USE OF ERP MARKERS IN PATIENTS WITH WHIPLASH AND CONCUSSION WITH COGNITIVE COMPLAINS

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Introduction

Deficits in attention, executive function and memory are frequently found in patients with history of Traumatic Brain Injury (TBI). Electrophysiological markers such as Event-related Potentials (ERP) may be helpful in revealing cognitive deficits not detected in routine neuroimaging studies.

Concussion may lead to changes in cerebral physiology that can be captured by ERP. ERP are the result of an averaged EEG signal time-locked to the onset of a given stimulus. ERP have different components labeled according to their polarity and the time of occurrence.

Previous studies have shown effects of concussion on P3 responses on ERP with decreased amplitude and/or prolonged latency that may persist after several years.The P3 component of the ERP can be divided in P3b which is evoked in response to an infrequent stimulus with a centroparietal location, and P3a is evoked by a novel stimuli with a frontocentral location. A third ERP response that may be affected in concussion patients is the N2 response which appears just before the P3 and localizes in the frontocentral area and seems to relate to inhibition control.

Whiplash injuries have been previously described in neuropsychological data meta-analysis associated with disturbance in attention, working memory, executive function, visuomotor tracking and immediate recall. Previous study have shown similar cognitive impairment in patient after mild traumatic brain injury and whiplash injury including speed of information processing, visuospatial abilities and verbal fluency. In addition, both whiplash injury and concussion have been shown to alter processing of the middle-latency somatosensory evoked potential N60 in the acute post traumatic period suggesting similar underlying mechanism of rotational mild traumatic brain injury.

Objectives

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We used an automated Event Related Potentials (ERP) technique to assess cognitive complains in patients with Traumatic Brain Injury (TBI), and investigate whether neurophysiological testing is a more sensitive measure of abnormalities than standard neuroimaging techniques in this population

Materials & Methods

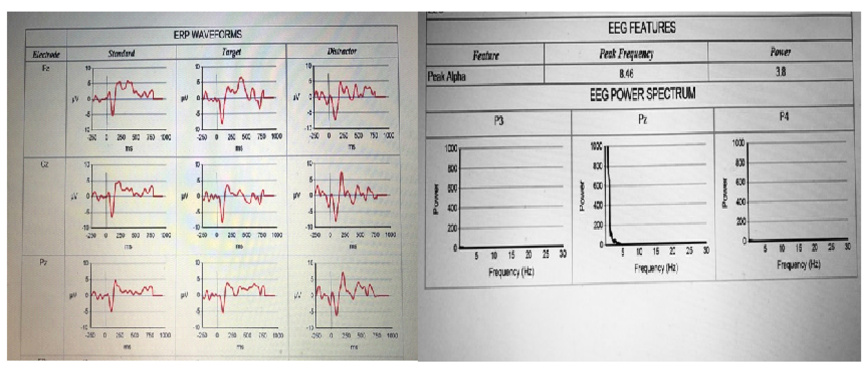
Patients with a history of subacute and chronic TBI, mild to moderate-severe injuries and cognitive complains underwent an auditory oddball ERP paradigm in conjunction with neuro imaging studies. The stimuli for the ERP comprised of standard tones (1000hz), target tones (2000hz) and unexpected distractor tones (white noise), that were played with probabilities of .75, .15 and.10. Tones were presented in a pseudorandom order, so that target and distractor tones were never presented sequentially. Instruction was given to the patients to respond to the target stimuli by pressing a button with their dominant hand. For each test 400 stimuli were presented binaurally through ear phones at 70-dB volume. The tone duration for each stimulus was 100 ms with rise and falltimes of 10ms. The interstimulus interval was between 1.5 and 2 sec. During the examination patients sat comfortably in a chair in an office room under regular lighting conditions.

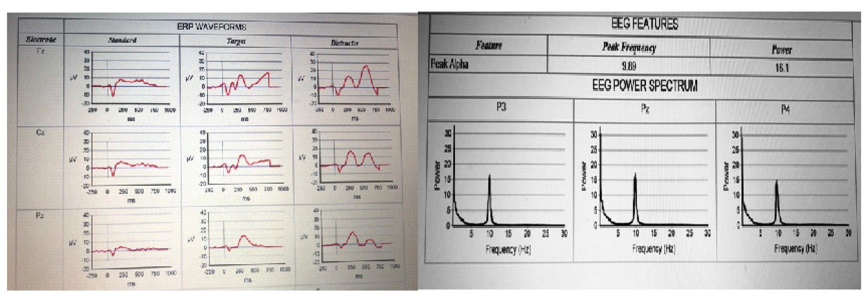
Electroencephalographic (EEG) activity was recorded from 7 electrode sites (Fz, Cz, Pz, F3, P3, F and P4) of the international 10-20 system using a COGNISION Headset (Neuronetrix). Electrodes were referenced to averaged mastoids (M1,M2) and Fpz served as the common electrode. Impedance was automatically checked. Data were collected from -240 to 1000 ms around the stimuli, digitized at 125 hz , and bandpass filtered from 0.3 to 35 hz. Trial sets of a deviant tone and preceding standards that contain artifacts were immediately repeated. Trial averaging and extraction of ERP measures were automatically performed by the COGNISION software. EEG data from each trial were baseline corrected using the prestimulus period. For standard tones, only the trials immediately preceding target and distractor stimuli were averaged. During data preprocessing, recordings that exceeded two times the root mean square value for the EEG test data, or with wrong button presses were rejected and excluded from averaging. ERP waves that averaged less than 20 trials after preprocessing were eliminated from all analysis.

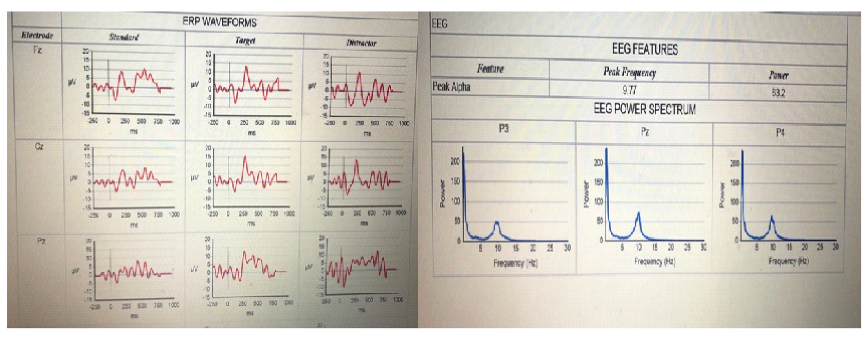
Peak amplitude of the ERP features was measured as the difference between prestimulus baseline and maximum peak amplitude. Peak latency was defined as the time point corresponding to the maximum amplitude. Peak latency was defined as the time point corresponding to the maximum amplitude and was calculated relative to the stimulus onset. P50 and N100 were measured from all stimuli. P200 was measured from standard and target tones. N200, P3b, and slow wave were measured from the target tone and P3a from the distractor tone.

Accuracy and reaction time of button presses were also analyzed. Accuracy was calculated as the percent of correct responses to target tones, whereas false alarms indicated button presses to nontargets. Reaction time was calculated as the time from the stimulus onset to button press. Median reaction time was calculated for each subject to limit the influence of any other reaction times.

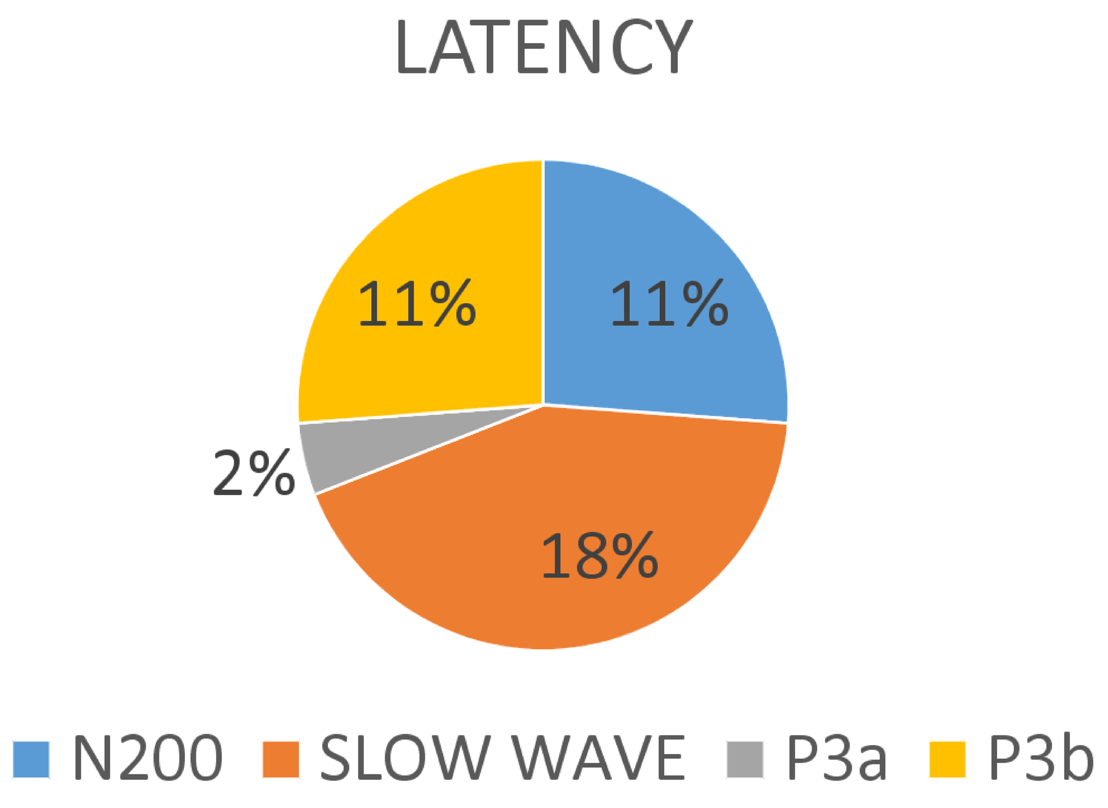
Results

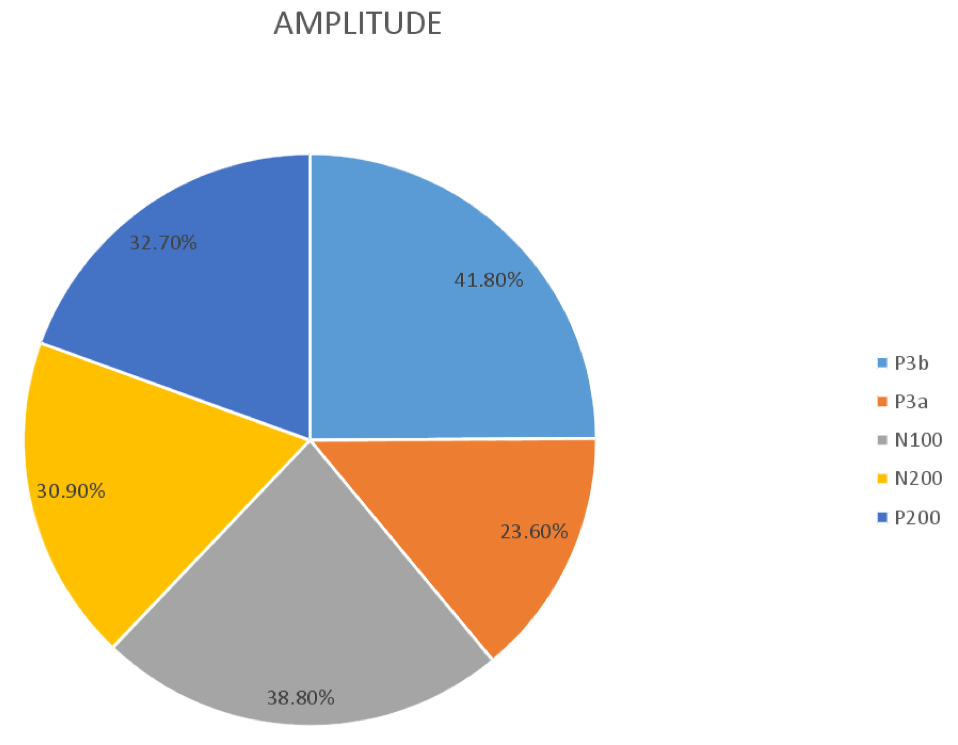






1. Decreased in P3a and P3b amplitude after MVA . MRI with signs of mild axonal diffuse injury
2. Unremarkable ERP after withplash injury
3. Decreased N100 N200 amplitude after whiplash injury





Of the 55 reported cases, 29 suffered whiplash type of injury, 8 had a fall,

9 hit head on the window and/or airbag ,

3 were hit by a car, 3 were assaulted , one hit head in the counter , 2 fell from bike .

MRI brain in 32 were unremarkable or showed age related changes.

Head CT revealed subarachnoid hemorrhage in one, subdural hematoma in four, one had occipital fracture, two had soft tissue edema, two had MRI showing signs of diffuse axonal injury, two had MRI with frontal contusions.

The time of the performance of the COGNISION was in the first month in 16 cases, between 1-3 months in 19, 3-6 months were 14, 4 between 6-12 months , one 2 years and one with recurrent concussions through the past several years.

ERP responses revealed decreased amplitude of P3b in 23(41.8%), P3a in 13 cases (23.6%).

P3b latency was prolonged in 7 (12.7%) and P3a in 5 (9%).

Median reaction time was prolonged in 25 studies (45,4%).

N100 amplitude was diminished in 21 cases (38.8%) and N200 was lower in 17 (30.9%).

P200 amplitude was decreased in 18 (32.7%).

Slow wave latency was prolonged in 12 (21.8%).

EEG peak alpha was decreased in 14 (25.4%).

New Section

DISCUSSION

The peak amplitude is a measure of focal attention and tends to correlate with executive function. The P3a latency reflects orientation to a non target deviant stimulus.

N200 is a negative peak that immediately precedes the P3b and is linked to cognitive processes of stimulus identification and distinction.

N100 reflects bottom up information such as stimulus characteristics and is modulated by attention and memory changes .

The slow wave is a negative deflection that follows the P3b and reflects a final stage of stimulus evaluation. The slow wave latency is affected by task difficulty.

Previous studies have demonstrated decreased in P300 amplitude after TBI as well as N200 amplitude, with memory deficit correcting in some with the reduced P300 amplitude.

The presence of ERP changes related to the time of injury has been controversial with some data showing reversal over time while others point to a persistent abnormally years after the injury in spite of unremarkable neuropsychological evaluation.

The most common used neuroimaging techniques underestimate the degree of injury as they do not evaluate for diffuse axonal injury except for diffusion tensor imaging which is mostly done in research setting.

In this series of cases with whiplash with cognitive complains imaging with MRI and or CT were unremarkable in all except two cases with P3a, P3b and N100 amplitude decreased in more than 30% of them. Median reaction time was also frequently prolonged indicating slowing of processing speed.

P3b amplitude is determined by the amount of attentional resources allocated when working memory is updated. P3a is associated with engagement of attention and processing of novelty.

N100 amplitude is also modulated by attention and memory-related variables.

P200 reduced amplitude also contributes to slower reaction time and reduced accuracy in stimulus classification.

Latencies abnormalities were less common.

Slow wave latency prolongation was the most commonly seen. And is affected by task difficulty. P3b latency reflects stimulus evaluation and classification speed.

The few cases with more significant neurological and neuroimaging abnormalities secondary to the injury may have more frequent abnormalities in the ERP but they were a very small sample. Furthermore, age and background history were not considered which may limit the findings. However, the vast majority did not have significant comorbidities.

CONCLUSION

Analysis of ERP data provides valuable information in patients with cognitive complains after TBI, even in mild cases of whiplash injury, particularly when standard neuroimaging studies are non revealing. Further data in a larger population and longitudinal study are suggested.

References

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