Concussions in athletes produce brain dysfunction as revealed by event-related potentials

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We have used event-related potentials (ERP) to assess cerebral activity following mild traumatic brain injuries in 20 college athletes practising contact sports. Concussion victims showed a striking decrease in P300 amplitude, an effect presumed to reflect alterations in attentional-cognitive processes. Moreover, the degree of impairment was strongly related to the severity of post-concussion symptoms. Our data suggest that concussions cause objectively measurable changes in the electrophysiological markers of brain activity and hence in the functions of the structures from which they originate. ERPs may thus constitute a reliable method to accurately monitor the clinical course and recovery of head injuries in athletes. *NeuroReport* 11:4087–4092 © 2000 Lippincott Williams & Wilkins.

Key words: Electrophysiology; Mild traumatic brain injury; P300; Sports

INTRODUCTION

As many as 300 000 sports-related concussions are identified each year in the USA although this number certainly underestimates the incidence as this injury is underreported [1]. The number and severity of concussions that one can safely sustain is not known but important short- and long-term cognitive sequelae from mild traumatic brain injury (MTBI) have been documented in athletes [2,3]. It has also been suggested that this type of injury may constitute a predisposing condition for important neuropathological diseases such as Parkinsonism or Alzheimer's disease [4,5]. At the present time, however, the quantification of brain dysfunction following concussions in athletes has been both inconsistent and inconclusive.

Athletes who suffer a concussion generally complain of various symptoms, such as dizziness or headaches, that are often disruptive in their everyday lives and may interfere with the practice of their sport. Researchers, physicians, team trainers and the athletes themselves are frequently faced with the problem of assessing the severity of these important indicators of brain trauma. This may lead to a trivialization of the short- and long-term consequences such that premature return to play may be advised and little follow-up is undertaken to verify whether long-term damage has been sustained. This is in part due to the lack of objective and robust methods to evaluate how concussions affect brain activity. For example, clinical evaluation of MTBI using neuroimaging techniques such as CT scans frequently show normal patterns and are thus of little value in diagnosis and management [6]. Recent studies [7] suggest that a single mild head injury in athletes causes cognitive/information processing deficits that can be documented with neuropsychological tests within 24 h of the injury. However, even in cases where deficits are detected, rapid return to pre-concussion performance often takes place within the next 5–10 days, even though the subjects are still symptomatic. This may be due in part to the inevitable practice effects inherent to psychological testing [2,7]. Neurophysiological techniques have also attempted to accurately measure the effects of concussions. Although the existence of close correlations between clinical and neurophysiological findings following severe head injuries have been demonstrated in several studies [8] conclusions are still equivocal for MTBI. For instance, electroencephalographic (EEG) recordings have been reported to be of little value in the assessment of MTBIs [9].

Here, we report that concussions lead to changes in brain electrophysiological activity and that these modifications can be measured reliably and objectively using event-related potentials (ERPs). The ERPs represent the averaged EEG signal time-locked to the onset of a given stimulus and consist of different components labelled by their polarity (P for positive or N for negative) and their time of occurrence in milliseconds (e.g. P300). In the present task, two stimuli with different probabilities of occurrence were presented. The infrequent stimulus (the so-called oddball) generally elicits a P300 deflection ~300 ms after stimulus

onset, which has a higher peak amplitude than that evoked by the frequent one. Using this paradigm, our results indicate that concussion victims show a decrease in P300 amplitude, a wave component presumed to reflect attentional-cognitive processes [10]. This decrease is seen for periods ranging from one week to at least 6 months after a concussion. Moreover, the degree of impairment is strongly related to the severity of post-concussion symptoms (headaches, dizziness, etc.).

SUBJECTS AND METHODS

Subjects: In order to maintain sample homogeneity, data from 12 of the 47 initial male participants were rejected either because of age ($\geqslant 25$), academic background (< 13 years of education), etiology of concussion (accidents or falls that did not occur within a sports context) and time elapsed since the last concussion (maximum of 2 years). Technical difficulties during recordings prevented the use of data obtained from five additional subjects. Three equal groups of subjects were thus tested in the present study ($n = 30$). All were McGill University athletes, practising contact sports (football $n = 16$, hockey $n = 10$, rugby $n = 1$, soccer $n = 2$, wrestling $n = 1$) who were referred by their athletic trainer and/or team physician. One group was composed of 10 athletes who had never sustained a concussion and they served as control subjects. The second group consisted of 10 athletes who suffered a concussion between 1 month and 2 years before testing (mean ($\pm$ s.d.) 9.75 ± 7.75) months but were asymptomatic at the time of recording. Subjects of the third group ($n = 10$) sustained a concussion 1 week to 6 months prior to testing (mean 1.7 ± 1.95 months) and were symptomatic at the time of the recording. The three groups did not differ in terms of age (mean 21.5, 21.4 and 21.6 years, respectively; $F = 0.081$; $p = 0.922$) or education level (mean 15.6, 15.5 and 15.4 years, respectively; $F = 0.069$; $p = 0.934$).

A standardized concussion history form was administered to obtain information regarding number and description (e.g. confusion, retrograde and/or anterograde amnesia, loss of consciousness) of all concussions ever sustained. On average, participants from the asymptomatic concussion group reported having experienced 2.6 concussions (range 1–4) and those from the symptomatic group, 3.2 concussions (range 1–7). Severity of the latest concussion was classified by a neurosurgeon (KJ) using the practice parameters of the American Academy of Neurology. Hence, a grade 1 concussion corresponded to a state of transient confusion, with no loss of consciousness (LOC), and symptoms or mental status abnormalities which disappeared within 15 min. Grade 2 referred to a state of transient confusion, with no LOC, and symptoms or mental status abnormalities which did not disappear within 15 min. Grade 3 concussion was characterized by a brief LOC. Using these criteria, the second group (asymptomatic concussion group) had a concussion score of 1.8 ± 0.63 whereas that of the third group (symptomatic concussion group) was 2.1 ± 0.57. CT scans showed no abnormalities and, of the eight symptomatic subjects that underwent MRIs using T1, PdT2 and FLAIR sequences, all were reported as normal except for one subject who showed two hyperintense foci, one in the right frontal subcortical white matter and the other in the anterior third of the left corona radiata.

The severity of the symptoms was assessed by a concussion symptoms scale consisting of 19 of the most common post-concussion symptoms (e.g. headache, dizziness and trouble falling asleep). The severity of each symptom was rated on a scale ranging from 0 (none) to 6 (severe), for a maximum score of 114. Subjects from the symptomatic concussion had a score of 29.45 ± 20.25 on this scale. All participants were also administered a battery of neuropsychological tests ($\sim$30 min in length) adapted from the one used by the National Football League [7], which included a test of orientation, the Hopkins Verbal Learning Test (verbal learning, delayed memory), the Color Trails Parts I and II (visual scanning and executive functions), the Controlled Oral Word Association Test (COWAT, word fluency), the Symbol Digit Modalities Test (SDMT, information processing speed), the Ruff Figural Fluency Test, and the PSU Symbol Cancellation Task. With respect to normative data taking into account age, gender and education, performance on those tests was normal for all subjects.

Approval for this research with human subjects was granted from the Ethics committee of the McGill Medicine Sports Center. Each participant provided written informed consent for voluntary participation.

ERP recording procedure: All subjects were tested using the ERP visual oddball paradigm [11]. In ERP research, the oddball paradigm is one of the most extensively used methods to explore neural substrates of human cognitive processes [10,12]. During the task, a circle (frequent stimulus, diameter, 1.5 cm, probability of occurrence, 0.75) and a star (rare stimulus, composed of three intersecting lines, 1 cm each, probability of occurrence, 0.25) were presented in the center of a monitor for 100 ms. The test comprised a total of 280 trials and conditions were mixed randomly with a variable ISI between 2200 and 2800 ms. Subjects were instructed to press a left button at the presentation of one category of stimulus (rare) and a right button for the other category (the order was alternated for each successive subject). Data acquisition was made possible by an InstEP system that was also used to trigger the computer controlling stimulus presentation. The EEG was recorded from 30 tin electrodes mounted in an E-Cap (Electro-Cap International Inc.). The electrodes were placed according to the guidelines for standard electrode position of the American EEG Society [13] at Fp1, Fp2, AF3, AF4, F7, F3, FZ, F4, F8, FC3, FC4, T7, C3, C1, CZ, C2, C4, T8, TP7, CP3, CP4, TP8, P7, P3, PZ, P4, P8, O1, OZ, and O2. All electrodes were referenced to linked earlobes and their impedances were kept below 5 KΩ, with no noticeable asymmetry in resistance. To control for eye artefacts, the horizontal electro-oculogram (EOG) electrodes were placed at the outer canthus of each eye and for the vertical EOG, they were placed above and below the right eye, in line with the pupil when looking straight ahead.

Data extraction and analysis: Only the ERP and reaction time (RT) results obtained during the successful trials (on average, 90% accuracy level) were submitted to analysis. Epochs contaminated by blinks or eye movement artefacts

were corrected offline using a dynamic regression of the EOG on the EEG in the frequency domain. However, an additional 5% of trials were rejected because the artefacts were too important to be corrected. Overall, every subject had epochs derived from 80–85% of trials, i.e. a minimum of 204 trials. All signals were amplified through a SAI amplifier with a gain of 10 000 (EEG) and 3500 (EOG) and a band-pass between 1 and 30 Hz. The EEG was averaged, offline, time-locked to the stimulus with epochs of a total sweep time of 2048 ms at a sampling rate of 250 Hz. The remaining artefacts in the EEG $>150\,\mu V$ at any electrode that were not correlated with eye movements were automatically rejected from averaging after the EOG corrections. The highest ERP deflection occurring between 300 and 500 ms post-stimulus was positive in all subjects and thus corresponded to a P300 wave component. No negative deflection was seen within the time-window specified above. The P300 amplitude, as well as its latency, were computed at each of the 28 recording sites. For statistical comparisons, the data were analyzed using the StatMap3D program for topographical analysis (DigiMed Systems Inc.) dedicated to functional brain imaging using EEG data. The mapping program allows the representation of the actual voltage distribution on the scalp in a three dimensional fashion based on spline interpolation. These topographical procedures allowed comparisons of the relative P300 amplitude evoked by the rare and frequent stimuli, using Student's *t*-test analyses for each group separately. Moreover, the ERP data to the rare and frequent condition was submitted separately to a multiple one-way ANOVA (SPSS-Windows). Reaction times, computed between stimulus onset and button press, were submitted to the same statistical analyses.

RESULTS

The amount of underlying cortical positive activation (P300) elicited by the frequent and rare stimuli for each of the three groups is illustrated in Fig. 1 in the form of a color gradient. The differences between the P300 amplitude related to the frequent and rare stimuli are clearly not the same in the three groups. In fact, a main group effect was found indicating that the symptomatic group displayed a smaller P300 amplitude, in all conditions and electrodes, than the other two groups ($F=6.42$; $p<0.05$). As illustrated in Fig. 1, the no-concussion group (Fig. 1a) shows a very strong and diffuse oddball effect, with most brain regions exhibiting a stronger P300 amplitude for the rare stimulus than for the frequent one. This difference was shown to be significant using *t*-tests (see significance levels in Fig. 1). Similarly, the asymptomatic group (Fig. 1b) demonstrated a P300 oddball effect. By contrast, the symptomatic group (Fig. 1c) showed almost no oddball effect ($t>-2.96$, $p>0.05$).

To determine the significance of how oddball effect in the P300 amplitude was distributed over various brain regions, the scalp recordings were divided into six sub-

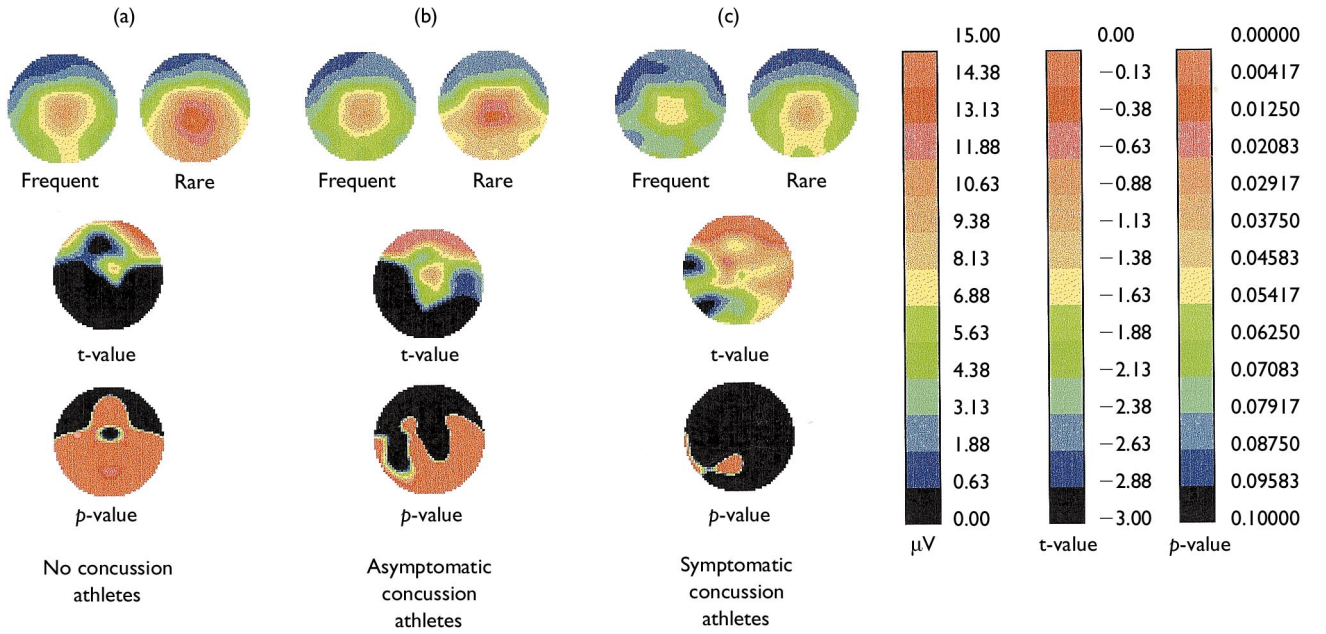

Fig. 1. Bidimensional view of the scalp distribution of the P300 component during the oddball task. Top three pairs of head representations: each pair shows the topographical maps of the mean voltage amplitudes (μV) for the frequent (left head) and rare (right head) stimuli. The leftmost bar chart presents activation in graduated fashion from red (highest positive activation) to black (least positive activation). Middle head representations: the scalp distribution differences between the two types of stimuli are represented as a color coded t-statistic. The middle bar chart presents these t-values in a graduated manner corresponding to the values that appear on the right of the bar. A t-value <-2.95 between the frequent and rare stimuli indicates a significant difference. Lower head representations: Probability values that the differences between the two conditions (frequent and rare) are significant. The corresponding color coded *p*-values are shown in a graduated manner on the rightmost bar chart. The differences between the P300 amplitude related to the frequent and rare stimuli are clearly not the same in the three groups. The rare stimulus condition elicits a larger P300 amplitude in the control group, followed by a weaker, though not statistically significant, response in the asymptomatic group and a significantly weaker response in the symptomatic group.

regions. These regions were pooled into frontal (af3, af4, f3, f4, f7, f8, and fz), central (cz, c1, c2, c3, c4, fc3, and fc4), parietal (cp3, cp4, p3, p4, and pz), occipital (o1, o2, and oz), right lateral (t8, p8, and tp8), and left lateral regions (t7, p7, tp7). Figure 2 shows that anterior regions were significantly different between the symptomatic and control groups for both rare (frontal: $F = 5.98$; $p < 0.05$ and central: $F = 8.83$; $p < 0.05$) and frequent stimuli (frontal: $F = 7.46$; $p < 0.05$ and central: $F = 10.27$; $p < 0.05$). In addition, the P300 amplitude over posterior and lateral regions

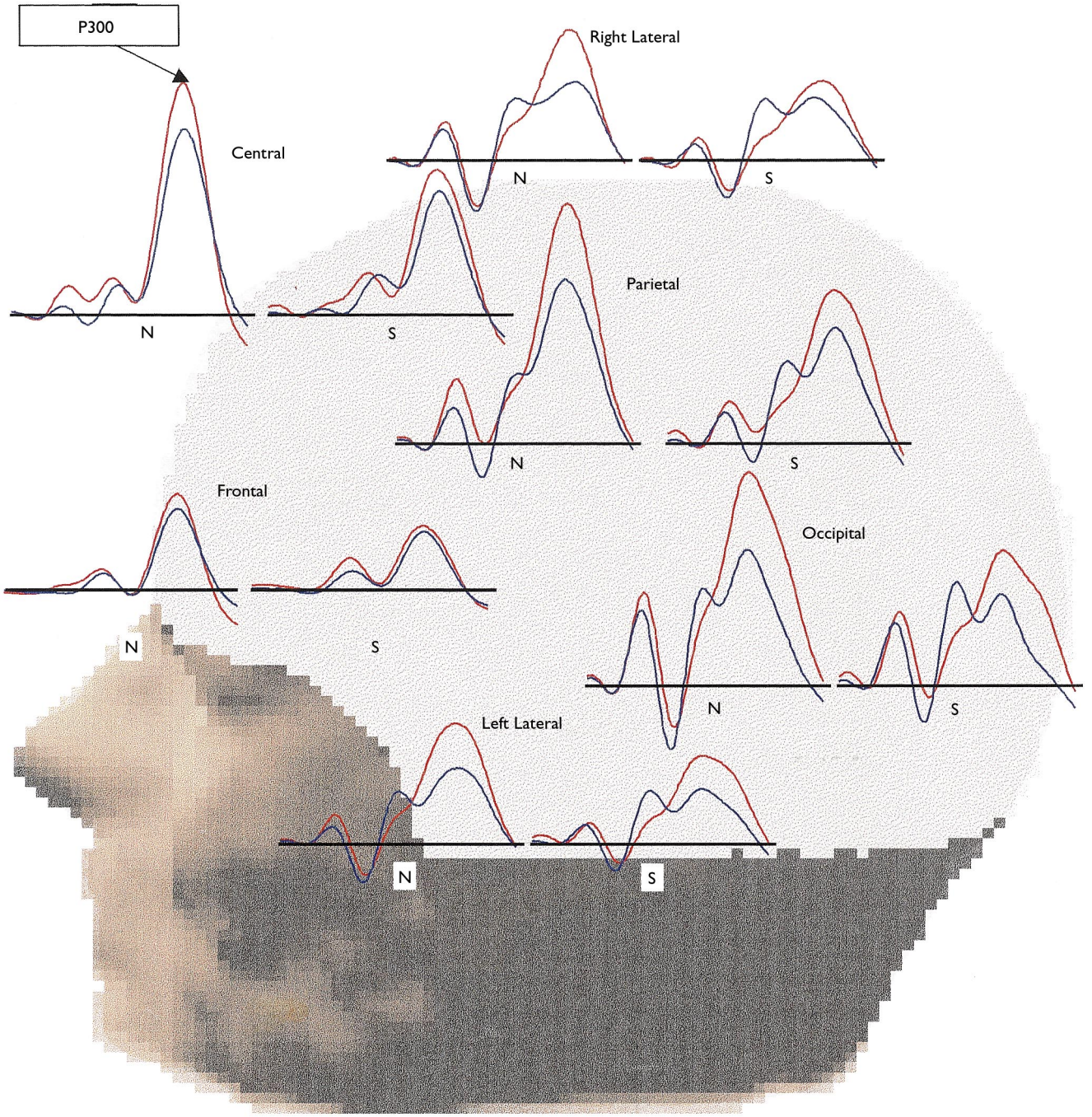

Fig. 2. Regional distribution of the evoked responses at six pooled electrode scalp regions in the symptomatic and no-concussion groups. The six regions include: frontal (af3, af4, f3, f4, f7, f8, and fz), central (cz, c1, c2, c3, c4, fc3, and fc4), parietal (cp3, cp4, p3, p4, and pz), occipital (o1, o2, and oz), right lateral (t8, p8, and tp8), and left lateral (t7, p7, tp7) regions. The P300 wave amplitudes are calculated on a base-to-peak measure The amplitude of the frontal and central regions were significantly different ($p < 0.05$) between the two groups for both rare ($p = 0.034$ and 0.011, respectively) and frequent ($p = 0.036$ and 0.028, respectively) stimuli. In addition, the P300 amplitude for the parietal ($p = 0.010$), occipital ($p = 0.017$), and right lateral regions ($p = 0.025$) were significantly different ($p < 0.05$) between the two groups for the rare stimuli. N, Non-concussion group; S, symptomatic group. Color code: red, rare stimulus; blue, frequent stimulus. Time scale = 500 ms. Amplitude − 3 to 15 μV.

was significantly different between symptomatic and control subjects in response to the rare stimuli (parietal: $F = 10.285$; $p < 0.05$; occipital: $F = 7.66$; $p < 0.05$, and right lateral: $F = 6.81$; $p < 0.05$). The difference between the two groups for the P300 amplitude of the left lateral region approached significance ($F = 3.48$, $p > 0.10$). The asymptomatic group did not differ from the no-concussion group with regard to the P300 amplitude over all scalp regions and experimental conditions.

The latency of the P300 wave was also computed to determine whether the decrease in P300 amplitude was specific to reduced cognitive processing of the information or to some generalized slowing down of brain activation. The latter was further assessed behaviorally by measuring the reaction time to the presentation of the stimulus. No significant differences were found between the three groups with respect to reaction time latency to both rare ($F = 1.28$; $p > 0.05$) and frequent stimuli ($F = 1.13$; $p > 0.05$). Similarly, no significant differences in P300 latency were observed between the three groups of athletes to both the rare ($F = 1.40$; $p > 0.05$) and the frequent stimuli ($F = 1.238$; $p > 0.05$).

Factors related to the decrease in amplitude of the oddball effect observed in symptomatic concussion victims were also assessed. Thus, the P300 amplitude of the frequent condition was subtracted from that of the rare condition, averaged for the 28 electrodes, and correlated with the severity of injury, number of injuries, time elapsed since injury, and clinical symptomatology in this concussion group. Symptomatology was the only factor that correlated significantly with the P300 oddball effect (Table 1). The negative correlation clearly indicates that the greater the symptoms the smaller the oddball effect.

The strong relationship between symptomatology and cognitive electrophysiological activation is also shown for illustrative purposes in a representative subject in Fig. 3a. This figure displays the oddball effect in a hockey player who was evaluated at two time intervals following a concussion. After 1 week, while still symptomatic, this subject showed an abnormally small oddball effect, which was moreover restricted to a limited area. One month later, when he no longer experienced any symptoms, a normal strong and diffuse oddball effect was seen. The re-establishment of the oddball effect, therefore, is closely associated with recovery.

The ERP technique as used here is thus quite sensitive to brain dysfunction. As a diagnostic tool, it also appears to offer an advantage when compared to neurobehavioral tests in that it is resistant to possible practice effects. To test this hypothesis, a college football player who never suffered a concussion underwent ERP recording twice to mimic the procedure used with concussion victims. The time interval between the two recordings was equivalent to that of the concussion victim depicted in Fig. 3a. Similar oddball effects were seen in this subject both times (see Fig. 3b), confirming that the oddball paradigm produces robust findings that do not habituate over repeated sessions [12].

Table 1. Correlations between P300 amplitude of the oddball effect (rare-frequent) and various concussion factors.

Factor	Pearson correlation (Rare−Frequent)	Significance (2-tailed) (Rare−Frequent)
Number of concussions	0.018	0.961
Severity of latest concussion	0.033	0.928
Time since concussion	−0.224	0.535
Symptomatology	−0.625*	0.053*

DISCUSSION

The main finding of the present study is that concussions in athletes produce brain dysfunctions which can be measured objectively using event-related potentials and the oddball paradigm. A clear difference in cortical activation was found between symptomatic concussion victims, on the one hand, and controls or asymptomatic subjects, on the other. Thus, the cortical marker of attentional-cognitive processes, namely the ERP response to the rarely presented stimulus, was smaller for almost all regions examined in subjects of the former group. In addition, a decrease in amplitude of the P300 wave related to the frequent stimuli was found in two sites. The fact that decreases in this indicator of electro-cortical activity was seen only in two sites is not really surprising. Intrinsically, processing of the

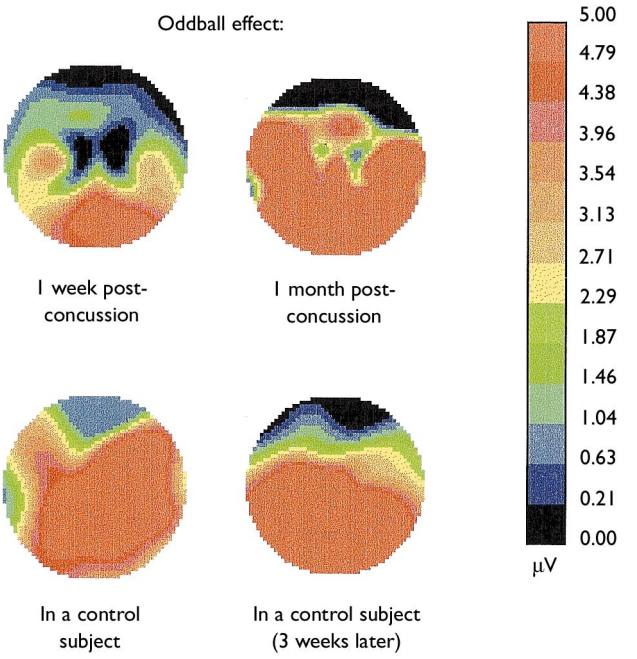

Fig. 3. Bidimensional view of the scalp distribution of the oddball effect in one concussed and one control athlete. The oddball effect was obtained by subtracting the P300 component elicited by the frequent stimulus from that of the rare stimulus in two subjects. This voltage difference is represented on the graduated scale of the bar chart. (**a**) Oddball effect in a hockey player who suffered a grade 1 concussion and who was evaluated one week post-concussion, at which time he was symptomatic (17 on the severity scale). This subject showed only a small oddball effect restricted to posterior areas. However, 1 month after the concussion, when no symptoms were present, a strong and diffuse oddball effect was seen. (**b**) Oddball effect in a control athlete, matched with this subject on the basis of sex, age, education and interval between recording. Similar oddball effects were seen in this subject at both recording sessions, confirming that there were no practice effects.

rare events relies heavily on attentional resources and is therefore extremely sensitive to brain dysfunction. By contrast, treatment of the frequent stimuli can be carried out in a more automatic mode. What is actually more meaningful is that there was a decrease in P300 amplitudes in the frontal and central regions following the presentation of the frequent stimuli. This possibly results from the fact that most of the head impacts involved the front of the head. Hence, these results showing important differences between symptomatic and control subjects even for the more automatic, frequent condition suggests that there may be a link between site of injury and its underlying abnormal electrophysiological activation.

The results showing that the latency of the P300 response was not affected in symptomatic subjects differ from those of other studies which reported a widespread decrease in P300 latency in mild head-injured subjects [8,14–16]. This discrepancy, however, is probably due to the fact that these studies used subjects whose injuries resulted from different impact factors (car accidents, falls, etc.). Moreover, because of the nature of the causal factors, many variables such as age, education level, type and severity of injury as well as time lag between injury and assessment were not as systematically controlled. In the present study, the fact that only the relative P300 amplitudes and not latencies or reaction times were reduced in the symptomatic group suggests that the deficits observed in these athletes are essentially related to cognitive-attentional processes.

Interestingly, neuropsychological testing carried out in the symptomatic group failed to bring out any attentional deficits. This result appears to be at variance with a recent study [2] that reported neuropsychological deficits on a test battery similar to the one used in the present experiment. It must be specified, however, that the effects shown in this study [2] were revealed by comparing pre- and post-concussion levels of performance. Furthermore, 1 week after the concussion, the deficits had abated, most subjects showing a return to baseline level. Our subjects were all examined $\geqslant 1$ week after their concussion, which may explain the fact that neuropsychological findings failed to differentiate the three groups of subjects.

It would appear, in fact, that neuropsychological testing may provide the most useful and sensitive information mainly within the context of a prospective approach, with baseline or pre-concussion data being gathered at the beginning of the sports season [7]. Indeed, individual players vary significantly with respect to their performance on tests of memory, attention/concentration and mental processing speed. Furthermore, they are often better on some of these measures than the general population, which makes any references to existing normative data inadequate [17]. For various reasons (cost, availability of qualified professionals, etc.), a pre-concussion assessment cannot be performed on every athlete who may be at risk of suffering a concussion. Moreover, monitoring of the recovery of functions would involve successive administration of the neuropsychological tests, which are not entirely resistant to practice effects. Hence, such prospective studies might show a return to baseline levels in spite of the fact that athletes continue to report postconcussion symptoms. For these reasons, the ERP technique, coupled with immediate postconcussion neuropsychological evaluation whenever possible, may provide the most sensitive measure of the cognitive effects of MTBI.

A strong relationship between symptomatology and cognitive electrophysiological activation was demonstrated in the present study. This high correlation between the two indicates that the severity of the symptoms might be a good predictor of brain electrophysiological dysfunction. The results suggest, therefore, that more emphasis should be placed on the monitoring of post-concussion symptoms over time with the use of a graded scale for each symptom so that they may be quantified and not simply left to the subjective evaluation of the athlete or the managerial staff.

CONCLUSION

The ERP results obtained in the present study show impaired brain functioning in athletes practising contact sports who are victims of concussions. The robustness and sensitivity of this technique suggest its usefullness in monitoring the clinical course and recovery of these athletes. Furthermore, ERPs constitute an objective test to validate symptomatology in athletes and assist in decisions concerning return to play. Hence the technique has important diagnostic potential and could provide safe return-to-play guidelines thereby attenuating and possibly preventing the appearance of long-term neurological and cognitive deficits.

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