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Evaluation of traumatic brain injury: Brain potentials in diagnosis, function, and prognosis

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ABSTRACT

The focus of this review is an analysis of the use of event-related brain potential (ERP) abnormalities as indices of functional pathophysiology in survivors of traumatic brain injury (TBI). TBI may be the most prevalent but least understood neurological disorder in both civilian and military populations. In the military, thousands of new brain injuries occur yearly; this lends considerable urgency to the use of highly sensitive ERP tools to illuminate brain changes and to address remediation issues. We review the processes thought to be indexed by the cognitive components of the ERP and outline the rationale for applying ERPs to evaluate deficits after TBI. Studies in which ERPs were used to clarify the nature of cognitive complaints of TBI survivors are reviewed, emphasizing impairment in attention, information processing, and cognitive control. Also highlighted is research on the application of ERPs to predict emergence from coma and eventual outcome. We describe primary blast injury, the leading cause of TBI for active duty military personnel in present day warfare. The review concludes with a description of an ongoing investigation of mild TBI, aimed at using indices of brain structure and function to predict the course of posttraumatic stress disorder. An additional goal of this ongoing investigation is to characterize the structural and functional sequelae of blast injury.

1. Introduction

A traumatic brain injury (TBI) occurs every 23 s in the United States (Brain Injury Association of America, 2007). In addition to hundreds of thousands of service members who have sustained TBI in recent years, the Centers for Disease Control and Prevention estimates that 1.7 million people in the United States sustain a TBI annually (Faul et al., 2010). Approximately 20% of these injuries are attributed to motor vehicle accidents (Faul et al., 2010), whereas the European Brain Injury Consortium estimated that more than half of all brain injuries in Europe resulted from "road traffic accidents" (Murray et al., 1999, p. 225). Other common causes of TBI include falls (35% of injuries in the United States) and striking/being struck by an object, including sports-related concussions (16% in the general population, 25% in those under the age of 14) (Faul et al., 2010).

Deficits after TBI vary in type and magnitude due to the strength of the injuring force and the locus and severity of the brain injury. The Department of Veterans Affairs/Department of Defense criteria for classifying a TBI as mild, moderate, or severe are based on the presence and duration of loss or alteration of consciousness and amnesia for the events surrounding the incident (see Table 1). In addition, score an the Glasgow Coma Scale (a behavioral assessment tool; Teasdale and Jennett, 1974) and neuroimaging results are considered (Management of Concussion/mTBI Working Group, 2009). Mild TBI (or "concussion") is the most common form of head injury; approximately 80 to 90% of head injuries are classified as mild (Cassidy et al., 2004; LaChapelle et al., 2008). Bazarian et al. (2005) estimated the annual incidence of mild TBI in civilian populations to be as high as one per 200 in the United States. There is abundant evidence that concussion alters brain potential indices of information processing; this research will be covered elsewhere in this publication (Broglio et al., 2011). The primary emphasis of the present review is on moderate to severe TBI.

There have been numerous scientific reports, some going back 50 years, linking TBI to cognitive impairment. Cognitive deficits following TBI include aspects of attention (Gentilini et al., 1989; Gronwall, 1976; Lezak et al., 2004; Mathias and Wheaton, 2007; Mirsky et al., 1991; Oddy et al., 1985; Reitan and Wolfson, 2000; Rosvold et al., 1956; Willmott et al., 2009) coupled with alterations in memory (Gronwall and Wrightson, 1981; Mathias and Wheaton, 2007; Oddy et al., 1985; Reitan and Wolfson, 2000; Ruff et al., 1989), problem solving (Cicerone and Wood, 1987; Dawson et al., 2004; Jarvie, 1960; Krpan et al., 2007; Levin et al., 1990; Temkin et al., 1995; Wayland and Taplin, 1985), language skills (Coelho et al., 1991, 1995, 2002; Davis and Coelho, 2004; Ellis and Peach, 2009; Hagen, 1984; Heilman et al., 1971; Holland, 1982; Stout et al., 2000; Wiig et al.,

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Table 1
Classification of TBI severity.[a]

Criteria	Severity		
	Mild	Moderate	Severe
Loss of consciousness (LOC)	0–30 min	>30 min but <24 h	>24 h
Alteration of consciousness/mental state	Brief, <24 h	>24 h	>24 h
Post-traumatic amnesia (PTA)	0–1 day	>1 and <7 days	>7 days
Glasgow Coma Scale (best score in the first 24 h)	13–15	9–12	<9
Structural neuroimaging	Normal	Normal or abnormal	Normal or abnormal

[a] Management of Concussion/mTBI Working Group, 2009.

1988; Yang et al., 2010), and cognitive control of behavior (Aubry et al., 2002; Collins et al., 1999; Ellemberg et al., 2007; Levin et al., 1987; Stuss et al., 1989). Information processing is slowed, often permanently, following the injury (Brouwer et al., 1989, 2002; Dikmen et al. 1986, 1995; Gentilini et al., 1989; Gronwall, 1989, Gronwall and Wrightson, 1981; Mathias and Wheaton, 2007; Ponsford and Kinsella, 1992; Reitan and Wolfson, 2000; Stuss et al., 1986, 1989; Willmott et al., 2009). Some cognitive deficits may be difficult or impossible to detect using standard neuroimaging methods. However, evoked potentials (EPs) and event-related brain potentials (ERPs) show promise in elucidating even subtle changes in sensory and cognitive processing.

2. Rationale for the use of ERPs to study cognitive sequelae of TBI

ERPs are one of the most informative and dynamic methods of monitoring the flow of information in the brain. The voltage deflections comprising the EP and ERP reflect the reception and evaluation of sensory information, as well as higher-level processing that involves selective attention, memory updating, semantic comprehension, and other types of cognitive activity. ERPs are linked in time with a physical event or mental activity. The ERP methodology is applicable to patients who are unable to respond orally or motorically, and thus provides a means to evaluate patients not suitable for conventional neuropsychological assessment.

An ERP component is defined by its positive or negative polarity,[1] amplitude, latency, scalp distribution, and relation to experimental variables. Components of the ERP are elicited in different paradigms and provide distinct types of information. Their sequence and latencies track the time course of processing activity in milliseconds (e.g., Duncan-Johnson, 1981; Duncan-Johnson and Donchin, 1982; McCarthy and Donchin, 1981; Näätänen et al., 1978; Sams et al., 1985). Their amplitudes indicate the extent of allocation of neural resources to specific cognitive processes required to analyze, categorize, and recognize stimuli (Donchin, 1981; Duncan-Johnson and Donchin, 1977, 1982; Näätänen, 1990; Näätänen and Picton, 1986; Pritchard et al., 1991; Ritter et al., 1979; Wickens et al., 1984). ERPs provide a non-invasive method of studying, with exceptional temporal resolution, information processing in the human brain.

3. Long latency ERP components used in TBI research

ERPs have been applied to TBI research to help elucidate and characterize deficits following brain injury. The cognitive ERP components applied most frequently to evaluate the effects of TBI include N100, mismatch negativity (MMN), N2b,[2] P3a,[3] P300,[4] error-related negativity (ERN), and post-error positivity (Pe). N100 reflects sensory processing of auditory stimuli (Davis and Zerlin, 1966; Näätänen and Picton, 1987), but is also sensitive to level of attention (Näätänen and Picton, 1987). Because the N100 component is primarily a sensory component, it is affected mainly by the physical characteristics of the eliciting auditory stimuli. The MMN is elicited by any discriminable change in a sequence of stimuli (Näätänen et al., 1978). This component is thought to reflect an automatic process that detects a difference between an incoming stimulus and the sensory memory trace of preceding stimuli. The MMN does not require conscious detection of a deviant stimulus.

N2b, P3a, and P300 are commonly elicited in the oddball paradigm, in which a random sequence of stimuli is presented. The stimuli can be classified into one of two or three categories, and the task is to classify the stimuli, either by counting or by pressing a button, to members of one category (the "target"). If members of the target category occur infrequently ("oddballs"), they will elicit N2b and P300. It is well established that the lower the probability of an attended stimulus, the larger the amplitude of P300 (Duncan-Johnson and Donchin, 1977). The N2b, P300, and P3a reflect aspects of information processing involved in stimulus discrimination, evaluation, and categorization (Clark et al., 1992; Courchesne et al., 1975; Duncan et al., 2003, 2009; Duncan-Johnson and Donchin, 1977, 1982; Näätänen and Picton, 1986; Ritter et al., 1982; Squires et al., 1975; Sutton and Ruchkin, 1984).

N2b is a component of negative polarity that is thought to reflect stimulus orienting (Czigler et al., 1996; Näätänen and Picton, 1986; Renault et al., 1982), recognition of stimulus relevance (Clark et al., 1992; Ritter et al., 1982; Spikman et al. 2004), and the conscious detection of deviance (Broglio et al., 2009; Duncan et al., 2005; Näätänen and Alho, 2004; Näätänen and Picton, 1986). It occurs approximately 200 ms after stimulus onset and is maximal over fronto-central brain regions (Spikman et al., 2004).

P300 is a positive-going component following N2b that is elicited by rare, attended stimuli (Duncan-Johnson and Donchin, 1977, 1982; Duncan et al., 2009; Johnson and Donchin, 1980; Johnson, 1989b; Kutas et al., 1977; Naito et al., 2005; Ruchkin et al., 1975; Sutton et al., 1965; Sutton and Ruchkin, 1984). It is typically elicited 300 ms or more after stimulus onset and is of maximal amplitude at centro-parietal electrode sites.

An additional component, P3a, can be elicited in the three-stimulus oddball task. This component reflects the identification and categorization of an unexpected, rare novel or deviant stimulus that does not require a response (the "no-go" stimulus; Courchesne et al., 1975; Snyder and Hillyard, 1976; Solbakk et al., 2002; Squires et al., 1975). In contrast to P300, which requires active attention to the eliciting stimuli, P3a can be elicited by attended or unattended sequences of stimuli. It is thought to be the neural correlate of the orienting response (Courchesne et al., 1975, Knight, 1984; Kok, 2001; Polich, 2007; Riggins and Polich, 2002; Rushby et al., 2005, Squires et al., 1975) and occurs somewhat earlier than P300, with a peak latency of 250–300 ms. It also has a more fronto-central distribution than P300 (Duncan et al., 2009; McDonald et al., 2010).

The error-related negativity (ERN) and post-error positivity (Pe) components have been used to evaluate deficits in cognitive control consequent to TBI. These ERP components are elicited by stimuli that provide feedback on task performance. The ERN is a negative response-locked ERP component elicited by incorrect responses. It

[1] Voltage difference between the recording and reference electrodes.
[2] The terms *N2b* and *N200* are used interchangeably in this review.
[3] The terms *P3a* and *novelty P3* are used interchangeably in this review.
[4] The terms *P300* and *P3b* are used interchangeably in this review.