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Optimizing detection and analysis of slow waves in sleep EEG

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HIGHLIGHTS

- We introduce an open-source toolbox for individual detection and analysis of slow waves in sleep electroencephalography.
- Novel and previously applied automatic detection algorithms are introduced and explored.
- Individual slow waves are detected in sleep recordings from participants along a large search-space of parameter settings.
- Properties of detected slow waves are compared across parameter settings on a range of outcome measures of interest.
- Visualization options for toolbox users are introduced, including the possibility to manual score sleep.

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ABSTRACT

Background: Analysis of individual slow waves in EEG recording during sleep provides both greater sensitivity and specificity compared to spectral power measures. However, parameters for detection and analysis have not been widely explored and validated.
New method: We present a new, open-source, Matlab based, toolbox for the automatic detection and analysis of slow waves; with adjustable parameter settings, as well as manual correction and exploration of the results using a multi-faceted visualization tool.
Results: We explore a large search space of parameter settings for slow wave detection and measure their effects on a selection of outcome parameters. Every choice of parameter setting had some effect on at least one outcome parameter. In general, the largest effect sizes were found when choosing the EEG reference, type of canonical waveform, and amplitude thresholding.
Comparison with existing method: Previously published methods accurately detect large, global waves but are conservative and miss the detection of smaller amplitude, local slow waves. The toolbox has additional benefits in terms of speed, user-interface, and visualization options to compare and contrast slow waves.
Conclusions: The exploration of parameter settings in the toolbox highlights the importance of careful selection of detection
Methods: The sensitivity and specificity of the automated detection can be improved by manually adding or deleting entire waves and or specific channels using the toolbox visualization functions. The toolbox standardizes the detection procedure, sets the stage for reliable results and comparisons and is easy to use without previous programming experience.

1. Introduction

For much of the 20th century sleep was considered to be a global phenomenon of the brain, and its macro-architecture was of primary interest (Jones, 2005; Saper et al., 2005; Siegel, 2009). The past few decades has witnessed a shift in interest to the spatial domain and local aspects of sleep (Krueger et al., 2008; Nobili et al., 2011; Vyazovskiy et al., 2011; Marzano et al., 2013). Much of the research into local patterns of sleep has used the measure of 'slow wave activity' (Werth et al., 1997; Huber et al., 2004; Stadelmann et al., 2013), reflective of the changes in the power spectra in the lower frequencies (typically around 1–4 Hz), measured across a whole night or single cycle of sleep. This measure is, however, underdetermined since both slow wave incidence and amplitude will affect power.

Slow waves can originate in a small region of the cortex and then propagate to other cortical regions based on both EEG and intracranial recordings (Amzica and Steriade, 1998). Therefore, there are,

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at least, five distinct ways in which local slow wave activity could increase or decrease (Massimini et al., 2004; Menicucci et al., 2009; Murphy et al., 2009): 1, origins and traveling parameters remain constant but there are local changes in the amplitudes of the slow waves as they travel over particular regions of the cortex; 2, there is an increase in the incidence of local waves which originate in that particular part of the cortex; 3, slow wave origins remain distributed but more waves travel to or through a specific area of the cortex; 4, there are local changes in the speed of propagation resulting in a frequency shift of power spectra; 5, some particular combination of the above factors. Notably, if any of the above mechanisms have opposing effects they may cancel out in the power spectra.

Conventional power-based methods are relatively easy to calculate as the appropriate tools have already been developed and standardized over time. Thus, results are relatively comparable across studies, in turn leading to power spectral measures being used repeatedly in research. Nevertheless, an examination of the properties of individual slow waves is now also possible and can yield an increase in specificity and sensitivity without the associated cost of having to perform new measurements (Riedner et al., 2007). For example, the analysis of the origin of slow waves revealed a local increase indicative of post-sleep learning in a visual perception task (Mascetti et al., 2013). Moreover, slopes of individual slow waves correlate with neural development (Fattinger et al., 2014), and epileptic spike waves can impair individual slow waves (Bölsterli Heinzle et al., 2014). The advent of parallel computing and the lower cost of technology has made individual waveform analysis practically feasible. However, the necessary tools for the detection of individual slow waves, and the subsequent calculation of their traveling parameters have not yet been made freely available, standardized, or validated. Moreover, tools have not been made sufficiently simple or generalized so that researchers and clinicians can easily explore their own data and have confidence in the results while also comparing them against set standards.

Here we describe an open source toolbox with the principal purpose of providing a reliable interface to detect and analyze individual slow waves found in EEG sleep recordings. The toolbox is version-controlled using git and freely available at https://github.com/Mensen/swa-matlab. The main goal of the current article is to introduce the main features of the toolbox for slow-wave detection. Secondly, we use several full-night sleep recordings to examine how a large search-space of different parameter settings influence the detection and properties of slow waves. While this is not intended to be an extensive overview of how to most accurately detect slow waves, it is meant to showcase the toolbox's functionality, typical work-flow, and visualization capabilities while making the user aware of the strengths and weaknesses of various settings and what aspects to consider when analyzing recordings of their own.

2. Materials and methods

2.1. Toolbox overview

2.1.1. Sleep scoring

Given that different types of waves in sleep occur during different periods, detection can be improved by parsing the night into its various sleep stages. To this end a user-friendly interface was created for the manual visual scoring of sleep stages and arousal events of high-density EEG channels. This has previously been available primarily through proprietary software in certified sleep centers and only once specified channels from the high-density caps had been exported. This set of toolbox functions allows for the on-line adjustment of displayed channels and specified references, as well as individual channel filtering options for each channel displayed. Navigation and sleep scoring can be performed using the mouse or keyboard keys (e.g. left and right arrows to navigate, number keys to indicate sleep stage). Importantly, the data used for scoring can be loaded directly from the original recording and is saved in the same file. This is a useful feature, as the file sizes for long recordings of high-density channels are typically in the 5–20 Gb range. This feature also reduces the number of copies necessary while simultaneously maintaining a controlled history of processing. Similarly, the scoring toolbox uses dynamic memory mapping to load into random-access-memory (RAM) only the part of the file that is currently displayed (e.g. 8 channels of 30 s duration). This feature allows for the scoring of files on a typical computer where the amount of RAM memory may be smaller than the dataset one needs to score. Since filtering is only applied to the displayed portion of data, and not the raw data itself, this graphical user interface (GUI) is also a good way to visualize raw recordings and mark artifacts manually, prior to any preprocessing methods. Channel montages and filtering options are saved within the file and can be used with other datasets to keep the settings consistent across participants or recording nights.

2.1.2. Wave detection

The detection of slow waves, regardless of specific settings, follows 4 key stages.

1 Calculation of the canonical wave(s).
2 Detection of individual slow waves within the canonical wave(s).
3 Detection of corresponding waves within the actual channels.
4 Examination of each wave for its traveling streams and its properties.

There are two conceptually distinct approaches available for the calculation of the canonical wave: either the mean activity over a specified region; or the negative envelope of the channels. The simplest canonical wave can be created by calculating the mean activity over a single circular region of the electrode array, defining its center and radius. Alternatively, multiple canonical waves can be computed by taking the mean activity of distinct regions. Regions can be specified over the mid-line, leading to a frontal, central and posterior canonical time series. Another option is to calculate the mean activity of four regions equidistant around the center, as was done in the original slow wave detection algorithm (Massimini et al., 2004). These four regions can be arranged as a square (left/right; frontal/posterior), or as a diamond (single frontal and posterior regions; left and right central region). Users may also directly specify their own canonical wave.

One issue with regional methods is that local waves outside the specified region will not be represented in the canonical wave and therefore have no chance of being detected. Thus, only waves that pass through a substantial portion of at least one of the regions can be detected – a source of bias that may underestimate the amount of locality in sleep. Conversely, if a single region is too large, then the mean activity within the region may no longer be representative and waves could be missed (see Supplementary Fig. 1 for comparison of regional methods). Secondly, such a method does not scale well to more sparsely recorded arrays where those predefined regions may only contain a few channels.

A solution is to calculate the negative envelope of all channels. This is akin to examining the butterfly plot (overlaying all channels) and tracing the negative contour. Here, we calculate the mean activity of the most negative 2.5% of channels at each sample independently in the time series. The advantage is that the most negative portion can potentially come from any channel in the dataset and is not restricted to a particular region. Furthermore, a single canonical wave is representative of the entire