NEUROPHYSIOLOGICAL ANOMALIES IN SYMPTOMATIC AND ASYMPTOMATIC CONCUSSED ATHLETES

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OBJECTIVE: Concussion in sports is a problem of such magnitude that improvements in diagnosis and management are desirable. The aim of the present study was to investigate the effect of concussion on event-related potentials, in symptomatic as well as in asymptomatic athletes.

METHODS: Twenty symptomatic and asymptomatic athletes who sustained a concussion were compared with 10 control athletes in a modified auditory Oddball task. The task included a sequence of tones containing standard and deviant stimuli. Participants were asked to respond to the target tone presented in the left ear and to ignore tones presented in the right ear. The electroencephalogram was recorded from 28 electrodes during the task.

RESULTS: The results showed a reduction in the amplitude of N1, P2, and P3 components in symptomatic and asymptomatic athletes in comparison with control athletes. No between-group differences were observed in reaction times or in latency of the event-related potentials components, except for P3 latency, in which the controls showed shorter latency than the concussed groups.

CONCLUSION: Concussions seem to produce deficits in the early and late stages of auditory information processing, which possibly reflect impaired brain functioning in symptomatic and asymptomatic concussed athletes. The fact that asymptomatic athletes have an electrophysiological profile similar to that of symptomatic athletes challenges the validity of return-to-play guidelines for which the absence of symptoms is a major issue.

KEY WORDS: Athletic injury, Concussion, Event-related potentials, Neuropsychology

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Concussions represent as many as 300,000 sport-related injuries in the United States (45). This incidence is certainly underestimated, because only a small percentage of concussions are reported because athletes may not recognize that they have sustained a concussion. The occurrence of concussions in contact sports is a problem of such magnitude that improvements in diagnosis and management are desirable.

According to the agreement reached at the First International Symposium on Concussion in Sport (9), the definition of concussion should include the following five criteria: 1) the concussion can be caused by a direct blow to the head or another place on the body with an impulsive force transmitted to the head; 2) the concussion results in immediate and short-lived deterioration of neurological functions; 3) the concussion can result from neuropathological changes, but the acute clinical symptoms reflect a functional disorder rather than structural damages; 4) the concussion can result in various clinical symptoms of variable severities, which imply or do not imply a loss of consciousness (LOC); and 5) the concussion is generally associated with normal structural neuroimaging results.

Approximately 40% of concussed athletes will develop postconcussion symptoms, such as headaches, drowsiness, dizziness, irritability, and sleep disorders (19), as well as neuropsychological deficits, such as memory problems and difficulty concentrating (8, 14, 27). The return-to-play decision is generally made if the athlete no longer reports symptoms after the concussion (6), has normal neurological and radiological examinations, and if the neu-

ropsychological data show a return to baseline performance (12). It is generally considered that the absence of symptoms during a few days and normal neuropsychological performances reflect a total brain recovery. In recent studies, it has been observed that concussed athletes show a return to neuropsychological baseline performances approximately 1 week after the concussion (5, 8, 26, 30), but it is not known if a week is sufficient to allow a complete brain recovery. The return-to-play decision is extremely important, because if athletes return to play with their concussions unresolved, they may still have cerebral, metabolic, or processing dysfunctions that increase the risk for permanent injury or, more rarely, for the second-impact syndrome (7, 42).

Cognitive event-related potentials (ERPs) seem to be sensitive in the evaluation of concussion effects by allowing the detection of attention and information processing deficits (17). ERPs represent the averaged electroencephalogram (EEG) signal recorded after the presentation of stimuli, and consist of various components named according to their polarity (P, positive; N, negative) and their latency (e.g., N1 is the first negative component to appear after the presentation of a stimulus). Each component is associated with a specific level of information processing.

The best-known paradigm among the tasks used in ERP is the Oddball paradigm (35). It consists of the presentation of two categories of stimuli having different probabilities of occurrence (frequent and rare stimuli). The appearance of the rare stimulus generally elicits a strong, positive P3 wave over the central and parietal electrodes at 300 to 600 milliseconds after the stimulus presentation. Contrary to earlier components, such as N1, which reflects automatic information processing, P3 represents cognitive and attentional processing. In fact, the amplitude of the P3 component reflects the amount of attentional resource allocated in a task or the degree and quality of information processing (22, 48), whereas its latency is associated with the stimulus classification speed (23, 29, 36). In patients with attentional deficit and hyperactive disorder, a reduced P3 is generally found (3a). Studying the effects of concussions on athletes with a visual Oddball task, Dupuis et al. (11) found a reduction in the amplitude of the P3 component in symptomatic athletes compared with asymptomatic and control participants. Recently, Lavoie et al. (24) found similar results in college athletes in a more-demanding visual Oddball task, in which an attenuation of the P3 component was again observed in concussed athletes; the reduction was more marked in symptomatic than in asymptomatic athletes. The effects of repetitive concussions in athletes have also been studied with ERP. Gaetz et al. (16) found that junior hockey athletes who sustained three or more concussions presented a prolonged P3 latency in visual ERP in comparison with athletes who had no concussion history. Thus, in athletes, the presence of symptoms and the number of concussions previously sustained seem to predict the P3 characteristics in Oddball paradigms (11, 16, 24).

The effects of sport-related concussion have not been investigated at the level of early ERP components, which reflect automatic attentional processes. Deficits in early stages of information processing may be the cause of the late attention-related P3 anomalies observed in concussed athletes. In electrophysiological auditory tasks, the early components include the N1, which occurs between 50 and 150 milliseconds, and is mainly determined by the stimulus physical features (33). The following positive component, the P2, occurs between 100 and 300 milliseconds and represents the inhibition of a stimulus that has to be ignored. Moreover, in a dichotic paradigm, when participants have to ignore one of the two auditory channels, stimuli presented in the attended channel evoke a negative response (Nd) in comparison with stimuli presented in the unattended channel (32).

Within the context of sport activities, there are many instances in which attention is being greatly solicited. A return to play occurring within a period in which subclinical symptoms are still present after a concussion may lead to suboptimal performances and, perhaps, a greater risk of sustaining further injuries. The aim of the present study was, therefore, to better characterize the electrophysiological, and, hence, the attentional changes that may be induced by concussions in symptomatic, and especially in asymptomatic athletes, within the context of an attentionally challenging task. We hypothesized that a task requiring a high level of cognitive processing should highlight deficits in early (automatic attention level) as well as in late (volitional attention level) ERP components in concussed athletes. More specifically, we hypothesized that the deficits observed in concussed athletes should be characterized by a reduction in the amplitude of early and late ERP components. Furthermore, because of its attentional load, this highly demanding task should reveal subclinical deficits in athletes who do not report symptoms, but these deficits should be less severe than those observed in symptomatic athletes.

PATIENTS AND METHODS

Participants

Thirty athletes who sustained a sport concussion were evaluated. Nine of these athletes were excluded because they showed EEG artifacts caused by important eye or head movements, and one athlete was excluded because he was taking medication at the time of evaluation. Therefore, a total of 20 concussed athletes were included in this study. They were athletes in professional (n = 12) or university and semiprofessional (n = 8) leagues, and were playing hockey (n = 17), football (n = 2), or soccer (n = 1). All athletes were referred by their team physician. They were divided into two groups of 10 athletes according to the presence or absence of reported symptoms at the time of the ERP recording. The Post-Concussion Symptoms (PCS) Scale was used to assess symptom severity. This questionnaire is a list of common symptoms that athletes have to rate according to severity on a scale varying from 0 to 6, for a maximum score of 114. The two concussed groups were compared with a control group of 10

athletes from the University of Montreal teams (volleyball, n = 7; tennis, n = 3) matched for age, sex, and handedness, and who never sustained a concussion. We decided not to include athletes from contact sports, such as soccer and football, in the control group, because it has been demonstrated that symptoms of concussion may not be recognized by many football and soccer players (10). None of the athletes was taking medication known to affect EEG, attentional functions, or reaction times (RTs).

All participants underwent a short neuropsychological evaluation consisting of an adaptation of the National Football League battery, excluding verbal tests, because of the variability in the first language (25). The battery included the Color Trail Test (visual attention and inhibition), the Ruff Figural Fluency Test (assessing nonverbal fluency and mental flexibility), the Symbol Digit Modality Test (SDMT; measuring information processing speed and nonverbal incidental learning), and the Pennsylvania State University cancellation task (evaluating information processing speed and visual attention). Concussion severity was determined by the team physician according to criteria provided by the American Academy of Neurology (3). Hence, a Grade 1 concussion corresponded to a state of transient confusion, with no LOC, and mental status abnormalities that disappeared within 15 minutes. Grade 2 referred to a state of transient confusion, with no LOC, and mental status abnormalities that did not disappear within 15 minutes. Finally, a Grade 3 concussion was characterized by a brief LOC.

Approval for this research was granted from the Ethics Committee of the University of Montreal. Each participant provided written informed consent for voluntary participation.

Stimuli and Procedures

All athletes were tested via a modified auditory Oddball paradigm. We presented a dichotic sequence of standard and deviant tones in earphones, in which the standard stimulus (1000-Hz tone) appeared in 75% (n = 240) of the trials, whereas the deviant stimulus (1100-Hz tone) was presented in 25% (n = 80) of the trials. All stimuli lasted 50 milliseconds and had an intensity of 80 dB SPL. Interstimulus intervals varied randomly between 1200 and 1400 milliseconds, and a total of 320 tones were presented. In the randomized sequence of tones, all deviant tones were separated by at least one standard tone. Participants were asked to ignore tones presented in the right ear and to pay attention to tones presented in the left ear. Thus, the right ear was labeled the unattended channel and the left ear as, the attended channel. Participants pressed a key with their right hand when they perceived the high tone in the left ear. Sound conception, stimulus presentation, and data acquisition were made using an InstEP system v3.3 (InstEP Systems, Ottawa, Canada). Participants were seated in an adjustable chair in a faradized room. The experimenter kept visual and verbal contacts with the participants using a camera and a two-way intercom. The same experimenter gave all instructions to the participants.

Electrophysiological Recordings

The EEG was recorded from 28 tin electrodes in an E-Cap (Electro-Cap International Inc., Eaton, OH), which were placed according to the guideline for standard electrode position (15) at AF3, AF4, Fz, F3, F4, F7, F8, Fc3, Fc4, Cz, C1, C2, C3, C4, Cp3, Cp4, T7, T8, Tp7, Tp8, Pz, P3, P4, P7, P8, Oz, O1, and O2. All electrodes were referred to linked earlobes, with a forehead ground, and the impedance was kept below 5 kΩ. Horizontal and vertical electro-oculograms (EOG) were recorded using four 9-mm tin electrodes placed at the outer canthus of each eye for horizontal EOG, and infraorbitally and supraorbitally to the right eye for vertical EOG. The EEG and EOG signals were amplified, respectively, with a gain of 10,000 and 3500, with a bandpass between 0.01 and 100 Hz, and were digitized continuously at a sampling rate of 256 Hz, with a 100-millisecond prestimulus baseline.

Data Analysis

Only successful trials were submitted to analysis, and trials on which either the EEG or EOG artifacts exceeded ± 100 μV were rejected automatically. The EEG was averaged time-locked to the stimulus for each type of stimuli: standard stimuli in the unattended channel, deviant stimuli in the unattended channel, standard stimuli in the attended channel, and deviant stimuli in the attended channel. Additional filters were applied on average ERPs (0.01–30 Hz, 12 dB/octave). Amplitude was measured relative to the mean of the prestimulus baseline. Latency was defined as the maximum positive or negative amplitude within the latency window on predefined electrodes for each component. The N1 component was defined as the negative-going peak within the latency window of 50 to 150 milliseconds, and was analyzed on six electrodes in which N1 is clearly observed (Fz, Cz, F3, F4, C3, and C4). Because the P2 component is generally observed for standard stimuli in the unattended condition in centroparietal regions, it was only analyzed for this condition on six electrodes (Cz, Pz, C3, C4, P3, and P4) between 100 and 300 milliseconds. The Nd component was obtained by subtracting the standard unattended stimulus waveform to the standard attended stimulus waveform in centroparietal electrodes. No distinction was made between an early and a late Nd component, because an overlap of these two subcomponents was observed in most athletes. Latencies and amplitudes of the highest negative peak were measured in the 150- to 350 millisecond latency window on six electrodes (Cz, Pz, C3, C4, P3, and P4). The P3 component was defined as the largest positive peak within 300 to 550 milliseconds, and was measured in the attended channel, for deviant and standard stimuli on six electrodes in which this component is usually maximal (Cz, C3, C4, Pz, P3, and P4). P3 was not analyzed in the unattended channel because, as is often the

TABLE 1. Demographic and clinical profile of the participants[a]

Variable	Control athletes	Asymptomatic athletes	Symptomatic athletes	*P*-value ANOVA
No. of subjects	10	10	10	N/A
Men, women (no.)	9, 1	9, 1	10, 0	N/A
Age (yr)	22.0 ± 1.8	26.1 ± 6.1	25.7 ± 7.0	NS
Education (yr)	14.3 ± 1.6	15.4 ± 2.9	11.6 ± 2.1	0.003
Last concussion severity (grade)	N/A	2.2 ± 0.6	2.6 ± 0.5	NS
Time since concussion (wk)	N/A	5.3 ± 3.1	15.1 ± 16.6	NS
Total no. of concussions	N/A	3.5 ± 3.3	5.1 ± 3.8	N/A
Total no. of LOC	N/A	0.5 ± 0.5	1.3 ± 1.4	NS

[a] ANOVA, analysis of variance; N/A, not applicable; NS, not significant; LOC, loss of consciousness.

TABLE 2. Symptoms reported at the time of evaluation[a]

Symptom	Control athletes (1)	Asymptomatic athletes (2)	Symptomatic athletes (3)	*P*-value ANOVA	*P* value 1 versus 2	*P* value 2 versus 3	*P* value 1 versus 3
Low energy	0.8 ± 1.5	1.0 ± 1.0	4.0 ± 1.3	<0.0001	NS	0.0002	0.0001
Feeling pressure in head	0.3 ± 1.0	1.1 ± 1.2	3.5 ± 1.7	<0.0001	NS	0.001	0.0001
Sleeping more than usual	0.0 ± 0.0	0.3 ± 1.0	3.4 ± 1.8	<0.0001	NS	0.0001	0.0001
Headaches	0.2 ± 0.4	1.2 ± 0.9	3.3 ± 1.3	<0.0001	NS	0.0002	0.0001
Difficulty concentrating	0.6 ± 1.3	0.7 ± 1.1	3.1 ± 0.7	<0.0001	NS	0.0002	0.0002
Nervous/anxious	0.6 ± 1.1	0.9 ± 1.3	2.9 ± 1.8	0.002	NS	0.01	0.003
Sensitivity to light	0.0 ± 0.0	0.5 ± 1.0	2.9 ± 2.0	<0.0001	NS	0.0008	0.0002
Feeling like "in a fog"	0.0 ± 0.0	0.7 ± 1.3	2.8 ± 1.2	<0.0001	NS	0.0003	0.0001
Feeling slowed down	0.7 ± 1.3	0.6 ± 1.0	2.8 ± 0.9	<0.0001	NS	0.0003	0.0005
Irritability	0.3 ± 0.7	0.3 ± 1.0	2.7 ± 2.0	0.0003	NS	0.001	0.001
Trouble falling asleep	0.2 ± 0.6	0.8 ± 1.5	2.5 ± 1.7	0.002	NS	0.02	0.002
Dizziness	0.0 ± 0.0	1.0 ± 1.3	2.0 ± 1.5	0.002	NS	NS	0.001
Sensitivity to noise	0.3 ± 1.0	0.6 ± 1.0	2.6 ± 2.1	NS			
Difficulty remembering	0.3 ± 1.0	0.6 ± 1.0	2.5 ± 2.0	NS			
Drowsiness	0.9 ± 1.7	0.5 ± 1.0	2.5 ± 1.2	NS			
More emotional than usual	0.3 ± 1.0	0.5 ± 1.0	2.2 ± 1.7	NS			
Sadness	0.3 ± 1.0	1.0 ± 1.6	2.0 ± 1.9	NS			
Balance problem	0.0 ± 0.0	0.6 ± 1.0	1.9 ± 1.9	NS			
Numbness/tingling	0.0 ± 0.0	0.3 ± 1.0	1.1 ± 1.3	NS			
Nausea	0.0 ± 0.0	0.4 ± 1.0	0.5 ± 1.0	NS			
Vomiting	0.1 ± 0.3	0.3 ± 1.0	0.1 ± 0.3	NS			

[a] ANOVA, analysis of variance; NS, not significant.

case (37), this component was absent in a high proportion of athletes.

Statistical Analyses

Group differences for concussion characteristics, symptoms, RT, RT variability, and accuracy in detecting target tones were analyzed with one-way analyses of variance (ANOVA) with planned comparisons, and a Bonferroni correction was applied because multiple tests were performed. Latencies and amplitudes for the N1 and P3 components were analyzed with two-way ANOVA with one factor (Control/Asymptomatic/Symptomatic: Group) and two repeated measures (Deviant/Standard: Stimulus and Electrode). Nd and P2 components were analyzed with one-way ANOVA with one factor (Group) and one repeated measure (Electrode). Simple effect analyses were performed to decompose any interaction effects. A Greenhouse-Geisser correction for sphericity was applied to all repeated measures. Pearson correlation coefficients were used to measure the relationships between ERP components and concussion characteristics, symptoms, neuropsychological results, and RT. To correct for multiple analyses, correlations were considered significant at $P < 0.01$.

RESULTS

Participant Characteristics

Demographic and clinical data of the selected participants are presented in *Table 1*. A group difference was found in the number of years of education ($F_{2,27} = 7.54$; $P < 0.01$), in which symptomatic participants had less education than asymptomatic and control participants. However, no significant correlations were observed between education and ERP characteristics. No between-group differences were found with regard to the last concussion severity, the total number of concussions sustained, the time between the last concussion and testing, and the total number of LOC episodes associated with a concussion.

Symptoms were measured with the PCS scale, and results are presented in *Table 2*. A significant group difference was observed in the PCS total score ($F_{2,27} = 52.9$; $P < 0.0025$). Self-reported symptomatic athletes had higher scores than the other two groups ($P < 0.0025$) and no difference was observed between asymptomatic and control athletes (total score for control athletes, 5.9 ± 9.7; asymptomatic athletes, 7.9 ± 5.7; symptomatic athletes, 51.4 ± 15.76). More symptoms related to sleep and vigilance (trouble falling asleep, sleeping more than usual, and difficulty concentrating) were reported in symptomatic athletes in comparison with asymptomatic and control athletes ($P < 0.0025$). Psychological symptoms (low energy, irritability, and nervousness), headaches, and sensitivity to light were also more prevalent in symptomatic athletes than in the two other groups ($P < 0.0025$). Symptomatic athletes showed more dizziness ($P < 0.0025$) than control athletes, but the two concussed groups did not differ with regard to these symptoms.

The athletes showed a similar performance on all neuropsychological tests, except a trend for the SDMT ($F_{2,23} = 4.96$; $P = 0.02$), in which symptomatic athletes tended to complete fewer items than the other two groups.

Electrophysiological Study: Behavioral Results

In the modified Oddball task, RT could not be recorded in two symptomatic athletes because of technical problems. The results for all other participants are presented in *Table 3*. Symptomatic athletes showed slower RT than control participants in response to the target stimulus, but this difference failed to reach significance when the Bonferroni correction was applied ($F_{2,25} = 4.12$; $P = 0.03$). RT variability during the Oddball task was more pronounced in symptomatic than in control athletes ($F_{2,25} = 6.48$; $P < 0.005$). No differences were observed between the asymptomatic athletes and the two other groups with respect to RT or RT variability, and were either between-group differences observed in the number of detected targets or false alarms. In fact, even if symptomatic athletes made, on average, more false alarms than the two other groups, the difference did not reach significance because of the important intersubject variability observed in all groups.

ERP Data

Grand-average ERP waveforms for standard and deviant stimuli in the attended and the unattended channels are represented in *Figures 1* and *2*. No between-group difference was observed in the number of EEG epochs included for the analyses, except that symptomatic participants had fewer trials than the two other groups in the deviant attended condition ($F_{2,27} = 5.77$; $P < 0.01$). Because no group difference was found in the number of detected trials, the difference in the number of EEG epochs was caused mainly by movement and ocular artifacts.

Unattended Channel

The results presented in this section include the ERP signals to both the standard and deviant stimuli that athletes had to ignore. Overall, a clear frontocentral N1 component was identified for

TABLE 3. Results obtained in the neuropsychological tests[a]

Tasks	Control athletes	Asymptomatic athletes	Symptomatic athletes	*P*-value ANOVA
Color trials				
Trail A	23.9 ± 5.8	24.3 ± 10.3	30.9 ± 11.3	NS
Trail B	51.1 ± 6.5	56.7 ± 12.0	67.1 ± 23.4	NS
Ruff figural fluency test				
Number of designs	117.4 ± 24.7	112.2 ± 10.7	99.9 ± 22.3	NS
Error ratio	0.0 ± 0.0	0.1 ± 01	0.1 ± 01	NS
Symbol digit modalities test				
Number of symbols	63.6 ± 4.1	63.9 ± 5.8	51.9 ± 13.9	0.02
Errors	1.5 ± 1.7	1.1 ± 1.5	0.8 ± 1.3	NS
PSU cancellation task				
Number of symbols	63.8 ± 11.7	59.2 ± 8.6	52.1 ± 10.9	NS
Errors	1.8 ± 1.9	1.4 ± 2.1	3.2 ± 2.2	NS

[a] ANOVA, analysis of variance; NS, non significant; PSU, Pennsylvania State University.

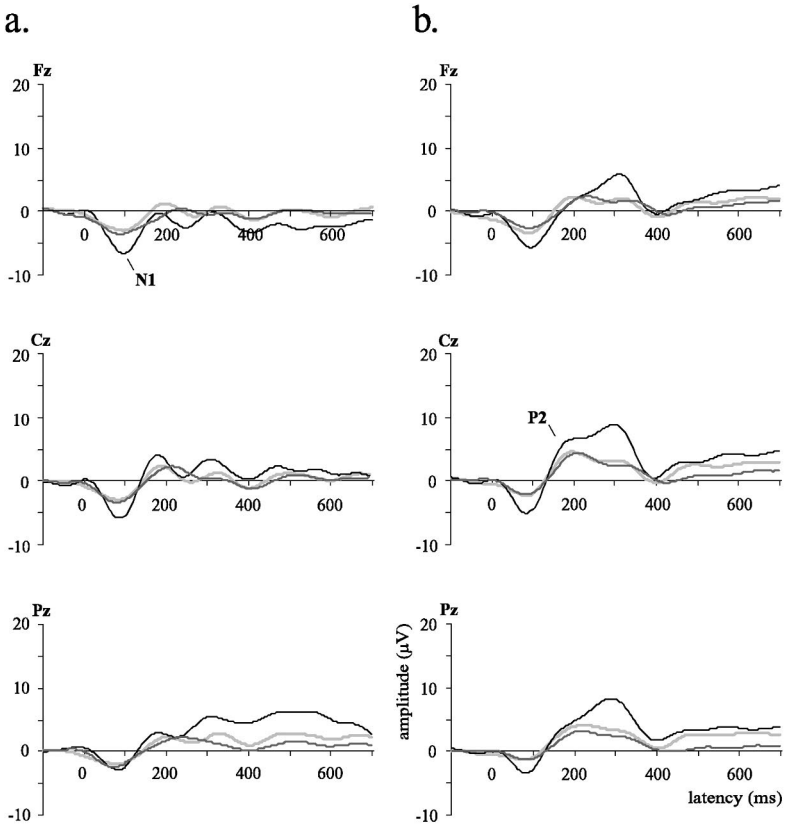

FIGURE 1. *ERP waveforms in response to deviant* (A) *and standard* (B) *stimuli presented in the unattended channel for control* (black)*, symptomatic* (dark gray)*, and asymptomatic* (light gray) *groups.*

both types of stimuli in all groups (*Fig. 1*), whereas a central P2 component was observed in response to standard stimuli only.

N1 Amplitude

The analyses revealed a between-group difference in the amplitude of the N1 component ($F_{2,25} = 7.88$; $P < 0.01$). Control athletes showed higher N1 amplitude than both concussed groups ($P < 0.01$), and no difference was found between asymptomatic and symptomatic athletes.

N1 Latency

No between-group difference was obtained in the N1 latency, and the latency of this component did not differ in response to standard and deviant stimuli.

P2 Amplitude

Because the P2 peak could not be clearly distinguished in some athletes (three concussed athletes and three control athletes), no peak analysis was performed. Thus, mean amplitudes were calculated for two consecutive latency windows: 100 to 200 milliseconds and 200 to 300 milliseconds. In the earlier window, no between-group difference was found in the P2 mean amplitude. In the 200- to 300-millisecond latency window, an interaction was found between Group and Electrode ($F_{10,135} = 2.47$; $P = 0.02$; $\varepsilon = 0.72357$). Control athletes showed higher P2 mean amplitudes than symptomatic athletes for all electrodes ($P < 0.05$). By contrast, no difference was observed between control and asymptomatic athletes, except on Cz, in which the control group showed a higher P2 mean amplitude than asymptomatic athletes ($P < 0.01$).

Attended Channel

Average ERP waveforms for the standard and deviant (target) stimuli presented to the attended channel are depicted in *Figure 2*.

N1

No between-group differences were observed with respect to N1 amplitude. Contrary to the results obtained in the unattended channel, similar N1 amplitudes were found for deviant and standard stimuli in the attended channel. No Group or Electrode effects were observed for the N1 latency.

P3 Amplitude

Regardless of the group, a smaller P3 component was observed for standard than for deviant stimuli, and this difference was intensified for parietal electrodes in comparison with central electrodes (Stimulus by Electrode interaction: $F_{5,115} = 12.11$; $P < 0.0001$; $\varepsilon = 0.602$). The amplitude of the P3 component showed a Group by Stimulus interaction ($F_{2,23} = 3.88$; $P < 0.05$). Planned comparisons revealed that the control group had a higher P3 amplitude in comparison with the two concussed groups ($P < 0.001$), and this between-group difference was accentuated for deviant stimuli ($P < 0.001$) in comparison with standard stimuli ($P < 0.001$). A Group by Electrode interaction was also found ($F_{10,115} = 2.94$; $P < 0.05$; $\varepsilon = 0.3795$), with more prominent group differences being observed for parietal than for central electrodes. However, these differential site responses were found only when comparing the controls with the two concussed groups; no such differential pattern was found between the asymptomatic and symptomatic athletes.

P3 Latency

The ANOVA revealed a Group by Electrode interaction ($F_{10,110} = 4.14$; $P < 0.01$; $\varepsilon = 0.58872$). The control athletes displayed shorter P3 latencies than the concussed athletes over the central, but not the parietal, electrodes. No between-group differences were found between asymptomatic and symptomatic athletes with respect to the P3 latency. Independently of the group, deviant and standard stimuli led to similar P3 latencies.

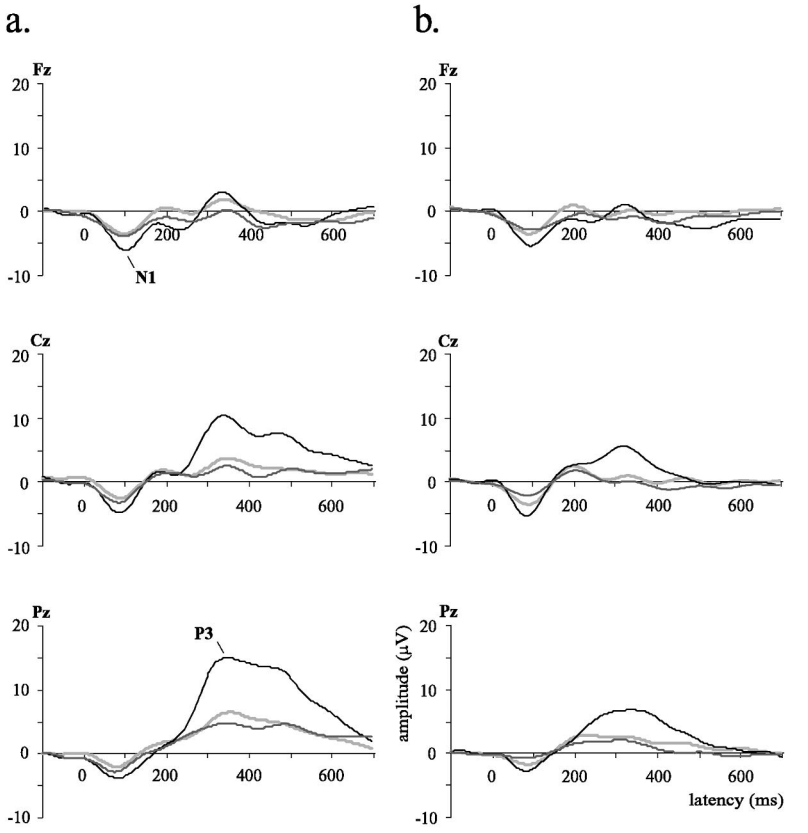

FIGURE 2. *ERP waveforms in response to deviant* (A) *and standard* (B) *stimuli presented in the attended channel for control* (black)*, symptomatic* (dark gray)*, and asymptomatic* (light gray) *groups.*

Comparison between the Unattended and Attended Channels

Nd

Both the symptomatic and asymptomatic athletes tended to show smaller amplitudes for the Nd component than the control group, but this difference failed to reach significance (control athletes, −5.8 μV; asymptomatic athletes, −3.6 μV; and symptomatic athletes, −4.0 μV; $F_{2,27} = 2.53$; $P = 0.1$). The Nd latency did not differ among the three groups.

Relation between Symptoms, Concussion Characteristics, and ERP Components

A significant negative relationship was found between the presence of some symptoms and the ERP characteristics. In fact, headaches and difficulties concentrating were both negatively correlated with the amplitude of the P3 component (headaches: $r = -0.55$, $P < 0.01$; difficulties concentrating: $r = -0.51$, $P < 0.01$). RT and RT variability obtained during the modified Oddball paradigm also showed a negative correlation with the amplitudes of the P2 component (RT: $r = -0.62$; $P < 0.001$, RT variability: $r = -0.58$, $P < 0.01$) and the P3 component (RT: $r = -0.63$, $P < 0.01$; RT variability: $r = -0.62$, $P < 0.01$). Thus, athletes having slower RT and/or greater RT variability showed smaller ERP amplitudes. The only neuropsychological test that correlated with ERP characteristics was the Pennsylvania State University cancellation task, in which a better performance was associated with a higher P3 amplitude in response to the target stimulus ($r = 0.71$; $P < 0.001$).

The number of concussions sustained by each athlete, the number of LOC, the concussion severity, and the delay between the concussion and the ERP recording were not correlated with ERP characteristics, except for the P2 mean amplitude, which correlates negatively with the number of LOC ($r = -0.613$; $P < 0.01$).

DISCUSSION

The present study investigated the effects of concussions on attentional functions and information processing using ERPs. The aim was to create a sufficiently difficult task to measure the presence of subclinical electrophysiological deficits in concussed athletes, be they symptomatic or not. The results showed a reduction in the amplitude of the N1, P2, and P3 auditory components and a prolonged P3 component in both the symptomatic and asymptomatic concussed athletes.

Concussion and Behavioral Performance

The behavioral results obtained in our study, especially the high false alarm rate, confirm the difficulty of the task. However, the RT and the number of correctly detected targets did not allow us to distinguish the three groups of athletes. The absence of a significant group difference in RT is somewhat surprising because symptomatic and asymptomatic concussed athletes reported to feel slowed down in comparison with control athletes. The high heterogeneity of RT in both concussed groups may explain the reason why only a trend was observed when we compared the groups. Symptomatic athletes did show a greater RT variability than the other two groups, a finding in keeping with the results obtained by Dupuis et al. (11) in symptomatic concussed athletes using a visual Oddball task. Makdissi et al. (28) also observed greater RT variability in concussed athletes. Such a significant RT variability in symptomatic athletes could reflect attentional fluctuations during the task.

In sport-related concussions, studies investigating short-term neuropsychological deficits generally showed a return to normal performance within 1 week after the concussion (8, 12, 13). In our study, the SDMT was the only test revealing a slower processing

speed in symptomatic than in asymptomatic and control athletes. These results are concordant with those obtained by Bernstein (4) in patients with mild traumatic brain injury (TBI) tested 8 years after their brain injury. Their performance was normal on all neuropsychological tests, except on the SDMT, in which patients showed a reduced information processing speed in comparison with controls. Similarly, Echemendia and Cantu (12) studied the neuropsychological impact of concussions in 29 athletes tested 2 hours, 48 hours, 1 week, and 1 month after injury. At the longest time interval after concussion (1 mo), no cognitive deficits were reported, except for a lower performance in the SDMT. These results, as well as ours, confirm that the SDMT is one of the most sensitive neuropsychological tests in assessing the short- and long-term cognitive effects of concussions.

ERPs

The ERP task used in the present study allowed the evaluation of information processing under both attended and unattended conditions. This paradigm, thus, provides an assessment of selective attention as well as the ability to inhibit irrelevant information under situations requiring sustained attention. The electrophysiological results indicate that, in comparison with nonconcussed athletes, asymptomatic as well as symptomatic concussed athletes present a reduction in the amplitude of early and late ERP components, which are presumed to reflect both automatic and volitional attentional processing. These results are somewhat surprising, because the asymptomatic athletes did not report more symptoms than control athletes on the PCS scale. Moreover, the ERP waveforms obtained in both concussed groups were similar for the four types of stimuli. These findings suggest that, even in the absence of overtly reported symptoms, concussions may induce anomalous neurophysiological patterns in response to attention-demanding tasks.

The present study is the first to have explored information processing in an unattended condition in sports-related concussions. Deficits occurring early in the information processing stages (i.e., between 50 and 150 ms after the stimulus onset) and related to preattentional processes were observed in concussed athletes and were characterized by a reduction in the amplitude of the N1 component. The same pattern was found at the P2 level, with the concussed athletes showing an abnormal electrophysiological response to stimuli that they had to ignore. Previous studies investigating the effects of mild and moderate TBI, 1 to 10 years after an accident (mostly motor vehicle accidents), also showed a reduction of the P2 component under the unattended condition (40). Taken together, these results and ours reflect an abnormal orientation response to nonpertinent information after a concussion.

After severe TBI, patients show a slow down in cortical responses as reflected by a delayed P3 component, often accompanied by longer RT (17, 34, 40). However, results are more heterogeneous with patients with mild TBI, in whom, some studies reported a prolonged P3 latency (39, 41, 47), whereas other studies (11, 24, 38, 43) showed similar P3 latencies in TBI patients and controls. This latency reflects the moment when the stimulus is being evaluated and categorized (28) and is usually related to information processing speed. In the present study, an increased P3 latency in concussed athletes was only observed in central electrodes and not in parietal electrodes, in which the P3 is generally maximal. No group difference was obtained in the RTs; in fact, concussed athletes did not show longer response times. Moreover, the latency of the earlier components (N1 and P2) was comparable in the concussed and control groups. Taken together, our results indicate that the processing of auditory information is not slowed down in concussed athletes.

In the condition in which selective attention had to be maintained, an important reduction in P3 amplitude was observed in both concussed groups, especially in response to the target stimulus. Similar results were observed in two studies that investigated the effects of sport-related concussions on visual ERP (11, 24) and in patients having undergone a mild (16, 39, 47), moderate, or severe TBI in situations other than sports (44, 46). The particularity of our study is that athletes who report no symptoms had a P3 reduction similar to that observed in patients who report cognitive symptoms. The P3 component represents the amount of attentional resources allocated for a specific stimulus (22, 48). The reduction in amplitude of this component may reflect either a difficulty to allocate an adequate level of attention during the task and/or attentional fluctuations during the task. The first explanation is less probable, because the behavioral performance (RT, omission, and false-alarm rates) did not distinguish concussed and control athletes. However, the concussed athletes showed a greater RT variability, which was also related to the reduction in P3 amplitude. Similar results have been obtained by Segalowitz et al. (44), who reported that the amplitude of the P3 component was associated with RT variability only in patients with TBI, but not in control participants. The present result suggests that the concussed athletes are more at risk of accidents in the practice of their sport when they return to play, because they have difficulties maintaining their attention when a high level of concentration is required.

The finding of ERP abnormalities in asymptomatic athletes has not been consistently reported in previous studies. In fact, symptomatic athletes usually display more deficits than asymptomatic athletes, at least in the visual Oddball tasks that have been performed in our laboratory (11, 24). In these two previous studies, the delay intervening between the concussion and ERP recording was longer in the asymptomatic than in the symptomatic athletes, a condition that could have accounted for the limited amount of electrophysiological anomalies observed in the asymptomatic athletes. This is not the case in the present experiment: the two groups did not differ with respect to the time interval since the last concussion. One must acknowledge, however, that this delay was relatively short in the present study (5 wk, on average) and that brain adjustment to the traumatic event may not have reached its full term. However, this interval was sufficient to allow an

almost full neuropsychological recovery, and it is certainly longer than the prescribed 1-week symptom-free return-to-play guideline. These athletes may display deficits only in more challenging cognitive tasks and perform normally in easier ones.

The methods used to analyze the effects of concussions generally consist of a short neuropsychological evaluation, a neurological examination, and neuroimaging techniques (20). The structural neuroimaging techniques, such as computed tomographic and magnetic resonance imaging scans, are usually not very useful, rarely revealing structural brain abnormalities in the case of concussions (18), except for single-photon emission computed tomographic brain perfusion imaging, in which abnormalities were found in more than 50% of patients with mild TBI who had normal computed tomographic scans (1, 2, 21). Thus, neuropsychology has had an important influence on the return-to-play decisions, particularly if a baseline is performed before the beginning of the sports season. However, neuropsychological tests may be less sensitive then the ERP technique, because they may reveal normal performances even though electrophysiological brain activity does reflect cognitive deficits.

Limitations of the Study

Obviously, the present study presents some limitations, which have to be considered. First, only auditory attention has been evaluated in this experiment. Previous ERP studies conducted with concussed athletes have used visual stimuli (11, 16, 24), but no study has yet combined visual and auditory stimulation, both of which are essential to the practice of sports. Second, ERP recordings were performed only once after concussion, thus preventing an assessment of its recovery course. It is, therefore, difficult to determine, at the present time, whether the abnormal electrophysiological pattern seen in this study is reversible or not. Third, we also observed a group difference in the education level, in which symptomatic athletes had a lower education level than the other two groups. Although education may act as a confounding variable, no correlation was observed between the number of years of education and ERP characteristics in the present study. However, further studies should examine whether education plays a protective role with respect to the intensity of postconcussive symptoms in athletes. Finally, although careful statistical steps were taken to ensure the validity of our results, our sample size was relatively small. We do think, however, that this pilot study could lead to the development of a multicenter trial, which could prove to be extremely useful in the context of contact sports.

Clinical Implications

The fact that asymptomatic athletes have an electrophysiological profile similar to that of symptomatic athletes challenges the validity of return-to-play guidelines for which the absence of symptoms is a major issue. Sports medicine physicians should, therefore, exert prudence in their return-to-play decisions, even when concussed athletes report no symptoms and have normal neuropsychological evaluation. A premature return-to-play may induce a worse performance and cause other sports-related accidents. We think that the ERP technique is a sensitive tool that may be used in association with neuropsychological evaluation to guide the return-to-play decisions in concussed athletes.

REFERENCES

1. Abdel-Dayem HM, Abu-Judeh HH, Kumar M, Atay S, Naddaf S, el-Zeftawy H, Luo HM, Abdel-Dayem JQ: SPECT brain perfusion abnormalities in mild or moderate traumatic brain injury. **Clin Nucl Med** 23:309–317, 1998.
2. Abu-Judeh HH, Parker R, Singh M, el-Zeftawy H, Atay S, Kumar M, Naddaf S, Aleksic S, Abdel-Daymen AM: SPET brain perfusion imaging in mild traumatic brain injury without loss of consciousness and normal computed tomography. **Nucl Med Commun** 20:505–510, 1999.
3. American Academy of Neurology: Practice parameter: The management of concussion in sports (summary statement)—Report of the quality standards subcommittee. **Neurology** 48:581–585, 1997.

3a. Barry RJ, Johnstone SJ, Clarke AR: A review of electrophysiology in attention-deficit/hyperactivity disorder: II. Event-related potentials. **Clin Neurophysiol** 114:184–198, 2003.

4. Bernstein DM: Information processing difficulty long after self-reported concussion. **J Int Neuropsychol Soc** 8:673–682, 2002.
5. Bleiberg J, Cernich AN, Cameron K, Sun W, Peck K, Ecklund PJ, Reeves D, Uhorchak J, Sparling MB, Warden DL: Duration of cognitive impairment after sports concussion. **Neurosurgery** 54:1073–1078, 2004.
6. Cantu RC: Return to play guidelines after a head injury. **Clin Sports Med** 17:45–60, 1998.
7. Cantu RC: Second-impact syndrome. **Clin Sports Med** 17:37–44, 1998.
8. Collins MW, Grindel SH, Lovell MR, Dede DE, Moser DJ, Phalin BJ, Nogle S, Wasik M, Cordry D, Daugherty KM, Sears SF, Nicolette G, Indelicato P: Relationship between concussion and neuropsychological performance in college football players. **JAMA** 282:964–970, 1999.
9. Concussion in Sport Group: Summary and agreement statement of the 1st international symposium on concussion in sport, Vienna 2001. **Clin J Sport Med** 12:6–11, 2002.
10. Delaney JS, Lacrois VJ, Leclerc S, Johnston K: Concussions among university football and soccer players. **Clin J Sport Med** 12:331–338, 2002.
11. Dupuis F, Johnston KM, Lavoie M, Lepore F, Lassonde M: Concussions in athletes produce brain dysfunction as revealed by event-related potentials. **Neuroreport** 11:4087–4092, 2000.
12. Echemendia RJ, Cantu RC: Return to play following sports-related mild traumatic brain injury: The role for neuropsychology. **Appl Neuropsychol** 10:48–55, 2003.
13. Echemendia RJ, Julian LJ: Mild traumatic brain injury in sports: Neuropsychology's contribution to a developing field. **Neuropsychol Rev** 11:69–88, 2001.
14. Echemendia RJ, Putukian M, Mackin RS, Julian L, Shoss N: Neuropsychological test performance prior to and following sports-related mild traumatic brain injury. **Clin J Sport Med** 11:23–31, 2001.
15. Electrode Position Committee: American Electroencephalographic Society guidelines for standard electrode position nomenclature. **J Clin Neurophysiol** 8:200–202, 1991.
16. Gaetz M, Goodman D, Weinberg H: Electrophysiological evidence for cumulative effects of concussion. **Brain Inj** 14:1077–1088, 2000.
17. Gaetz M, Weinberg H: Electrophysiological indices of persistent post-concussion symptoms. **Brain Inj** 14:815–832, 2000.
18. Haydel MJ, Preston CA, Mills TJ, Luber A, Blaudeau E, DeBlieux PM: Indications for computer tomography in patients with minor head injury. **N Engl J Med** 343:100–105, 2000.

19. Ingebrigtsen T, Waterloo K, Marup-Jensen S, Attner E, Romner B: Quantification of post-concussion symptoms 3 months after minor head injury in 100 consecutive patients. **J Neurol** 245:609–612, 2001.
20. Johnston KM, Ptito A, Chankowsky J, Chen JK: New frontiers in diagnostic imaging in concussive head injury. **Clin J Sport Med** 11:166–175, 2001.
21. Kant R, Smith-Seemiller L, Isaac G, Duffy J: Tc-HMPAO SPECT in persistent post-concussion syndrome after mild head injury: Comparison with MRI/CT. **Brain Inj** 11:115–124, 1997.
22. Kramer AF, Strayer DL: Assessing the development of automatic processing: An application of dual-task and event-related brain potential methodologies. **Biol Psychol** 26:231–267, 1988.
23. Kutas M, McCarthy G, Donchin E: Augmenting mental chronometry: The P300 as a measure of stimulus evaluation time. **Science** 197:792–795, 1977.
24. Lavoie ME, Dupuis F, Johnston KM, Lassonde M: Visual P300 effect beyond symptoms in concussed college athletes. **J Clin Exp Neuropsychol** 26:55–73, 2004.
25. Lovell MR, Collins MW: Neuropsychological assessment of the college football player. **J Head Trauma Rehabil** 13:9–26, 1998.
26. Macciocchi SN, Barth JT, Alves W, Rimel RW, Jane JA: Neuropsychological functioning and recovery after mild head injury in collegiate athletes. **Neurosurgery** 39:510–514, 1996.
27. Maddocks D, Saling M: Neuropsychological deficits following concussion. **Brain Inj** 10:99–103, 1996.
28. Makdissi M, Collie A, Maruff P, Darby DG, Bush A, McCrory P, Bennell K: Computerised cognitive assessment of concussed Australian rules footballers. **Br J Sports Med** 35:354–360, 2001.
29. McCarthy G, Donchin E: A metric for thought: A comparison of P300 latency and reaction time. **Science** 211:77–80, 1981.
30. McCrea M, Guskiewicz KM, Marshall SW, Barr W, Randolph C, Cantu RC, Onate JA, Yang J, Kelly JP: Acute effects and recovery time following concussion in collegiate football players: The NCAA Concussion Study. **JAMA** 290:2556–2563, 2003.
31. *Deleted in proof.*
32. Näätänen R: The role of attention in auditory information processing as revealed by event-related potentials and other brain measures of cognitive function. **Behav Brain Sci** 13:201–288, 1990.
33. Näätänen R, Picton T: The N1 wave of the human electric and magnetic response to sound: A review and an analysis of the component structure. **Psychophysiol** 24:375–425, 1987.
34. Papanicolaou AC, Levin HS, Eisenberg HM, Moore BD, Goethe KE, High WM: Evoked potential correlates of posttraumatic amnesia after closed head injury. **Neurosurgery** 14:676–678, 1984.
35. Picton TW: The P300 wave of the human event-related potential. **J Clin Neurophysiol** 9:456–479, 1992.
36. Polich J: Attention, probability, and task demands as determinants of P300 latency from auditory stimuli. **Electroencephalogr Clin Neurophysiol** 63: 251–259, 1986.
37. Polich HK, McIsaac J: Comparison of auditory P300 habituation from active and passive conditions. **Int J Psychophysiol** 17:25–34, 1994.
38. Potter DD, Bassett MR, Jory SH, Barret K: Changes in event-related potentials in a three-stimulus auditory oddball task after mild head injury. **Neuropsychologia** 39:1464–1472, 2001.
39. Pratap-Chand R, Sinniah M, Salem FA: Cognitive evoked potential (P300): A metric for cerebral concussion. **Acta Neurol Scand** 78:185–189, 1988.
40. Reinvang I, Nordby H, Nielsen CS: Information processing deficits in head injury assessed with ERPs reflecting early and late processing stages. **Neuropsychologia** 38:995–1005, 2000.
41. Sangal RB, Sangal JA: Closed head injury patients with mild cognitive complaints without neurological or psychiatric findings have abnormal visual P300 latencies. **Biol Psychiatry** 39:305–307, 1996.
42. Saunders RL, Harbaugh RE: The second impact in catastrophic contact-sports head trauma. **JAMA** 254:538–539, 1984.
43. Segalowitz SJ, Bernstein DM, Lawson S: P300 Event-related potential decrements in well-functioning university students with mild head injury. **Brain Cogn** 45:342–356, 2001.
44. Segalowitz SJ, Dywan J, Unsal A: Attentional factors in response time variability after traumatic brain injury: An ERP study. **J Int Neuropsychol Soc** 3:95–107, 1997.
45. Thurman DJ, Branche CM, Sniezek JE: The epidemiology of sports-related traumatic brain injuries in the United States: Recent developments. **J Head Trauma Rehabil** 13:1–8, 1998.
46. Unsal A, Segalowitz SJ: Sources of P300 attenuation after head injury: Single-trial amplitude, latency jitter, and EEG power. **Psychophysiol** 32: 249–256, 1995.
47. von Bierbrauer A, Weissenborn K: P300 after minor head injury: A follow-examination. **Acta Neurol Belg** 98:21–26, 1998.
48. Wickens C, Kramer A, Vanasse L, Donchin E: Performance of concurrent tasks: A psychophysiological analysis of the reciprocity of information-processing resources. **Science** 221:1080–1082, 1983.

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COMMENTS

Gosselin et al. report interesting findings utilizing cognitive event-related potentials (ERPs) to evaluate the effects of sports-related concussion. The ERPs represent an averaged electroencephalogram (EEG) signal, which is recorded subsequent to presenting stimuli related to a specific level of information processing. Analyzing in particular a P3 wave that is recorded over the central and parietal electrodes, they are able to access cognitive and intentional processing. Previous studies have also corroborated athletic concussion that P3 latency in visual ERP was predictive of symptomatic athletic concussion. Their study included 20 concussed athletes, of which 12 were professional and eight were semi-professional in hockey (17), football (2), and soccer (1). EEG was recorded from 28 electrodes in a standardized array, while subjects were presented with various standard and deviant stimuli. The electrophysiological results showed that both asymptomatic and symptomatic concussed athletes had a reduction in amplitude of early and late ERP components. Thus, without the concussed athlete obviously being symptomatic, there are documented anomalous neurophysiological deficits in response to attention-demanding tasks. The authors also suggest that not only is there the risk for repetitive or cumulative injury with an unappreciated deficit in cerebral processing, but that an athlete may also experience difficulty with attention-related activities when a high level of concentration is required.

In summary, I believe that this is intriguing and provocative research that will lead us to further refine and define the deficits in cerebral processing that may occur secondary to mild traumatic brain injury. The suggestion that ERP techniques may be more sensitive than standardized or computerized neuropsychological testing needs further evaluation and clinical application. However, we are always interested in more sophisticated and objective measures of ongoing cerebral dysfunction in any patient, but especially in an athlete who will most often experience further head impacts and either subconcussive or concussive phenomena.

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The authors used a classical advanced form of auditory evoked potential to assess auditory attention and information gaiting in young athletes who had sustained a concussion. The principal finding suggests that the clinical examination is insensitive to detect cognitive deficits after an injury. This conclusion should serve as a warning to all athletes, trainers, and sports medicine physicians who perform routine assessment based on the clinical examination, which is insufficient to detect brain dysfunction after a concussion. It is unclear what short-term or long-term risks are associated with this dysfunction or how long the risk exists. However, it is clear that the return-to-play guidelines should include the requirement of objective diagnostic testing of brain cognitive function rather than a simple clinical examination. This call for objective measures will likely go unheeded, and it is our duty to inform our sports medicine colleagues of this need.

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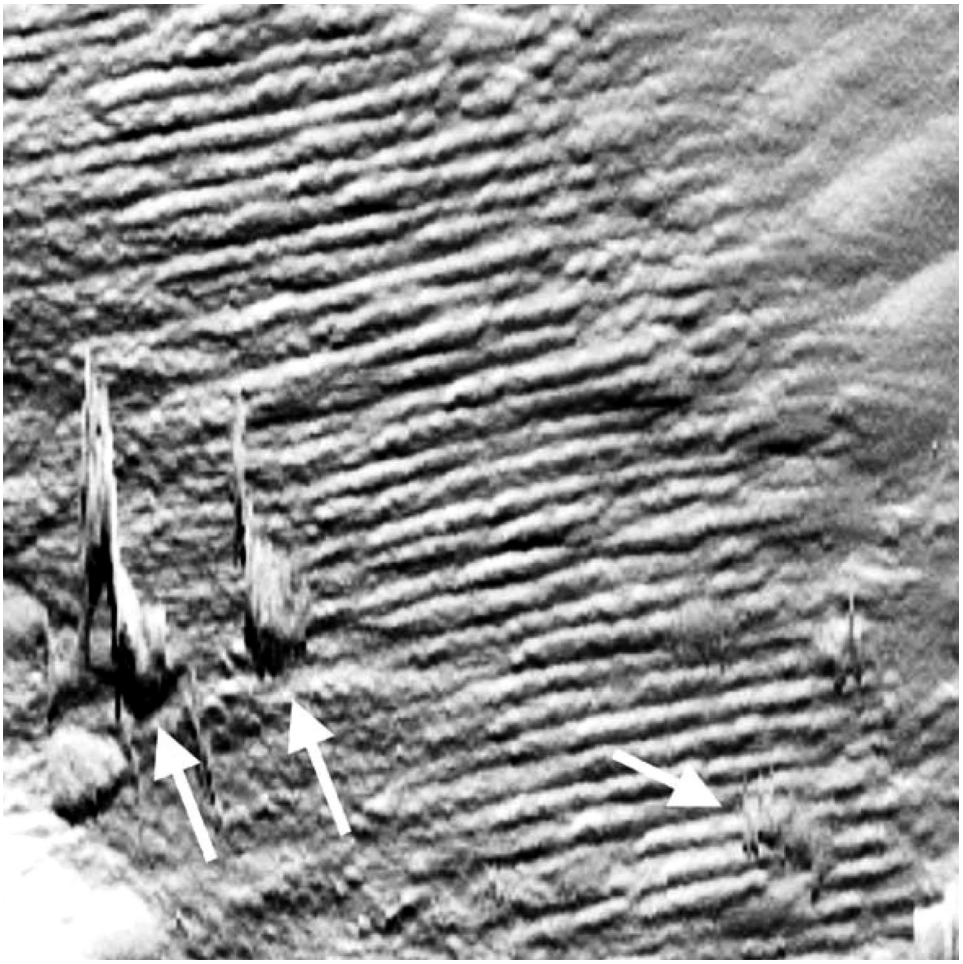

Enlarged view of the chemically treated bacterium after an atomic force microscope tip (AFM) removed the smooth cell membrane. A portion of the outer cell wall was removed exposing the peptidoglycan strands beneath (middle of image). Some of the original surface is visible in the upper right corner, while fragments of the cell wall that were removed remain visible within the exposed area as indicated by the arrows. (Firtel M, Henderson G, Sokolov I. Nanosurgery: observation of peptidoglycan strands in Lactobacillus helveticus cell walls. ***Ultramicroscopy.*** *2004 Nov;101(2–4):105–9.)*