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Tracking the recovery of visuospatial attention deficits in mild traumatic brain injury

Charlene I. Halterman, Jeanne Langan, Anthony Drew, Erika Rodriguez, Louis R. Osternig,
Li-Shan Chou and Paul van Donkelaar

Department of Human Physiology and Institute of Neuroscience, University of Oregon, Eugene, Oregon, USA

Correspondence to: Paul van Donkelarr
E-mail: paulvd@darkwing.uoregon.edu

The goal of the current investigation was to probe the deficits in the alerting, orienting and executive components of visuospatial attention in individuals who have recently suffered a mild traumatic brain injury (mTBI) and to assess the rate and degree of recovery for each of these components over a month post-injury. A group design was employed to assess and compare the performance of participants (12 males, 8 females; mean age: 21 ± 1.74 years) identified with mTBI relative to control subjects matched for gender, age, height, weight and activity level. Participants performed the attentional network test, designed to isolate the constituents of attention into alerting, orienting and executive components. Reaction times (RTs) and response accuracy were the main dependent variables. The results showed that the orienting and executive components were significantly affected by mTBI immediately after the injury, whereas the alerting component was not. Furthermore, participants with mTBI recovered from the deficits in the orienting component of attention within a week of their injury, whereas the deficits in the executive component remained throughout the month post-injury. In addition, the RT cost to generate accurate compared with inaccurate responses was significantly larger in participants with mTBI than in controls, and this difference was maintained throughout the 1 month testing period. These findings indicate that the regions of the brain associated with the orienting and executive components of visuospatial attention may be most susceptible to neural damage resulting from mTBI. Moreover, the lack of recovery in the executive component indicates that the degree and time course for recovery may be regionally specific.

Keywords: attention; mTBI; executive function; recovery

Abbreviations: ANT = attentional network test; mTBI = mild traumatic brain injury; RT = reaction time

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Introduction

Concussion, or mild traumatic brain injury (mTBI), is defined as any transient neurological dysfunction that results from a biomechanical force to the head (Giza and Hovda, 2001). A variety of studies examining the effects of mTBI have demonstrated that both diffuse axonal injury and/or focal lesions can result from an impact to the head (Kant *et al.*, 1997; Hofman *et al.*, 2002; Lorberboym *et al.*, 2002; Chen *et al.*, 2003). Although the list of symptoms resulting from mTBI runs the gamut from mild to severe, it is widely held that an alteration in consciousness in and of itself is sufficient to meet the criterion for diagnosis.

Deficits in attention are often observed in individuals who have recently suffered an mTBI. Research has illustrated that participants with mTBI often struggle to maintain or appropriately allocate their attentional resources while performing one or more concurrent tasks (Stuss *et al.*, 1989*a, b*; Ponsford and Kinsella, 1992; Cicerone, 1996; Spikman *et al.*, 1996; Chan, 2002; Chan *et al.*, 2003; Felmingham *et al.*, 2004). The visuospatial orienting of attention comprises disengagement, movement and re-engagement components that are associated through unique but interconnected neural networks (Fan *et al.*, 2002). Specific regions of the brain that have been implicated for their respective roles in these attentional networks include the parietal, frontal, temporal and cingulate cortices in addition to the midbrain (Posner and Petersen, 1990). Research on the process of shifting and re-engaging of attention has illustrated that activity of the superior parietal lobule, intraparietal sulcus of the posterior parietal cortex (PPC), frontal eye fields (FEF) and cingulate gyrus may be critical to the control of this behaviour (Nobre *et al.*, 1997; Kim *et al.*, 1999; Vandenberghe *et al.*, 2001). Furthermore, lesions of the parietal lobe lead to deficits in the ability to disengage attention from the location of a cue, whereas lesions in the frontal or temporal lobes and mid-brain create no such deficits (Posner *et al.*, 1984, 1987). Additionally, a searching component of attention has been localized to activity in the prefrontal cortex (PFC), especially within the dorsomedial and ventrolateral regions (Daffner *et al.*, 2000; Nobre *et al.*, 2004).

Based upon these previous studies, it is our belief that it is possible to identify regions of the brain with greater susceptibility to injury induced by a traumatic blow to the head. These regions at greater risk for injury may be associated with the generation of specific deficits when comparing performance of concussed individuals with age-matched controls.

To investigate this proposal we employed the attentional network test (ANT) developed by Fan and colleagues (Fan *et al.*, 2002) designed to separate the three main components of visuospatial attention. Specifically, the ANT assesses specific aspects of the alerting, orienting and executive components of attention. The alerting component functions to maintain vigilance or arousal throughout performance of a continuous task. The orienting component of attention facilitates covert shifts of attentional resources to a desired spatial location that allows an increase in processing speed for the detection and/or perception of targets appearing within that region of space. The executive component of attention plays a critical role in the capacity to resolve conflict and efficiently switch between tasks requiring unique sets of responses or behaviours for their performance.

Clinicians are commonly required to assess the recovery of participants with mTBI through application of a number of different clinical tests. However, it is unclear whether these tests are stringent enough to provide sufficient assessment of recovery. In our previous publication (van Donkelaar *et al.*, 2005) we examined the attentional deficits caused by an mTBI within the first 48 h of injury through comparison of performance on the ANT to matched controls. This investigation demonstrated that participants with mTBI displayed slower reaction times (RTs) due to deficits in both the orienting and executive components of attention, whereas the alerting component appeared normal. The aim of the current investigation is to thoroughly probe the rate and degree of recovery of visuospatial attention following mTBI throughout a 1 month post-injury period. For this purpose, participants with mTBI were compared with age-matched healthy controls in performance on the ANT at four points within a month of the injury.

Methods

Participants

Twenty participants who suffered an mTBI [12 males, 8 females; mean age: 21 ± 1.74 years (age range: 18–24 years); education: 16 ± 1.65 years] were identified from within the University of Oregon student population. A majority of participants were associated with intercollegiate, club, or intramural sports or recreational activities. All participants were initially recruited for testing within 2 days following the injury (mean elapsed time: 37 ± 11.5 h; range: 12–50 h) after identification by certified athletic trainers and/or attending medical doctors in the university intercollegiate athletic programme or the student health centre. Subsequent testing occurred 7, 14 and 28 days after the injury. The source of the injury ranged from impacts to the head occurring during sporting activities to accidental falls and collision with inanimate and/or stationary objects (*see* Table 1). The severity of the injury was categorized by the attending certified athletic trainers and/or medical doctors in accordance with the definitions originated by the American

Table 1 Demographic data for participants with concussion

Subject	Age (years)	Gender	Height (cm)	Weight (kg)	Time since injury (h)	Sport activity	Cause of injury
1	23	M	203	121	46	Basketball	Knee to head
2	19	M	194	89	24	Football	Helmet to helmet
3	23	M	180	79	24	N/A	Fall
4	22	M	187	109	42	Football	Helmet to helmet
5	19	F	171	89	46	Rugby	Knee to head
6	21	M	172	72	43	Tennis	Blunt injury
7	20	F	172	69	50	Volleyball	Fall
8	20	M	190	128	43	Football	Helmet to helmet
9	22	M	191	100	48	Football	Knee to helmet
10	18	F	164	70	12	N/A	Fall
11	22	F	169	65	48	N/A	Fall
12	19	F	165	61	36	Soccer	Head to head
13	21	F	153	73	45	N/A	Bicycle accident
14	18	F	174	72	42	N/A	Blunt injury
15	23	M	164	56	38	N/A	Fall
16	22	M	194	145	41	Football	Helmet to helmet
17	21	M	196	140	28	Football	Knee to helmet
18	21	M	186	94	48	Rugby	Head to head
19	20	M	157	64	20	N/A	Fall
20	24	F	172	47	20	N/A	Fall

Academy of Neurology (1997). A Grade 1 mTBI was assigned if the participant was disoriented as to time and place for <15 min. A Grade 2 mTBI was assigned if the participant remained disoriented for >15 min. Only individuals with Grade 1 or Grade 2 mTBIs were included in this study. Individuals with a rating of Grade 3, demarcated by a loss of consciousness for any period of time, or individuals who had incurred a previous mTBI within the last 6 months were excluded from participating in the study. Age-matched [mean age: 21 ± 1.81 years (age range: 18–24)], gender-matched (12 males, 8 females), activity level-matched (e.g. football players were matched with teammates who played the same position) and education level-matched (16 ± 1.68 years) control participants were located from within the same university population and tested at the same intervals. Individual control participant was paired with a matched participant with mTBI. All of the participants signed an informed consent form prior to partaking in the study and the local university human subjects compliance committee approved the experimental protocol.

Testing procedures

Participants performed the ANT that was designed by Fan and colleagues (Fan *et al*., 2002) for the purpose of assessing the three major components of visuospatial attention; alerting, orienting and executive function. Throughout each testing session, participants were seated ~50 cm in front of a computer monitor. Subjects were presented with visual targets subtending ~1° of visual angle to which they responded. Figure 1A illustrates the basic characteristics of a representative trial. At the onset of each trial a central fixation crosshair was displayed. On 75% of trials a precue (asterisk) was displayed briefly (100 ms) after a variable delay (400–1600 ms). Conversely, on the remaining trials no precue was presented. After a fixed delay (400 ms) a target arrow pointing to the left or right was displayed either 5° above or below the central fixation crosshair. Participants were instructed to press the left or right mouse button corresponding to the direction of the arrow as quickly and accurately as possible. The target arrow disappeared when either the subject responded or after 1700 ms, whichever occurred first.

The precue could appear in one of three configurations (Fig. 1B). Trials with a spatially informative precue were characterized by the appearance of the asterisk at the location where the subsequent target arrow would appear. These 'spatial precue' trials were always valid since the precue never appeared at a location at which the target did not subsequently appear. In trials containing a 'double precue', two asterisks were displayed 5° above and 5° below the central fixation crosshair. During trials incorporating a 'central precue', the asterisk was presented at the same location as the central fixation point. In conjunction with these precue arrangements, the target arrow likewise was displayed in one of three configurations (Fig. 1C). The target arrow could be displayed alone ('neutral' trials) or flanked on either side by a total of four arrows of the same size (two on the left and two on the right of the target arrow). During trials with flanker arrows, the arrows could be 'congruent', where flanker arrows pointed in the same direction as the target arrow, or 'incongruent' where the flanker arrows pointed in the opposite direction to the target arrow. The three different target types, congruent, incongruent and neutral, were equally distributed in trials containing each of the different precue conditions.

All participants completed a series of 24 practice trials with visual feedback concerning RT and accuracy prior to data collection. The experimental testing consisted of three blocks of experimental trials comprising 96 trials each (4 cue conditions × 2 target locations × 2 target directions × 3 flanker conditions × 2 trials). Experimental trials were pseudo-randomized and contained no visual feedback.

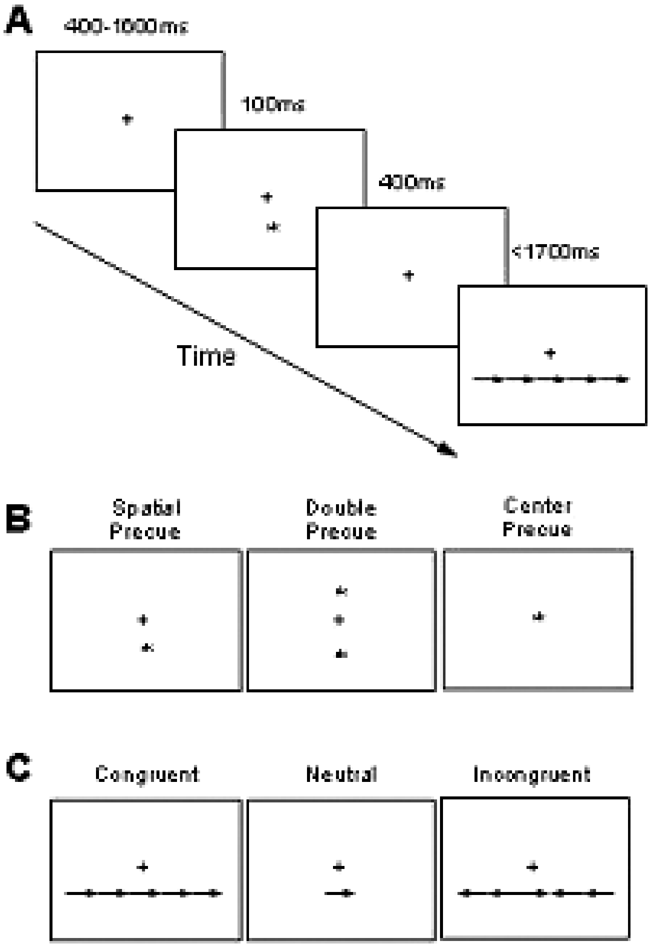

Fig. 1 Events occurring during the trials. (**A**) Sequence of events in a typical trial. Plus sign: fixation cross; asterisk: precue; arrows: target. Participants responded to the appearance of the target arrow by pressing the corresponding button on the mouse. In this example, the right mouse button would be pressed. (**B**) Precue configurations. *Left*: spatially informative precue; *middle* and *right*: spatially uninformative precues. On some trials, no precue was given. (**C**) Target configurations. *Left*: congruent targets; *middle*: neutral target; *right*: incongruent targets.

Data analysis

The primary dependent variables of interest were the median RT on accurate trials and error rate. RTs were calculated as the time from onset of the target arrow to the time when the mouse button was pressed. Error rate was designated as the percentage of trials within a condition where the subject responded incorrectly by pressing the wrong mouse button. In addition, to characterize the intrasubject variability within each group the coefficient of variation was calculated across the different combinations of conditions. The alerting, orienting and executive components of attention were calculated as median RT differences across relevant conditions following the same reasoning employed by Fan and colleagues (Fan *et al*., 2002). The

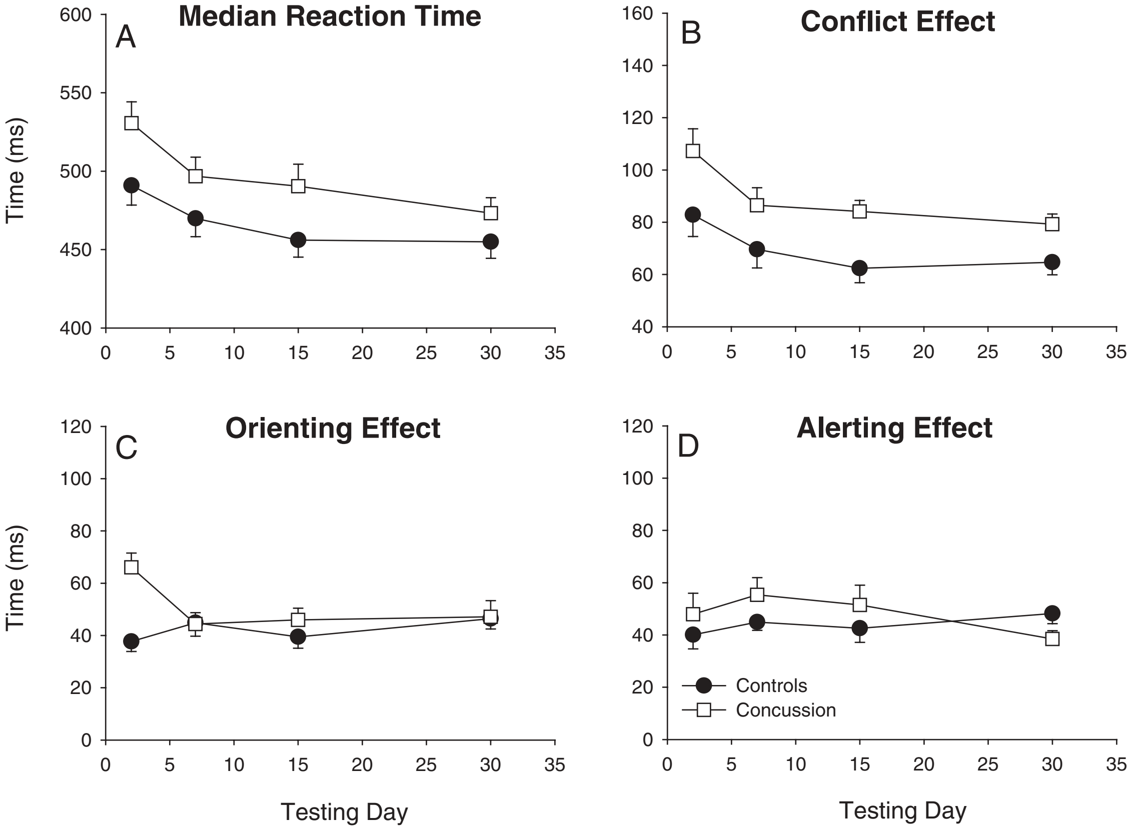

Fig. 2 (**A**) Median RT across all combinations of conditions for each respective day of testing for controls (filled circles) and participants with concussion (open squares). (**B**) Conflict Effect: Mean RT difference between congruent and incongruent target conditions for participants with concussion and controls across the four testing sessions. (**C**) Orienting Effect: Mean RT difference between spatial cue and centre cue conditions for controls versus participants with concussion across the four testing days. (**D**) Alerting Effect: Mean RT difference between double cue and no cue conditions for controls versus participants with concussion across the 4 days of testing. Error bars, one intersubject standard error.

alerting effect was evaluated by subtracting the median RT during double precue trials from the median RTs on no precue trials, regardless of the target configuration. This subtraction represents the benefit in RT, associated with knowing the target would appear exactly 400 ms later. The orienting effect was calculated by taking into account median RTs in trials with the spatial precue. Although this precue communicates when the target arrow will appear, it also indicates the exact location where the target will be displayed. Therefore, the orienting effect was evaluated by taking the difference between the median RTs of centre precue trials and the median RT of spatial precue trials. Trials containing either the centre or spatial precues alert the subject to the appearance of the subsequent target. Therefore, the subtraction of the RTs from these conditions represents the decrease in RT associated with the awareness of the precise location at which the subsequent target would be presented. The conflict effect, employed to appraise the executive component of attention, involves calculating the difference between the median RT for responses to congruent versus incongruent targets. This calculation determines the influence of facilitating or distracting information on RT, respectively. Analyses of variance were performed to investigate the differences within each attentional component across the various conditions. Specifically, 2 (subject group) × 4 (testing day) mixed model ANOVAs were performed to assess the differences between groups and across testing days for each component of attention, as well as for evaluation of RT differences for accurate versus inaccurate responses and error rates.

Results

Figure 2 displays the main results for overall median RTs, and for each of the three effects evaluating the components of attention (alerting, orienting and conflict). Figure 2A shows the overall median RT from all conditions combined across the four testing days. The results demonstrate that there is a significant group effect [$F(1,7) = 12.4$, $P = 0.001$], as well as a significant day effect [$F(3,7) = 5.7$, $P = 0.001$]. This indicates that controls were significantly faster than participants with mTBI in their RT and that both groups improved their RTs during the 1 month of testing. Furthermore, the lack of a significant interaction between subject group and testing days indicates that despite the improvements in RTs the differences between the groups were maintained across the 1 month period. Figure 2B displays the difference in median RTs for trials with congruent and incongruent target configurations, a calculation to estimate the executive component of attention (conflict effect). Statistical analysis revealed a significant group [$F(1,7) = 18.7$, $P = 0.001$] and day [$F(3,7) = 5.6$, $P = 0.001$] effect analogous to that observed for overall RT. This illustrates that participants with mTBI had a significantly larger conflict effect than controls and that across the 1 month testing period both groups reduced the size of the conflict effect. However, the lack of a significant interaction revealed that the differences between the subject groups were maintained throughout the month of recovery post-injury. To assess the orienting component of attention the median RTs for responses to spatially informative precues were subtracted from those to centre cues (spatially uninformative) (Fig. 2C). Statistical assessment demonstrated that there was a significant group effect [$F(1,7) = 6.8$, $P = 0.01$], but not a significant day effect. There was, however, a significant interaction between group and day [$F(3,7) = 3.97$, $P = 0.009$]. This implies that although there was initially a significant difference in the orienting effect between the two subject groups, during the month of post-injury testing the recovery allowed resolution of the deficits associated with the orienting of attention in participants with mTBI. Finally, to assess the alerting component of attention, the median RTs in conditions with a double precue were subtracted from median RTs in the no precue conditions (Fig. 2D). Statistical evaluation demonstrated that there were no significant differences in the alerting effect between the subject groups or across the testing days. In addition, for each of these effects there were no significant effects for the coefficient of variation measure indicating that the response variability across subjects within each group was similar.

Two additional assessments were performed to compare participants with mTBI and controls in terms of the difference in RTs during the generation of accurate compared with inaccurate responses, as well as their respective error rates on incongruent trials. The RT assessment demonstrated a significant group effect [$F(1,7) = 12.91$, $P = 0.001$] (Fig. 3). This indicates that participants with mTBI took significantly longer to prepare accurate compared with inaccurate responses relative to controls. The lack of a significant interaction between group and day implies that there was no recovery in this difference across the four testing sessions. The error rate evaluation examined the error rates of the participants with mTBI and control subjects during incongruent trials. This analysis yielded no significant group or testing day effects, implying that participants with mTBI and control subjects are equally accurate across the different trial types. Furthermore, this comparable performance in participants with mTBI and controls was maintained across the month post-injury. Thus, there is no interaction of the error rates and RTs, meaning that neither the participants with mTBI nor the controls adopted a strategy of focusing primarily on accuracy or speed at the expense of performance on the other factor. Again, the coefficient of variation measures for this data were similar for the two subject groups indicating that the within group variability was similar.

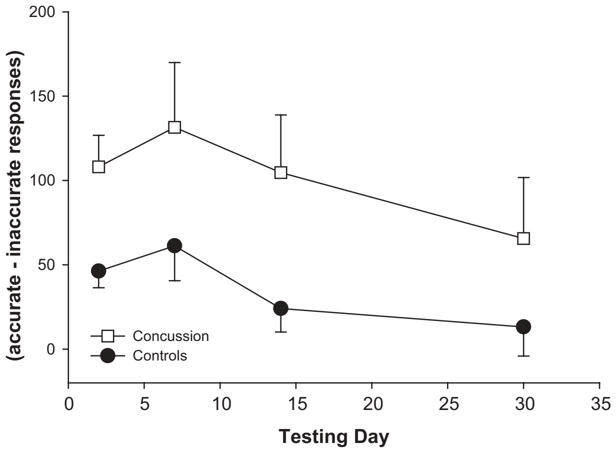

Fig. 3 Influence of response accuracy on RTs in trials testing the executive effect. The mean RT difference in accurate versus inaccurate responses during trials with the incongruent target configuration. Error bars, one intersubject standard error.

Discussion

This investigation employed the ANT to evaluate the affect of mTBI on the various components of visuospatial attention. In summary, the orienting component of attention was mildly affected, the executive component was substantially affected and there was no significant affect upon the alerting component of attention. There was no significant difference in the error rates for participants with mTBI and controls. However, there was a significant difference in the RTs associated with generation of accurate versus inaccurate responses between participants with mTBI and controls, and this difference was maintained throughout the period of testing.

The orienting component of the ANT evaluates the ability of the participant to make covert shifts of attentional resources to the cued spatial location, which in turn leads to quicker processing of the subsequent target appearing at that location. The decrease in RT as a result of this type of spatially informative cueing is acknowledged as a manifestation of the human capacity to shift attention and engage it at a cued location prior to onset of the target at that location (Posner, 1980). In our research, we demonstrated that participants with mTBI were significantly different from control subjects in their ability to use the spatially informative precues within the first 2 days after the injury. However, by the end of the first week post-injury the participants with mTBI performed similarly to controls. This line of evidence implies that suffering an mTBI hinders the ability to disengage, shift and re-engage attention at the cued location and, thus, the injury must affect regions of the brain associated with the spatial orienting of attention during the early period immediately following the injury. Specifically, regions involved in re-engagement of attention such as the superior parietal lobule and intraparietal sulcus of the PPC, FEF and cingulate gyrus may all be affected to some degree by mTBI (Nobre *et al.*, 1997; Kim *et al.*, 1999; Vandenberghe *et al.*, 2001; Yantis *et al.*, 2002). Furthermore, the searching component associated with orienting of attention is believed to involve PFC areas (Daffner *et al.*, 2000), including dorsomedial and ventrolateral prefrontal regions (Nobre *et al.*, 2004), and these regions may likewise be vulnerable during the first few days after the injury.

The executive component of the ANT assesses the capacity to use relevant information and ignore irrelevant information in order to facilitate the production of appropriate responses. Participants with mTBI had a significantly reduced capacity to disregard the irrelevant distractor stimuli during the incongruent trials resulting in markedly increased RTs. This RT cost was particularly evident when comparing accurate versus inaccurate responses with this target configuration. This result is in agreement with prior studies investigating the distractibility of participants with mTBI (Ponsford and Kinsella, 1992; Stuss *et al.*, 1989*a, b*). Furthermore, because there was no interaction between group and day for each of these executive component measures, there was no evidence to support a recovery of this function in the participants with mTBI during the 1 month post-injury. The anterior cingulate cortex (ACC) is the primary region of the brain implicated in the activity of ignoring distracting or irrelevant stimuli (Casey *et al.*, 2000; Fan *et al.*, 2003; Weissman *et al.*, 2003). Based on the current evidence, it appears that the ACC may be particularly susceptible to injury via mTBI and the damage created may take more time to resolve relative to the other attentional components localized to different regions of the brain.

The alerting component of the ANT functions to assess the participants' capacity to use precues providing temporal, but not spatial, information to prepare the appropriate response. The term 'phasic alertness' has been used to describe the benefit gained by the use of such precue information (Sturm *et al.*, 1999). However, participants with mTBI in our study benefited to a similar degree to controls from the alerting precue. This indicates that the mTBI investigated in the current study is not sufficient to produce substantial alterations in the participants' ability to maintain vigilance and/or arousal during performance of the ANT. Sturm and colleagues (Sturm *et al.*, 1999) implicated the ascending noradrenergic system arising from the locus coeruleus in the brainstem as having a pivotal role in maintaining alertness. Therefore, this region of the brain may be less susceptible to damage resulting from mTBI. Furthermore, our results regarding alertness are in accordance with a variety of other studies that likewise found no differences between participants with mTBI and controls in similar assessments of this component of attention (Stuss *et al.*, 1989*a, b*; Ponsford and Kinsella, 1992; Spikman *et al.*, 1996; Felmingham *et al.*, 2004). It is somewhat surprising that the alerting component of attention was unaffected by mTBI, however, this may reflect specific task constraints rather than any lack of functional deficit. For example, we used a constant foreperiod with this version of the ANT. It is possible that alerting deficits would be more likely to be revealed with a variable foreperiod including trials with cue-target intervals of up to 2–3 s. This may be especially apparent if the variability of response latencies was assessed as opposed to the median response latency (Stuss *et al.*, 1989*a*).

Be that as it may, the fact that we have shown significant differences in the behaviour of participants with mTBI relative to that of controls even a month after the injury demonstrates that with this very mild form of brain injury caution is warranted when making decisions regarding a return to normal activities. Although our results are statistically significant—for example, the conflict effect difference was $\sim$20 ms—one may question whether they are of sufficient clinical significance to affect day-to-day life in our participants. Although we did not measure any such deficits quantifiably, anecdotal reports from the participants themselves indicated that there were some difficulties, such as lack of concentration, dizziness and memory problems, that lingered for variable periods of time during the 1 month testing period. In addition, we have shown that participants with mTBI have gait deficits that are exacerbated in dual-task contexts and remain present for at least a month (Parker *et al.*, 2005*a*). Such difficulties are especially important to monitor for the athletes in our study who participate in sports that expose them to the risk of subsequent brain injuries.

Another issue to consider is the fact that we used a matched control group as a basis of comparison rather than directly contrasting pre-injury and post-injury performance of our participants with mTBI. This may result in effects that are due to the predisposition of individuals who suffer an mTBI rather than caused by the mTBI itself. This was partially controlled for by using control participants who were matched on a number of different criteria, including the actual activity (and even the specific position played in the case of team sports athletes). Moreover, the fact that different recovery patterns were observed across the different attentional components and that the orienting effect in particular returned to normal levels implies that the two participant groups were well matched and that the observed effects were caused by the injury rather than the result of a predisposing characteristic of individuals who suffer an mTBI.

The underlying causes of mTBI vary from one individual to the next and, as such, there most probably was a large variety of damage to the brain across the participants in this study. We did not attempt to confirm this with structural brain imaging (MRI or CT scans), although the utility of this approach is questionable with the mild form of brain injury being studied in this investigation (Hughes *et al.*, 2004). One prediction based on the heterogeneous nature of the putative damage is that the responses of the participants with mTBI should have been more variable than that observed in the controls. However, analysis of the coefficient of variation across the different combinations of conditions for each dependent variable did not reveal any significant group differences. Thus, despite the high likelihood that different regions of the brain were affected in the participants with mTBI, their overall performance as a group was relatively consistent.

In conclusion, this study illustrated that the orienting and executive components of visuospatial attention are especially vulnerable to injury caused by mTBI and that the executive component exhibits deficits even a month after the injury. By contrast, the alerting component of attention is relatively immune to the negative affects of mTBI, at least at the levels of severity encountered in this study. It is widely held that these components of attention involve functionally distinct, although interconnected, networks within the brain. Therefore, based on the current evidence we believe that some regions of the brain are more at risk than others following an mTBI and that the degree and rate of recovery varies from region to region. Future studies using functional MRI should be completed to more clearly map these functional deficits onto alterations in the patterns of activity in specific networks of brain regions and include follow-up tests after a longer period of recovery (i.e. 3–6 months). Information such as this could be useful in the future in leading to a refined approach to both diagnosis and treatment of mTBI.

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