The Effects of Sub-Clinical EEG on Cognition; A Case of Two Patients with JME

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Received date: Apr 10, 2014, Accepted date: May 22, 2014, Published date: May 27, 2014

Abstract

It is increasingly becoming apparent that patients with Juvenile Myoclonic Epilepsy (JME) experience difficulties with various aspects of cognition. Studies that have attempted to find specific seizure-related factors contributing to and predicting cognitive dysfunction have provided conflicting and inconclusive results. In this brief paper we aimed to discuss the nature and context of sub-clinical EEG activity on cognition in JME using two individual cases. It seems that the potential ‘mechanism’ for cognitive impairments in JME is unlikely to be solely attributable to the effects of paroxysmal discharges and further research is required to clarify the longer term, cumulative effects of a range of factors that may help to explain such deficits in cognitive functioning.

Keywords: Juvenile myoclonic epilepsy; Cognition; Sub clinical; EEG

Introduction

EEG activity over the frontal and parietal regions are thought to map onto the seizure pathway in JME [1]. A number of neuropsychological deficits have therefore been identified, potentially impacting on personality and social functioning [2]. Whilst most previous studies have focussed on executive functioning, recent attention has been drawn to other aspects of cognition [3].

Epileptiform discharges that are not accompanied by obvious clinical events are cautiously termed ‘sub-clinical’ and include spike, spike-wave, polyspike-wave and sharp wave discharges. Sensitive neuropsychological analyses indicate brief episodes of impaired cognitive function during such discharges [4] using more sophisticated video-EEG methods, which are not detectable by routine clinical observations. This momentary cognitive deficit has been described as “transient cognitive impairment (TCI)” and confirmed in a number of studies. TCI’s are thought to be limited to the actual period in which the sub-clinical discharge occurred without any ‘pre- or post-discharge’ effects [5].

The extent of cognitive impairment during such discharges varies according to the type of discharge and its localisation, with the number of spike components and the involvement of fronto-central regions being very important [6]. However, it is more readily detected during generalised spike-wave discharges lasting more than 3 seconds, than with focal activity as originally documented by Aarts and colleagues [7].

In JME, Matsuoka and colleagues [8] demonstrated that sub-clinical discharges were almost exclusively precipitated by mental activities, using video-EEG methods. Such tasks included reading, writing, written arithmetic calculation, mental arithmetic calculation, and spatial construction. In a later they stated that action-programming tasks (mental activities using hands such as writing, written calculations and spatial construction) produced the most discharges followed by thinking-type tasks (mental tasks such as mental calculation and reading), which is in keeping with the hypothesis of motor system hyper-excitability in JME.

Overall, studies that have attempted to find specific seizure-related factors contributing to and predicting cognitive dysfunction have provided conflicting and inconclusive results. Therefore, the occurrence of sub-clinical EEG discharges and their relation to impairments in cognitive performance in JME remains largely unstudied. In this brief report we therefore aimed to discuss the nature and context of sub-clinical EEG activity on cognition in JME using two individual cases.

Methods

In the original study [3], eight sibling pairs, one in each pair with JME, were compared with 16 controls matched for age, sex, ethnicity, and educational level. All participants underwent a detailed neuropsychological assessment under standard 40 minute video-EEG conditions. The measures included tests of intelligence, visual-spatial skills, language, memory, attention and reaction time, and executive functioning. Only two patients with JME (out of eight) exhibited sub-clinical EEG activity in the patient group and are described here.

Case Reports

Patient A

In the first case study of a 31-year-old right-handed Caucasian female (Patient A), the video EEG analysis indicated a number of sub-clinical discharges occurring mostly in two tests assessing verbal learning memory and sustained attention for verbal information.
California Verbal Learning Test-II; CVLT-II and Digit Span; WMS-III respectively). The recall of this information appeared to vary depending on the nature and type of discharge.

Video EEG

Three discharges occurred during the verbal learning task (Figure 1). These three discharges occurred exactly at the point of being presented a word on the list learning task, at different intervals. On two occasions the patient was able to recall the words and the subclinical discharges (a sharp wave and spike and slow wave) when higher in amplitude over the fronto-central regions. On the third occasion, where the word was not recalled, the generalised spike and wave discharge was higher in amplitude within the right central areas of the fronto-central regions.

The other three discharges (Figure 2) occurred during the digit span task. Again, three discharges occurred exactly at the point of being presented a number on the task at different intervals. On two occasions the patients was able to recall the number and the spike and wave discharges were higher in amplitude over the left fronto-central regions. On the third occasion, when the number was not recalled, the generalised spike and wave discharge was again higher in amplitude within the right central areas of the fronto-central regions.

In the second case (Patient B); a 25-year-old, right-handed Caucasian male had exhibited significant difficulties in a number of tasks. That said, the occurrence of sub-clinical activity did not appear to affect his performance on the measures during which this activity occurred (Rey Complex Figure Test and Spatial Span).

Video EEG

Patient B experienced two episode of generalised spike wave discharges; each occurring outside of any learning task (Figure 2). The first spike wave discharge was categorised as having fronto-central predominance and lasted less than one second. This occurred as he was drawing the figure from memory. The second discharge lasted approximately four seconds; again it was generalised in nature with predominance over the fronto-central regions with high amplitude over this region during the Spatial Span sub-test. He performed within the normal range on both these tests.

Discussion

It would appear that paroxysmal generalised discharges, with predominately higher amplitude over the fronto-central regions, when occurring at the point of learning impaired performance in Patient A. This is in contrast to other types of discharges that coincided at the same point of learning as highlighted in both cases here. This would be in keeping with the work of Aldenkamp et al. [5], but also extends the original findings made by Aarts et al. [7] as such impairments can occur with specific discharges lasting as little as one second and not necessarily the three or more seconds they purported. This may be explained by the advances in current video-EEG methodology, which is more sophisticated and accurate.

In Patient B, the occurrence of subclinical activity had no bearing on performance on the task during which it occurred. Instead, we found evidence to support the original results by [8] whereby tasks requiring spatial construction precipitated sub-clinical activity in select JME populations (as detailed in the full study by the authors)[8]. This is thought to be associated with the pathophysiology of myoclonic seizures and recent neuroimaging data has implicated increased functional connectivity between prefrontal cognitive areas and motor system in JME. Koepp et al. [9] have recently suggested that the altered structural connectivity of the supplementary motor area in JME can help us understand the relationship between seizure type and explain the seizure provoking mechanisms in such patients [9].

Given these brief findings it is unlikely we can assume that specific and timely sub-clinical activity accounts for the overall trend of reduced performances in cognitive functioning and general IQ in people with JME when compared to controls [3]. Other explanations in the current literature speculate that the long term effects of clinical seizures, genetic heterogeneity, effects of medication and the underlying brain abnormalities may also be significant. It is possible too that existing methodological variations with regards to assessing for the precipitatory or inhibitory effects do not account for the ‘spontaneous’ occurrences of discharges in people with JME. It is perhaps likely that a combination of these factors offer plausible alternatives to ‘transient cognitive impairment’ as an important mechanism for impaired cognition in JME.
References


