International Journal of Psychophysiology 79 (2011) 89–96

Contents lists available at ScienceDirect

International Journal of Psychophysiology

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

Mild traumatic brain injury: Graph-model characterization of brain networks for episodic memory

Vasso Tsirka [a,*], Panagiotis G. Simos [b], Antonios Vakis [a], Kassiani Kanatsouli [a], Michael Vourkas [c], Sofia Erimaki [a], Ellie Pachou [a], Cornelis Jan Stam [d], Sifis Micheloyannis [a]

[a] Department of Medicine, Clinical Research Laboratory Widén, University of Crete, 71409 Iraklion/Crete Greece
[b] Department of Psychology, University of Crete, Rethymnon/Crete, Greece
[c] Technological Educational Institute, Iraklion/Crete, Greece
[d] Department of Clinical Neurophysiology, VU University Medical Center, Amsterdam, The Netherlands

ARTICLE INFO

Article history:
Received 21 September 2009
Received in revised form 6 September 2010
Accepted 14 September 2010
Available online 21 September 2010

Keywords:
Small-World Networks
Graph theory
Synchronization likelihood
Mild traumatic brain injury
Episodic memory
Declarative memory

ABSTRACT

Episodic memory is among the cognitive functions that can be affected in the acute phase following mild traumatic brain injury (MTBI). The present study used EEG recordings to evaluate global synchronization and network organization of rhythmic activity during the encoding and recognition phases of an episodic memory task varying in stimulus type (kaleidoscope images, pictures, words, and pseudowords). Synchronization of oscillatory activity was assessed using a linear and nonlinear connectivity estimator and network analyses were performed using algorithms derived from graph theory. Twenty five MTBI patients (tested within days post-injury) and healthy volunteers were closely matched on demographic variables, verbal ability, psychological status variables, as well as on overall task performance. Patients demonstrated sub-optimal network organization, as reflected by changes in graph parameters in the theta and alpha bands during both encoding and recognition. There were no group differences in spectral energy during task performance or on network parameters during a control condition (rest). Evidence of less optimally organized functional networks during memory tasks was more prominent for pictorial than for verbal stimuli.

1. Introduction

Mild Traumatic Brain Injury (MTBI) is the most common cause of brain insult. According to the Mild Traumatic Brain Injury Committee of the Head Injury Interdisciplinary Special Interest Group (American Congress of Rehabilitation Medicine; Kay et al., 1993), a patient with traumatically induced disturbance of brain functions with loss of consciousness for 30 min or less, posttraumatic amnesia not greater than 24 h and an initial Glasgow Coma Scale score of 13–15, is considered to have mild traumatic brain injury. MTBI may affect many cognitive functions, including attention (Alexander, 1995; Binder et al., 1997; De Monte et al., 2006; Vanderploeg et al., 2005; Voller et al., 1999). Memory is also affected and apart from the abundant reports concerning working memory deficits (Levin et al., 1987; Ruff et al., 1989; Vanderploeg et al., 2005), there are also reports of deficits in episodic memory, including verbal learning (De Monte et al., 2006; Ruff et al., 1989; Voller et al., 1999) and visual memory (Levin et al., 1987; Raskin, 2000; Ruff et al., 1989). For instance, Ruff et al. (1989) followed 32 MTBI patients between 7 days and three months following injury. Whereas patients as a group scored significantly lower than a control group at the initial assessment on the Mattis–Konver Verbal Learning and Memory Test and the Benton Visual Retention Test, these differences were minimized at follow-up. There are also reports for a general reduction in processing speed, especially in the acute phase following a MTBI, which is more prominent during difficult, cognitively demanding tasks (e.g. Gentilini et al., 1989; Gronwal, 1989; Landre et al., 2006). These deficits, however, are often very mild and not clinically significant at the individual patient level. In one of the few studies of material-specific episodic memory difficulties in the acute phase following MTBI, Tsirka et al. (2010) examined 26 MTBI patients and 26 age-, education, and IQ-matched controls on a series of neuropsychological tests evaluating primary and secondary memory, executive functions, and verbal fluency. Participants were also tested on experimental episodic memory tasks involving words, pseudowords, pictures of common objects and abstract kaleidoscopic images. In addition to reduced performance on standardized episodic memory and executive measures, MTBI patients showed evidence of increased response bias during recognition. The presumed difficulties among MTBI patients were more evident on tasks involving pictorial and, especially complex, abstract, stimuli, such as pictures and kaleidoscope images.

The present study explores potential correlates of the relatively subtle, task-specific changes in performance reported by Tsirka et al.

* Corresponding author. Mitropolitou Kallidou 5, Thessaloniki 54655, Greece. Tel.: +30 6944686948.
E-mail address: tsirkav@yahoo.com (V. Tsirka).

0167-8760/$ – see front matter © 2010 Elsevier B.V. All rights reserved.
doi:10.1016/j.ijpsycho.2010.09.006

(2010) on EEG measures obtained during performance of the same tasks. Several investigations have applied electrophysiological methods (EEG, MEG, and ERPs) to study brain function in MTBI (e.g. Ford and Khalil, 1996; Gaetz et al., 2000; Gaetz, 2002; Lewine et al., 1999; Nuwer et al., 2005; Pointinger et al., 2002; Gaetz and Bernstein, 2001; Nuwer, 1997; Wallace et al., 2001; Thatcher et al., 1989), although EEG studies of memory task-related changes in MTBI are scarce. In normative studies, episodic memory has been studied extensively with the majority of studies focusing on EEG oscillations in the alpha and theta bands (e.g., Doppelmayr et al., 1998; Klimesch et al., 2001a, 2008; Sauseng et al., 2008).

Recently developed methods of network analysis applied to bioelectrical signals have emerged as promising tools for the evaluation of brain function in real time. Instead of focusing on regional task-specific changes in EEG parameters, like power measures, these methods rely on the premise that the brain is a complex network of interconnected regions, each hosting one or more neurophysiological processes, which are engaged in unison in order to accomplish a particular psychological function. One of these measures, synchronization likelihood (SL), in contrast to traditional coherence measures, is sensitive to both linear and nonlinear statistical independencies between a time series within a dynamic system (Stam and van Dijk, 2002). SL can then be used to evaluate the properties of hypothetical, underlying neural networks using mathematical models provided by graph theory. A graph is a network model characterized by nodes (vertices) and connections (edges) between nodes. For EEG data, nodes are represented by electrode sites, whereas SL values for each and every pair of electrodes serve as the edges of the graph model. Widely known direct indices of network organization provided by graph-model algorithms are the clustering coefficient (*Cp*) and characteristic path length (*Lp*). The former is an index of the connectedness between neighbouring nodes (if A connects to B and C, what is the chance that B and C will be interconnected as well). The latter is the average shortest path connecting any two vertices; the number of edges it contains indicates the length of a path. *Lp* is an indicator of the overall connectedness (integration) of the graph. These two measures form the basis for computing an index of “small-world” network (SWN) organization (Humphries and Gurney, 2008). A SWN is an ideal network model consisting of several local and a few random distant connections and is characterized by a high clustering coefficient and a short path length. Optimal SWN organization has been found to characterize anatomical, hemodynamic, and electrophysiological data obtained from healthy individuals (Bullmore and Sporns, 2009; Micheloyannis et al., 2006b; Stam and Reijneveld, 2007). Optimally functioning network models, such as those computed from multielectrode, surface EEG recordings are believed to reflect optimally organized, underlying brain circuits engaged during performance of a particular function—in the present study, memory encoding and recognition. Whether this is indeed the case is an empirical question which should be reassessed in each study. An indirect approach to establishing the validity of this assumption is to demonstrate significant associations between network model parameters during performance of memory tasks and memory ability measures obtained independently. Secondary, episodic memory functions such as those tapped by the task used in the present study are suitable for this purpose, as they require engagement of a tightly interconnected set of brain areas (for a recent review see Dash et al., 2006). In contrast, brain dysfunction is expected to alter network structure, generally in the direction of less optimal SWN organization, indicating more “random” networks. Binary, unweighted graph parameters are more commonly used in relevant EEG studies, with weighted graphs emerging more recently as a method of choice, as they specify indices of the strength of modelled connections (Alstott et al., 2009; Bassett and Bullmore, 2009; Micheloyannis et al., 2006a; Ponten et al., 2009; Rubinov et al., 2009; Stam et al., 2009).

Here we employ a variety of EEG-derived measures, including power in individually-determined frequency bands (according to Klimesch et al., 1994, 1996; Klimesch, 1999), Synchronization Likelihood, clustering, path length, and SWN (using both weighted and unweighted calculation methods). The main goal of the study was to assess global cortical connectivity and network organization in the acute phase of MTBI in comparison to age-, education-, gender-, and IQ-matched, neurologically healthy control participants. Estimates of network organization in the same subjects were obtained at rest and during the encoding and recognition phases of the same episodic memory tasks reported by Tsirka et al. (2010). The MTBI patients were expected to differ from control participants over a wide range of frequencies including theta and three, individually-determined alpha sub-bands. The role of stimulus type was also examined. It was expected that, during encoding and recognition of pictorial stimuli, especially of the more abstract kaleidoscope images, findings will be indicative of deviating from the optimal small-world configuration i.e. of less optimal network organization in MTBI patients.

2. Methods

2.1. Participants

The patient group consisted of 25 individuals (23 right handed and 2 left handed, including 19 men and 6 women) who had sustained mild TBI with a mean age of 26.82 years (SD 8.58) and an average of 11.84 (SD 2.85) years of education. The control group consisted of 25 healthy volunteers (23 right handed and 2 left handed, including 19 men and 6 women) with a mean age of 27.1 years (SD 8.79) and an average of 11.76 (SD 2.85) years of education. None of the participants had a history of neurological (including previous TBI) or systemic disease that could affect cognitive function, drug or alcohol abuse, hearing problems, or family history of an inheritable neurological disease. They all had normal or corrected to normal vision. All participants had Greek as their primary language and they were informed about the procedures involved in the study, which had been earlier approved by the Ethics Committee of the University of Crete. All participants gave written informed consent. Patients were excluded if they had reported sleep deprivation or alcohol use before the test sessions. The patients were recruited upon admission to the Neurosurgical Emergency Department if they had Glasgow Coma Scale (GCS) >13, loss of consciousness (LOC) <30 min, Post Traumatic Amnesia (PTA) <24 h, no focal neurological signs and a normal CT scan. Data collection was performed within 23 days post-injury (21 patients were tested within one week post-injury, two patients were tested within two weeks, and the remaining two within three weeks post-injury).

Control subjects were volunteers matched to each patient on the basis of age, gender, handedness, years of education, geographical origin, and general cultural background. They were recruited among family members and friends of the MTBI patients. Participants completed a medical and family history questionnaire and were screened using a series of scales and psychometric tests. These tests provided a comprehensive description of patients' cognitive status at the time of the examination. Screening tests included the Galveston Orientation and Amnesia Test (GOAT, administered only to patients) assessing orientation to place, time, person and also retrograde and anterograde amnesia, the Mini Mental State Examination (MMSE), the Edinburgh Handedness Inventory, the Hamilton Depression Scale, the Hamilton Anxiety Scale, and the Adult ADHD (Attention Deficit Hyperactivity Disorder) Self-Report Scale Symptom Checklist. The Vocabulary and Similarities subtests from the Greek adaptation of the Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 1999) were used as indices of crystallized intelligence, which was least likely to be affected by the injury. The two groups did not differ on age ($p>0.9$), education ($p>0.9$), scores on the Hamilton anxiety ($p>0.9$),