifacts, fNIRS is suitable: (i) for a wide variety of populations (e.g., clinical patients, infants, elderly people), (ii) for bedside monitoring, and (iii) for those experimental situations that cannot be easily recreated within the physical constraints of an fMRI scanner because require the volunteer to have unconstraint physical

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movements (Scholkmann et al., 2014a; Quaresima and Ferrari, 2016). In fact, while motion artifacts can represent a major obstacle both for fMRI and electrophysiological techniques, such as electroencephalography (EEG) measurements, fNIRS is more robust against this issue and thus more suitable for tasks involving unconstrained physical movements. The development of wireless, miniaturized and fiberless fNIRS systems, opens up the way to more ecological applications in neuroscience, especially for those situations in which experiments conducted in the real-world are needed (Burgess et al., 2006; McKendrick et al., 2016; Pinti et al., 2015a).

For instance, mental workload and situation awareness in augmented reality wearable displays (ARWDs) are assessed traditionally by questionnaires administered during task probes, pauses or at the end of the experiment. However, these measures are less ecologically valid than measures taken in dynamic situations with mobile participants. Thanks to the new generation of wearable fNIRS devices, we have demonstrated their applicability for monitoring prefrontal cortex activation in freely moving subjects outside the lab (Pinti et al., 2015a); and recently, others (McKendrick et al., 2016) were able to assess mental workload and situation awareness during navigation in ARWDs in similar naturalistic situations. Wearable fNIRS devices can also be used in non-invasive Brain Computer Interface (BCI) systems to detect task-related brain activations in less restrained situations and control external devices for e.g. neuro-rehabilitation, communication or motor restoration (see Naseer and Hong (2015) for a review). In addition, monitoring brain activity in real life scenarios may also be particularly important in the study of executive functions, the high-level processes used to control and organise other mental processes in order to enable flexible goal-directed behaviour (Gilbert and Burgess, 2008; Lezak, 1995; Miller and Cohen, 2001). Previous studies have suggested that standard lab-based neuropsychological tests may be insensitive to executive function difficulties of patients with frontal lobe lesions, which can be revealed in more naturalistic real-world tasks (Burgess et al., 2006; Shallice and Burgess, 1991). Motivated by this, our team demonstrated the feasibility of investigating one aspect of executive function (prospective memory) using a fiberless and wearable fNIRS system (Pinti et al., 2015a). This allowed the measurement of prefrontal cortex hemodynamics of freely moving participants performing a prospective memory experiment outside the lab.

So far, fNIRS has been used mostly to monitor functional brain activity in response to computer-based cognitive tasks in conventional laboratory settings. Given the slow nature of the hemodynamic response, fNIRS and fMRI lab-based protocols are designed very similarly (Strangman et al., 2002). Lab-based experiments are usually structured as event- or block-related designs, in which task periods are spaced out by low-level baseline periods and stimuli are repeated multiple times in order to maximize the Signal-to-Noise ratio (SNR).

In the early stages of fNIRS research, brain activation was assessed typically by visual inspection or application of thresholds to the signals (Benaron et al., 2000; Murata et al., 2002; Tak and Ye, 2014). However, in order to get more rigorous and statistically meaningful interpretation of fNIRS data, the main approaches that have been adopted to infer changes in functional activity are averaging techniques, General Linear Models (GLM) and data-driven methods. The averaging approach consists in averaging signals across task and rest periods and in assessing brain activation by statistically testing (e.g., through *t*-tests or ANOVAs) the difference between task and rest average values. The advantage of these methods is that they do not have to make very accurate assumptions about the timing and/or the shape of the haemodynamic signal; however, the disadvantage is that they do not make use of the high temporal resolution of fNIRS (Tak and Ye, 2014). By contrast, the GLM method overcomes this issue and considers the entire fNIRS time course, providing more statistical power. The GLM is a well-established regression approach widely used for fMRI data analysis (Friston et al., 1994a), which has been extended for fNIRS applications, as both techniques recover the hemodynamic response. In the GLM analysis, fNIRS data are regressed using a linear combination of explanatory variables (i.e., regressors) plus an error term. Such task-related regressors are created by convolving boxcar functions, which reflect the experimental design, with a hemodynamic response function (HRF). The beginning and end of each function event is coded by the shape of the boxcar function, or, in the limiting case of an event with duration zero, a delta function. The design matrix is comprised by task-related regressors plus a constant term and models the expected hemodynamic response to the assigned cognitive task. However, whilst the GLM method presents different advantages, assumptions have to be made on the shape and timing of the HRF (Tak and Ye, 2014). Other data-driven approaches have been proposed as well for the analysis of task-evoked activity measured through fNIRS, such as Principal Component Analysis (PCA), Independent Component Analysis (ICA) and Task-Related Component Analysis (TRCA). These methods do not make any a-priori hypothesis of the HRF shape and rely on the assumption that fNIRS data are a mixture of task-related and task-unrelated components (Tanaka et al., 2013). Through these approaches, fNIRS data are decomposed into independent components assuming statistical independence between source signals. Task-related components are then identified, for example using a threshold of the mean inter-trial cross-correlation (Patel et al., 2011), maximizing the inter-trial covariance (Tanaka et al., 2013) or maximizing both inter-trial correlations and the covariance between HbO_2 and HHb (Tanaka et al., 2014).

However, in order to create the boxcar function in the GLM approach, to compute task and rest mean values in the averaging method or to calculate the inter-trial correlations in data-driven methods, the timing of the event onsets must be known. In lab-based experiments such a timeline is established and controlled, the trial order is known a-priori and all the stimuli timings are triggered and recorded. However, this is not necessarily the case in real-world experiments conducted outside the lab, which are designed to be more ecological and to mirror real-life situations, without predetermined and controlled stimulus presentation. Whilst rules and some explicit targets can be used, the timing control can be very unpredictable. For example, in our previous study (Pinti et al., 2015a), participants were asked to perform a task in which they were required to remember delayed intentions (i.e. prospective memory) whilst walking freely in an outdoor environment. They were left free to accomplish the task without significant restraints, encountering different type of stimuli (e.g., obstacles, people, sounds, and so on) while they walked, looked around, crossed the streets and interacted with the environment. In addition, inter-subject variability needs to be taken into account as each participant is exposed to different stimuli and can use his/her own strategy to accomplish the task. Functional events in the real-world thus originate from the integration of complex and highly variable behaviours, which may be hard to identify from e.g., the behavioural analyses of video recordings. The identification of the event onsets from video examinations can be extremely difficult, time consuming and, sometimes, inaccurate as, for instance, it can be hard to predict if the real functional event in a freely moving participant occurs when they see the target stimulus or when they reach it.

In order to automatically disentangle these events and improve the identification of various behavioural actions through assessment of behavioural data (such as video recordings), in this study we propose a novel GLM-based method for the Automatic IDentification of functional Events (AIDE) that statistically detects functional events directly from fNIRS neuroimaging data. Rather than taking the standard approach of starting with a predetermined experimental design and investigating the effects of its events on haemodynamic activity, here we take the opposite approach of starting with neuroimaging data and seeking to identify the occurrence of experimental events on the basis of it. This algorithm is based on the GLM model and identifies functional events by evaluating the best fit between different models of functional activity, assembled considering all the possible combina-