Journal of Neuroscience Methods 224 (2014) 66–78

Contents lists available at ScienceDirect

Journal of Neuroscience Methods

journal homepage: www.elsevier.com/locate/jneumeth

Computational Neuroscience

An automated approach towards detecting complex behaviours in deep brain oscillations

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HIGHLIGHTS

- Extracting event-related potentials (ERPs) from neurological rhythms related to complex/gross movements is addressed.
- Gross movements are challenging given complexity, information depth, and limited data from surgically implanted electrodes.
- Approach is tested in bilateral recordings of LFPs during simultaneous head, extremity, and trunk motions.
- Despite these interfering signals, the algorithm is able to correctly detect events across the four brain sites.
- Methodology functions in real-time, as only a single trial ERP is required, with detection algorithm calculated causally.

ARTICLE INFO

Article history:
Received 29 June 2013
Received in revised form
19 November 2013
Accepted 20 November 2013

Keywords:
Event detection
Event-related potentials
Deep brain implants
Sensory motor control
Movement related potentials
Sub-thalamic nucleus (STN)
Pedunculopontine nucleus (PPN)

ABSTRACT

Extracting event-related potentials (ERPs) from neurological rhythms is of fundamental importance in neuroscience research. Standard ERP techniques typically require the associated ERP waveform to have low variance, be shape and latency invariant and require many repeated trials. Additionally, the non-ERP part of the signal needs to be sampled from an uncorrelated Gaussian process. This limits methods of analysis to quantifying simple behaviours and movements only when multi-trial data-sets are available. We introduce a method for automatically detecting events associated with complex or large-scale behaviours, where the ERP need not conform to the aforementioned requirements. The algorithm is based on the calculation of a detection contour and adaptive threshold. These are combined using logical operations to produce a binary signal indicating the presence (or absence) of an event with the associated detection parameters tuned using a multi-objective genetic algorithm. To validate the proposed methodology, deep brain signals were recorded from implanted electrodes in patients with Parkinson's disease as they participated in a large movement-based behavioural paradigm. The experiment involved bilateral recordings of local field potentials from the sub-thalamic nucleus (STN) and pedunculopontine nucleus (PPN) during an orientation task. After tuning, the algorithm is able to extract events achieving training set sensitivities and specificities of [87.5 ± 6.5, 76.7 ± 12.8, 90.0 ± 4.1] and [92.6 ± 6.3, 86.0 ± 9.0, 29.8 ± 12.3] (mean ± 1 std) for the three subjects, averaged across the four neural sites. Furthermore, the methodology has the potential for utility in real-time applications as only a single-trial ERP is required.

1. Introduction

Detection of neuronal events relating to modulations in brain states is of fundamental importance in the field of neuroscience. These generally follow from a change in environmental stimuli, which can be of varying complexity. Such events can be detected within a neural signal or rhythm, highlighting stereotypical responses and correlations between the neurological phenomenon, physical or pathological response and spatiotemporal neuroanatomical relationships. This modulation in the brain's state generally manifests as an event-related potential (ERP) within a specific neurological rhythm (Bressler, 2002). By examining these evoked potentials in terms of event-related synchronisation (ERS) and/or de-synchronisation (ERD), useful insights about the nature

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0165-0270/$ – see front matter © 2013 Elsevier B.V. All rights reserved.
http://dx.doi.org/10.1016/j.jneumeth.2013.11.019

and timing of these events and how they sub-serve sensorimotor, perceptual or pathological processes can be elucidated (Luck, 2005; Paradiso et al., 2003; Rajdev et al., 2010). The majority of research regarding ERP's relates to movement or visual responses triggered using cued, self-paced or imagined stimuli (Dandekar et al., 2007; Niazi et al., 2011; Paradiso et al., 2004). As such, their associated potentials can be sub-categorised as movement-related potentials (MRP) or visually-evoked potentials (VEP) and occur within specific cortical–subcortical neural circuits. For instance the Bereitschaftspotential (BP) also known as the pre-motor potential is a measure of the neural activity exhibited in the motor cortex preceding a volitional muscle contraction. Epileptiform activities are a common pathological event potential and indicate the clinical onset of seizures (Osorio et al., 1998; Rajdev et al., 2010).

The majority of ERP research is performed using electroencephalographic (EEG) scalp electrodes on healthy individuals (Acunzo et al., 2012; Dandekar et al., 2007; Luck, 2005). As such, the ERP is generally buried in noise with a very low signal-to-noise ratio (SNR). This is mainly attributed to the fact that the EEG signal represents an amalgamation of far-field potentials which are heavily attenuated due to transmission through the cranium and scalp. Therefore, to extract the ERP, many trials need to be conducted so that the resulting waveforms can be averaged allowing the random brain activity to be cancelled out and the signal of interest exposed (Luck, 2005). This is under the assumption that the signal of interest is event-locked with invariant latency and shape, and that the remainder of the signal constitutes noise approximated by a zero-mean independent Gaussian process.

More recently, the exploration of MRPs captured within deep brain structures has been explored (Alegre et al., 2005; Paradiso et al., 2004, 2003; Tsang et al., 2010). This is due to recent developments in functional neurosurgery, specifically, clinical implantation of deep brain stimulation (DBS) electrodes, for example, within the Basal Ganglia structure providing therapeutic relief of Parkinsonian symptoms (Cassidy et al., 2002; Jenkinson et al., 2005; Pereira et al., 2011; Priori et al., 2002; Stefani et al., 2007). The same DBS electrodes can be used to record local field potentials (LFP) and/or action potentials thus providing higher spatial resolution than corresponding EEG scalp electrodes. This allows researchers to explore various motor and behavioural paradigms with a high degree of spatial and temporal resolution. Such studies have included defined finger, wrist, foot and pointing movements, to name a few and have helped to highlight the role of these subcortical structures within a variety of sensorimotor control loops (DeLong and Wichmann, 2007; Mena-Segovia et al., 2004).

The basal ganglia–brainstem system (BG–BS) plays an important role in the control of various types of behavioural expression (Mena-Segovia et al., 2004; Takakusaki et al., 2004). It also plays a significant role in both automatic and voluntary control processes including rhythmic limb movements and adjustment of postural tone during locomotion. Central to this neural architecture is the pedunculopontine nucleus (PPN) which provides dense efferent and afferent connections between the two subsystems (Jenkinson et al., 2009; Nandi et al., 2002). The PPN modulates its activity in response to locomotion and voluntary arm motions (Tsang et al., 2010). Dysfunction of the PPN structure has been highlighted as a possible cause of a variety of clinical Parkinson's disease (PD) symptoms, including gait freezing and a decrease in vestibular control (Jacobs and Horak, 2007; Shoushtarian et al., 2011; Thevathasan et al., 2012). Despite its active role in neurophysiology, the PPN has only recently been explored with regards to PD, DBS and LFP signal analysis (Androulidakis et al., 2008; Thevathasan et al., 2012; Tsang et al., 2010). Furthermore, research pertaining to both the basal ganglia and PPN structures and linking this to movement, balance and gait function has so far been minimal. The majority of research regarding LFPs and deep brain recordings has generally been on individual brain structures usually from electrodes placed in the sub-thalamic nucleus (STN) or globus pallidus interna (GPi) as these are established targets for therapeutic application of functional DBS (Burgess et al., 2010; Singh et al., 2011; Stefani et al., 2007; Wei et al., 2010).

The majority of motor paradigms tested have involved small and discrete bodily movements, corresponding to fine motor skills which allow for high subject and thus inter-trial repeatability. This increases the probability of the associated waveform being event-locked to the stimulus and physical response, with invariable latency and shape. However, the ERP will generally have a much smaller SNR and thus inter-trial averaging becomes essential. In recent years, the exploration of more complex movement and behavioural paradigms have become of interest (do Nascimento et al., 2005; Shoushtarian et al., 2011; Thevathasan et al., 2012). These include the study of gross movement behaviours such as gait, locomotion and postural control, where multiple muscle synergies and neural control loops are engaged. Examples of such movements include walking, turning and balancing (involving vestibular functions) and standing up/sitting down. This leads to higher SNR associated with the evoked response due to an increased rate in neural firing within the specific cortical–subcortical network. If enough excitatory neural pathways are activated then the ERP signal will no longer be buried in noise. However, the shape and latency invariance of the ERP is generally compromised due to both intrinsic/extrinsic noise and variability. The intrinsic noise component constitutes internal near-field volumetric activity which is generated from simultaneously occurring brain responses and to some extent may be correlated to the gross ERP. The extrinsic noise component comprises measurement errors and far-field volumetric effects (such as those experienced in EEG signals) and therefore can be assumed Gaussian. While it is still of great interest to extract these complex behaviours related ERP, a different approach is required.

In this paper we outline an approach whereby events related to gross movements and behaviours are able to be extracted from neural signals in an automated and systematic fashion. Here we define a gross neural response as one which produces an ERP not completely buried within intrinsic and/or extrinsic noise. This will be at the cost of high inter-trial variability thus preventing standard ERP methods to be employed. Furthermore, this work significantly differs from standard real-time single-trial evoked potential studies such as those utilised in brain computer interface (BCI) applications. This is because current research into self-paced BCI systems is based on either very simple movements and/or motor imagery whereas gross and unstructured movements are rarely explored (Borisoff et al., 2004; Fatourechi et al., 2008; Niazi et al., 2011). The signal analysis method and data collection process in self-paced BCI applications can be designed concurrently, allowing them to be based on predefined input behaviours from the user. Instead, this work explores real life scenarios where the behaviours are freely moving, unstructured and highly complex. The exploration of these sorts of behaviours is rare in existing literature and would never be used within BCI paradigms. As such the proposed methods need to be designed in a flexible manner and data-driven to allow for the exploration of unknown signal distributions.

In the next section, the automated detection methodology is introduced with the binary decision output based on the combination of a decision envelope and adaptive threshold. The detection algorithm is validated on a data-set collected from patients with PD who have undergone bilateral DBS electrode placement within both the STN and PPN substructures. Post-operative LFP signals were recorded whilst the subjects participated in a turning and balance experiment. The parameters of the detection algorithm are optimised using a multi-objective genetic algorithm in response to motion data collected from the head and trunk of the subject. In