Neurocomputing 74 (2011) 1301–1314

Contents lists available at ScienceDirect

Neurocomputing

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

A variational Bayesian approach for the robust analysis of the cortical silent period from EMG recordings of brain stroke patients

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ARTICLE INFO

Available online 22 February 2011

Keywords:
Multivariate time series
Manifold learning
Variational Bayesian generative topographic mapping
Index of variability
Electromyography
Brain stroke
Cortical silent period

ABSTRACT

Transcranial magnetic stimulation (TMS) is a powerful tool for the calculation of parameters related to the intracortical excitability and inhibition of the motor cortex. The cortical silent period (CSP) is one such parameter that corresponds to the suppression of muscle activity for a short period after a muscle response to TMS. The duration of the CSP is known to be correlated with the prognosis of brain stroke patients' motor ability. Current methods for the estimation of the CSP duration are very sensitive to the presence of noise. A variational Bayesian formulation of a manifold-constrained hidden Markov model is applied in this paper to the segmentation of a set of multivariate time series (MTS) of electromyographic recordings corresponding to stroke patients and control subjects. A novel index of variability associated to this model is defined and applied to the detection of the silent period interval of the signal and to the estimation of its duration. This model and its associated index are shown to behave robustly in the presence of noise and provide more reliable estimations than the current standard in clinical practice.

1. Introduction

The field of clinical neurology often deals with complex data that require advanced data analysis techniques with capabilities beyond those of traditional statistics. In particular, the acquisition of physiological data of motor activity resulting from cognitive processes is usually fraught with measurement artifacts and noise. This noise must be processed using robust procedures in order to extract usable knowledge. This is the case not only for the purpose of research but also for the routine medical practice.

In electromyographical (EMG) recordings, the electrical muscle activity resulting from the activity of motor neurons is recorded from the skin surface above the muscle, and not at the muscle itself, in order to avoid unnecessary discomfort in the analyzed subject. EMG recordings are very sensible to muscle activation, and it is very important to maintain the muscle in a state of relaxation during data collection. In clinical neurology research, the majority of subjects participating in the studies are patients affected by a given pathology. This often makes data acquisition, processing, and analysis rather difficult undertakings. For the reasons outlined above, physiological data in general and EMG data, which are the concern of this paper, in particular, should benefit from the development and use of data analysis models that behaved robustly in the presence of noise.

This paper analyzes data from brain stroke patients. A brain stroke is the rapidly developing loss of brain functions due to disturbance in the blood supply to the brain. The majority of stroke patients suffer motor disabilities as a result. The recovery of the motor skills strongly depends on the rehabilitation performed in the acute phase of stroke (under 6 months after stroke).

Many studies of neural plasticity in stroke patients have shown correlations between brain parameters (obtained through neuropsychological tests and brain stimulation techniques) and the prognosis of the patient (i.e., the prediction of functional recovery after the acute stroke phase). Transcranial magnetic stimulation (TMS) is a non-invasive brain stimulation method used to excite neurons. With TMS, brain activity can be triggered with minimal discomfort, and the functionality of the circuitry and connectivity of the brain can thus be studied. This technique has its more obvious application in motor cortex analysis. In brain stimulation using TMS, EMG can be used to register the signal of the corresponding muscle activation. Through this signal, several excitatory and inhibitory parameters can be studied. One of the most important inhibitory parameters is the cortical silent period (CSP) [1]. The CSP is a refractory period in the EMG signal, elicited after motor cortex stimulation with voluntary pre-activation of the target muscle.

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doi:10.1016/j.neucom.2010.12.006

The duration of this de-activation interval is an important parameter in the study of stroke, as research has provided evidence that the CSP shortens during the recovery of the affected limbs, making it a reliable indicator of therapeutic progress [2,3]. EMG recordings of stroke patients are often difficult in both acute and chronic patients. Some stroke patients have great difficulty in maintaining the muscle contraction in any stable way. As a result, some spurious low-amplitude EMG activity is likely to be detected during the CSP, making its analysis difficult.

Several attempts to define methods for the accurate estimation of the CSP duration have been made [4–6] with varying success. The CSP measuring methods in common use, though, are known to yield a significant error due to their sensitivity to noise, which is commonplace in this kind of data. Therefore, no fully satisfactory answer to the accurate estimation of CSP as yet been provided. This limitation calls for the development of EMG signal analysis methods capable of dealing with noise through effective regularization and, more specifically, methods for the robust estimation of the CSP in EMG recordings.

For this, we resort in this paper to a manifold-constrained hidden Markov model, which formulation within a variational Bayesian framework imbues it with regularization properties that minimize the negative effect of the presence of noise in the EMG MTS. A novel index of variability is defined for this model. It is shown to be capable of estimating the duration of the CSP by accurately pinpointing its offset time. This model and its associated index are shown in this study, through several experiments, to provide more reliable estimations than the current standard in clinical practice.

2. Medical background

2.1. Brain stroke

A stroke is the rapidly developing loss of brain functions due to disturbance in the blood supply to the brain. As a result, the affected area of the brain is unable to function. This can lead, for instance, to inability to move one or more limbs on one side of the body; to cognitive impairments such as inability to understand or formulate speech (aphasia); or to inability to perceive one side of the visual field (homonymous hemianopsia).

The prognosis of stroke patients is uncertain: About 10% of people who have an ischemic stroke recover almost all normal function, whereas about 25% recover most of it. About 40% show moderate to severe impairments requiring special care, and up to 10% require care in a nursing home or other long-term care facility. Most of the impairments that remain after 12 months become permanent.

2.2. Rehabilitation from brain stroke

Disability associated with hemiplegia or hemiparesis markedly limits independent living and social participation in at least half of all stroke survivors [7]. Reduced levels of exercise and daily activity as a consequence of the disability can increase risk factors for recurrent stroke and associated cardiovascular disease. Within days after the onset of a stroke, clinicians can begin to promote functional recovery in their patients.

Initial motor gains after stroke might result from the resolution of reversible injuries to neurons and glia. Reorganization of spared assemblies of neurons that represent motor actions within the sensorimotor cortex, as well as in transcortical, ascending and descending pathways, seems to accompany further improvements in motor skills [7]. Contributions from more widely distributed cortical and subcortical regions, including cerebral systems for perception, attention, motivation, executive planning, working memory, as well as explicit and implicit learning, may be required to compensate for strategies that the injured brain can no longer support. The ability to strengthen muscles and reach an appropriate level of cardiovascular fitness also depends on these non-motor systems.

In some animal models of stroke, M1 and related motor cortices and the spinal cord evolve robust changes in their structure and function in response to specific types of motor training. Skills training induces the creation of new synaptic connections, as well as synaptic potentiation and reorganization of movement representations within the motor cortex. This plasticity supports the production and refinement of skilled movement sequences.

The biological responses to exercise in patients are likely to depend on how long after stroke the exercise is initiated, the amount of exercise administered, and the duration and type of the task practiced by patients. In terms of improving daily functioning, task-specific training seems to benefit stroke patients more than general exercise does. One of the problems in demonstrating the specific effects in practice of any given task across rehabilitation trials has been the low intensity of training, which might limit the robustness of outcomes [8]. In addition, responsiveness to training has been observed mostly in patients who have retained reasonable motor control.

However, the effectiveness of classical approaches in rehabilitation methods, such as rehabilitation based on repetitive manipulation of objects and movement training of the affected side, has been found to be quite limited [9]. As a result, a need for efficient motor rehabilitation approaches still remains.

New rehabilitation methods, such as constraint-induced therapy, which consist on the use of the impaired extremity while immobilizing the healthy one for several hours per day, have been shown to lead to functional reorganization. In this field, animal studies have provided evidence that cortical plasticity is increased by the behavioral relevance of the stimulation and its motivational value.

2.3. Transcranial magnetic stimulation and the cortical silent period

Transcranial magnetic stimulation can be applied in several ways and at different levels of the nervous system. The TMS of the cerebral cortex is quite different from that of other parts of the nervous system: The EMG responses to cortical stimulation are more complex than those following the peripheral stimulation. Not only excitatory effects but also inhibitory effects can be elicited. This characteristic is used to investigate cerebral functions other than those of the motor cortex [10].

When an individual is instructed to maintain muscle contraction and a single supra-threshold TMS pulse is applied to the motor cortex contralateral to the target muscle, the EMG activity is arrested for a few hundred milliseconds [11]. This period of EMG suppression is referred to as a CSP, normally defined as the time from the end of the motor evoked potential (MEP) to the return of voluntary EMG activity. However, the definition of the end of the MEP is, at times, difficult. In order to circumvent this difficulty, some investigators have defined the CSP as the interval from stimulus delivery to the return of voluntary activity [12]. Silent periods of abnormally short or long duration are observed in patients with various movement disorders [13].

Classen and co-workers [14] investigated patients after acute stroke, who showed hemiparesis and a long duration of the silent period, but normal MEP amplitude in the affected side. These patients had impaired movement initiation, inability to maintain a constant force, and impaired movement of individual fingers that resembled motor neglect. The CSP duration decreased with clinical improvement.