Clinical Neurophysiology 126 (2015) 959–966

Contents lists available at ScienceDirect

Clinical Neurophysiology

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

EEG predictors of outcome in patients with disorders of consciousness admitted for intensive rehabilitation

Sergio Bagnato *, Cristina Boccagni, Antonino Sant'Angelo, Caterina Prestandrea, Roberta Mazzilli, Giuseppe Galardi

Unit of Neurophysiology and Unit for Severe Acquired Brain Injury, Rehabilitation Department, Fondazione Istituto San Raffaele G. Giglio, Cefalù (PA), Italy

ARTICLE INFO

Article history:
Accepted 5 August 2014
Available online 1 September 2014

Keywords:
Vegetative state
Unresponsive wakefulness syndrome (UWS)
Minimally conscious state (MCS)
EEG amplitude
EEG frequency
EEG reactivity
EEG scale

HIGHLIGHTS

- EEG amplitude, frequency, and reactivity are related to clinical outcomes in patients with severe disorders of consciousness.
- Their prognostic value increases if they are combined with a new Amplitude–Frequency–Reactivity score.
- Standard EEG descriptors are useful to define a prognosis in patients with disorders of consciousness.

ABSTRACT

Objective: This study examined the prognostic value of standard EEG in patients with unresponsive wakefulness syndrome (UWS) or in a minimally conscious state (MCS).
Methods: EEGs recorded at admission in 106 patients with UWS or in a MCS were analyzed retrospectively. EEG amplitude, dominant frequency, and reactivity to stimuli were correlated to patient outcomes according to the Coma Recovery Scale Revised (CRS-R). In 101 patients, data were integrated to generate a novel Amplitude–Frequency–Reactivity (AFR) scale, with scores ranging from 3 to 7.
Results: Patients with reduced amplitudes showed less improvement in CRS-R scores at 3 months compared to patients with normal amplitudes. Delta, theta, and alpha frequencies were associated with the least, intermediate, and the greatest improvement in CRS-R scores, respectively. Patients with EEG reactivity showed greater improvements in CRS-R scores than patients without reactivity. The AFR scores for these patients were correlated with outcomes.
Conclusions: Reduced EEG amplitudes and delta frequencies correlated with worse clinical outcomes, while alpha frequencies and reactivity correlated with better outcomes. AFR scores allowed more delineated descriptions of outcomes in patients with normal amplitude, theta frequency, and no reactivity.
Significance: Standard EEG descriptors are related to the 3-month outcomes in patients with disorders of consciousness.

1. Introduction

Patients who survive acute brain injuries can develop severe disorders of consciousness such as unresponsive wakefulness syndrome (UWS, formerly known as vegetative state) or a minimally conscious state (MCS). UWS is a condition similar to coma, where patients exhibit no signs of awareness of themselves or their environment. Unlike comas however, they do exhibit functions such as eye opening, indicating recovery of the ascending reticular activating system of the brain (Royal College of Physicians, 2003; Laureys et al., 2010; Giacino et al., 2014). UWS can persist indefinitely or evolve towards recovery of consciousness to varying degrees. The first stage of recovery from UWS is MCS. Transition into a MCS starts when patients show minimal but definite behavioral evidence of self awareness or environmental awareness such as ocular fixation, localization of noxious stimuli, intelligible verbalization,

* Corresponding author. Address: Rehabilitation Department, Fondazione Istituto "San Raffaele-G. Giglio", Viale G. Giardina, Cefalù (PA), 90015, Italy.
E-mail address: sergiobagnato@gmail.com (S. Bagnato).

http://dx.doi.org/10.1016/j.clinph.2014.08.005
1388-2457/

intentional communication, or the ability to follow simple commands (Giacino et al., 2002). MCS can persist indefinitely or progress to further recovery of conscious awareness, denoting the emergence from MCS (E-MCS) (Giacino et al., 2002). Because the mechanisms underlying the recovery from UWS and MCS are largely unknown (Bagnato et al., 2013), their prognosis is particularly challenging, which is frustrating for physicians and distressing for patients' relatives.

Several recent studies have shown that standard electroencephalogram (EEG) is a useful tool to assess patients with UWS or in a MCS (Bagnato et al., 2010; Boccagni et al., 2011; Logi et al., 2011). In these studies, EEGs were evaluated with qualitative scales, such as the Synek scale (Synek, 1988), which assigns scores related to outcomes. However, there are drawbacks to using this method or any other EEG scale that is available for patients with severe disorders of consciousness, as they were specifically developed for patients in a coma (Synek, 1988; Scollo-Lavizzari and Bassetti, 1987; Rae-Grant et al., 1991; Young et al., 1997). The pathophysiology of coma (a deficit of arousal systems) (Young, 2009) is very different from that of UWS or MCS, in which arousal is recovered but a complete or partial lack of awareness is a typical feature (Monti et al., 2010; Bagnato et al., 2013). Moreover, some EEG scales require significant skill to use. For example, the Synek scale used in previous studies (Bagnato et al., 2010; Boccagni et al., 2011; Logi et al., 2011; Estraneo et al., 2013) identifies 5 grades and 10 subgrades of abnormalities, but it can be difficult to assign a specific prognostic value to each subgrade. In addition, recent studies reported conflicting data on the prognostic value of EEG evaluated with the Synek scale in patients with hypoxic brain injury (Boccagni et al., 2011; Estraneo et al., 2013). Although these data may be justified with different study designs (i.e., short-term vs. long-term evaluation), the lack of specificity of the Synek scale (which was developed for patients in comas rather than for patients with UWS or in a MCS) should be taken into account. Furthermore, the Synek scale includes some EEG patterns (e.g., theta coma and alpha coma) that are not found in disorders of consciousness following a coma.

Rather than assessing specific EEG patterns (e.g., burst-suppression, background slowing, alpha-coma, or theta-coma) in patients with disorders of consciousness, it may be more useful to utilize standard EEG descriptors that may be easily assessed by visual examination (i.e., amplitude, frequency, and reactivity) (Kaplan and Benbadis, 2013). This confers a number of advantages both in clinical practice and in research. First, a patient may exhibit several different EEG patterns within a single recording (Bauer et al., 2013) but data on background amplitude (reduced/normal), dominant frequency band (delta/theta/alpha), and reactivity (absent/present) is readily obtained from almost all EEG recordings. Second, the pathophysiological significance and the prognostic value of these descriptors were well established in the acute phase of patients with brain injuries: (1) the reduction of EEG background amplitude is associated with poor outcomes in comatose patients after cardiac arrest (Synek, 1988; Cloostermans et al., 2012; Hofmeijer et al., 2014; Sadaka et al., in press); (2) increases in theta and delta band frequencies with the disappearance of alpha band frequencies is associated with poor prognoses (Scollo-Lavizzari and Bassetti, 1987; Synek, 1988); and (3) EEG reactivity to external stimuli is associated with favorable outcomes upon hospital discharge (Howard et al., 2012), and absent reactivity predicts an increased mortality rate (Rossetti et al., 2010). Third, previous studies showed that, after visual examination, there are no EEG patterns that could be considered specific for UWS or MCS (Kulkarni et al., 2007; Bagnato et al., 2010; Boccagni et al., 2011). Furthermore, some researchers have concluded that EEG findings in UWS "are heterogeneous and too variable to be of diagnostic value" (Kulkarni et al., 2007). Fourth, with only a few exceptions (i.e., the burst-suppression pattern), there is no standard nomenclature for most of these EEG patterns and similar EEG findings are described using different terms among various studies. On the contrary, EEG recordings can be described unambiguously by combining a few standard descriptors (i.e., amplitude, frequency, and reactivity) and by using a standard terminology (Hirsch et al., 2013; Kaplan and Benbadis, 2013); however, their prognostic value remains scarcely known.

The aim of this study was to describe standard EEG findings in terms of its classical descriptors, i.e., amplitude, frequency, and reactivity, in a large population of patients with UWS or in a MCS. These findings were correlated with patient outcomes, to evaluate the prognostic capabilities of EEG and to derive a novel scale for specifically assessing patients affected by severe disorders of consciousness.

2. Methods

This study was performed according to the Helsinki Declaration and was approved by the ethics committee of the Fondazione Istituto San Raffaele G. Giglio (Cefalù, Italy). Only information present in the clinical files of patients was used.

2.1. Patients

This retrospective study was conducted on 106 consecutive patients (71 males and 35 females; mean age 39.1 ± 16.5 years) admitted to our Unit for Severe Acquired Brain Injury (USABI) between January 2005 and June 2013 for intensive rehabilitation following an acute brain injury (mean time from the brain injury to admission 45.5 ± 24.4 days). A total of 59 patients with UWS and 47 in a MCS participated in the study (see Supplementary Table S1 for more detailed descriptions). All patients who fulfilled the following criteria were included in the study: (1) a diagnosis of UWS or MCS upon admission to our department after a traumatic brain injury (TBI), stroke, or cerebral hypoxic event; (2) hospitalization in our department for at least 3 consecutive months; and (3) availability of the Coma Recovery Scale Revised (CRS-R) (Giacino et al., 2004) score at admission and after 3 months. Patients with a previous history of epilepsy, TBI, stroke, cerebral hypoxia, neurodegenerative diseases, tumors, or infections of the central nervous system were excluded.

2.2. Clinical and EEG evaluations

A diagnosis of UWS or MCS was made after evaluations that were performed upon admission and during the subsequent 2 days by a multidisciplinary team (neurologist, neuropsychologist, and speech therapist) according to the diagnostic criteria for UWS and MCS (Royal College of Physicians, 2003; Giacino et al., 2002). Diagnoses were confirmed by CRS-R scores (Giacino et al., 2004). The CRS-R provides criteria for a diagnosis of UWS, MCS, and E-MCS. It has been identified as the most reliable tool to assess patients with disorders of consciousness, both in clinical practice and research (Seel et al., 2010; La Porta et al., 2013). The CRS-R consists of 29 hierarchically organized items grouped into 6 subscales addressing auditory, visual, motor, oromotor/verbal, communication, and arousal functions. Each subscale provides increasing scores that allow identifying UWS, MCS, or E-MCS through clinical diagnostic criteria (Giacino et al., 2004). The total score can be used to track changes in the level of consciousness over time. In general, an increasing score indicates a trend toward an improvement in the level of consciousness, but it cannot be unequivocally associated to a particular level of consciousness. The total CRS-R score, which ranges from 0 (comatose state) to