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Impacts fonctionnels du traumatisme craniocérébral léger sur la vision et l'équilibre postural chez l'adulte

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Thèse présentée à la Faculté des études supérieures
en vue de l'obtention du grade de PhD
en sciences biomédicales

Août 2015

Résumé

Le traumatisme craniocérébral léger (TCCL) a des effets complexes sur plusieurs fonctions cérébrales, dont l'évaluation et le suivi peuvent être difficiles. Les problèmes visuels et les troubles de l'équilibre font partie des plaintes fréquemment rencontrées après un TCCL. En outre, ces problèmes peuvent continuer à affecter les personnes ayant eu un TCCL longtemps après la phase aiguë du traumatisme. Cependant, les évaluations cliniques conventionnelles de la vision et de l'équilibre ne permettent pas, la plupart du temps, d'objectiver ces symptômes, surtout lorsqu'ils s'installent durablement. De plus, il n'existe pas, à notre connaissance, d'étude longitudinale ayant étudié les déficits visuels perceptifs, en tant que tels, ni les troubles de l'équilibre secondaires à un TCCL, chez l'adulte. L'objectif de ce projet était donc de déterminer la nature et la durée des effets d'un tel traumatisme sur la perception visuelle et sur la stabilité posturale, en évaluant des adultes TCCL et contrôles sur une période d'un an. Les mêmes sujets, exactement, ont participé aux deux expériences, qui ont été menées les mêmes jours pour chacun des sujets.

L'impact du TCCL sur la perception visuelle de réseaux sinusoïdaux définis par des attributs de premier et de second ordre a d'abord été étudié. Quinze adultes diagnostiqués TCCL ont été évalués 15 jours, 3 mois et 12 mois après leur traumatisme. Quinze adultes contrôles appariés ont été évalués à des périodes identiques. Des temps de réaction (TR) de détection de clignotement et de discrimination de direction de mouvement ont été mesurés. Les niveaux de contraste des stimuli de premier et de second ordre ont été ajustés pour qu'ils aient une

visibilité comparable, et les moyennes, médianes, écarts-types (ET) et écarts interquartiles (EIQ) des TR correspondant aux bonnes réponses ont été calculés. Le niveau de symptômes a également été évalué pour le comparer aux données de TR. De façon générale, les TR des TCCL étaient plus longs et plus variables (plus grands ET et EIQ) que ceux des contrôles. De plus, les TR des TCCL étaient plus courts pour les stimuli de premier ordre que pour ceux de second ordre, et plus variables pour les stimuli de premier ordre que pour ceux de second ordre, dans la condition de discrimination de mouvement. Ces observations se sont répétées au cours des trois sessions. Le niveau de symptômes des TCCL était supérieur à celui des participants contrôles, et malgré une amélioration, cet écart est resté significatif sur la période d'un an qui a suivi le traumatisme.

La seconde expérience, elle, était destinée à évaluer l'impact du TCCL sur le contrôle postural. Pour cela, nous avons mesuré l'amplitude d'oscillation posturale dans l'axe antéropostérieur et l'instabilité posturale (au moyen de la vitesse quadratique moyenne (VQM) des oscillations posturales) en position debout, les pieds joints, sur une surface ferme, dans cinq conditions différentes : les yeux fermés, et dans un tunnel virtuel tridimensionnel soit statique, soit oscillant de façon sinusoïdale dans la direction antéropostérieure à trois vitesses différentes. Des mesures d'équilibre dérivées de tests cliniques, le *Bruininks-Oseretsky Test of Motor Proficiency 2nd edition* (BOT-2) et le *Balance Error Scoring System* (BESS) ont également été utilisées. Les participants diagnostiqués TCCL présentaient une plus grande instabilité posturale (une plus grande VQM des oscillations posturales) que les participants contrôles 2 semaines et 3 mois après le traumatisme, toutes

conditions confondues. Ces troubles de l'équilibre secondaires au TCCL n'étaient plus présents un an après le traumatisme. Ces résultats suggèrent également que les déficits affectant les processus d'intégration visuelle mis en évidence dans la première expérience ont pu contribuer aux troubles de l'équilibre secondaires au TCCL. L'amplitude d'oscillation posturale dans l'axe antéropostérieur de même que les mesures dérivées des tests cliniques d'évaluation de l'équilibre (BOT-2 et BESS) ne se sont pas révélées être des mesures sensibles pour quantifier le déficit postural chez les sujets TCCL.

L'association des mesures de TR à la perception des propriétés spécifiques des stimuli s'est révélée être à la fois une méthode de mesure particulièrement sensible aux anomalies visuomotrices secondaires à un TCCL, et un outil précis d'investigation des mécanismes sous-jacents à ces anomalies qui surviennent lorsque le cerveau est exposé à un traumatisme léger. De la même façon, les mesures d'instabilité posturale se sont révélées suffisamment sensibles pour permettre de mesurer les troubles de l'équilibre secondaires à un TCCL. Ainsi, le développement de tests de dépistage basés sur ces résultats et destinés à l'évaluation du TCCL dès ses premières étapes apparaît particulièrement intéressant. Il semble également primordial d'examiner les relations entre de tels déficits et la réalisation d'activités de la vie quotidienne, telles que les activités scolaires, professionnelles ou sportives, pour déterminer les impacts fonctionnels que peuvent avoir ces troubles des fonctions visuomotrice et du contrôle de l'équilibre.

Mots-clés : Traumatisme craniocérébral léger (TCCL), intégration visuomotrice, stimuli visuels, premier ordre, second ordre, mouvement, temps de réaction, équilibre, instabilité posturale

Abstract

Mild traumatic brain injury (mTBI) has complex effects on several brain functions that can be difficult to assess and follow-up. Visual and balance problems are frequently reported after an mTBI. Furthermore, these problems can still affect mTBI individuals far beyond the acute stage of injury. However, standard clinical assessments of vision and balance most often fail to objectivize these symptoms, especially if they are lingering. Moreover, to our knowledge, no longitudinal study investigated either mTBI-related deficits of visual perception *per se*, or mTBI-related balance deficits in adults. The aim of this project was to determine the nature and duration of the effects of such a traumatism on visual perception as well as on postural stability, by evaluating mTBI and control adults over a one-year period. Exactly the same subjects participated in both experiments, which took place on the same days for every subject.

The impact of mTBI on the visual perception of sine-wave gratings defined by first-and second-order characteristics was, first, investigated. Fifteen adults diagnosed with mTBI were assessed at 15 days, 3 months and 12 months after injury. Fifteen matched controls followed the same testing schedule. Reaction times (RTs) for flicker detection and motion direction discrimination were measured. Stimulus contrast of first- and second-order patterns was equated to control for visibility, and correct-response RT means, standard deviations (SDs), medians, and interquartile ranges (IQRs) were calculated. The level of symptoms was also evaluated to compare it to RT data. In general in mTBI, RTs were longer and more variable (ie.,

larger SDs and IQRs), than those of controls. In addition, mTBI participants' RTs to first-order stimuli were shorter than those to second-order stimuli, and more irregular for first- than for second-order stimuli in the motion condition. All these observations were made over the 3 sessions. The level of symptoms observed in mTBI was higher than that of control participants and this difference did also persist up to one year after the brain injury, despite an improvement.

The second experiment, then, investigated the impact of mTBI on postural control. To achieve that, antero-posterior body sway amplitude (BSA) and postural instability (given by body sway velocity root mean square, vRMS) during upright stance, feet together, on a firm surface, were measured in five different conditions: with eyes closed and in a 3D virtual reality tunnel, either static or sinusoidally moving in the antero-posterior direction at 3 different velocities. Balance measures derived from clinical tests, *Bruininks-Oseretsky Test of Motor Proficiency 2nd edition* (BOT-2) and *Balance Error Scoring System* (BESS), were also used. Participants diagnosed with mTBI exhibited more postural instability (i.e. higher body sway vRMS) than control participants at 2 weeks and at 3 months post-injury, regardless of the testing condition. These mTBI-related balance deficits were no longer present one year post-injury. These results also suggest that visual processing impairments revealed in the first experiment might have contributed to mTBI-related balance deficits. Antero-posterior BSA as well as measures derived from clinical tests for balance assessment did not appear to be sensitive enough to quantify postural deficits of mTBI participants.

The combination of RT measures with particular stimulus properties appeared

to be a highly sensitive method for measuring mTBI-induced visuomotor anomalies, and to provide a fine probe of the underlying mechanisms when the brain is exposed to mild trauma. Likewise, postural instability measures prove to be sensitive enough for measuring mTBI-induced balance deficits. Developing screening tests in this respect intended for early post-mTBI use would be of interest. Also, studying relationships of such deficits with performance in daily life activities, such as school, work, or sports, is crucial in order to determine the functional impacts of these alterations in visuomotor and balance functions.

Keywords: mild traumatic brain injury (mTBI), visuomotor integration, visual stimuli, first-order, second-order, motion, reaction time, balance, postural instability

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Liste des sigles

ANOVA : Analysis of variance

BESS : Balance Error Scoring System

BOT-2 : Bruininks-Oseretsky Test of Motor Proficiency 2nd edition

BSA : Body sway amplitude

CAARS-S: S : Conners' Adult ADHD Rating Scale–Self-report: Short Version

CT Scan : Computerized tomography scan

EC : Eyes closed

ED : Emergency department

EEG : Électroencéphalogramme, ou électroencéphalographie (ou tout équivalent en anglais)

EIQ : écarts interquartiles

EMS : Emergency medical service

ET : écarts-types

FDT : Frequency Doubling Technology

FOF : First-order flicker

FOM : First-order motion

GCS : Glasgow Coma Scale

HSCM : Hôpital du Sacré-Cœur de Montréal

IQR : Interquartile range

LOC : Loss of consciousness

mTBI : Mild brain traumatic injury

MUHC : McGill University Health Centre

PCSS-R : Post-Concussion Symptom Scale – Revised

PTA : Post-traumatic amnesia

RT : Reaction time

RTIQR : Reaction time interquartile range

RTSD : Reaction time standard deviation

SAH : Subarachnoid hemorrhage

SD : Standard deviation

SE : Standard error

SOF : Second-order flicker

SOM : Second-order motion

TCCL : Traumatisme craniocérébral léger, ou traumatisé craniocérébral léger

TDM : Tomodensitométrie

TONI-3 : Test of Nonverbal Intelligence – Third Edition

TR : Temps de réaction

VQM : Vitesse quadratique moyenne

vRMS : Velocity root mean square

WHO : World Health Organization

Remerciements

Tout d'abord, j'aimerais remercier Jocelyn Faubert, mon directeur de thèse. Merci, Jocelyn, de m'avoir proposé ce projet de recherche. Merci pour ton soutien et ta grande disponibilité. Merci également de m'avoir laissé autant de latitude dans mon travail.

Merci à mon codirecteur, Robert Forget. Merci, Robert, pour ton soutien, ton aide, ton temps et ta patience. Merci aux autres membres de la grande équipe qui a collaboré à ce projet : Michelle McKerral et Isabelle Gagnon (chercheuses principales), Thomas Romeas (coordonnateur du projet), Dr Jean-François Giguère (HSCM), Isabelle Roy et Ariane Demers (recrutement, HSCM), Lisa Grilli (recrutement, MUHC).

Merci aux membres du laboratoire Faubert que j'ai eu le plaisir de côtoyer. Merci notamment aux personnes qui m'ont aidé dans ce projet. Merci à Rémy Allard, pour avoir pris le temps de répondre à toutes mes questions et m'avoir aidé à orienter ma réflexion. Merci également à David Nguyen-Tri ; merci pour ton énorme travail de relecture. Merci à Claudine Habak, pour la relecture et tes précieux conseils. Merci enfin à Isabelle Legault, bras droit et cerveau gauche de Jocelyn : merci, Isabelle, pour ta très grande efficacité.

Merci à mes parents, mes frères et sœurs, et mes neveux et nièces. Merci à tous pour votre inestimable soutien.

Merci à mes amis, et notamment François et Guillaume. Merci d'avoir été là chaque fois que j'en avais besoin.

Merci à Pascale Dauthuile et Christian Dotter qui m'ont encouragé dès le début dans ce long périple au Canada. Je vous en serai éternellement reconnaissant.

Enfin, merci à Mélanie « Papagena » de m'avoir soutenu et supporté.

Chapitre 1 : Introduction

1. Le traumatisme craniocérébral léger

Il est communément admis que le traumatisme craniocérébral léger (TCCL) est une perturbation *transitoire* des fonctions du système nerveux central générée par une accélération ou une décélération subite de la tête (Carroll et al., 2004; Gaetz, 2004; G. L. Iverson, 2005; R. M. Ruff et al., 2009; Shaw, 2002; Viano, Casson, & Pellman, 2007). C'est principalement de la nature transitoire des effets du TCCL qui sera traité dans cette thèse.

1.1. Aspects mécanique, anatomique et biologique

Lorsque la tête est mise en mouvement ou arrêtée brutalement, le cerveau, qui est maintenu dans la boîte crânienne avec un certain degré de liberté, est à son tour mis en mouvement. Du fait de sa relative liberté de mouvement et de son inertie par rapport au reste du crâne, le cerveau suit le mouvement de la tête avec un léger retard. Il est alors secoué dans la boîte crânienne, et si le choc est suffisamment violent, il entre en contact avec la voûte crânienne qui limite sa course (Bain, Raghupathi, & Meaney, 2001; Bayly et al., 2005; Bigler, 2007, 2008; Evans, 2004; Gaetz, 2004; Ivarsson, Viano, & Lovsund, 2002; Nishimoto & Murakami, 1998; Ropper & Gorson, 2007; Shaw, 2002; Viano et al., 2005).

De par ses propriétés viscoélastiques, le parenchyme cérébral subit, lors de cet ébranlement, des déformations par étirement et par compression (Bayly et al., 2005; Nishimoto & Murakami, 1998). Les mécanismes de coup et de contrecoup sont

responsables de l'écrasement du cortex contre la voûte crânienne (Shaw, 2002). De petites contusions corticales circonscrites sont associées à ces mécanismes (Lee et al., 2008). Les zones généralement touchées sont les cortex frontal, temporal et occipital (Bayly et al., 2005; Bigler, 2007; Datta, Pillai, Rao, Kovoor, & Chandramouli, 2009; Gaetz, 2004; Lee et al., 2008). Les élongations affectent notamment la substance blanche. Elles participent à l'étirement et à la désorganisation des axones. Il s'agit d'une atteinte diffuse communément appelée traumatisme axonal diffus ou lésion axonale diffuse (Bain et al., 2001; Gaetz, 2004; G. L. Iverson, 2005; Maxwell, Povlishock, & Graham, 1997; Nishimoto & Murakami, 1998; Shaw, 2002; Topal et al., 2008). Dans certains cas, à l'interface entre les substances blanche et grise, en raison de la différence de densité et d'organisation de ces deux parties du tissu nerveux, on remarque des déconnexions sous-corticales (Bigler, 2008; Gaetz, 2004). Les principales structures de la substance blanche affectées par ces étirements sont le corps calleux, le fornix, et la substance blanche sous-corticale, tant à un niveau profond qu'à l'interface entre les substances blanche et grise (Bayly et al., 2005; Bigler, 2008; Nishimoto & Murakami, 1998). D'autres structures situées à la jonction du télencéphale et du tronc cérébral, le diencéphale et le mésencéphale, subissent également des déformations par étirement et compression, lors des oscillations du cerveau dans la boîte crânienne (Bayly et al., 2005; Ropper & Gorson, 2007). Dans les cas de TCCL, on retrouve rarement des hémorragies (Bigler, 2008; G. L. Iverson, 2005; Lee et al., 2008; Topal et al., 2008). Il s'agit le plus souvent de pétéchies localisées notamment au niveau du corps calleux. Elles résultent des déformations subies par le cerveau ainsi que des interactions entre le corps calleux et la faux du

cerveau (Bayly et al., 2005; Bigler, 2007). Tous ces dommages mécaniques associés au TCCL restent relativement petits, voire microscopiques, et dispersés dans le parenchyme cérébral. En effet, la physiopathologie du TCCL se résume généralement à des perturbations physiologiques des neurones plutôt qu'à leur destruction (G. L. Iverson, 2005; Lee et al., 2008; Marion, 1998).

Les déformations du cerveau déclenchent une cascade de processus biochimiques qui commence par la libération anarchique de neurotransmetteurs et le déclenchement de flux ioniques désordonnés (Bigler, 2007, 2008; Gaetz, 2004; G. L. Iverson, 2005; Lee et al., 2008; Maxwell et al., 1997; Shaw, 2002; Topal et al., 2008). Ces processus vont avoir comme premier effet d'amener le potentiel de membrane des neurones à un état d'hyperpolarisation situé largement en dessous de sa valeur de repos. Pendant la période relativement courte de restauration de ce potentiel de membrane, l'activité neuronale est abolie (Shaw, 2002). Le retour à l'homéostasie nécessite un accroissement de l'activité métabolique qui se prolonge plusieurs minutes après le choc. Cette hyperactivité métabolique conduit à un épuisement des ressources énergétiques (Shaw, 2002), et se fait, par ailleurs, dans le contexte d'une diminution du flux sanguin cérébral, diminution qui, elle, va durer plusieurs jours (G. L. Iverson, 2005). Les déséquilibres ioniques, qui, eux aussi, durent plusieurs jours, vont également avoir une incidence directe sur la diminution de la production d'énergie et affecter le fonctionnement métabolique mitochondrial (G. L. Iverson, 2005; Maxwell et al., 1997). Enfin, l'augmentation de calcium intracellulaire participe à la destruction des microtubules et à la compaction des neurofilaments, ce qui a pour

effet de perturber, voire d'interrompre, le transport axonal (Bigler, 2008; Gaetz, 2004; G. L. Iverson, 2005; Maxwell et al., 1997).

1.2. Aspects fonctionnels et symptômes

Les conséquences visibles d'un TCCL sont les signes fonctionnels qui le suivent, plutôt que les lésions mineures et autres dommages microscopiques résultant des processus mécaniques ou physiologiques qui le caractérisent. Ainsi, les signes et symptômes généralement constatés immédiatement après un TCCL sont : la perte de connaissance, la confusion, une période d'amnésie des événements entourant l'impact, des troubles de l'équilibre ou un étourdissement, des vomissements et des maux de tête (Carroll et al., 2004; Evans, 2004; Fife & Kalra, 2015; R. M. Ruff et al., 2009; Shaw, 2002).

Les événements qui se passent au niveau cérébral ainsi que leurs liens avec les signes fonctionnels et les symptômes du TCCL ne sont pas encore précisément connus (Gaetz, 2004; Shaw, 2002). Les explications physiopathologiques des signes secondaires à un TCCL sont pour le moment théoriques. Aussi, les définitions du TCCL considèrent-elles, principalement, les signes visibles (Carroll et al., 2004; Marshall et al., 2015; Shaw, 2002).

1.3. Définition de l'Organisation mondiale de la santé

L'Organisation mondiale de la santé (OMS) définit le TCCL de la façon suivante (Carroll et al., 2004) :

« Un TCCL est une lésion cérébrale aiguë résultant du transfert à la tête d'énergie mécanique provenant de forces physiques externes. Les critères opérationnels permettant son identification clinique sont : (i) au moins un des signes suivant : confusion ou désorientation, perte de connaissance d'au plus 30 minutes,

amnésie post-traumatique de moins de 24 heures, et/ou tout autre déficit neurologique, comme des signes focaux, des convulsions et des lésions intracrâniennes ne nécessitant pas de chirurgie ; (ii) un score de coma de Glasgow de 13-15, 30 minutes après l'accident ou plus tard à l'admission dans un service médical. Ces manifestations du TCCL ne doivent pas être dues à la prise de drogue, d'alcool ou de médicaments, ni être causées par d'autres lésions ou gestes posés pour soigner d'autres lésions (comme des lésions systémiques, des lésions de la face ou une intubation), ni être causées par d'autres problèmes (comme un trauma psychologique, la barrière de la langue ou des conditions médicales coexistantes), ni être causées par une blessure craniocérébrale pénétrante. »[1]

Cette définition a été établie notamment dans le but d'apporter davantage d'homogénéité dans la recherche sur les TCCL, afin d'être en mesure de mieux cerner et caractériser ce type de traumatisme. En effet, parmi les études présentes dans la littérature scientifique, les critères utilisés pour définir et établir ce qu'est un TCCL sont variables. Également, certaines études, notamment celles relatives aux commotions cérébrales dans le sport, ne donnent ou ne considèrent aucune définition du TCCL (Carroll et al., 2004).

1.4. Prise en charge du TCCL

La prise en charge médicale d'individus ayant subi un TCCL a lieu généralement lors de la phase aiguë du traumatisme et relève alors de services d'urgence (Borg et al., 2004; Fayol, Carriere, Habonimana, & Dumond, 2009; R. M. Ruff et al., 2009). La mission de tels services est d'écarter tout risque vital. L'essentiel est alors de déterminer quels sont les individus qui se présentent, à première vue, comme des TCCL et sont à risque d'avoir des lésions intracrâniennes évolutives

[1] Traduit de l'anglais

impliquant la nécessité du recours à la chirurgie (Borg et al., 2004; Fayol et al., 2009). Le diagnostic de TCCL apparaît dans ce contexte comme un diagnostic d'exclusion. Aussi, lorsque le diagnostic de TCCL est posé avec certitude, le suivi ne relève plus d'un service d'urgence.

En effet, le caractère transitoire du TCCL implique qu'il est sans gravité, c'est-à-dire notamment qu'il ne constitue pas une menace vitale, et qu'il n'est pas suivi de séquelles (G. L. Iverson, 2005). Au niveau cérébral, les dommages causés lors d'un TCCL sont mineurs, rarement visibles à l'imagerie cérébrale (Gaetz, 2004; Lee et al., 2008; Lewine et al., 2007; P. M. Rees, 2003; Topal et al., 2008) et ne requièrent pas de chirurgie. Aussi, les conséquences d'un tel traumatisme étant considérées comme étant bénignes et de courte durée, il n'existe pas vraiment de consensus de protocole de suivi ou de prise en charge (c'est-à-dire de traitement ou de rééducation) d'un TCCL (Fayol et al., 2009; Leddy, Kozlowski, Fung, Pendergast, & Willer, 2007). Ce qui est préconisé, la plupart du temps, est l'éducation de l'individu blessé et de son entourage ainsi que le traitement des symptômes, au besoin (Marshall et al., 2015; McAllister & Arciniegas, 2002). Finalement, le plein retour aux activités est jugé possible après la disparition des premiers symptômes, soit généralement dans les jours qui suivent le traumatisme (G. L. Iverson, 2005; Marshall et al., 2015). La question demeure cependant : y a-t-il persistance de certaines dysfonctions malgré la disparition des symptômes ?

1.5. Épidémiologie

Dans un rapport établi en 2004 (Cassidy et al., 2004), l'OMS estime que les TCCL représentent de 70 à 90% de tous les traumatismes craniocérébraux qui font

l'objet d'une prise en charge médicale. Chez les adultes ayant subi un TCCL, le taux de prise en charge hospitalière est d'environ 100 à 300/100 000 individus chaque année. Cependant, sachant que de nombreux cas de TCCL ne sont pas vus en milieu hospitalier, le taux d'incidence réel des TCCL excèderait probablement les 600/100 000 individus par an.

1.6. Résolution du TCCL et symptômes post-commotionnels persistants

Les premiers effets d'un TCCL, comme les maux de tête, étourdissements, vomissements et troubles cognitifs, disparaissent généralement en quelques jours ou semaines (Naunheim, Matero, & Fucetola, 2008). Ainsi, la grande majorité des individus ayant subi un TCCL retrouvent, au bout de 1 à 3 mois, un niveau de fonctionnement comparable à celui qu'ils avaient avant le traumatisme (G. L. Iverson, 2005; Marshall et al., 2015).

Cependant, l'idée de résolution relativement rapide et sans séquelles des déficits fonctionnels secondaires à un TCCL est encore sujette à caution. Il arrive, en effet, dans 5 à 20% des cas, que certains symptômes, physiques, émotionnels ou cognitifs, perdurent au-delà de trois mois après le traumatisme, à un niveau invalidant (Bigler, 2008; Evans, 2004; G. Iverson, 2007; G. L. Iverson, 2005; Konrad et al., 2011; Lewine et al., 2007; McAllister & Arciniegas, 2002; P. M. Rees, 2003; R. J. Rees & Bellon, 2007; Ropper & Gorson, 2007; R. Ruff, 2005; R. M. Ruff, 2011; Shaw, 2002; Sheedy, Geffen, Donnelly, & Faux, 2006; Sheedy, Harvey, Faux, Geffen, & Shores, 2009; Willer & Leddy, 2006). On parle alors de syndrome post-commotionnel (SPC, ou de syndrome post-commotionnel persistent).

D’un autre côté, la persistance de symptômes suivant un TCCL suscite, elle aussi, la controverse, notamment parce que les symptômes concernés ne sont pas propres au TCCL, ou encore parce que l’état de morbidité psychique prétraumatique n’est pas toujours connu (Bigler, 2008; G. L. Iverson, 2005; Leddy et al., 2007; McAllister & Arciniegas, 2002; R. Ruff, 2005). Aussi, une attribution erronée de certains symptômes au TCCL est possible plusieurs mois après un tel traumatisme. Cela explique notamment la variabilité des proportions de cas de SPC rapportées dans la littérature scientifique (Bigler, 2008; G. L. Iverson, 2005; R. Ruff, 2005).

Par ailleurs, des déficits cognitifs (Kumar, Rao, Chandramouli, & Pillai, 2009; Malojcic, Mubrin, Coric, Susnic, & Spilich, 2008; Vanderploeg, Curtiss, & Belanger, 2005), sensorimoteurs (Gagnon, Forget, Sullivan, & Friedman, 1998; Gagnon, Friedman, Swaine, & Forget, 2001; Gagnon, Swaine, Friedman, & Forget, 2004a; Slobounov, Cao, Sebastianelli, Slobounov, & Newell, 2008; Slobounov, Tutwiler, Sebastianelli, & Slobounov, 2006), visuomoteurs (Gagnon, Swaine, Friedman, & Forget, 2004b) et perceptifs visuels (Brosseau-Lachaine, Gagnon, Forget, & Faubert, 2008) ont été mis en évidence au-delà de la période supposée de rémission, chez des individus ayant eu un TCCL, et qui parfois même ne ressentaient plus de symptômes (Slobounov et al., 2008; Slobounov, Wu, et al., 2006). Mais ces déficits persistants, généralement subtils, ne sont pas, la plupart du temps, décelés par les tests cliniques qui paraissent insuffisamment sensibles pour cela (Fayol et al., 2009; Fife & Kalra, 2015; G. L. Iverson, 2005; McCrea et al., 2003).

Le fait qu’aucun déficit ne soit clairement identifiable, sur le plan clinique, plusieurs jours après un TCCL, soulève plusieurs questions. Il y a d’abord la reprise

des activités (travail ou activité physique). La disparition des symptômes est-elle suffisante pour permettre une pleine reprise de ces activités ? Ensuite, dans le cas de la persistance de symptômes, il n'est possible que de s'en remettre au patient et de faire au mieux pour traiter ses symptômes plutôt que leurs causes. Finalement, compte tenu des données épidémiologiques et du fait que sa physiopathologie est encore mal connue, le TCCL constitue un problème majeur de santé publique (Carroll et al., 2004). Aussi, la conception de tests cliniques sensibles aux déficits subtils secondaires à un TCCL apparaît nécessaire, afin de pouvoir mieux identifier et prendre en charge ce type de traumatisme, notamment dans les jours qui suivent sa phase aiguë et plus tard lorsque des symptômes persistent.

2. Perception visuelle et traumatisme craniocérébral léger

Outre les voies visuelles rétino-corticales (De Moraes, 2013; Krainik, Feydy, Colombani, Helias, & Menu, 2003; McKerral, Lepore, & Lachapelle, 2001), une grande partie du cerveau comporte des réseaux neuronaux impliqués dans la perception visuelle (Billino, Braun, Bremmer, & Gegenfurtner, 2011; Dumoulin, Baker, Hess, & Evans, 2003; Dupont, Sary, Peuskens, & Orban, 2003; Farivar, 2009; Kalaycioglu, Nalcaci, Schmiedt-Fehr, & Basar-Eroglu, 2009; Noguchi, Kaneoke, Kakigi, Tanabe, & Sadato, 2005; Sunaert, Van Hecke, Marchal, & Orban, 2000; Vaina & Soloviev, 2004; Vakalopoulos, 2005). Compte tenu de cela et du caractère diffus des dommages cérébraux engendrés par un TCCL (Kirov et al., 2013; Topal et al., 2008), il est raisonnable de supposer qu'un ou plusieurs des réseaux impliqués dans

la perception visuelle soient touchés suite à un tel traumatisme, et que cela se traduise par des déficits perceptifs visuels.

2.1. Perception visuelle

La perception visuelle d'un stimulus repose sur ses attributs. On distingue les attributs de premier ordre et ceux de second ordre. Les attributs de 1er ordre, la luminance et la couleur, ont des propriétés dites simples ou linéaires et qui peuvent être analysées dans le domaine de Fourier. Les attributs de 2d ordre, la texture, la profondeur et le mouvement de 1er ordre, ont des propriétés dites complexes ou non linéaires et qui ne peuvent être analysées dans le domaine de Fourier.

Une façon de concevoir un stimulus de 1er ordre est d'additionner un signal sinusoïdal de luminance et un signal de bruit de luminance moyenne constante (Allard & Faubert, 2006; Brosseau-Lachaine et al., 2008) (*Figure 1*). Le signal résultant est un signal de bruit dont la luminance moyenne varie de façon sinusoïdale. On parle alors de modulation de luminance. Cette variation de la luminance d'un tel stimulus de 1er ordre permet au système visuel d'en déterminer les caractéristiques spatio-temporelles grâce à des détecteurs sensibles aux variations d'énergie lumineuse dans le signal au cours d'une seule étape de filtrage (Chubb & Sperling, 1988; Lu & Sperling, 2001).

Pour concevoir un stimulus de 2d ordre, il est possible de partir des mêmes signaux de luminance (signal sinusoïdal et signal de bruit) que ceux utilisés pour créer un stimulus de 1er ordre ; l'opération consiste alors à les multiplier l'un par l'autre (Allard & Faubert, 2006; Brosseau-Lachaine et al., 2008). Le signal résultant est un signal de bruit de luminance moyenne constante et dont le contraste de

luminance varie suivant une succession de « ventres » et de « nœuds ». Les « ventres » correspondent aux zones où le contraste est le plus important entre les points de bruit, et les « nœuds » correspondent aux zones où le contraste est le plus faible entre les points de bruit. On parle alors de modulation de contraste. Comme la luminance moyenne d'un tel stimulus de 2^d ordre est constante, les détecteurs du système visuel sensibles aux variations de luminance ne permettent pas de déterminer les caractéristiques spatiales de ce stimulus. La détermination des caractéristiques spatiales d'un tel stimulus de 2^d ordre passe d'abord par une étape de filtrage qui consiste à analyser les variations locales de contraste de luminance entre les points de bruits (Chubb & Sperling, 1988; Lu & Sperling, 2001) (*Figure 2*). Le signal est ensuite rectifié et passe finalement par une étape de filtrage qui permet d'extraire l'enveloppe du signal (c'est-à-dire sa forme globale consistant en une succession de « ventres » et de « nœuds »), et donc d'en déterminer les caractéristiques spatiales (Chubb & Sperling, 1988; Lu & Sperling, 2001).

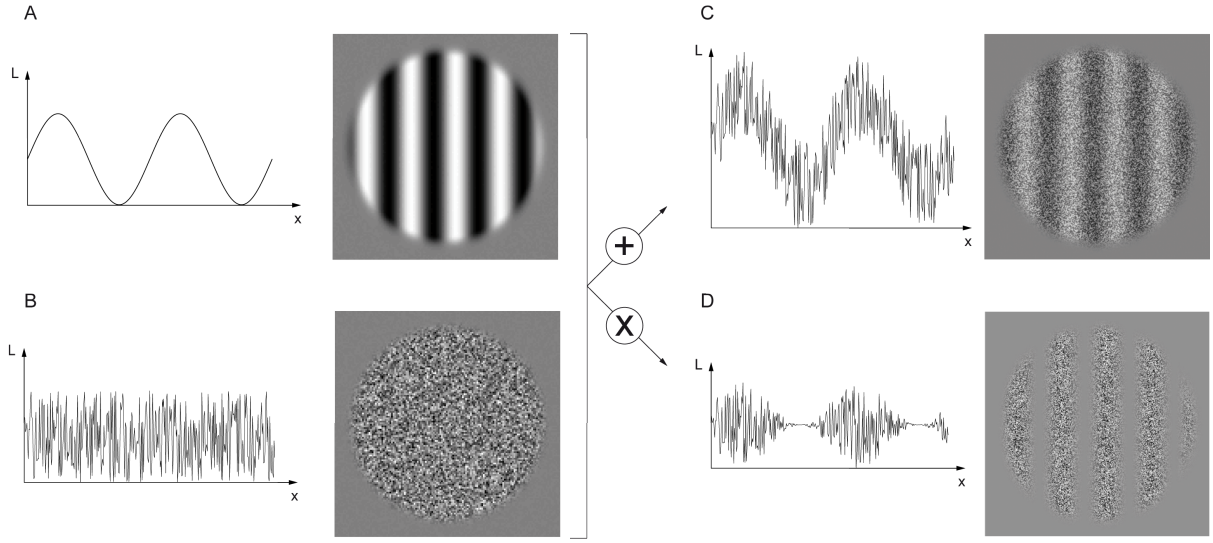

Figure 1. Exemples de stimuli de 1er et de 2^{d} ordre.

A : profil du signal et image d'un réseau sinusoïdal de luminance ; B : profil du signal et image d'un patron de bruit de luminance ; C : profil du signal et image d'un stimulus de 1er ordre obtenu par addition des signaux présentés en A et B ; D : profil du signal et image d'un stimulus de 2^{d} ordre obtenu par multiplication des signaux présentés en A et B.

Deux mécanismes distincts permettent donc l'analyse visuelle des caractéristiques spatiales des stimuli de 1er et de 2^{d} ordre, et la perception visuelle des stimuli de 2^{d} ordre, par rapport à celle des stimuli de 1er ordre, nécessitant des processus additionnels (Cavanagh & Mather, 1989; Chubb & Sperling, 1988; Sukumar & Waugh, 2007). Cela explique notamment le fait que le système visuel présente une moins grande sensibilité pour les stimuli de 2^{d} ordre que pour ceux de 1er ordre (Allard & Faubert, 2006; Armstrong, Maurer, & Lewis, 2009; Bertone, Hanck, Cornish, & Faubert, 2008; Habak & Faubert, 2000; Hutchinson & Ledgeway, 2006; Schofield & Georgeson, 2000).

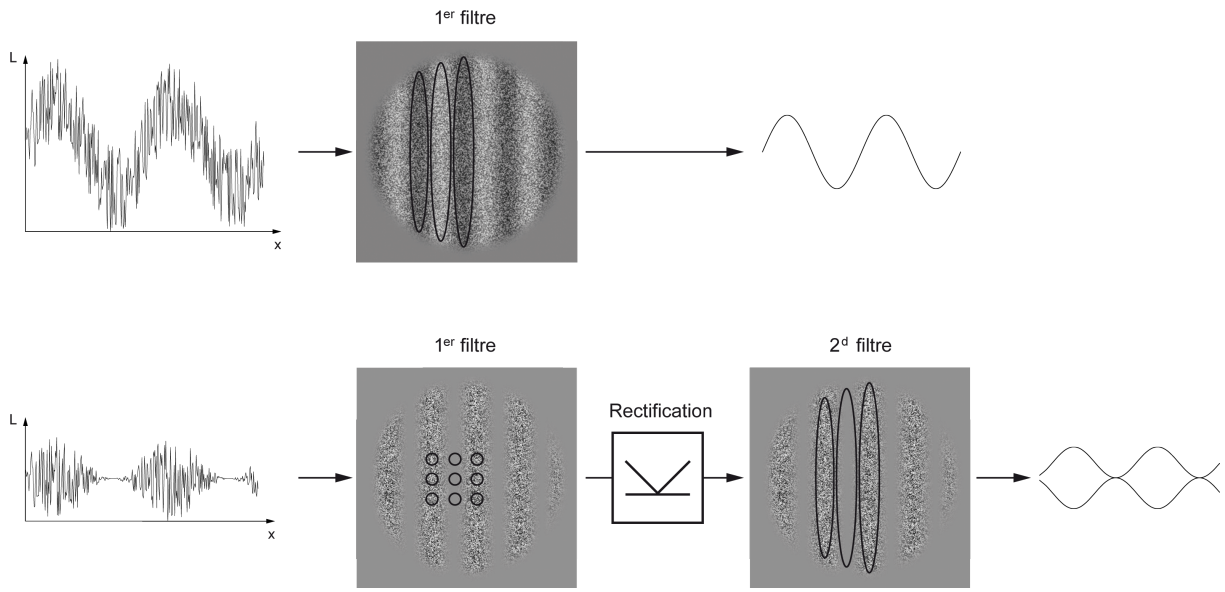

Figure 2. Traitement visuel des stimuli de 1er et de 2^{d} ordre.

Si la perception du mouvement (analyse visuelle des caractéristiques spatio-temporelles) des stimuli de 1er ordre se fait par le biais de récepteurs sensibles aux variations d'énergie lumineuse du signal, donc suivant des mécanismes de détection automatiques, la perception du mouvement des stimuli de 2^{d} ordre, elle, requiert des processus attentionnels, plus complexes (Allard & Faubert, 2013b; Cavanagh, 1992; Lu & Sperling, 2001), qui succèdent aux étapes d'extraction des caractéristiques spatiales du signal. Aussi, comme cela a été démontré par la mesure de temps de réaction, la discrimination de la direction du mouvement de stimuli de 1er ordre se fait plus rapidement que celle de stimuli de 2^{d} ordre (Ledgeway & Hutchinson, 2008). Il faut noter ici que, à basses fréquences spatiales et temporelles, la perception du mouvement des stimuli de 1er ordre peut aussi, lorsqu'elle est expérimentalement perturbée (par la superposition d'un autre stimulus, par exemple), passer par des processus attentionnels suivant l'extraction des caractéristiques spatiales du signal.

Cependant, lorsqu'un stimulus de 1er ordre est présenté seul, la perception du mouvement relève essentiellement de mécanismes automatiques de détection.

Il faut également noter que, dans le cas des stimuli de 2d ordre, la discrimination de direction de mouvement nécessite un niveau de contraste plus élevé que celui requis pour la détection d'orientation (stimuli statiques), alors que dans le cas des stimuli de 1er ordre, la discrimination de direction de mouvement se fait à un niveau de contraste inférieur à celui requis pour la détection d'orientation (Armstrong et al., 2009; Smith & Ledgeway, 1997).

Enfin, la perception du mouvement de stimuli de 2d ordre dépend de mécanismes neuronaux distincts (Ellemberg et al., 2003; Ledgeway & Hutchinson, 2008) et implique des circuits neuronaux plus étendus que celle de stimuli de 1er ordre (Ashida, Lingnau, Wall, & Smith, 2007; Billino et al., 2011; Dumoulin et al., 2003; Noguchi et al., 2005; Smith, Greenlee, Singh, Kraemer, & Hennig, 1998; Sukumar & Waugh, 2007; Vaina & Soloviev, 2004).

2.2. Déficits perceptifs visuels suite à un traumatisme craniocérébral léger

Une première étude a montré que la perception visuelle de stimuli de 2d ordre, avec et sans mouvement, était affectée chez des enfants ayant subi un TCCL, et que les déficits observés persistaient au moins jusqu'à 3 mois après le traumatisme, et ce malgré la disparition des symptômes (Brosseau-Lachaine et al., 2008). Cette étude présente aussi comme intérêt le fait d'être longitudinale : les enfants TCCL ont été évalués à une, 4 et 12 semaines après l'accident, et les enfants contrôles ont été évalués à des intervalles de temps semblables. La période de 4 semaines suivant le TCCL est généralement considérée comme une période de récupération qui s'achève

par la résolution des symptômes et la possibilité de retour normal aux activités physiques pour les enfants (Swaine & Friedman, 2001), et la disparition des symptômes est généralement considérée complète à 12 semaines suivant le TCCL (Levin et al., 1987). Autrement dit, l'étude de Brosseau-Lachaine et al. (2008) a permis de mettre en évidence la présence de déficits de la perception visuelle suivant un TCCL à une période où la récupération fonctionnelle est censée être complète.

Une deuxième étude, menée sur des adultes ayant subi un traumatisme craniocérébral et utilisant les potentiels évoqués visuels (PEV) (Lachapelle, Ouimet, Bach, Ptito, & McKerral, 2004), a montré que des déficits affectant la perception des stimuli définis par la texture (nécessitant des processus complexes) pouvaient persister plusieurs mois, voire plusieurs années, après l'accident. Elle a aussi montré que la perception de stimuli de « bas niveau »[1] (définis par la luminance) pouvait également être affectée suite à un traumatisme craniocérébral, et que, dans ce cas, la perception des stimuli de « plus haut niveau »[2] était systématiquement affectée. Cependant, les traumatisés crâniens ayant participé à cette étude avaient subi des atteintes cérébrales de degrés divers (sévère, modéré ou léger), et le nombre trop faible de participants dans chaque catégorie n'a pas permis de dégager des conclusions s'appliquant plus spécifiquement à l'une ou l'autre de ces catégories. D'autre part, les participants blessés de cette étude n'ont été testés qu'une seule fois

[1] « *Low level »,* dans le texte original.
[2] « *Higher level »*, dans le texte original

et à des périodes allant de 2 à 39 mois suivant leur accident. Ces différences de temps impliquent possiblement des niveaux de récupération des blessures différents, ce qui ajoute encore à l'hétérogénéité de l'échantillon.

Une troisième étude, menée sur des adultes ayant subi un TCCL et utilisant les PEV ainsi que des temps de réaction enregistrés dans le cadre d'une tâche cognitive, a également montré, avec les PEV, que la perception de stimuli définis par leur texture était affectée suite à un TCCL (Lachapelle, Bolduc-Teasdale, Ptito, & McKerral, 2008). En outre, cette étude a montré, toujours à l'aide des PEV, la présence de déficits chez les TCCL, en comparaison des participants contrôles, lors de l'exécution d'une tâche cognitive simple. Cependant, les temps de réaction enregistrés au cours de cette même tâche n'ont pas permis d'établir de différence entre les TCCL et les participants contrôles. Là encore, les participants n'ont été testés qu'une seule fois et à des périodes différentes, allant de 1 à 18 mois, suite à leur traumatisme, ce qui pourrait impliquer une certaine hétérogénéité quant au niveau de récupération des fonctions testées.

Enfin, d'autres études menées sur des adultes ayant subi un TCCL ont utilisé des mesures de temps de réaction associées à des tâches visuelles lors de tests cognitifs ou neuropsychologiques. Il s'agissait de mesures de temps de réaction liés à l'apparition du stimulus (aussi appelés temps de réaction simple), ou de temps de réaction liés à un jugement répondant à des règles définies par l'expérimentateur (aussi appelés temps de réaction de choix). Les résultats dans ce domaine présentent une certaine variabilité. En effet, des études ont montré que le TCCL était associé à des temps de réaction significativement plus longs, soit pour des temps de

réaction simple (Bryan & Hernandez, 2011), soit pour des temps de réaction de choix (Halterman et al., 2006). D'autres chercheurs ont trouvé que les temps de réaction de choix, mais pas ceux de réaction simple, étaient significativement plus longs chez des sujets ayant subi un TCCL (Tinius, 2003). D'autres chercheurs encore n'ont trouvé qu'une tendance au ralentissement des sujets ayant subi un TCCL, qu'il s'agisse de temps de réaction simple ou de temps de réaction de choix (Malojcic et al., 2008). Finalement, d'autres chercheurs n'ont trouvé aucune différence significative entre les mesures de temps de réaction de choix des sujets ayant subi un TCCL et celles des sujets contrôles (Larson, Clayson, & Farrer, 2012; Pontifex et al., 2012; Pontifex, O'Connor, Broglio, & Hillman, 2009). Cette variabilité pourrait être imputée, notamment, à la grande variabilité, dans certains groupes de sujets ayant subi un TCCL, concernant le temps écoulé depuis la commotion cérébrale au moment du recrutement (Larson et al., 2012; Malojcic et al., 2008; Pontifex et al., 2012; Pontifex et al., 2009; Tinius, 2003). D'autre part, ces études avaient pour objectif de mettre en évidence des déficits cognitifs ou attentionnels et non des déficits affectant la perception visuelle en soi. Donc, bien que les temps de réaction ainsi mesurés dépendaient d'indices visuels, l'emphase était mise davantage sur l'aspect cognitif ou attentionnel des tâches à effectuer que sur les caractéristiques (attributs, contraste, fréquences spatiale et temporelle) des stimuli utilisés.

Aussi, il n'existe pas à notre connaissance d'étude longitudinale ayant étudié la présence, la nature et la durée de déficits relatifs à la vitesse du traitement de l'information visuelle des stimuli de 1er et 2^{d} ordres, suite à un TCCL chez l'adulte.

3. Contrôle postural et traumatisme craniocérébral léger

Le contrôle postural associe les voies afférentes provenant du système visuel, du système vestibulaire et du système somatosensoriel (pour la proprioception), pour produire une réponse motrice appropriée (Dieterich & Brandt, 2015; Peterka, 2002). Ainsi, une grande partie du cerveau se trouve impliquée dans le contrôle postural (Guldin & Grusser, 1998; Uesaki & Ashida, 2015; zu Eulenburg, Caspers, Roski, & Eickhoff, 2012; Zwergal et al., 2012). Comme dans le cas de la perception visuelle à proprement parler, vu le caractère diffus des dommages cérébraux engendrés par un TCCL (Kirov et al., 2013; Topal et al., 2008), il est raisonnable de supposer qu'un ou plusieurs des réseaux impliqués dans le contrôle postural soient touchés suite à un tel traumatisme, et que cela se traduise par une certaine instabilité posturale.

3.1. Vision et contrôle postural

La vision a un rôle important dans le maintien de l'équilibre postural. En effet, les informations visuelles et vestibulaires notamment sont traitées ensemble dans des aires corticales secondaires (Dieterich & Brandt, 2015; Guldin & Grusser, 1998; Zwergal et al., 2012). Aussi, en l'absence d'indices visuels, l'instabilité posturale augmente (Slobounov, Sebastianelli, & Hallett, 2012; Slobounov, Sebastianelli, & Moss, 2005). D'autre part, dans un environnement parfaitement immobile, il est possible d'induire une réponse posturale orientée chez des individus se tenant debout, en leur présentant une scène visuelle en mouvement (Piponnier, Hanssens, & Faubert, 2009; Slobounov, Tutwiler, et al., 2006).

Dans ce contexte, le flux optique est un paradigme intéressant. Il s'agit d'un type d'information visuelle dynamique et complexe. Le flux optique représente

également une stimulation écologique, car il reproduit la perception visuelle du mouvement propre liée à la navigation dans un environnement, et qui peut être expérimentée dans des situations comme la marche (Gibson, 1979; Slobounov, Wu, et al., 2006).

3.2. Troubles de l'équilibre postural suite à un traumatisme craniocérébral léger

Suite à un TCCL, les problèmes d'équilibre et l'étourdissement font partie des symptômes les plus fréquemment rapportés (Fife & Kalra, 2015). De plus, la présence de déficits de l'équilibre postural a été mise en évidence après un TCCL (Findling, Schuster, Sellner, Ettlin, & Allum, 2011; Geurts, Knoop, & van Limbeek, 1999; Geurts, Ribbers, Knoop, & van Limbeek, 1996; Guskiewicz, Ross, & Marshall, 2001; Kaufman et al., 2006; King et al., 2014; McCrea et al., 2003; Slobounov et al., 2005; Slobounov, Tutwiler, et al., 2006; Sosnoff, Broglio, & Ferrara, 2008; Sosnoff, Broglio, Shin, & Ferrara, 2011), y compris chez des individus n'ayant aucun symptôme (Slobounov et al., 2008; Slobounov et al., 2012; Slobounov, Sebastianelli, & Newell, 2011; Thompson, Sebastianelli, & Slobounov, 2005). Ces déficits de stabilité posturale sont évidents dans la phase aiguë du TCCL (Fife & Kalra, 2015), quelle que soit la façon de les mesurer ou la population concernée (Guskiewicz et al., 2001; McCrea et al., 2003; Sheedy et al., 2006; Sheedy et al., 2009; Slobounov, Tutwiler, et al., 2006). Chez les étudiants appartenant à des équipes sportives universitaires ou collégiales, l'utilisation de tests cliniques a montré que de tels déficits duraient de 3 à 5 jours (Guskiewicz et al., 2001; McCrea et al., 2003), alors que des mesures dérivées de la cinématique du contrôle postural (comme la vitesse moyenne des oscillations posturales ou l'aire de déplacement du centre de masse du

corps) ont permis de mettre en évidence des déficits jusqu'à 30 jours après le traumatisme (Slobounov et al., 2008; Slobounov, Tutwiler, et al., 2006). Par ailleurs, chez des individus issus de la population générale, des mesures dérivées de la cinématique du contrôle postural ont montré que des troubles de l'équilibre relatifs à un TCCL pouvaient persister des mois, voire des années, après le traumatisme (Findling et al., 2011; Geurts et al., 1999; Geurts et al., 1996; Kaufman et al., 2006).

Deux études longitudinales on suivi le cours de la récupération des déficits posturaux suite à un TCCL. Ces études concernaient toutes deux des étudiants-athlètes. La première (McCrea et al., 2003) s'est déroulée sur une période de 90 jours. Elle utilisait un test clinique du contrôle de la stabilité posturale, des tests neuropsychologiques et un questionnaire d'évaluation subjective des symptômes post-commotionnels. Cette étude a montré que les symptômes et les déficits fonctionnels relatifs à la cognition et à l'équilibre postural ne duraient pas plus d'une semaine après le traumatisme.

La seconde étude (Slobounov et al., 2012) combinait des mesures EEG liées au contrôle postural et des mesures dérivées de la cinématique du contrôle postural, sur une période d'un an. Les mesures EEG ont été utilisées pour déterminer le niveau de diminution (en pourcentage) du spectre de puissance du rythme alpha lors du passage de la position assise à la position debout, avec les yeux fermés pour les deux positions. La diminution de puissance dans le spectre du rythme alpha est considérée par ces chercheurs comme un indicateur des déficits du contrôle postural chez les personnes ayant subi un TCCL (Thompson et al., 2005). Cette étude incluait également des mesures prises avant le traumatisme, qui reflétaient un niveau de

fonctionnement normal des participants. Les données cinématiques ont montré que les déficits posturaux duraient moins de 30 jours, alors que les données EEG ont montré que certains sujets en particulier n'étaient pas retournés, au bout d'un an, au niveau auquel ils étaient avant leur accident. La proportion d'individus concernés par ces déficits de l'activité EEG liée au contrôle postural n'était pas indiquée dans cette étude.

Ainsi, il semble que davantage d'études longitudinales soient nécessaires pour établir le temps nécessaire pour récupérer d'un TCCL (Sosnoff et al., 2011).

4. Présentation du projet

Les hypothèses principales de ce projet étaient, d'une part, que les adultes ayant eu un TCCL présenteraient des déficits perceptifs visuels relatifs au traitement des stimuli complexes (c'est-à-dire de 2^{d} ordre) ainsi que des déficits de l'équilibre postural, et, d'autre part, que ces déficits seraient toujours présents un an après le traumatisme.

Le premier article avait trois objectifs principaux. Il s'agissait d'abord de vérifier si les déficits visuels affectant la perception des stimuli de 2^{d} ordre observés chez les enfants ayant subi un TCCL (Brosseau-Lachaine et al., 2008) étaient également présents chez les adultes ayant subi pareil traumatisme. Le deuxième objectif était de vérifier si ces déficits perdureraient au bout d'un an de suivi, ou si la récupération serait totale à ce moment-là. Finalement, cette première étude avait pour but d'évaluer le lien entre le niveau des symptômes rapportés et les déficits visuels observés, pour notamment vérifier si les diminutions éventuelles des symptômes et

des déficits étaient corrélées, et savoir si la récupération du TCCL serait totale (c'est-à-dire aboutirait à la disparition complète des symptômes et déficits) un an après le traumatisme. Pour répondre à ces objectifs, nous avons effectué des mesures de temps de réaction de détection (temps de réaction simple) et de discrimination de direction de mouvement (temps de réaction de choix) avec des stimuli dynamiques de 1er et de 2^{d} ordre, et évalué le niveau des symptômes pour le comparer aux données comportementales. Ces mesures ont été effectuées à trois périodes de temps définies et identiques pour tous les participants, sur une période d'un an.

Le second article avait d'abord pour but de déterminer si des déficits du contrôle postural semblables à ceux trouvés chez les étudiants-athlètes en station debout (McCrea et al., 2003; Slobounov et al., 2012) seraient également présents chez des individus adultes TCCL dans la population générale. Ensuite, il s'agissait de voir si ces déficits persisteraient jusqu'à un an après le TCCL. L'équilibre postural a été évalué en utilisant des mesures dérivées de tests cliniques, et des mesures dérivées de la cinématique du contrôle postural réalisées dans un environnement virtuel tridimensionnel immersif. Ces mesures ont également été effectuées à trois reprises sur une période d'un an, suivant les mêmes périodes de temps que l'expérience précédente.

Les mêmes sujets, exactement, ont participé aux deux expériences. Toutes les mesures de temps de réaction et d'équilibre postural ont été prises les mêmes jours pour chacun des participants.

Chapitre 2 : Article 1

First- and second-order stimuli reaction time measures are highly sensitive to mild traumatic brain injuries

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Abstract

Mild traumatic brain injury (mTBI) has subtle effects on several brain functions that can be difficult to assess and follow-up. We investigated the impact of mTBI on the perception of sine-wave gratings defined by first-and second-order characteristics. Fifteen adults diagnosed with mTBI were assessed at 15 days, 3 months and 12 months after injury. Fifteen matched controls followed the same testing schedule. Reaction times (RTs) for flicker detection and motion direction discrimination were measured. Stimulus contrast of first- and second-order patterns was equated to control for visibility, and correct-response RT means, standard deviations (SDs), medians, and interquartile ranges (IQRs) were calculated. The level of symptoms was also evaluated to compare it to RT data. In general in mTBI, RTs were longer, and SDs as well as IQRs larger, than those of controls. In addition, mTBI participants' RTs to first-order stimuli were shorter than those to second-order stimuli, and SDs as well as IQRs larger for first- than for second-order stimuli in the motion condition. All these observations were made over the 3 sessions. The level of symptoms observed in mTBI was higher than that of control participants and this difference did also persist up to one year after the brain injury, despite an improvement. The combination of RT measures with particular stimulus properties is a highly sensitive method for measuring mTBI-induced visuomotor anomalies, and provides a fine probe of the underlying mechanisms when the brain is exposed to mild trauma.

Key words: first-order, second-order, motion, reaction time, mTBI

1. Introduction

Mild TBI constitutes a serious public health concern. It accounts for about 80% of *all treated* traumatic brain injuries, which represent 100-300/100 000 individuals per year, while the actual incidence of mTBI is estimated to be higher than 600 individuals/100 000 (Cassidy et al., 2004). The diagnosis, prognosis and therapeutic management of mTBI rely mostly on the observation of the first signs and symptoms following injury, rather than the direct and objective examination of microscopic cerebral lesions or brain function (G. Iverson, 2007; Kontos et al., 2012; Leddy et al., 2007; Naunheim et al., 2008; P. M. Rees, 2003; R. J. Rees & Bellon, 2007; Ropper & Gorson, 2007; Sheedy et al., 2006; Sheedy et al., 2009; Willer & Leddy, 2006). The time needed for symptoms to resolve is also taken into account *a posteriori* for diagnostic purposes, and is eventually used to revise prognosis and treatment (G. Iverson, 2007). In the absence of objective observations, clearly understanding symptomatology and functional deficits left by an mTBI, as well as their potential persistence over time, remains difficult and may be impossible.

There is now clear evidence that mTBI results in brain deformations that affect white and grey matters as well as their interface, and cerebral vascular tissue (Bain et al., 2001; Bayly et al., 2005; Bigler, 2007, 2008; Evans, 2004; Gaetz, 2004; Ivarsson et al., 2002; Nishimoto & Murakami, 1998; Ropper & Gorson, 2007; Shaw, 2002; Viano et al., 2005). Resulting metabolic disorders lead to physiological dysfunctions (Bigler, 2007; Gaetz, 2004; G. L. Iverson, 2005; Lee et al., 2008; Maxwell et al., 1997; Shaw, 2002; Topal et al., 2008). Although the physical signs left by such a diffuse injury often remain undetectable by conventional investigation tools (e.g. CT scan) (Gaetz,

2004; Lee et al., 2008; Lewine et al., 2007; P. M. Rees, 2003; Topal et al., 2008), they can result, in the short and/or long term, in cognitive and/or emotional disorders and/or other disabling symptoms that have an impact on daily activities (Bigler, 2008; Evans, 2004; Kontos et al., 2012; R. J. Rees & Bellon, 2007; Ropper & Gorson, 2007; Shaw, 2002). Moreover, although symptoms and functional disorders are most often transient (Naunheim et al., 2008), in some individuals they can persist to diverse degrees and over long time-periods (Bigler, 2008; Evans, 2004; G. Iverson, 2007; G. L. Iverson, 2005; Konrad et al., 2011; Lewine et al., 2007; McAllister & Arciniegas, 2002; P. M. Rees, 2003; R. J. Rees & Bellon, 2007; Ropper & Gorson, 2007; R. Ruff, 2005; R. M. Ruff, 2011; Shaw, 2002; Sheedy et al., 2006; Sheedy et al., 2009; Willer & Leddy, 2006).

A broad part of the brain is involved in visual perception (Billino et al., 2011; Dumoulin et al., 2003; Dupont et al., 2003; Farivar, 2009; Kalaycioglu et al., 2009; Noguchi et al., 2005; Sunaert et al., 2000; Vaina & Soloviev, 2004; Vakalopoulos, 2005). Given the diffuse nature of brain alterations produced by an mTBI, one or several networks involved in vision could be affected following mTBI, leading to visual perception deficits.

The visual perception of a stimulus relies on its attributes, which fall into two broad categories. First-order attributes (luminance and colour) have simple or linear properties that can be processed in Fourier domain. Second-order attributes (texture, depth and motion) have complex or non-linear properties that cannot be processed in Fourier domain. Two distinct mechanisms allow for processing of first- and second-order stimuli, the latter necessitating additional steps (Cavanagh & Mather, 1989;

Chubb & Sperling, 1988; Sukumar & Waugh, 2007). As a result, the visual system has a lower sensitivity for second-order than for first-order stimuli (Allard & Faubert, 2006; Armstrong et al., 2009; Bertone et al., 2008; Habak & Faubert, 2000; Hutchinson & Ledgeway, 2006; Schofield & Georgeson, 2000).

Visual motion perception of first- and second-order stimuli also relies on two distinct mechanisms (Cavanagh & Mather, 1989; Chubb & Sperling, 1988; Gegenfurtner & Hawken, 1996; Hutchinson & Ledgeway, 2006; Ledgeway & Hutchinson, 2005; Smith & Ledgeway, 1997). Motion perception of second-order stimuli is based essentially on attentional processes, whereas that of first-order stimuli rests on a more automatic detection mechanism (Allard & Faubert, 2013b; Cavanagh, 1992; Lu & Sperling, 2001). Consequently, as already evidenced by reaction time (RT) measures, motion direction discrimination is faster for first- than for second-order stimuli (Chakor, Bertone, McKerral, Faubert, & Lachapelle, 2005; Ledgeway & Hutchinson, 2008). It is also noteworthy that, in the case of second-order stimuli, motion direction discrimination necessitates a greater modulation depth than that required for orientation discrimination (static stimuli), while in the case of first-order stimuli motion direction discrimination is possible at a lower modulation depth than orientation discrimination (Armstrong et al., 2009; Smith & Ledgeway, 1997). Finally, motion perception of second-order stimuli depends on distinct neural mechanisms (Ellemberg et al., 2003; Ledgeway & Hutchinson, 2008), and recruits broader neuronal networks than those dedicated to first-order motion perception (Ashida et al., 2007; Billino et al., 2011; Dumoulin et al., 2003; Noguchi et al., 2005; Smith et al., 1998; Sukumar & Waugh, 2007; Vaina & Soloviev, 2004).

Therefore, it seems that RT measures related to motion direction discrimination of first- and second-order stimuli are of particular interest to objectively assess the presence of diffuse microscopic lesions that could affect the visual system following an mTBI.

One study showed that perception of second-order stimuli, whether static or moving, was altered in children having sustained an mTBI. Observed visual deficits also persisted at least 3 months after the injury, even if symptoms had resolved (Brosseau-Lachaine et al., 2008). This study is particularly interesting because it is longitudinal: mTBI children were evaluated at 1, 4 and 12 weeks after their injury, as were matched controls.

The objectives of this study were: (1) to determine if the visual deficits affecting perception of first- and second-order stimuli observed in children having sustained an mTBI (Brosseau-Lachaine et al., 2008) are also present in adults having sustained such trauma; (2) to assess if these deficits persist over a one year period following the injury; (3) to evaluate the link between the severity of symptoms and visual deficits. To achieve these goals we consequently: (1) measured detection and motion direction discrimination RTs with dynamic first- and second-order stimuli; (2) evaluated the level of symptoms to compare it to RT data; and (3) repeated these measures at 3 pre-defined time periods identical for all subjects over a one year period.

2. Material and methods

This study received approval from the institutional research ethics boards of the Hôpital du Sacré-Cœur de Montréal (HSCM), McGill University Health Centre (MUHC), and Université de Montréal.

2.1. Participants

Two groups of 15 subjects (2 females, 13 males) each ranging in age from 17.8 to 39.8 years participated in this study: a group of subjects having sustained an mTBI (mean age at first testing session: 29.2 ± 6.8 years old), and a group of control subjects matched for age (29.3 ± 6.8 years old at first testing session), sex, handedness, and, whenever possible, education level. Prior to their participation in this study, all subjects gave their written informed consent. Subjects were clearly informed that they could leave the study whenever they wanted to do so, without prejudice.

Subjects in the mTBI group were volunteers recruited following their admission to emergency departments (ED) of HSCM, and of the Montreal Children's Hospital of the MUHC. They were eligible if: (1) they had received a diagnosis of mTBI from a physician at the ED (criteria used for this diagnostic were based on the WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury definition of mTBI (Carroll et al., 2004; R. M. Ruff et al., 2009)); (2) the mTBI was not concomitant with any substance consumption affecting alertness or arousal state; (3) there was no more than one mTBI in the past 12 months; (4) they had no problematic alcohol consumption; (5) they were not consuming substance on consistent basis; (6) they

had no premorbid psychiatric or learning disorders; (7) they had no fractures or cut preventing their participation in experimentations; (8) they were aged 17-40. Coordinators of trauma programs obtained a first consent from each subject of the mTBI group, giving the first author the authorisation to contact them by phone. This phone interview was used to further screen subjects, carefully confirming that inclusion criteria (2 to 7) listed above were fulfilled and that subjects were fluent in French or English.

None of the mTBI participants were engaged in litigation or compensation issues.

The characteristics of participants of mTBI group are displayed in *Table 1*.

Subjects of the control group were recruited among patients of the Université de Montréal School of Optometry Clinic, friends of mTBI participants, and the general population. Prior to participation, control subjects also underwent a phone screening. They had to fulfil the same criteria as mTBI subjects, and their medical history also had to be clear of mTBI.

mTBI patients prior to their brain injury had occupational statuses, sports practices and means of transportation very similar to those of subjects of the control group. Therefore, subjects of the control group were exposed to the same risks of mTBI (predisposing factors and injury-related stress) than the mTBI patients previous to their brain injury. Moreover, each control subject was recruited within two months after the recruitment of the corresponding mTBI subject.

Prior to participating in the study and at every visit, subjects of both groups underwent a complete optometric examination including the assessment of visual acuity, refraction, binocular vision (extra-ocular motility and stereoscopic vision), and ocular

health (pupillary reflex, examination of anterior segment and fundus), as well as a screening evaluation of the central 20 degrees of monocular visual fields with Frequency Doubling Technology (FDT) (screening mode of C-20 FDT program; perimeter Humphrey-Welch Allyn, Inc., Shakeneatles Falls, NY) (Wadood, Azuara-Blanco, Aspinall, Taguri, & King, 2002). Participants had a visual acuity of 6/6 or better, and wore a refractive correction to achieve this visual acuity level whenever necessary. Further, their binocular vision, ocular health and central visual fields were within normal limits.

Sex	*Cause of injury*	*GCS score*		*LOC*	*PTA*	*CT Scan*
		EMS	*ED*			
M	Car to car rear impact; ~ 40 km/h; backseat passenger – wearing seatbelt	15	15	1 min	≤ 1 min	N/D
M	Punch to the face and left mastoid process	15	15	2 min	< 5 min	–
M	Hockey tackling; probably hit in the face with hockey stick – wearing helmet	N/D	15	15 sec	≤ 1 min	N/D
M	Hockey; fall on the back left-side of the head – no helmet	N/D	15	40 sec	1-2 min	Parietal SAH; non significant lesion
M	Car to car near-side impact – wearing seatbelt	15	15	Not reported	Probable ≤ 1 min	No traumatic intracerebral lesion
M	Soccer: ball to face hit	N/D	15	+	+	N/D
M	Rollerblade: fall – wearing helmet	15	15	–	5 min	Normal
M	Car to pylon near-side impact; ~ 70 km/h – wearing seatbelt, airbags deployed	15	15	+	< 6 h	No traumatic intracerebral lesion
F	Highway, car to truck accident: spinning and multiple hits (truck and guardrail barrier); ~ 110 km/h – wearing seatbelt, airbags deployed	N/D	15	N/D	until EMS arrival (minutes)	Normal (reported by patient; medical file not available)
F	Loss of motor scooter control and fall; ~ 40 km/h – wearing helmet	14	15	+	until Police arrival (minutes)	No traumatic intracerebral lesion
M	Kung Fu training: kick to the face	N/D	15	Not asked	< 1 min	N/D
M	Bike accident; hit by a car – no helmet	N/D	15	N/D	20 min	–
M	Bike fall – no helmet	14	14	–	+	No traumatic intracerebral lesion
M	Bike accident; front impact with a, car – no helmet	15	15	< 1 min	until EMS arrival (minutes)	Negligible right frontal SAH
M	Fall down a scaffold; 1.5 m high – no helmet	N/D	15	No LOC validated by physician	≤ 1 min	Traumatic SAH

Table 1. Characteristics of mTBI participants

GCS: Glasgow Coma Scale; EMS: Emergency medical service (on site of accident); ED: Emergency department; LOC: Loss of consciousness; PTA: Post-traumatic amnesia; N/D: not documented; SAH: subarachnoid hemorrhage; +: positive for clinical sign but unknown duration; -: negative.

RT measures as well as self-reported symptoms ratings were taken at 2 weeks (session A), 3 months (session B) (G. Iverson, 2007; Leddy et al., 2007; Ropper & Gorson, 2007; R. Ruff, 2005; Willer & Leddy, 2006) and 1 year (session C) (Bigler, 2008; G. L. Iverson, 2005; Konrad et al., 2011; Marshall, Bayley, McCullagh, Velikonja, & Berrigan, 2012; McAllister & Arciniegas, 2002; P. M. Rees, 2003; R. J. Rees & Bellon, 2007) after the injury for mTBI subjects, and at equivalent times for control subjects (*Table 2*).

Session	mTBI group				Control group		
	N*	Time post-injury	Time post-session A	Age	N*	Time post-session A	Age
A	15	16.3 ± 3.3	$T_A = 0$	29.2 ± 6.8	15	$T_A = 0$	29.3 ± 6.8
B	15	90.9 ± 4.0	$T_B = 74.7 \pm 4.1$	29.4 ± 6.5	15	$T_B = 77.0 \pm 2.2$	29.6 ± 6.6
C	15	364.9 ± 2.5	$T_C = 348.7 \pm 4.6$	30.1 ± 6.5	15	$T_C = 350.8 \pm 4.8$	30.3 ± 6.6

Table 2. Session times

Session times (days) and age of participants (years): means ± standard deviation (SD). No significant difference was found between groups for B ($F(1, 28) = 3.845$, $p = 0.060$) and C ($F(1, 28) = 1.557$, $p = 0.222$) session times. No significant difference was found between groups for age at session A ($F(1, 28) = 0.004$, $p = 0.948$), B ($F(1, 28) = 0.005$, $p = 0.946$ and C ($F(1, 28) = 0.005$, $p = 0.946$). * The same subjects participated in the 3 sessions for both groups; there were 2 females and 13 males in each group for the three sessions.

All participants were administered the Test of Nonverbal Intelligence – Third Edition (TONI-3) (Brown, Sherbenou, & Johnsen, 1997) at their first testing session. Standard score had to be at least of 85 to participate in the study. This test was also administered to ensure that both groups had comparable levels of general cognitive skills. A one-way ANOVA (*Group* factor) showed no significant IQ difference ($F(1, 29) = 0.462$, $p = 0.502$) between mTBI (Mean Scaled Score ± SD = 110.40 ± 14.22) and control (107.13 ± 12.02) groups (Fisher, Ledbetter, Cohen, Marmor, & Tulsky, 2000). Finally, to make sure there was no attention deficit, each participant had to fill the Conners' Adult ADHD Rating Scale–Self-report: Short Version (CAARS-S: S) (Conners, 1997). All participants obtained T-Scores within the mean range or below, confirming the absence of overt attention deficits in both groups.

2.2. Device

RT measures took place in a dark room where the monitor screen was the only light source. Stimuli were presented on a 17'' CRT screen (6307-BTN Lenovo™) at a refresh rate of 100 Hz, and a viewing distance of 114 cm. The screen was gamma corrected and calibrated using a Minolta CS100 photometer. An Intel® Core™ 2 Duo, 2.33 GHz with an NVIDIA Quadro® NVS 290 graphic card computed the stimuli.

2.3. Stimuli

Stimuli were sine-wave achromatic gratings with a spatial frequency of 0.5 cycle per degree. These gratings consisted of a static 2 dimensions grey-scale noise carrier either luminance- (first-order; obtained by adding a sinusoidal signal to a noise signal) or contrast-modulated (second-order; obtained by multiplying a sinusoidal envelope

by the noise carrier) (Allard & Faubert, 2006, 2013b; Brosseau-Lachaine et al., 2008) (*Figure 1*). Noise carrier was set to 50% Michelson contrast. Stimuli were presented in a circular window, 10º in total diameter, with a plateau of 8º in diameter and a Gaussian edge (0.5º SD). Screen background was set to a mean luminance of 22 cd/m^2. Each noise carrier pixel subtended 0.016º x 0.016º (0.96' x 0.96') (Smith & Ledgeway, 1997).

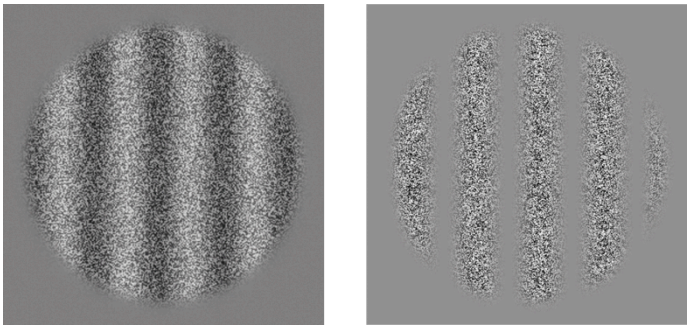

Figure 1. First- and second-order stimuli

Examples of first- (left) and second-order (right) stimuli.

Gratings were either pattern-reversal flickering (*Flicker* condition) or drifting to the right or left (*Motion* condition) at a temporal frequency of 2 Hz (Allard & Faubert, 2013a, 2013b). Motion direction varied randomly from trial to trial, with the same probability for each direction. In each condition an equal number of first- and second-order stimuli were presented in random order. In combination with modulation types, there were 4 experimental conditions: first- and second-order *Flicker* (FOF and SOF), and first- and second-order *Motion* (FOM and SOM).

The stimuli were supra-threshold. Their visibility (related to modulation depth) has also been equated by setting luminance modulation depth at 12.5% (first-order

stimuli) and contrast modulation depth at 100% (second-order stimuli). These modulation depths were chosen because they were supra-threshold by a factor of about 10 for both modulation types (considering threshold levels for static stimuli), ensuring that all participants were able to easily perceive the stimuli (Armstrong et al., 2009; Brosseau-Lachaine et al., 2008; Hutchinson & Ledgeway, 2006; Ledgeway & Hutchinson, 2008).

2.4. Reaction time measurements procedure

Trial blocks (*Flicker*/*Motion*) were displayed in random order.

Flicker and *Motion* conditions consisted of 4 blocks of 100 trials each (i.e. 200 trials per condition, modulation and session). Sporadically, for technical reasons or punctual participant failures to comply with instructions, the number of trials per condition, modulation and session was inferior to 200 (either 150, 197 or 198 trials).

Subjects started each block by pressing the left mouse button. Within each block, trials were linked together in the following manner: a black cross appeared for 125 ms in the centre of the screen uniformly grey; then the cross disappeared, the screen remaining uniformly grey, for 500 to 1000 ms (random duration, depending on refresh rate); the stimulus was then presented for 1000 ms; the trial finally ended with a uniform grey screen, for 125 ms. The cross indicated where to maintain fixation.

Each block lasted around 5 minutes. To prevent fatigue, subjects could take a 1 to 2 minutes break after each block. Thus total duration for RT measures was around 40 to 50 minutes.

Subjects were instructed to maintain fixation at the centre of the screen and to give their responses using a computer mouse the way they were used to do it (all of them used the mouse with the right hand, even those who were left-handed).

The *Flicker* condition consisted of a simple detection task: subjects were instructed to left-click as soon as a stimulus appeared. The *Motion* condition consisted of a motion direction discrimination task: subjects were instructed to right- or left-click depending on motion direction and as soon as they perceived it. RTs were recorded during the stimulus presentation period.

RTs were not recorded for responses that were out of the stimulus presentation time period. RTs shorter than 150 ms were discarded from the analysis because it is an anticipated response faster than the shortest time necessary for simple detection (Chakor et al., 2005; Ellemberg et al., 2003; Korth, Rix, & Sembritzki, 2000; Kuba & Kubova, 1992; Lachapelle et al., 2004; Ledgeway & Hutchinson, 2008; Malojcic et al., 2008; McKerral et al., 2001; Prieto et al., 2007). For the *motion* condition, RTs associated with incorrect responses were also discarded from the analysis.

2.5 Self-reported symptoms recording

At each testing session, participants self-reported their symptoms using the Post-Concussion Symptom Scale – Revised (PCSS-R) (Lovell & Collins, 1998; Naunheim et al., 2008). Participants had to indicate in the 22 items list which symptoms (i.e. physical, cognitive, emotional/behavioural) they experienced during the last 24 hours and to rate their severity on a scale ranging from 0 to 6 (0: none; 1: mild; 2-4: moderate; 5-6: severe). The variable we retained for the analysis of the level of symptoms is the total score.

2.6 Reaction times statistical analysis

For each participant, and each of the four experimental conditions (*Flicker* first- and second-order, and *Motion* first- and second-order) at each session, we determined the mean, standard deviation (SD), median and interquartile range (IQR) for RTs. Thus we decided to take, for each distribution, two values of central tendency and their corresponding values of dispersion. The mean is usually used more frequently than the median. However, RT distribution is not symmetrical around its central tendency: higher values are more spread out than smaller ones. The median seems therefore more appropriate than the mean to estimate the central tendency of such a distribution, because it is less affected by the asymmetrical distribution of extreme values (Delorme, 2006). Moreover, removing RTs shorter than 150 ms has a lesser incidence on medians and IQRs than on means and SDs (Ulrich & Miller, 1994).

We also determined participation rates for both *Flicker* and *Motion* conditions, and accuracy rates for the *Motion* conditions (one per modulation type). We defined the participation rate as being the number of responses given during stimuli presentation periods and corresponding to RTs of 150 ms and more out of the total number of stimuli presented. In other words, participation rate is the percentage of responses given following instructions. For the *Motion* condition, we defined the accuracy rate as being the proportion of correct direction responses.

For each variable set (mean, SD, median, IQR), we performed a four-way (*Condition* (2) x *Modulation* (2) x *Session* (3) x *Group* (2)) mixed ANOVA. When decompositions were necessary to further explain interactions, other ANOVAs (mixed (between-within

subjects) or repeated measures (within subjects), depending on the case) were performed.

2.7 Self-reported symptoms statistical analysis

PCSS-R total scores were analysed using a two-way mixed ANOVA (*Session* (3) x *Group* (2)).

They were also used in two-tailed bivariate Pearson correlations in order to investigate and describe the relationship between:

- The level of post-concussive symptoms and RTs recorded for each session;
- The initial level of post-concussive symptoms (reported at session A) and RTs recorded at each session.

The Greenhouse-Geisser corrective factor was used for all the ANOVAs.

The overall significance level set at 5% was corrected for all correlations with Bonferroni correction for the number of conditions, giving a significance level of 1.25%.

3. Results

3.1. Participation and response accuracy

The four-way mixed ANOVAs (*Condition* (2) x *Modulation* (2) x *Session* (3) x *Group* (2)) performed respectively on *Participation* and *Accuracy* variables revealed no significant *Group* effect (*Participation*: $F(1, 28) = 0.207$, $p = 0.653$; *Accuracy*: $F(1, 28) = 0.090$, $p = 0.766$). These results indicate that participation and accuracy levels of mTBI and control participants were similar. They also demonstrate that RT tests were

easy enough to execute, and reinforce the validity of the following comparisons between mTBI and control groups.

3.2. Mean and median reaction times

The four-way mixed ANOVA (*Condition* (2) x *Modulation* (2) x *Session* (3) x *Group* (2)) performed on mean RTs revealed, first, a significant *Group* effect ($F(1, 28) = 5.167$, $p = 0.031$) indicating that mean RTs were longer for the mTBI than for the control group (*Figures 2 & 3*).

Moreover, a significant *Condition* effect ($F(1, 28) = 549.544$, $p < 0.0001$) indicated that mean detection RTs (*Flicker* condition) were shorter than mean motion direction discrimination RTs (*Motion* condition), for both groups. This result was expected owing to the difference of cognitive weight between tasks.

Mean RT analysis also revealed: (1) a significant *Modulation* effect ($F(1, 28) = 9.711$, $p = 0.004$), indicating that mean RTs for first-order stimuli differed significantly from those for second-order stimuli; (2) a significant interaction *Modulation* x *Group* ($F(1, 28) = 5.477$, $p = 0.027$), indicating that an mTBI has a larger effect on RTs for first- than for second-order stimuli; (3) a significant interaction *Condition* x *Modulation* ($F(1, 28) = 22.226$, $p < 0.0001$), indicating that margins observed between mean RTs related to first- and second-order stimuli significantly differed from the *Flicker* to the *Motion* condition; and (4) a significant interaction *Condition* x *Modulation* x *Group* ($F(1, 28) = 4.799$, $p = 0.037$). To further explain the *Modulation* factor main effect as well as the latter three interactions, we performed a three-way repeated measures ANOVA (*Condition* (2) x *Modulation* (2) x *Session* (3)) for each of the mTBI and control groups.

These latter analyses revealed a significant *Modulation* effect for the mTBI ($F(1, 14) = 8.975$, $p = 0.010$), but not for the control group ($F(1, 14) = 0.882$, $p = 0.364$). These results determine that margins observed between mean RTs related respectively to first- and second-order stimuli were significant for the mTBI group alone. These ANOVAs also showed a significant *Condition* x *Modulation* interaction ($F(1, 14) = 20.210$, $p = 0.001$) for the mTBI group, but not for the control group ($F(1, 14) = 3.882$, $p = 0.069$). These results demonstrate that differences observed between mean RTs related respectively to first- and second-order stimuli for *Flicker* condition significantly differed from those observed for *Motion* condition, for mTBI participants only. To further explain the *Condition* x *Modulation* interaction for the mTBI group, we performed a two-way repeated measures ANOVA (*Modulation* (2) x *Session* (3)).

This latter ANOVA showed a significant *Modulation* effect for the *Motion* ($F(1, 14) = 16.637$, $p = 0.001$), but not for the *Flicker* condition ($F(1, 14) = 0.276$, $p = 0.608$). This indicates that mean motion direction discrimination RTs for first-order stimuli were significantly shorter than for second-order stimuli, while mean detection RTs were relatively similar for both types of stimulus.

Finally, there was no significant *Session* effect on mean RTs ($F(2, 56) = 1.378$, $p = 0.261$), indicating that RTs did not significantly vary across testing sessions. This was true for both groups. However, a significant *Condition* x *Session* interaction ($F(2, 56) = 3.402$, $p = 0.043$) indicates that differences observed between mean RTs related to *Flicker* and *Motion* conditions varied between sessions. To better explain the latter interaction, we performed a three-way mixed ANOVA (*Modulation* (2) x *Session* (3) x *Group* (2)) for both *Flicker* and *Motion* conditions.

These latter analyses revealed a significant *Session* effect for the *Motion* ($F(2, 56) = 3.495$, $p = 0.039$), but not for the *Flicker* condition ($F(2, 56) = 0.260$, $p = 0.769$). Therefore, these results indicate that, for both groups, mean motion direction discrimination RTs significantly shortened from Session A to Session C, whereas mean detection RTs did not significantly vary from session to session. This can be due to a learning effect for both groups, and could also be due, to some extent to a lessening of visual perception deficits for mTBI subjects.

Median RTs analysis returned similar results (*not shown here*).

3.3. Reaction times standard deviations and interquartile ranges

A four-way mixed ANOVA (*Condition* (2) x *Modulation* (2) x *Session* (3) x *Group* (2)) revealed a significant *Group* effect on RT standard deviations (RTSDs), ($F(1, 28) = 5.170$, $p = 0.031$) (*Figures 2 & 3*). This result indicates that RTSDs were significantly larger for the mTBI than for the control group. In other words, RT distributions were further spread around their mean for the mTBI group.

Moreover, a main effect of the *Condition* factor on RTSDs turned out to be almost significant ($F(1, 28) = 4.132$, $p = 0.052$). This indicates that detection RTSDs tended to differ from motion direction discrimination RTSDs. For the control group, detection RTSDs clearly seemed shorter than motion direction discrimination RTSDs, whereas for mTBI group detection and motion direction discrimination RTSDs did not seem to differ.

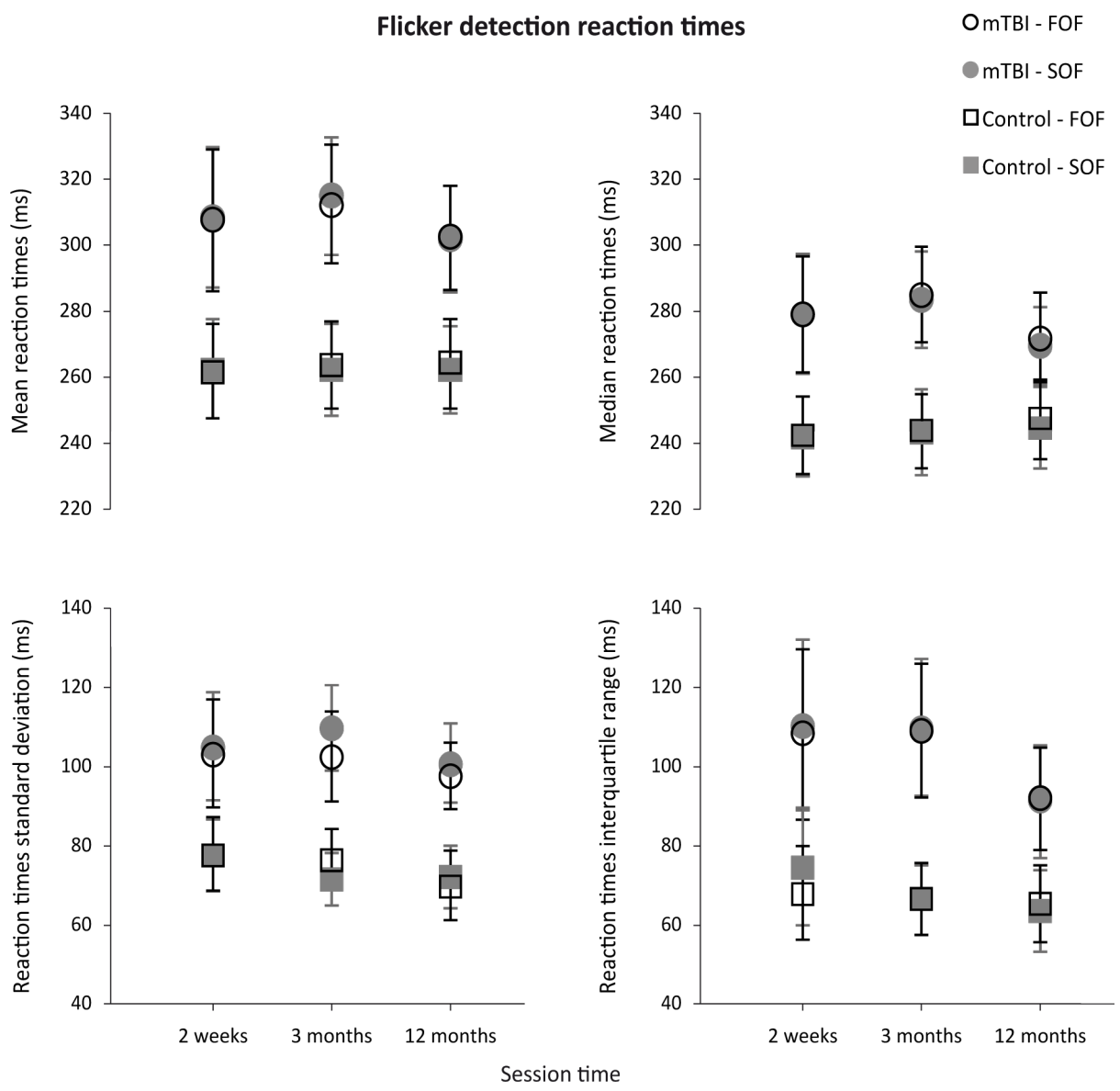

Figure 2. Flicker detection reaction times

Derived variables from **f**licker detection reaction time measures; Mean ± SE. FOF: first-order flicker; SOF: second-order flicker.

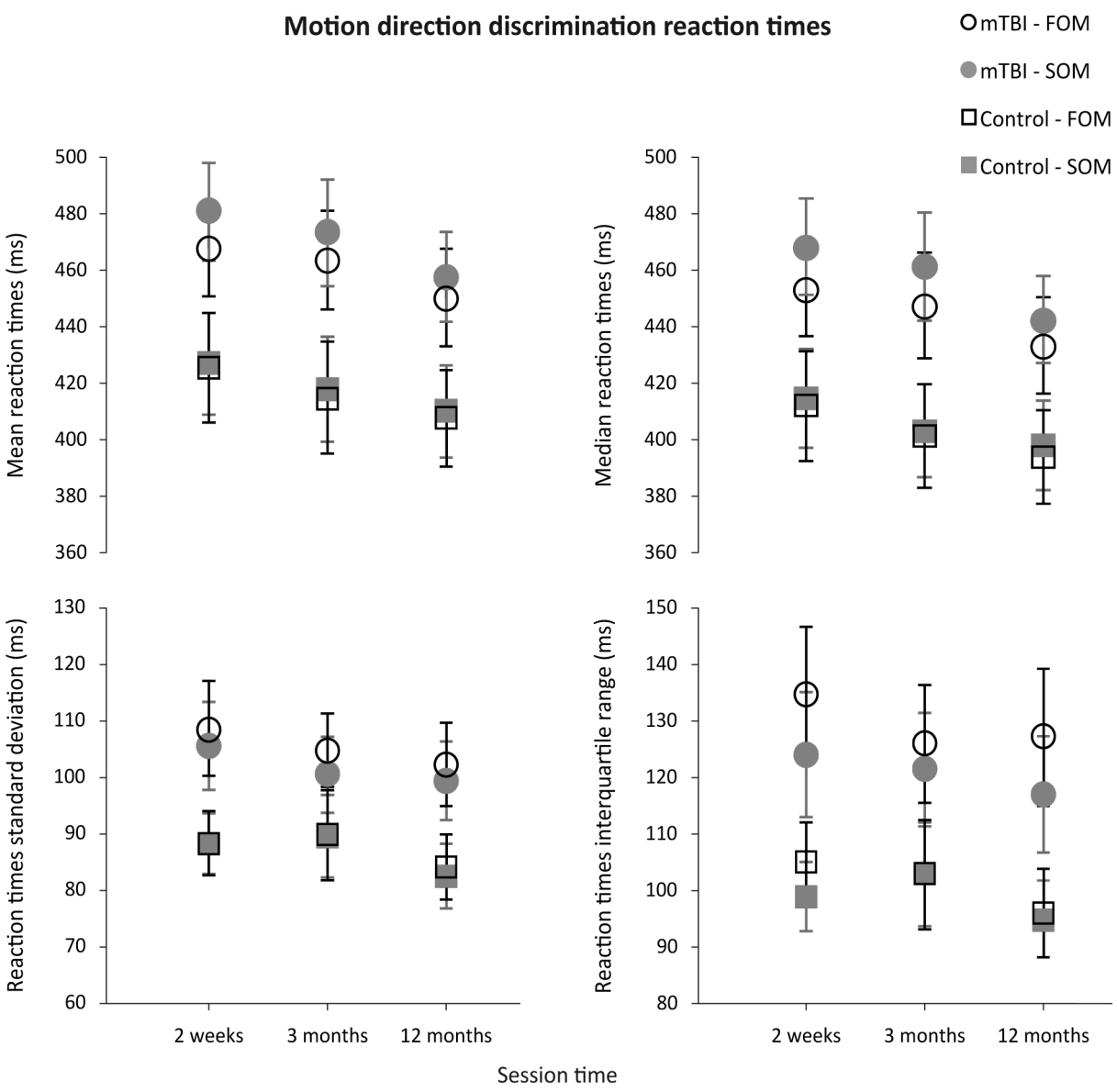

Figure 3. Motion direction discrimination reaction times

Derived variables from motion direction discrimination reaction time measures; Mean ± SE. FOM: first-order motion; SOM: second-order motion.

RTSDs analysis, revealed no significant *Modulation* effect ($F(1, 28) = 0.054$, $p = 0.818$), which indicates there was no difference between first- and second-order stimuli RTSDs. There was also no significant *Modulation* x *Group* interaction ($F(1, 28)$

= 0.261, p = 0.613), which indicates that the differences observed between RTSDs for first- and second-order stimuli did not significantly differ from one group to the other. However, RTSDs analysis showed: (1) a *Condition* x *Modulation* interaction (F(1, 28) = 4.189, p = 0.050), indicating that difference observed between RTSDs for first- and second-order stimuli were significantly different from *Flicker* to *Motion* condition; and (2) a *Condition* x *Modulation* x *Group* interaction (F(1, 28) = 4.943, p = 0.034). To better describe those two latter interactions as well as the almost significant effect of *Condition* factor, we performed a three-way repeated measures ANOVA (*Condition* (2) x *Modulation* (2) x *Session* (3)) for each of the mTBI and control groups.

These ANOVAs revealed a significant *Condition* effect (F(1, 14) = 10.030, p = 0.007) for the control but not for the mTBI group (F(1, 14) = 0.011, p = 0.920). These results suggest that detection RTSDs were significantly narrower than motion direction discrimination RTSDs for control group, whereas detection and motion direction discrimination RTSDs were similar for mTBI group. In other words, shorter mean RTs corresponded with a smaller dispersion for the control group, while dispersions around the mean were similar for short (*Flicker* condition) and long (*Motion* condition) RTs, in the mTBI group. These latter observations also explain why the *Condition* factor effect was almost significant in the four-way mixed ANOVA.

There was also a significant *Condition* x *Modulation* interaction (F(1, 14) = 6.686, p = 0.022) for the mTBI, but not for the control group (F(1, 14) = 0.025, p = 0.878). These results indicate that the margins observed between RTSDs respectively related to first- and second-order stimuli significantly differed between *Flicker* and *Motion* conditions for the mTBI group only. To further explain this latter interaction we applied

a two-way repeated measures ANOVA (*Modulation* (2) x *Session* (3)) to mTBI group data.

This latter ANOVA revealed a significant *Modulation* factor effect ($F(1, 14) = 4.726$, $p = 0.047$) for the *Motion* but not for the *Flicker* condition ($F(1, 14) = 2.429$, $p = 0.141$) for the mTBI group. These results finally indicate that motion direction discrimination RTSDs were significantly larger for first- than for second-order stimuli, while there was no significant difference between detection RTSDs related to first- or second-order stimuli. In the *Motion* condition, the shortest mean RTs (i.e. related to first-order stimuli) were associated with a larger dispersion in the mTBI group.

Finally, the four-way mixed ANOVA revealed no significant *Session* factor effect ($F(2, 56) = 1.726$, $p = 0.189$), and no significant *Condition* x *Session* interaction ($F(2, 56) = 0.028$, $p = 0.970$), which indicates that all previously described observations for the RTSDs did not significantly vary across sessions.

RTIQs analysis (4-way mixed ANOVA) slightly differed from RTSDs analysis as for the *Condition* factor effect and decompositions. Actually, it revealed a significant effect of *Condition* factor ($F(1, 28) = 23.985$, $p < 0.0001$), indicating that detection RTIQRs were significantly narrower than motion direction discrimination RTIQRs, for both groups (*Figures 2 & 3*). However, in spite of different decompositions, RTIQRs analysis led to the same conclusions as RTSDs analysis, and thus is not described further here.

3.4. Self-reported symptoms

The two-way mixed ANOVA (*Session* (3) x *Group* (2)) applied to PCSS-R total scores revealed a significant *Group* effect ($F(1, 28) = 12.614$, $p = 0.001$). However, this

analysis did return neither significant *Session* effect ($F(2, 56) = 1.816$, $p = 0.182$), nor significant *Session* x *Group* interaction ($F(2, 56) = 0.909$, $p = 0.387$). These results indicate that: (1) mTBI subjects had significantly more symptoms and/or symptoms of greater severity than control subjects; and (2) this difference between mTBI and control subjects did not significantly vary across sessions (*Figure 4*).

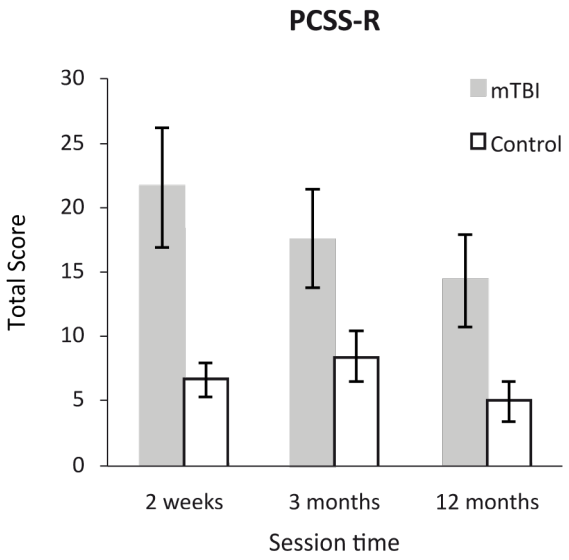

Figure 4. Post-concussion symptom scores

Post-concussion symptom scale-Revised Total scores; Mean ± SE.

We also sought to verify if there were correlations between: (1) RT variables (mean, SD, median and IQR) at each session and the level of symptoms at corresponding session times; and (2) between those same variables and the initial level of symptoms (i.e. determined at session A).

No correlation was found between the level of symptoms and RT variables for the control group.

3.5. Correlations between reaction times and level of symptoms at each session (mTBI group)

Session A. Mean and median RTs of the mTBI group for *Motion* condition (first- and second-order) are positively correlated with the level of symptoms (mean RTs: $r \geq 0.646$, $p \leq 0.009$; median RTs: $r \geq 0.637$, $p \leq 0.011$). No significant correlation ($p \leq 0.0125$) was found between level of symptoms and RT SDs and IQRs at session A.

Sessions B and C. No significant correlation was found between level of symptoms and RT variables

3.6. Correlations between reaction times and initial level of symptoms (mTBI group)

Session B. Mean RTs and RTSDs of the mTBI group of session B are positively correlated with the initial level of symptoms for all conditions (mean RTs: $r \geq 0.708$, $p \leq 0.003$; RTSDs: $r \geq 0.673$, $p \leq 0.006$). Median RTs are positively correlated with the initial level of symptoms for *Motion* condition (first- and second-order), and RTIQRs are positively correlated with the initial level of symptoms for *Flicker* condition (first- and second-order) and for first-order *Motion* condition (median RTs: $r \geq 0.702$, $p \leq 0.004$; RTIQRs: $r \geq 0.649$, $p \leq 0.009$).

Session C. The initial level of symptoms is positively correlated only with RTSDs for first-order *Flicker* ($r = 0.639$, $p = 0.010$).

4. Discussion

4.1. Visuomotor deficits related to motion processing after mTBI

Several conclusions have to be retained concerning the RT measures made in this study. Firstly, for all conditions and sessions, RTs were globally longer and more spread around the central tendency for mTBI than for control subjects. In other words, responses of mTBI participants were significantly slower and more variable than those of control subjects, even one year after brain injury. These results are in agreement with those of Hugenholtz, Stuss, Stethem, and Richard (1988), Stuss et al. (1989) and Beaupre, De Guise, and McKerral (2012). They highlight the presence of persisting deficits affecting neural networks involved in visual information detection, integration and interpretation, as well as in the related motor response as shown using RTs. Furthermore, the observed difference in processing speed between the two groups in this kind of simple task suggests that, at early visual perception stages, this slowing is probably due: (1) to longer processing steps leading to increasing delays during global processing; and/or (2) to defective links between these steps in mTBI individuals. The durable presence of such deficits lingering beyond 3 months after an mTBI is in agreement with the findings of Brosseau-Lachaine et al. (2008).

Secondly, concerning detection RTs, regardless of group, no difference was observed between first- and second-order stimuli. In other words, the discrepancies observed between detection RTs related to first- and second-order stimuli were similar in both groups. However, this task required giving a response as soon as the stimulus appeared. This means that the response speed resulted probably more from the detection of any change on the screen than from identification of the stimuli attributes.

Thirdly, concerning motion direction discrimination RTs three observations can be made. The first one is that they were longer than detection RTs, regardless of group or session. This can easily be explained by the fact that the processing load was greater for motion direction discrimination than for detection.

The second observation is, for control subjects, the absence of significant difference between choice RTs related respectively to first- and second-order stimuli, regardless of the variable (mean, median, SD, IQR), and in spite of the fact that central tendencies were greater for second- than for first-order stimuli. These results confirm that our modulation depth adjustment between first- and second-order stimuli allowed equating their visibility. These results are also in agreement, at least for these modulation depths, with RT measures reported by Ledgeway and Hutchinson (2008) as a function of stimuli attributes (first- vs. second-order) and contrast level.

Finally, the third observation concerns data of mTBI subjects. Two conclusions can be drawn. The first conclusion is that both the mean and the median RTs were significantly longer for second-order than for first-order stimuli, across all testing sessions. The second conclusion concerns RT SDs and IQRs. For motion direction discrimination RT SDs and IQRs were significantly larger for first- than for second-order stimuli. This second conclusion went against expectations: it was expected that the lower means and medians (i.e. corresponding to the shortest RTs and related to first-order stimuli) would be associated with a smaller dispersion. This is what we observed in the control group, where simple RTs, which were the shortest, were associated to a lesser dispersion than choice RTs. The validity of these findings is further reinforced by the fact that motion direction discrimination RTs of control group,

as well as detection RTs of both groups, did not reveal any difference related to stimuli attributes, regardless of the variable (mean, median, SD and IQR).

The finding that mean and median motion direction discrimination RTs of the mTBI group are longer for second- than for first-order stimuli is in agreement with the hypothesis of the existence of two separate mechanisms respectively dedicated to first- and second-order motion perception (Allard & Faubert, 2013b; Bertone & Faubert, 2003; Cavanagh, 1992; Cavanagh & Mather, 1989; Chubb & Sperling, 1988; Ledgeway & Hutchinson, 2008; Lu & Sperling, 2001). These observations indicate that more time is needed to discriminate motion direction for second- than for first-order stimuli. Finally, the fact that, for the mTBI group, motion direction discrimination RTs were longer for second- than for first-order stimuli indicates that the integration of complex stimuli (i.e. second-order) is more severely affected in individuals having sustained an mTBI. Our findings are therefore in agreement with the observations of Brosseau-Lachaine et al. (2008).

The finding that motion direction discrimination RT SDs and IQRs are greater for first- than for second-order stimuli for the mTBI group does not agree with the idea that, globally, shortest RTs should be associated with the smallest dispersion. This is what the data of control group indicates, when comparing simple to choice RTs. RT SDs and IQRs of mTBI group show a greater variability of RTs for first- than for second-order motion. It has been demonstrated that, for low spatial and temporal frequencies, motion of sine-wave luminance-defined gratings could be perceived either through a simple mechanism specific to such stimuli attributes, or through a more complex attention-based mechanism (Allard & Faubert, 2013a, 2013b; Allen & Ledgeway,

2003; Cavanagh, 1992; Lu & Sperling, 2001). The first mechanism, more automatic and requiring less complex processing, seems usually to be preferentially used, whatever the spatial or temporal frequency, for first-order motion processing. This mechanism is the fastest. The second mechanism, of higher perception level and requiring additional visual-attentional processes, seems to be associated only with low spatial and temporal frequencies (such as the ones we used here) and be the only one available for second-order motion stimuli perception. This mechanism is the slowest. The direction discrimination RT SDs and IQRs of both the mTBI and the control groups are in agreement with findings indicating that, at low spatial and temporal frequencies, both of the previously discussed mechanisms are available for first-order motion perception. These results also show that the fastest of those mechanisms is preferentially used in non-brain-injured adults. The greater variability of motion direction discrimination RTs for first- than for second-order stimuli in mTBI participants is compatible with the hypothesis of a first-order motion perception switching from a slower to another faster mechanism, following such a mild diffuse brain injury. Otherwise, the similar distributions of first- and second-order-related motion direction discrimination RTs in the control group may testify, in this particular case and given the equivalent visibility of stimuli attributes, to the systematic use of the fastest mechanism for first-order motion processing, and of the slowest mechanism for second-order motion processing. The greater dispersion of motion direction discrimination RTs related to first-order stimuli, in mTBI participants, could be the result of a combination of deficits affecting neural networks dedicated to each of these mechanisms as well as inhibitory neural networks, which may enable

selecting one or the other of these two pathways, without any parasitic or competitive interference of the other one. Another hypothesis would be that motion visual processing switches from one mechanism to the other whenever one is not able to efficiently process information, secondary to neurophysiological disorders that could temporally render inefficient such cerebral processes when used in a sustained fashion (as they probably were in such a task). Both of these hypotheses are compatible, in the first days after the mTBI, with the occurrence of neurophysiological disorders due to traumatic axonal injury and cerebrovascular damages (Bigler, 2007; Gaetz, 2004; G. L. Iverson, 2005; Lee et al., 2008; Maxwell et al., 1997; Shaw, 2002; Topal et al., 2008), and in a longer term with the brain atrophy that occurs in individuals having sustained an mTBI (Lewine et al., 2007; MacKenzie et al., 2002).

4.2. Visual perception deficits and level of symptoms following mTBI

The level of self-reported symptoms using the PCSS-R remained significantly higher for mTBI than for control subjects across sessions. Consequently, we investigated if there was any relationship between level of symptoms and RTs.

No statistically significant correlation was established between these variables for control group participants, regardless of the session.

In mTBI group participants, there was a link between level of symptoms and mean and median RTs in the first days following the brain injury. However, significant correlations between symptoms at the time of testing and RT measures disappeared 3 months after the injury. The level of symptoms 15 days after injury positively correlated with mean and median RTs recorded at the same period for *Motion* conditions (first- and second-order). These correlations for data gathered at 15 days

following brain injury could indicate that level of symptoms and deficits associating visual perception and motor response requiring a choice may have, to some extent, a common neurophysiological origin, soon after the brain injury.

Three months after mTBI, significant correlations between level of symptoms and RTs were no longer found. These results indicate that RTs shortened more than the level of symptoms decreased for the mTBI group. These findings are in agreement with those of Naunheim et al. (2008) who found that, in the first 6 hours following an mTBI, the general cognitive status and performances to attention tests improved faster than the level of symptoms deceased. Our results are also in agreement with those of other researchers who showed that, in some cases, the persistence of some particular post-concussive symptoms for months, and even years, after mTBI was associated with usually subtle cognitive deficits (Beaupre et al., 2012; Cicerone & Azulay, 2002; Konrad et al., 2011; Lewine et al., 2007; Ruffolo, Friedland, Dawson, Colantonio, & Lindsay, 1999). Other factors than that related directly to the brain injury may also have contributed to the lack of correlation between level of symptoms and reaction time measures at 12 months post-injury. Our results show that although symptoms are still present months after the injury they are no more related to the RT responses.

Considering correlations between the initial level of symptoms and RT variables, we can see that 4 out of 16 were significant at session A, they were globally (13/16) significant at session B, and only 1 out of 16 was significant at session C. These findings seem to be attributable to some variability in the time course of recovery from visuomotor deficits resulting from an mTBI. The fact that correlations between initial

level of symptoms and RTs were stronger for data related to session B than for those related to session A indicates that the shortening of RTs and the narrowing of their distribution from session A to B were relatively more pronounced in mTBI individuals having a lower initial level of symptoms, or that these two phenomena concerned only initially less symptomatic subjects. From session B to C, the number of significant correlations between the initial level of symptoms and RTs largely decreased. This suggests that, from session B to C, the shortening of RTs and the narrowing of their dispersion were relatively larger in subjects having a higher initial level of symptoms, or that these two phenomena were found only in the initially more symptomatic subjects. In other words, RTs were even longer and their dispersion even greater when the initial level of symptoms was high, and the decrease in visuomotor deficits revealed by RTs was even faster when initial level of symptoms was low. These time course recovery differences among mTBI participants depending on injury severity have also been observed in children aged from 8 to 15 over a one-year period (Yeates et al., 2009). Likewise, Iverson (2007), in a study on athletes aged from 13 to 19, showed that participants whose recovery was longer were also those who had the worst performances on neuropsychological tests and a higher level of symptoms on average, 72 hours after the mTBI. Finally and similarly, other authors showed that individuals having sustained an mTBI and who had the worst performances on neuropsychological and balance tests at emergency department[1] assessment, had

[1] ED, dans le texte original

persisting symptoms one (Sheedy et al., 2006) and three months later (Sheedy et al., 2009).

Conclusions drawn from correlations between RT variables and level of symptoms had an essentially descriptive goal, as this can eventually become highly relevant for clinical practice. Given that these results showed some heterogeneity, they should be interpreted with caution, particularly because: (1) the assessment of level of symptoms is subjective in nature; (2) there is variability over time (in the short term) in the presence and severity of symptoms, especially at three months and one year after the mTBI, whereas the PCSS-R assesses self-reported symptoms only over the last 24 hours; (3) the symptoms listed in the PCSS-R are not entirely specific to mTBI, although they have been shown to be more frequent, as well as sensitive and specific in mTBI, in comparison to moderate-severe TBI or trauma controls at similar time points post-injury, or to normal control (Dikmen, Machamer, Fann, & Temkin, 2010; Gordon, Haddad, Brown, Hibbard, & Sliwinski, 2000); (4) the neurophysiological disorders behind symptoms and the visuomotor deficits demonstrated by RT measures may perhaps not be related entirely to the same brain areas and/or tissues (Bigler, 2007; de Guise et al., 2010; Lachapelle et al., 2008; Lachapelle et al., 2004; McAllister & Arciniegas, 2002).

4.3. Limitations

Ideally, a larger sample size would have been preferable, especially to draw more general conclusions and establish sub-categories in terms of concussion type or level of symptoms, for instance. However, strictly respecting all inclusion and exclusion criteria, particularly regarding the absence of alcohol or drug abuse, made recruitment

rather difficult. Moreover, as the willingness to participate in research is less in patients who fully recover, this may result in an underestimation of the recovery after an mTBI as measured with RTs (Lingsma et al., 2015).

It would also have been preferable that none of the participants belonging to the mTBI group have a previous medical history of mTBI (a year or more prior to inclusion in the study, according to our inclusion/exclusion criteria). However, this was found for only two subjects, and thus results of the entire mTBI group cannot be ascribed to this.

Finally, due to relatively long periods between each testing session, it was not impossible that subjects sustained another mTBI in the course of the present study. However, this was verified before the second and third testing sessions. None of the subjects belonging to the control group reported having sustained an mTBI during the whole study period. In the mTBI group however, one subject reported, at session C, having being concussed on a soccer field 6 weeks after the session B. He reported having neither loss of consciousness nor post-traumatic amnesia following this injury. He reported his symptoms (nausea, dizziness, confusion and fatigue) to have lasted about one to two months. Finally, he said having stopped all sport activities after this incident (i.e. for over a 7.5 months period). At the third session, he reported being clear from all symptoms (nausea, dizziness, confusion and fatigue). His data gathered at session C were compared to those recorded at previous sessions and to those of other mTBI group participants. As no aberration was found this way in his latter data, we decided to include them in the study.

5. Conclusion

In the present study, RT measures related to first- and second-order stimuli reveal the presence of subtle visual perception deficits induced by an mTBI, and affecting high-level as well as low-level processing steps. Moreover, our findings related to motion direction discrimination RTs showed that visuomotor deficits affected high-level more than low-level processes. Finally, these deficits and level of symptoms observed in mTBI participants did persist up to one year after the brain injury. This reveals that, even though after an mTBI there is a lessening of visuomotor deficits as well as a decrease in the level of symptoms, the recovery from such a brain injury one year later does not reach the functional level that can be observed in a non-brain-injured population.

Visual perception deficits induced by an mTBI prove to be detectable by tasks relying on the analysis of first- and second-order motion perception. Developing screening tests in this respect intended for early post-mTBI use would be of interest. Furthermore, further studying relationships of such deficits with performance in daily life activities such as school, work, or sports is crucial in order to determine the functional impacts of these alterations in visuomotor functions.

Acknowledgements

David Nguyen-Tri (programming and English proof-reading)

Isabelle Roy & Ariane Demers (HSCM), Lisa Grilli (MUHC) (recruitment of participants)

Thomas Romeas (School of Optometry, Université de Montréal) (project coordinator)

Rémy Allard and Frédéric Poirier (comments on the manuscript)

Claudine Habak (English proof-reading and comments on the manuscript)

The Canadian Institutes of Health Research (funding of the study, MOP-18004)

All the participants that participated in this study.

Author Disclosure Statement

No competing financial interests exist.

References

Adams, C. W., Bullimore, M. A., Wall, M., Fingeret, M., & Johnson, C. A. (1999). Normal aging effects for frequency doubling technology perimetry. *Optom Vis Sci, 76*(8), 582-587.

Allard, R., & Faubert, J. (2006). Same calculation efficiency but different internal noise for luminance- and contrast-modulated stimuli detection. *J Vis, 6*(4), 322-334. doi:10.1167/6.4.3

Allard, R., & Faubert, J. (2013a). No dedicated second-order motion system. *J Vis, 13*(11). doi:10.1167/13.11.2

Allard, R., & Faubert, J. (2013b). No second-order motion system sensitive to high temporal frequencies. *J Vis, 13*(5). doi:10.1167/13.5.4

Allard, R., Lagace-Nadon, S., & Faubert, J. (2013). Feature tracking and aging. *Front Psychol, 4*, 427. doi:10.3389/fpsyg.2013.00427

Allen, H. A., & Ledgeway, T. (2003). Attentional modulation of threshold sensitivity to first-order motion and second-order motion patterns. *Vision Res, 43*(27), 2927-2936.

Armstrong, V., Maurer, D., & Lewis, T. L. (2009). Sensitivity to first- and second-order motion and form in children and adults. *Vision Res, 49*(23), 2774-2781. doi:10.1016/j.visres.2009.08.016

Ashida, H., Lingnau, A., Wall, M. B., & Smith, A. T. (2007). FMRI adaptation reveals separate mechanisms for first-order and second-order motion. *J Neurophysiol, 97*(2), 1319-1325. doi:10.1152/jn.00723.2006

Bain, A. C., Raghupathi, R., & Meaney, D. F. (2001). Dynamic stretch correlates to both morphological abnormalities and electrophysiological impairment in a model of traumatic axonal injury. *J Neurotrauma, 18*(5), 499-511. doi:10.1089/089771501300227305

Bayly, P. V., Cohen, T. S., Leister, E. P., Ajo, D., Leuthardt, E. C., & Genin, G. M. (2005). Deformation of the human brain induced by mild acceleration. *J Neurotrauma, 22*(8), 845-856. doi:10.1089/neu.2005.22.845

Beaupre, M., De Guise, E., & McKerral, M. (2012). The Association between Pain-Related Variables, Emotional Factors, and Attentional Functioning following Mild Traumatic Brain Injury. *Rehabil Res Pract, 2012*, 924692. doi:10.1155/2012/924692

Bell, D. R., Guskiewicz, K. M., Clark, M. A., & Padua, D. A. (2011). Systematic review of the balance error scoring system. *Sports Health, 3*(3), 287-295. doi:10.1177/1941738111403122

Bertone, A., & Faubert, J. (2003). How is complex second-order motion processed? *Vision Res, 43*(25), 2591-2601.

Bertone, A., Hanck, J., Cornish, K. M., & Faubert, J. (2008). Development of static and dynamic perception for luminance-defined and texture-defined information. *Neuroreport, 19*(2), 225-228. doi:10.1097/WNR.0b013e3282f48401

Bigler, E. D. (2007). Anterior and middle cranial fossa in traumatic brain injury: relevant neuroanatomy and neuropathology in the study of neuropsychological outcome. *Neuropsychology, 21*(5), 515-531. doi:10.1037/0894-4105.21.5.515

Bigler, E. D. (2008). Neuropsychology and clinical neuroscience of persistent post-concussive syndrome. *J Int Neuropsychol Soc, 14*(1), 1-22. doi:10.1017/S135561770808017X

Billino, J., Braun, D. I., Bremmer, F., & Gegenfurtner, K. R. (2011). Challenges to normal neural functioning provide insights into separability of motion processing mechanisms. *Neuropsychologia, 49*(12), 3151-3163. doi:10.1016/j.neuropsychologia.2011.07.009

Brosseau-Lachaine, O., Gagnon, I., Forget, R., & Faubert, J. (2008). Mild traumatic brain injury induces prolonged visual processing deficits in children. *Brain Inj, 22*(9), 657-668. doi:10.1080/02699050802203353

Brown, L., Sherbenou, R. J., & Johnsen, S. K. (1997). Test of Nonverbal Intelligence: : A language-free measure of cognitive ability—Third Edition.

Bruininks, R. H., & Bruininks, B. D. (2005). Bruininks–Oseretsky Test of Motor Proficiency (2nd Edition).

Bryan, C. J., & Hernandez, A. M. (2011). Predictors of post-traumatic headache severity among deployed military personnel. *Headache, 51*(6), 945-953. doi:10.1111/j.1526-4610.2011.01887.x

Carroll, L. J., Cassidy, J. D., Holm, L., Kraus, J., Coronado, V. G., & Injury, W. H. O. C. C. T. F. o. M. T. B. (2004). Methodological issues and research recommendations for mild traumatic brain injury: the WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury. *J Rehabil Med*(43 Suppl), 113-125.

Cassidy, J. D., Carroll, L. J., Peloso, P. M., Borg, J., von Holst, H., Holm, L., . . . Injury, W. H. O. C. C. T. F. o. M. T. B. (2004). Incidence, risk factors and prevention of mild traumatic brain injury: results of the WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury. *J Rehabil Med*(43 Suppl), 28-60.

Cavanagh, P. (1992). Attention-based motion perception. *Science, 257*(5076), 1563-1565.

Cavanagh, P., & Mather, G. (1989). Motion: the long and short of it. *Spat Vis, 4*(2-3), 103-129.

Chakor, H., Bertone, A., McKerral, M., Faubert, J., & Lachapelle, P. (2005). Visual evoked potentials and reaction time measurements to motion-reversal luminance- and texture-defined stimuli. *Doc Ophthalmol, 110*(2-3), 163-172. doi:10.1007/s10633-005-3694-8

Chubb, C., & Sperling, G. (1988). Drift-balanced random stimuli: a general basis for studying non-Fourier motion perception. *J Opt Soc Am A, 5*(11), 1986-2007.

Cicerone, K. D., & Azulay, J. (2002). Diagnostic utility of attention measures in postconcussion syndrome. *Clin Neuropsychol, 16*(3), 280-289. doi:10.1076/clin.16.3.280.13849

Conners, C. K. (1997). Conner's Rating Scales - Revised Technical Manual. *Toronto, Ontario, Canada: Multi-Health Systems Inc.*

Daniel, P. M., & Whitteridge, D. (1961). The representation of the visual field on the cerebral cortex in monkeys. *J Physiol, 159*, 203-221.

de Guise, E., Lepage, J. F., Tinawi, S., LeBlanc, J., Dagher, J., Lamoureux, J., & Feyz, M. (2010). Comprehensive clinical picture of patients with complicated vs uncomplicated mild traumatic brain injury. *Clin Neuropsychol, 24*(7), 1113-1130. doi:10.1080/13854046.2010.506199

De Moraes, C. G. (2013). Anatomy of the visual pathways. *J Glaucoma, 22 Suppl 5*, S2-7. doi:10.1097/IJG.0b013e3182934978

Delorme, A. (2006). Statistical methods. *Encyclopedia of Medical Device and Instrumentation* (Vol. 6, pp. 240-264): Wiley Interscience.

DeMatteo, C., Greenspoon, D., Levac, D., Harper, J. A., & Rubinoff, M. (2014). Evaluating the Nintendo Wii for assessing return to activity readiness in youth

with mild traumatic brain injury. *Phys Occup Ther Pediatr, 34*(3), 229-244. doi:10.3109/01942638.2014.885103

Dieterich, M., & Brandt, T. (2015). The bilateral central vestibular system: its pathways, functions, and disorders. *Ann N Y Acad Sci, 1343*, 10-26. doi:10.1111/nyas.12585

Dikmen, S., Machamer, J., Fann, J. R., & Temkin, N. R. (2010). Rates of symptom reporting following traumatic brain injury. *J Int Neuropsychol Soc, 16*(3), 401-411. doi:10.1017/S1355617710000196

Draganski, B., Ashburner, J., Hutton, C., Kherif, F., Frackowiak, R. S., Helms, G., & Weiskopf, N. (2011). Regional specificity of MRI contrast parameter changes in normal ageing revealed by voxel-based quantification (VBQ). *Neuroimage, 55*(4), 1423-1434. doi:10.1016/j.neuroimage.2011.01.052

Dumoulin, S. O., Baker, C. L., Jr., Hess, R. F., & Evans, A. C. (2003). Cortical specialization for processing first- and second-order motion. *Cereb Cortex, 13*(12), 1375-1385.

Dupont, P., Sary, G., Peuskens, H., & Orban, G. A. (2003). Cerebral regions processing first- and higher-order motion in an opposed-direction discrimination task. *Eur J Neurosci, 17*(7), 1509-1517.

Eikema, D. J., Hatzitaki, V., Tzovaras, D., & Papaxanthis, C. (2012). Age-dependent modulation of sensory reweighting for controlling posture in a dynamic virtual environment. *Age (Dordr), 34*(6), 1381-1392. doi:10.1007/s11357-011-9310-9

Ellemberg, D., Lavoie, K., Lewis, T. L., Maurer, D., Lepore, F., & Guillemot, J. P. (2003). Longer VEP latencies and slower reaction times to the onset of second-order motion than to the onset of first-order motion. *Vision Res, 43*(6), 651-658.

Evans, R. W. (2004). Post-traumatic headaches. *Neurol Clin, 22*(1), 237-249, viii. doi:10.1016/S0733-8619(03)00097-5

Farivar, R. (2009). Dorsal-ventral integration in object recognition. *Brain Res Rev, 61*(2), 144-153. doi:10.1016/j.brainresrev.2009.05.006

Faubert, J. (2002). Visual perception and aging. *Can J Exp Psychol, 56*(3), 164-176.

Faubert, J., & Allard, R. (2004). Effect of visual distortion on postural balance in a full immersion stereoscopic environment. In A. J. Woods, Merrit, J. O., Benton, S. A. & Bolas, M. T. (Ed.), *Stereoscopic displays and virtual reality systems XI, Proceedings of SPIE IS&T Electronic Imaging, SPIE, 5291* (pp. 491–500).

Ferre, E. R., Walther, L. E., & Haggard, P. (2015). Multisensory interactions between vestibular, visual and somatosensory signals. *PLoS One, 10*(4), e0124573. doi:10.1371/journal.pone.0124573

Fife, T. D., & Kalra, D. (2015). Persistent vertigo and dizziness after mild traumatic brain injury. *Ann N Y Acad Sci, 1343*, 97-105. doi:10.1111/nyas.12678

Findling, O., Schuster, C., Sellner, J., Ettlin, T., & Allum, J. H. (2011). Trunk sway in patients with and without, mild traumatic brain injury after whiplash injury. *Gait Posture, 34*(4), 473-478. doi:10.1016/j.gaitpost.2011.06.021

Fisher, D. C., Ledbetter, M. F., Cohen, N. J., Marmor, D., & Tulsky, D. S. (2000). WAIS-III and WMS-III profiles of mildly to severely brain-injured patients. *Appl Neuropsychol, 7*(3), 126-132. doi:10.1207/S15324826AN0703_2

Gaetz, M. (2004). The neurophysiology of brain injury. *Clin Neurophysiol, 115*(1), 4-18.

Gagnon, I., Forget, R., Sullivan, S. J., & Friedman, D. (1998). Motor performance following a mild traumatic brain injury in children: an exploratory study. *Brain Inj, 12*(10), 843-853.

Gagnon, I., Swaine, B., Friedman, D., & Forget, R. (2004). Children show decreased dynamic balance after mild traumatic brain injury. *Arch Phys Med Rehabil, 85*(3), 444-452.

Gegenfurtner, K. R., & Hawken, M. J. (1996). Perceived velocity of luminance, chromatic and non-fourier stimuli: influence of contrast and temporal frequency. *Vision Res, 36*(9), 1281-1290.

Geurts, A. C., Knoop, J. A., & van Limbeek, J. (1999). Is postural control associated with mental functioning in the persistent postconcussion syndrome? *Arch Phys Med Rehabil, 80*(2), 144-149.

Geurts, A. C., Ribbers, G. M., Knoop, J. A., & van Limbeek, J. (1996). Identification of static and dynamic postural instability following traumatic brain injury. *Arch Phys Med Rehabil, 77*(7), 639-644.

Gibson, J. J. (1979). *The ecological approach to visual perception*. Boston: Houghton Mifflin.

Giorgio, A., Santelli, L., Tomassini, V., Bosnell, R., Smith, S., De Stefano, N., & Johansen-Berg, H. (2010). Age-related changes in grey and white matter structure throughout adulthood. *Neuroimage, 51*(3), 943-951. doi:10.1016/j.neuroimage.2010.03.004

Gordon, W. A., Haddad, L., Brown, M., Hibbard, M. R., & Sliwinski, M. (2000). The sensitivity and specificity of self-reported symptoms in individuals with traumatic brain injury. *Brain Inj, 14*(1), 21-33.

Greffou, S., Bertone, A., Hanssens, J. M., & Faubert, J. (2008). Development of visually driven postural reactivity: a fully immersive virtual reality study. *J Vis, 8*(11), 15 11-10. doi:10.1167/8.11.15

Guerraz, M., Thilo, K. V., Bronstein, A. M., & Gresty, M. A. (2001). Influence of action and expectation on visual control of posture. *Brain Res Cogn Brain Res, 11*(2), 259-266.

Guldin, W. O., & Grusser, O. J. (1998). Is there a vestibular cortex? *Trends Neurosci, 21*(6), 254-259.

Guskiewicz, K. M., Ross, S. E., & Marshall, S. W. (2001). Postural Stability and Neuropsychological Deficits After Concussion in Collegiate Athletes. *J Athl Train, 36*(3), 263-273.

Habak, C., & Faubert, J. (2000). Larger effect of aging on the perception of higher-order stimuli. *Vision Res, 40*(8), 943-950.

Haibach, P. S., Slobounov, S. M., & Newell, K. M. (2008). The potential applications of a virtual moving environment for assessing falls in elderly adults. *Gait Posture, 27*(2), 303-308. doi:10.1016/j.gaitpost.2007.04.004

Halterman, C. I., Langan, J., Drew, A., Rodriguez, E., Osternig, L. R., Chou, L. S., & van Donkelaar, P. (2006). Tracking the recovery of visuospatial attention deficits in mild traumatic brain injury. *Brain, 129*(Pt 3), 747-753. doi:10.1093/brain/awh705

Harmon, K. G., Drezner, J. A., Gammons, M., Guskiewicz, K. M., Halstead, M., Herring, S. A., . . . Roberts, W. O. (2013). American Medical Society for Sports

Medicine position statement: concussion in sport. *Br J Sports Med, 47*(1), 15-26. doi:10.1136/bjsports-2012-091941

Heltemes, K. J., Holbrook, T. L., Macgregor, A. J., & Galarneau, M. R. (2012). Blast-related mild traumatic brain injury is associated with a decline in self-rated health amongst US military personnel. *Injury, 43*(12), 1990-1995. doi:10.1016/j.injury.2011.07.021

Hugenholtz, H., Stuss, D. T., Stethem, L. L., & Richard, M. T. (1988). How long does it take to recover from a mild concussion? *Neurosurgery, 22*(5), 853-858.

Hutchinson, C. V., & Ledgeway, T. (2006). Sensitivity to spatial and temporal modulations of first-order and second-order motion. *Vision Res, 46*(3), 324-335. doi:10.1016/j.visres.2005.03.002

Ivarsson, J., Viano, D. C., & Lovsund, P. (2002). Influence of the lateral ventricles and irregular skull base on brain kinematics due to sagittal plane head rotation. *J Biomech Eng, 124*(4), 422-431.

Iverson, G. (2007). Predicting slow recovery from sport-related concussion: the new simple-complex distinction. *Clin J Sport Med, 17*(1), 31-37. doi:10.1097/JSM.0b013e3180305e4d

Iverson, G. L. (2005). Outcome from mild traumatic brain injury. *Curr Opin Psychiatry, 18*(3), 301-317. doi:10.1097/01.yco.0000165601.29047.ae

Iwasaki, S., & Yamasoba, T. (2015). Dizziness and Imbalance in the Elderly: Age-related Decline in the Vestibular System. *Aging Dis, 6*(1), 38-47. doi:10.14336/AD.2014.0128

Jiang, Y., Luo, Y. J., & Parasuraman, R. (2009). Neural correlates of age-related reduction in visual motion priming. *Neuropsychol Dev Cogn B Aging Neuropsychol Cogn, 16*(2), 164-182. doi:10.1080/13825580802348588

Kalaycioglu, C., Nalcaci, E., Schmiedt-Fehr, C., & Basar-Eroglu, C. (2009). Corpus callosum has different channels for transmission of spatial frequency information. *Brain Res, 1296*, 85-93. doi:10.1016/j.brainres.2009.08.018

Kaufman, K. R., Brey, R. H., Chou, L. S., Rabatin, A., Brown, A. W., & Basford, J. R. (2006). Comparison of subjective and objective measurements of balance disorders following traumatic brain injury. *Med Eng Phys, 28*(3), 234-239. doi:10.1016/j.medengphy.2005.05.005

King, L. A., Horak, F. B., Mancini, M., Pierce, D., Priest, K. C., Chesnutt, J., . . . Chapman, J. C. (2014). Instrumenting the balance error scoring system for use with patients reporting persistent balance problems after mild traumatic brain injury. *Arch Phys Med Rehabil, 95*(2), 353-359. doi:10.1016/j.apmr.2013.10.015

Kirov, II, Tal, A., Babb, J. S., Reaume, J., Bushnik, T., Ashman, T. A., . . . Gonen, O. (2013). Proton MR spectroscopy correlates diffuse axonal abnormalities with

post-concussive symptoms in mild traumatic brain injury. *J Neurotrauma, 30*(13), 1200-1204. doi:10.1089/neu.2012.2696

Kleffelgaard, I., Roe, C., Soberg, H. L., & Bergland, A. (2012). Associations among self-reported balance problems, post-concussion symptoms and performance-based tests: a longitudinal follow-up study. *Disabil Rehabil, 34*(9), 788-794. doi:10.3109/09638288.2011.619624

Konrad, C., Geburek, A. J., Rist, F., Blumenroth, H., Fischer, B., Husstedt, I., . . . Lohmann, H. (2011). Long-term cognitive and emotional consequences of mild traumatic brain injury. *Psychol Med, 41*(6), 1197-1211. doi:10.1017/S0033291710001728

Kontos, A. P., Elbin, R. J., Schatz, P., Covassin, T., Henry, L., Pardini, J., & Collins, M. W. (2012). A revised factor structure for the post-concussion symptom scale: baseline and postconcussion factors. *Am J Sports Med, 40*(10), 2375-2384. doi:10.1177/0363546512455400

Korth, M., Rix, R., & Sembritzki, O. (2000). The sequential processing of visual motion in the human electroretinogram and visual evoked potential. *Vis Neurosci, 17*(4), 631-646.

Krainik, A., Feydy, A., Colombani, J. M., Helias, A., & Menu, Y. (2003). [Functional anatomy of the central nervous system]. *J Radiol, 84*(3), 285-297.

Kuba, M., & Kubova, Z. (1992). Visual evoked potentials specific for motion onset. *Doc Ophthalmol, 80*(1), 83-89.

Lachapelle, J., Bolduc-Teasdale, J., Ptito, A., & McKerral, M. (2008). Deficits in complex visual information processing after mild TBI: electrophysiological markers and vocational outcome prognosis. *Brain Inj, 22*(3), 265-274. doi:10.1080/02699050801938983

Lachapelle, J., Ouimet, C., Bach, M., Ptito, A., & McKerral, M. (2004). Texture segregation in traumatic brain injury--a VEP study. *Vision Res, 44*(24), 2835-2842. doi:10.1016/j.visres.2004.06.007

Lange, R. T., Iverson, G. L., & Rose, A. (2010). Post-concussion symptom reporting and the "good-old-days" bias following mild traumatic brain injury. *Arch Clin Neuropsychol, 25*(5), 442-450. doi:10.1093/arclin/acq031

Langrova, J., Kuba, M., Kremlacek, J., Kubova, Z., & Vit, F. (2006). Motion-onset VEPs reflect long maturation and early aging of visual motion-processing system. *Vision Res, 46*(4), 536-544. doi:10.1016/j.visres.2005.06.024

Larson, M. J., Clayson, P. E., & Farrer, T. J. (2012). Performance monitoring and cognitive control in individuals with mild traumatic brain injury. *J Int Neuropsychol Soc, 18*(2), 323-333. doi:10.1017/S1355617711001779

Leddy, J. J., Kozlowski, K., Fung, M., Pendergast, D. R., & Willer, B. (2007). Regulatory and autoregulatory physiological dysfunction as a primary

characteristic of post concussion syndrome: implications for treatment. *NeuroRehabilitation, 22*(3), 199-205.

Ledgeway, T., & Hutchinson, C. V. (2005). The influence of spatial and temporal noise on the detection of first-order and second-order orientation and motion direction. *Vision Res, 45*(16), 2081-2094. doi:10.1016/j.visres.2005.02.005

Ledgeway, T., & Hutchinson, C. V. (2008). Choice reaction times for identifying the direction of first-order motion and different varieties of second-order motion. *Vision Res, 48*(2), 208-222. doi:10.1016/j.visres.2007.11.008

Lee, H., Wintermark, M., Gean, A. D., Ghajar, J., Manley, G. T., & Mukherjee, P. (2008). Focal lesions in acute mild traumatic brain injury and neurocognitive outcome: CT versus 3T MRI. *J Neurotrauma, 25*(9), 1049-1056. doi:10.1089/neu.2008.0566

Levin, H. S., Mattis, S., Ruff, R. M., Eisenberg, H. M., Marshall, L. F., Tabaddor, K., . . . Frankowski, R. F. (1987). Neurobehavioral outcome following minor head injury: a three-center study. *J Neurosurg, 66*(2), 234-243. doi:10.3171/jns.1987.66.2.0234

Lewine, J. D., Davis, J. T., Bigler, E. D., Thoma, R., Hill, D., Funke, M., . . . Orrison, W. W. (2007). Objective documentation of traumatic brain injury subsequent to mild head trauma: multimodal brain imaging with MEG, SPECT, and MRI. *J Head Trauma Rehabil, 22*(3), 141-155. doi:10.1097/01.HTR.0000271115.29954.27

Lingsma, H. F., Yue, J. K., Maas, A. I., Steyerberg, E. W., Manley, G. T., Cooper, S. R., . . . Yuh, E. L. (2015). Outcome Prediction after Mild and Complicated Mild Traumatic Brain Injury: External Validation of Existing Models and Identification of New Predictors Using the TRACK-TBI Pilot Study. *J Neurotrauma, 32*(2), 83-94. doi:10.1089/neu.2014.3384

Lovell, M. R., & Collins, M. W. (1998). Neuropsychological assessment of the college football player. *J Head Trauma Rehabil, 13*(2), 9-26.

Lu, Z. L., & Sperling, G. (2001). Three-systems theory of human visual motion perception: review and update. *J Opt Soc Am A Opt Image Sci Vis, 18*(9), 2331-2370.

MacKenzie, J. D., Siddiqi, F., Babb, J. S., Bagley, L. J., Mannon, L. J., Sinson, G. P., & Grossman, R. I. (2002). Brain atrophy in mild or moderate traumatic brain injury: a longitudinal quantitative analysis. *AJNR Am J Neuroradiol, 23*(9), 1509-1515.

Malojcic, B., Mubrin, Z., Coric, B., Susnic, M., & Spilich, G. J. (2008). Consequences of mild traumatic brain injury on information processing assessed with attention and short-term memory tasks. *J Neurotrauma, 25*(1), 30-37. doi:10.1089/neu.2007.0384

Marshall, S., Bayley, M., McCullagh, S., Velikonja, D., & Berrigan, L. (2012). Clinical practice guidelines for mild traumatic brain injury and persistent symptoms. *Can Fam Physician, 58*(3), 257-267, e128-240.

Marshall, S., Bayley, M., McCullagh, S., Velikonja, D., Berrigan, L., Ouchterlony, D., & Weegar, K. (2015). Updated clinical practice guidelines for concussion/mild traumatic brain injury and persistent symptoms. *Brain Inj, 29*(6), 688-700. doi:10.3109/02699052.2015.1004755

Maxwell, W. L., Povlishock, J. T., & Graham, D. L. (1997). A mechanistic analysis of nondisruptive axonal injury: a review. *J Neurotrauma, 14*(7), 419-440.

McAllister, T. W., & Arciniegas, D. (2002). Evaluation and treatment of postconcussive symptoms. *NeuroRehabilitation, 17*(4), 265-283.

McCrea, M., Guskiewicz, K. M., Marshall, S. W., Barr, W., Randolph, C., Cantu, R. C., . . . Kelly, J. P. (2003). Acute effects and recovery time following concussion in collegiate football players: the NCAA Concussion Study. *JAMA, 290*(19), 2556-2563. doi:10.1001/jama.290.19.2556

McKerral, M., Lepore, F., & Lachapelle, P. (2001). Response characteristics of the normal retino-cortical pathways as determined with simultaneous recordings of pattern visual evoked potentials and simple motor reaction times. *Vision Res, 41*(8), 1085-1090.

Naunheim, R. S., Matero, D., & Fucetola, R. (2008). Assessment of patients with mild concussion in the emergency department. *J Head Trauma Rehabil, 23*(2), 116-122. doi:10.1097/01.HTR.0000314530.30401.70

Nishiike, S., Nakagawa, S., Tonoike, M., Takeda, N., & Kubo, T. (2001). Information processing of visually-induced apparent self motion in the cortex of humans: analysis with magnetoencephalography. *Acta Otolaryngol Suppl, 545*, 113-115.

Nishimoto, T., & Murakami, S. (1998). Relation between diffuse axonal injury and internal head structures on blunt impact. *J Biomech Eng, 120*(1), 140-147.

Noguchi, Y., Kaneoke, Y., Kakigi, R., Tanabe, H. C., & Sadato, N. (2005). Role of the superior temporal region in human visual motion perception. *Cereb Cortex, 15*(10), 1592-1601. doi:10.1093/cercor/bhi037

Owsley, C. (2011). Aging and vision. *Vision Res, 51*(13), 1610-1622. doi:10.1016/j.visres.2010.10.020

Peterka, R. J. (2002). Sensorimotor integration in human postural control. *J Neurophysiol, 88*(3), 1097-1118.

Piponnier, J. C., Forget, R., Gagnon, I., McKerral, M., Giguere, J. F., & Faubert, J. (2015). First- and second-order stimuli reaction time measures are highly sensitive to mild traumatic brain injuries. *J Neurotrauma*. doi:10.1089/neu.2014.3832

Piponnier, J. C., Hanssens, J. M., & Faubert, J. (2009). Effect of visual field locus and oscillation frequencies on posture control in an ecological environment. *J Vis, 9*(1), 13 11-10. doi:10.1167/9.1.13

Pontifex, M. B., Broglio, S. P., Drollette, E. S., Scudder, M. R., Johnson, C. R., O'Connor, P. M., & Hillman, C. H. (2012). The relation of mild traumatic brain injury to chronic lapses of attention. *Res Q Exerc Sport, 83*(4), 553-559.

Pontifex, M. B., O'Connor, P. M., Broglio, S. P., & Hillman, C. H. (2009). The association between mild traumatic brain injury history and cognitive control. *Neuropsychologia, 47*(14), 3210-3216. doi:10.1016/j.neuropsychologia.2009.07.021

Prieto, E. A., Barnikol, U. B., Soler, E. P., Dolan, K., Hesselmann, G., Mohlberg, H., . . . Tass, P. A. (2007). Timing of V1/V2 and V5+ activations during coherent motion of dots: an MEG study. *Neuroimage, 37*(4), 1384-1395. doi:10.1016/j.neuroimage.2007.03.080

Raghuram, A., Lakshminarayanan, V., & Khanna, R. (2005). Psychophysical estimation of speed discrimination. II. Aging effects. *J Opt Soc Am A Opt Image Sci Vis, 22*(10), 2269-2280.

Rees, P. M. (2003). Contemporary issues in mild traumatic brain injury. *Arch Phys Med Rehabil, 84*(12), 1885-1894.

Rees, R. J., & Bellon, M. L. (2007). Post concussion syndrome ebb and flow: longitudinal effects and management. *NeuroRehabilitation, 22*(3), 229-242.

Ropper, A. H., & Gorson, K. C. (2007). Clinical practice. Concussion. *N Engl J Med, 356*(2), 166-172. doi:10.1056/NEJMcp064645

Ruff, R. (2005). Two decades of advances in understanding of mild traumatic brain injury. *J Head Trauma Rehabil, 20*(1), 5-18.

Ruff, R. M. (2011). Mild traumatic brain injury and neural recovery: rethinking the debate. *NeuroRehabilitation, 28*(3), 167-180. doi:10.3233/NRE-2011-0646

Ruff, R. M., Iverson, G. L., Barth, J. T., Bush, S. S., Broshek, D. K., Policy, N. A. N., & Planning, C. (2009). Recommendations for diagnosing a mild traumatic brain injury: a National Academy of Neuropsychology education paper. *Arch Clin Neuropsychol, 24*(1), 3-10. doi:10.1093/arclin/acp006

Ruffolo, C. F., Friedland, J. F., Dawson, D. R., Colantonio, A., & Lindsay, P. H. (1999). Mild traumatic brain injury from motor vehicle accidents: factors associated with return to work. *Arch Phys Med Rehabil, 80*(4), 392-398.

Salat, D. H. (2013). Imaging small vessel-associated white matter changes in aging. *Neuroscience*. doi:10.1016/j.neuroscience.2013.11.041

Schofield, A. J., & Georgeson, M. A. (2000). The temporal properties of first- and second-order vision. *Vision Res, 40*(18), 2475-2487.

Shaw, N. A. (2002). The neurophysiology of concussion. *Prog Neurobiol, 67*(4), 281-344.

Sheedy, J., Geffen, G., Donnelly, J., & Faux, S. (2006). Emergency department assessment of mild traumatic brain injury and prediction of post-concussion

symptoms at one month post injury. *J Clin Exp Neuropsychol, 28*(5), 755-772. doi:10.1080/13803390591000864

Sheedy, J., Harvey, E., Faux, S., Geffen, G., & Shores, E. A. (2009). Emergency department assessment of mild traumatic brain injury and the prediction of postconcussive symptoms: a 3-month prospective study. *J Head Trauma Rehabil, 24*(5), 333-343. doi:10.1097/HTR.0b013e3181aea51f

Slobounov, S., Cao, C., Sebastianelli, W., Slobounov, E., & Newell, K. (2008). Residual deficits from concussion as revealed by virtual time-to-contact measures of postural stability. *Clin Neurophysiol, 119*(2), 281-289. doi:10.1016/j.clinph.2007.10.006

Slobounov, S., Sebastianelli, W., & Hallett, M. (2012). Residual brain dysfunction observed one year post-mild traumatic brain injury: combined EEG and balance study. *Clin Neurophysiol, 123*(9), 1755-1761. doi:10.1016/j.clinph.2011.12.022

Slobounov, S., Sebastianelli, W., & Moss, R. (2005). Alteration of posture-related cortical potentials in mild traumatic brain injury. *Neurosci Lett, 383*(3), 251-255. doi:10.1016/j.neulet.2005.04.039

Slobounov, S., Sebastianelli, W., & Newell, K. M. (2011). Incorporating virtual reality graphics with brain imaging for assessment of sport-related concussions. *Conf Proc IEEE Eng Med Biol Soc, 2011*, 1383-1386. doi:10.1109/IEMBS.2011.6090325

Slobounov, S., Tutwiler, R., Sebastianelli, W., & Slobounov, E. (2006). Alteration of postural responses to visual field motion in mild traumatic brain injury. *Neurosurgery, 59*(1), 134-139; discussion 134-139. doi:10.1227/01.NEU.0000219197.33182.3F

Slobounov, S., Wu, T., Hallett, M., Shibasaki, H., Slobounov, E., & Newell, K. (2006). Neural underpinning of postural responses to visual field motion. *Biol Psychol, 72*(2), 188-197. doi:10.1016/j.biopsycho.2005.10.005

Smith, A. T., Greenlee, M. W., Singh, K. D., Kraemer, F. M., & Hennig, J. (1998). The processing of first- and second-order motion in human visual cortex assessed by functional magnetic resonance imaging (fMRI). *J Neurosci, 18*(10), 3816-3830.

Smith, A. T., & Ledgeway, T. (1997). Separate detection of moving luminance and contrast modulations: fact or artifact? *Vision Res, 37*(1), 45-62.

Sosnoff, J. J., Broglio, S. P., & Ferrara, M. S. (2008). Cognitive and motor function are associated following mild traumatic brain injury. *Exp Brain Res, 187*(4), 563-571. doi:10.1007/s00221-008-1324-x

Sosnoff, J. J., Broglio, S. P., Shin, S., & Ferrara, M. S. (2011). Previous mild traumatic brain injury and postural-control dynamics. *J Athl Train, 46*(1), 85-91. doi:10.4085/1062-6050-46.1.85

Stoffregen, T. A. (1985). Flow structure versus retinal location in the optical control of stance. *J Exp Psychol Hum Percept Perform, 11*(5), 554-565.

Stuss, D. T., Stethem, L. L., Hugenholtz, H., Picton, T., Pivik, J., & Richard, M. T. (1989). Reaction time after head injury: fatigue, divided and focused attention, and consistency of performance. *J Neurol Neurosurg Psychiatry, 52*(6), 742-748.

Sukumar, S., & Waugh, S. J. (2007). Separate first- and second-order processing is supported by spatial summation estimates at the fovea and eccentrically. *Vision Res, 47*(5), 581-596. doi:10.1016/j.visres.2006.10.004

Sunaert, S., Van Hecke, P., Marchal, G., & Orban, G. A. (2000). Attention to speed of motion, speed discrimination, and task difficulty: an fMRI study. *Neuroimage, 11*(6 Pt 1), 612-623. doi:10.1006/nimg.2000.0587

Swaine, B. R., & Friedman, D. S. (2001). Activity restrictions as part of the discharge management for children with a traumatic head injury. *J Head Trauma Rehabil, 16*(3), 292-301.

Tang, Y., & Zhou, Y. (2009). Age-related decline of contrast sensitivity for second-order stimuli: earlier onset, but slower progression, than for first-order stimuli. *J Vis, 9*(7), 18. doi:10.1167/9.7.18

Thompson, J., Sebastianelli, W., & Slobounov, S. (2005). EEG and postural correlates of mild traumatic brain injury in athletes. *Neurosci Lett, 377*(3), 158-163. doi:10.1016/j.neulet.2004.11.090

Thurrell, A. E., & Bronstein, A. M. (2002). Vection increases the magnitude and accuracy of visually evoked postural responses. *Exp Brain Res, 147*(4), 558-560. doi:10.1007/s00221-002-1296-1

Tinius, T. P. (2003). The intermediate visual and auditory continuous performance test as a neuropsychological measure. *Arch Clin Neuropsychol, 18*(2), 199-214.

Topal, N. B., Hakyemez, B., Erdogan, C., Bulut, M., Koksal, O., Akkose, S., . . . Korfali, E. (2008). MR imaging in the detection of diffuse axonal injury with mild traumatic brain injury. *Neurol Res, 30*(9), 974-978. doi:10.1179/016164108X323799

Tweedie, D., Milman, A., Holloway, H. W., Li, Y., Harvey, B. K., Shen, H., . . . Greig, N. H. (2007). Apoptotic and behavioral sequelae of mild brain trauma in mice. *J Neurosci Res, 85*(4), 805-815. doi:10.1002/jnr.21160

Uesaki, M., & Ashida, H. (2015). Optic-flow selective cortical sensory regions associated with self-reported states of vection. *Front Psychol, 6*, 775. doi:10.3389/fpsyg.2015.00775

Ulrich, R., & Miller, J. (1994). Effects of truncation on reaction time analysis. *J Exp Psychol Gen, 123*(1), 34-80.

Vaina, L. M., & Soloviev, S. (2004). First-order and second-order motion: neurological evidence for neuroanatomically distinct systems. *Prog Brain Res, 144*, 197-212. doi:10.1016/S0079-6123(03)14414-7

Vakalopoulos, C. (2005). Neural correlates of consciousness: a definition of the dorsal and ventral streams and their relation to phenomenology. *Med Hypotheses, 65*(5), 922-931. doi:10.1016/j.mehy.2005.05.016

Viano, D. C., Casson, I. R., & Pellman, E. J. (2007). Concussion in professional football: biomechanics of the struck player--part 14. *Neurosurgery, 61*(2), 313-327; discussion 327-318. doi:10.1227/01.NEU.0000279969.02685.D0

Viano, D. C., Casson, I. R., Pellman, E. J., Zhang, L., King, A. I., & Yang, K. H. (2005). Concussion in professional football: brain responses by finite element analysis: part 9. *Neurosurgery, 57*(5), 891-916; discussion 891-916.

Villemure, R., Nolin, P., & Le Sage, N. (2011). Self-reported symptoms during post-mild traumatic brain injury in acute phase: influence of interviewing method. *Brain Inj, 25*(1), 53-64. doi:10.3109/02699052.2010.531881

Wadood, A. C., Azuara-Blanco, A., Aspinall, P., Taguri, A., & King, A. J. (2002). Sensitivity and specificity of frequency-doubling technology, tendency-oriented

perimetry, and Humphrey Swedish interactive threshold algorithm-fast perimetry in a glaucoma practice. *Am J Ophthalmol, 133*(3), 327-332.

Wang, Y., Zhou, Y., Ma, Y., & Leventhal, A. G. (2005). Degradation of signal timing in cortical areas V1 and V2 of senescent monkeys. *Cereb Cortex, 15*(4), 403-408. doi:10.1093/cercor/bhh143

Willer, B., & Leddy, J. J. (2006). Management of concussion and post-concussion syndrome. *Curr Treat Options Neurol, 8*(5), 415-426.

Winter, D. A., Patla, A. E., Prince, F., Ishac, M., & Gielo-Perczak, K. (1998). Stiffness control of balance in quiet standing. *J Neurophysiol, 80*(3), 1211-1221.

Wright, M. J., & Johnston, A. (1983). Spatiotemporal contrast sensitivity and visual field locus. *Vision Res, 23*(10), 983-989.

Yamamoto, T., Smith, C. E., Suzuki, Y., Kiyono, K., Tanahashi, T., Sakoda, S., . . . Nomura, T. (2015). Universal and individual characteristics of postural sway during quiet standing in healthy young adults. *Physiol Rep, 3*(3). doi:10.14814/phy2.12329

Yang, Y., Liang, Z., Li, G., Wang, Y., & Zhou, Y. (2009). Aging affects response variability of V1 and MT neurons in rhesus monkeys. *Brain Res, 1274*, 21-27. doi:10.1016/j.brainres.2009.04.015

Yang, Y., Liang, Z., Li, G., Wang, Y., Zhou, Y., & Leventhal, A. G. (2008). Aging affects contrast response functions and adaptation of middle temporal visual

area neurons in rhesus monkeys. *Neuroscience, 156*(3), 748-757. doi:10.1016/j.neuroscience.2008.08.007

Yeates, K. O., Taylor, H. G., Rusin, J., Bangert, B., Dietrich, A., Nuss, K., . . . Jones, B. L. (2009). Longitudinal trajectories of postconcussive symptoms in children with mild traumatic brain injuries and their relationship to acute clinical status. *Pediatrics, 123*(3), 735-743. doi:10.1542/peds.2008-1056

Zhang, J., Wang, X., Wang, Y., Fu, Y., Liang, Z., Ma, Y., & Leventhal, A. G. (2008). Spatial and temporal sensitivity degradation of primary visual cortical cells in senescent rhesus monkeys. *Eur J Neurosci, 28*(1), 201-207. doi:10.1111/j.1460-9568.2008.06300.x

zu Eulenburg, P., Caspers, S., Roski, C., & Eickhoff, S. B. (2012). Meta-analytical definition and functional connectivity of the human vestibular cortex. *Neuroimage, 60*(1), 162-169. doi:10.1016/j.neuroimage.2011.12.032

Chapitre 3 : Article 2

Balance deficits in adults with mild traumatic brain injury revealed by postural instability measures

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Abstract

After a mild traumatic brain injury (mTBI), patients frequently complain of balance problems and/or dizziness, even beyond the acute stage of injury. However, standard clinical assessment of balance most often fails to objectivize these symptoms, especially if they are lingering. This study investigated the impact of mTBI on postural control. Fifteen adults (18 to 40 years old) diagnosed with mTBI were assessed at 15 days, 3 months and 12 months after injury. Fifteen matched non-injured controls followed the same testing schedule. Antero-posterior body sway amplitude (BSA) and postural instability (given by body sway velocity root mean square, vRMS) were measured in five different conditions: with eyes closed and in a 3D virtual reality tunnel, either static or sinusoidally moving in the antero-posterior direction at 3 different frequencies (0.125, 0.25 and 0.5 Hz). Measures derived from clinical balance tests were also used. Participants diagnosed with mTBI exhibited more postural instability (i.e. higher body sway vRMS) than control participants at 2 weeks and at 3 months post-injury, regardless of the testing condition. These mTBI-related balance deficits were no longer present one year post-injury. Results also showed that visual processing impairments might have contributed to mTBI-related balance deficits. Antero-posterior BSA as well as clinical tests were not sensitive enough to evidence mTBI-related balance deficits. It is concluded that postural instability deficits given by body sway vRMS are still present in young adults at 3 months but not at 12 months post mTBI.

Key words: mild traumatic brain injury (mTBI), balance, postural instability

1. Introduction

Accounting for about 80% of *all treated* traumatic brain injuries, and with an actual rate estimated to exceed 600/100 000 cases per year (Cassidy et al., 2004), mild traumatic brain injuries (mTBIs) constitute a major public health concern. The diagnosis, prognosis and initial treatment of an mTBI mostly rely upon functional signs and symptoms present at the acute stage rather than on an objective examination of microscopic brain lesions (G. Iverson, 2007; Kontos et al., 2012; Leddy et al., 2007; Naunheim et al., 2008; P. M. Rees, 2003; R. J. Rees & Bellon, 2007; Ropper & Gorson, 2007; Sheedy et al., 2006; Sheedy et al., 2009; Willer & Leddy, 2006), which remain most often undetectable with tools usually used for clinical investigation (e.g. CT scan) (Gaetz, 2004; Lee et al., 2008; Lewine et al., 2007; P. M. Rees, 2003; Topal et al., 2008).

Although functional signs and symptoms of mTBIs are generally transient (Harmon et al., 2013; Naunheim et al., 2008) and may resolve within a few days or weeks (McCrea et al., 2003), they can persist for months, even years in a significant proportion of individuals (Bigler, 2008; Evans, 2004; Findling et al., 2011; Geurts et al., 1999; Geurts et al., 1996; G. Iverson, 2007; G. L. Iverson, 2005; Kaufman et al., 2006; King et al., 2014; Kleffelgaard, Roe, Soberg, & Bergland, 2012; Konrad et al., 2011; Leddy et al., 2007; Lewine et al., 2007; Marshall et al., 2015; McAllister & Arciniegas, 2002; P. M. Rees, 2003; Ropper & Gorson, 2007; R. Ruff, 2005; R. M. Ruff, 2011; Shaw, 2002; Sheedy et al., 2006; Sheedy et al., 2009; Willer & Leddy, 2006). Unfortunately, most of the time, conventional clinical examination fails to objectivise the signs or deficits behind these symptoms (Evans, 2004; Fife & Kalra,

2015; King et al., 2014; Marshall et al., 2015). Hence, clearly understanding the symptomatology and the functional deficits related to an mTBI, as well as the time-course of their resolution or their potential persistence, remains elusive.

Among acute signs left by an mTBI and that can lead to long-lasting symptoms are dizziness and balance problems (Fife & Kalra, 2015; Findling et al., 2011; Geurts et al., 1999; Geurts et al., 1996; Kaufman et al., 2006; King et al., 2014; Kleffelgaard et al., 2012). Balance is maintained as a function of the vestibular, somatosensory (i.e. proprioceptive), and visual systems (Peterka, 2002). A broad part of the brain is involved in visual and somatosensory perception (Billino et al., 2011; Dumoulin et al., 2003; Dupont et al., 2003; Farivar, 2009; Ferre, Walther, & Haggard, 2015; Kalaycioglu et al., 2009; Nishiike, Nakagawa, Tonoike, Takeda, & Kubo, 2001; Noguchi et al., 2005; Slobounov, Wu, et al., 2006; Sunaert et al., 2000; Uesaki & Ashida, 2015; Vaina & Soloviev, 2004; Vakalopoulos, 2005), and the vestibular system comprises numerous structures scattered in the brain (Dieterich & Brandt, 2015; Guldin & Grusser, 1998; zu Eulenburg et al., 2012). Due to the diffuse nature of the brain lesions left by an mTBI (Bayly et al., 2005; Bigler, 2007; Gaetz, 2004; Lewine et al., 2007; Nishimoto & Murakami, 1998; Shaw, 2002; Topal et al., 2008; Viano et al., 2007; Viano et al., 2005), many of these structures along with their connections could be impaired by such an injury.

Postural instability measures have been shown to reveal balance deficits following an mTBI (Findling et al., 2011; Gagnon et al., 2004a; Geurts et al., 1999; Geurts et al., 1996; Guskiewicz et al., 2001; Kaufman et al., 2006; King et al., 2014; Kleffelgaard et al., 2012; McCrea et al., 2003; Sheedy et al., 2006; Sheedy et al., 2009; Sosnoff et

al., 2008), even in asymptomatic individuals (Slobounov et al., 2008; Slobounov et al., 2012; Slobounov et al., 2005; Slobounov et al., 2011; Slobounov, Tutwiler, et al., 2006; Thompson et al., 2005). However, there are still discrepancies concerning long-term balance deficits, as well as time-to-recovery. These discrepancies may arise in part from methodological issues. For instance, there are more studies having investigated balance deficits following mTBI in collegiate and university athletes (Guskiewicz et al., 2001; McCrea et al., 2003; Slobounov et al., 2008; Slobounov et al., 2012; Slobounov et al., 2005; Slobounov et al., 2011; Slobounov, Tutwiler, et al., 2006; Sosnoff et al., 2008; Sosnoff et al., 2011; Thompson et al., 2005) than in patients recruited from the general population (Findling et al., 2011; Geurts et al., 1999; Geurts et al., 1996; Kaufman et al., 2006; Sheedy et al., 2006; Sheedy et al., 2009). Also, some studies used cost-effective clinical tests like the Balance Error Scoring System (BESS) test (McCrea et al., 2003; Sheedy et al., 2006; Sheedy et al., 2009), while others used measures derived from body kinematics (Findling et al., 2011; Geurts et al., 1999; Geurts et al., 1996; Kaufman et al., 2006; Slobounov et al., 2008; Slobounov et al., 2012; Slobounov et al., 2005; Slobounov et al., 2011; Slobounov, Tutwiler, et al., 2006; Thompson et al., 2005). As for the time-course of recovery, or regarding the investigation of long-term balance deficit following mTBI, some studies used repeated measures at equal time-points for all participants (Guskiewicz et al., 2001; McCrea et al., 2003; Slobounov et al., 2012; Slobounov, Tutwiler, et al., 2006), while others comprised a single assessment at unequal times since injury between subjects (Geurts et al., 1999; Geurts et al., 1996; Kaufman et al., 2006; King et al., 2014; Sosnoff et al., 2011; Thompson et al., 2005).

Nevertheless, what emerges from the literature is that (1) balance deficits are noticeable in the acute stage following mTBI, regardless of the balance measures used and of the population category (Guskiewicz et al., 2001; McCrea et al., 2003; Sheedy et al., 2006; Sheedy et al., 2009; Slobounov, Tutwiler, et al., 2006; Sosnoff et al., 2008); (2) in concussed collegiate athlete populations, such deficits have been reported to last within 3 to 5 days using the BESS test (Guskiewicz et al., 2001; McCrea et al., 2003), and up to 30 days using body kinematics-derived measures (Slobounov et al., 2008; Slobounov, Tutwiler, et al., 2006), while in the general population they have been reported to last for months, even years, using body kinematics-derived measures (Findling et al., 2011; Geurts et al., 1999; Geurts et al., 1996; Kaufman et al., 2006). Unfortunately, concerning adult patients with mTBI from the general population no longitudinal study is available, and BESS test has been used only in the acute stage of the injury (Sheedy et al., 2006; Sheedy et al., 2009). In children with mTBI, balance deficits have been reported to persist 3 months after the injury using a clinical test, the Bruininks-Oseretsky Test of Motor Proficiency (BOTMP), and other measures that challenge postural stability (Gagnon et al., 2004a). Else, studies done on student athletes showed that mTBI-related symptoms resolved within 7 to 15 days post-injury (McCrea et al., 2003; Slobounov et al., 2012; Slobounov et al., 2005; Slobounov et al., 2011; Slobounov, Tutwiler, et al., 2006). Also, some studies investigating mTBI-related lingering balance (Slobounov et al., 2008) or postural-related (Thompson et al., 2005) deficits in student-athletes involved only asymptomatic participants, whereas concerning patients from the general population all studies recruited exclusively participants seeking care because they

had persisting disabling symptoms of impaired balance (Findling et al., 2011; Geurts et al., 1999; Geurts et al., 1996; Kaufman et al., 2006). Finally, the only posture-related measures that seem to allow tracking the time-course recovery (Slobounov et al., 2012) and also to provide insight into the subtle long-term deficits following mTBI in athletes, even in the absence of symptoms (Thompson et al., 2005), are EEG data. Two longitudinal studies have tracked the time-course of recovery of balance deficits following mTBI in adults, both of them involving collegiate athletes. The first-one (McCrea et al., 2003), using BESS and neuropsychological test measures, as well as self-reported symptoms questionnaire over a 90-day period, found all symptoms and functional impairments (cognitive and balance) to resolve by 7 days post-injury. The second-one (Slobounov et al., 2012) combined EEG and body kinematics-derived measures throughout a one-year period. EEG measures were used to determine alpha power decrease from sitting to standing posture (both postures with eyes closed). These researchers consider alpha power decrease as an index of postural control deficits following an mTBI (Thompson et al., 2005). They found balance deficits to last less than 30 days post-injury compared to baseline, as revealed by body kinematics-derived measures (increase of center of pressure area while standing upright with eyes closed as compared to eyes open), while EEG data revealed that most of mTBI participants whose posture-related cerebral activity changed by more than 20% seven days post-injury (proportion of mTBI participants not mentioned) did not returned to pre-injury level one year post-injury. It should be noticed here that the BESS test uses exclusively stances with eyes closed, and that EEG results of the second study (Slobounov et al., 2012) were done with eyes

closed. Moreover, still in the second study, no information is available about the visual environment or simulation used for kinematics-derived measures. Hence, the need for more longitudinal studies investigating the time-course of recovery and the possible lingering of balance deficits following mTBI seems obvious (Sosnoff et al., 2011).

The goal of this longitudinal study was to explore if different evaluations of postural balance are sensitive enough to detect deficits in upright stance in adults in the year following an mTBI. The specific objectives were: (1) to assess the effects of visual integration in a virtually controlled environment; (2) to evaluate specific items taken from standardised clinical tests of balance and reflecting varying levels of difficulty in balance control tasks; and (3) to determine if results of these evaluations vary at 2 weeks, 3 months and 12 months after the mTBI.

2. Material and method

This study received the approval from the institutional research ethics boards of the Hôpital du Sacré-Cœur de Montréal (HSCM), Montreal Children's Hospital of the McGill University Health Centre (MCH-MUHC), and Université de Montréal.

2.1. Participants

Two groups of 15 subjects each (2 females, 13 males), ranging from 17.8 to 39.8 years old, participated in this prospective longitudinal study: a group of subjects diagnosed with an mTBI (mean age at first testing session: 29.2 ± 6.8 years), and a group of control subjects matched for age (29.3 ± 6.8 years at first testing session),

sex, handedness (Dieterich & Brandt, 2015), and, whenever possible, education level. All subjects gave their informed consent prior to participating in this study.

Subjects in the mTBI group were volunteers recruited following their admission at the emergency department (ED) of HSCM, and of the MCH-MUHC. They were eligible if they fulfilled the following criteria: (1) diagnosis of mTBI from a physician at the ED (based on the WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury definition of mTBI (Carroll et al., 2004; R. M. Ruff et al., 2009)); (2) mTBI was not concomitant with any substance consumption affecting alertness or arousal state; (3) no mTBI other than the index injury in the last 12 months; (4) no problematic alcohol consumption; (5) no substance consumption on consistent basis; (6) no pre-injury diagnosed psychiatric or learning disorder; (7) no pre-injury vestibular and/or balance and/or musculoskeletal disorder ; (8) no fractures or cut preventing participation in experimentations; (9) being aged 17-40 years. Coordinators of trauma programs obtained a first consent from each subject of the mTBI group, giving the first author the authorisation to contact them by phone. This phone interview was aimed at carefully confirming that inclusion criteria 3 to 8 listed above were fulfilled and that subjects were fluent in French or English. None of the injured participants were engaged in litigation or compensation issues for their mTBI.

This report is part of a multidisciplinary project investigating long-lasting effects of mTBI in various fields connected to visual perception. All participants in this experiment also participated in another experiment previously reported and investigating visual perception and reaction time deficits following an mTBI. The

characteristics of participants of mTBI group can be found elsewhere (Piponnier et al., 2015).

Subjects of the control group were recruited among patients of the Université de Montréal School of Optometry Clinic and friends of mTBI participants. Prior to participation, control subjects also underwent a phone screening. They had to fulfil the same criteria as mTBI subjects, and their medical history also had to be clear of mTBI.

Prior to participating in the study and at every visit, subjects of both groups underwent a complete optometric examination (see Piponnier et al. (2015) for further details). Participants had a visual acuity of 6/6 or better. Their binocular vision, ocular health and central visual fields were within normal limits.

All participants were administered the Test of Nonverbal Intelligence – Third Edition (TONI-3) (Brown et al., 1997) at their first testing session. Standard score had to be at least of 85 to participate in the study. This test was also administered to ensure that both groups had comparable levels of general cognitive skills. A one-way ANOVA (*Group* factor) showed no significant IQ difference ($F(1, 29) = 0.462$, $p = 0.502$) between mTBI (Mean Scaled Score ± SD = 110.40 ± 14.22) and control (107.13 ± 12.02) groups (Fisher et al., 2000).

Finally, to make sure there was no attention deficit, each participant had to fill the Conners' Adult ADHD Rating Scale–Self-report: Short Version (CAARS-S: S) (Conners, 1997). All participants obtained T-Scores within the mean range or below, confirming the absence of overt attention deficits in both groups.

2.2. Apparatus

The main experiment was conducted in an EON Icube™ 3D virtual immersive environment. The EON Icube™ is a room where the visual scene is projected on 3 walls (1 front and 2 lateral walls) and the floor by four synchronized projectors (projectiondesign® F10). Two identical images, one for each eye, are displayed with a spatial disparity. Stereoscopic vision is made possible by the wear of stereoscopic LCD shutter glasses (CrystalEyes® 4s RealD). A motion tracking system (12 cameras OptiTrack™ Flex:V100r2; software: Tracking Tools 2.5) records the position and the orientation of the observer in space. This allows updating the image in real time as to maintain the viewing perspective of the observer (Piponnier et al., 2009). The EON Icube™ was under the computer control of an Intel Xeon E5530 (NVIDIA Quadro FX 5800 graphic card) along with four Hewlett Packard Z800 workstations.

2.3. Stimuli

We used a two-side open-ended tunnel oriented in the antero-posterior direction (*Figure 1*). The inner wall of this tunnel was covered with a black and white checkerboard. Each element of this checkerboard was a rectangle of 1 m long and 0.58 m wide. The virtual tunnel was 20 m long and 3 m in diameter. The background at the front extremity of the tunnel was black. Subjects were placed at 7 m from the virtual back extremity of the tunnel at the position z=0 (see equation of motion below). A red point of fixation subtending 29.5' was virtually located at 7 m from the subjects and at equal distance from the lateral wall (i.e. 1.5 m high and 1.5 m from the lateral wall). The tunnel was either static or sinusoidally moved on the antero-posterior axis

at three different frequencies (0.125, 0.25 and 0.5 Hz) and an amplitude of 2 m (± 1 m). The equation of motion of the tunnel is

$$z(t) = \frac{A}{2} \sin(\omega + \varphi),$$

where *z* is the position of the tunnel at time *t, A* is the amplitude (in meters), ω is the frequency (in Hertz) and φ is the phase (in degrees).

This optic-flow structure has been shown to be ecological (Daniel & Whitteridge, 1961; Gibson, 1979; Wright & Johnston, 1983). Moreover, it has been proven that the visual system was highly sensitive to such an optic-flow structure and consequently quite responsive to it with respect to the control of stance (Piponnier et al., 2009; Stoffregen, 1985; Uesaki & Ashida, 2015).

2.4. Procedure

Subjects were placed at 1.20 m from the front screen and at equal distance from lateral screens. They stood upright, barefoot, with feet together and arms crossed over the chest. They were asked to stand still and to stare at the point of fixation. Their body movements were assumed to correspond to those of an inverted pendulum as previously demonstrated in similar conditions (Faubert & Allard, 2004; Winter, Patla, Prince, Ishac, & Gielo-Perczak, 1998).

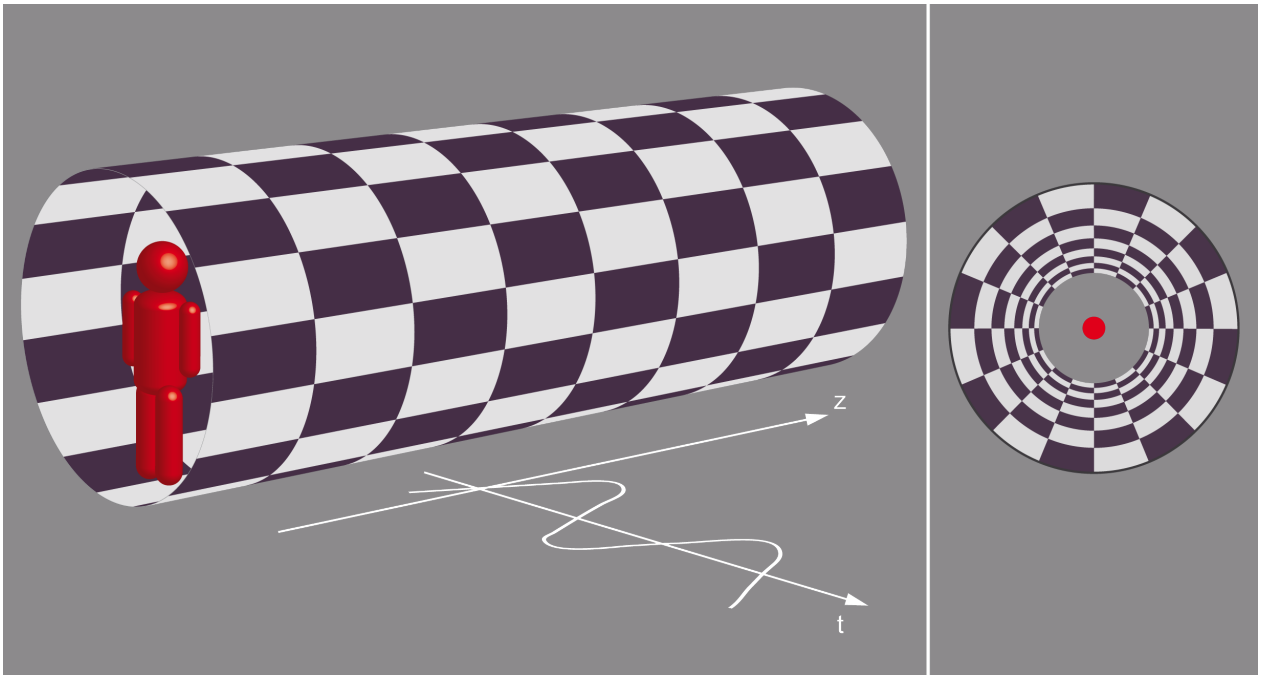

Figure 1. Schematic representation of the tunnel.

Left panel: side view in perspective with an illustration of the equation of motion; right panel: inner view.

At each testing session, the subjects performed a first trial with eyes closed. They then performed a series of 4 trials, eyes open. Three of these trials were optic flow (or dynamic) conditions (one per frequency, i.e., 0.125, 0.25, and 0.5 Hz), and the fourth one was a static tunnel condition. Conditions inside the series were randomly presented. Eyes closed and static tunnel conditions served as control conditions.

Each trial lasted 68 s. In the series, the inter-trial interval was 5 s. The position of each subject was recorded, by the motion tracking system, over the last 64 s of the trial with a sampling rate of 64 Hz.

Two outcome measures, antero-posterior body sway amplitude (BSA) and postural instability index of the subjects were computed from these recordings (Faubert &

Allard, 2004; Greffou, Bertone, Hanssens, & Faubert, 2008). The BSA corresponds to the amplitude of oscillation of the subject, in degrees, in the axis of motion and at the corresponding moving frequency of the tunnel. The postural instability is given by the body sway velocity root mean square (vRMS, in degrees per second (°/s)) at all the frequencies and in all directions in a horizontal plane except the frequency and direction of the moving tunnel.

2.5. Clinical balance tests

As a comparison purpose, we also used selected items from clinical tests: the Bruininks-Oseretsky Test of Motor Proficiency 2nd edition (BOT-2) (Bruininks & Bruininks, 2005) and the Balance Error Scoring System (BESS) (Bell, Guskiewicz, Clark, & Padua, 2011). The BOT-2 and its former version (BOTMP) have been used to assess balance in concussed paediatric populations (DeMatteo, Greenspoon, Levac, Harper, & Rubinoff, 2014; Gagnon et al., 1998). The BOT-2 has been chosen as the overall study included a paediatric sample whose measures will be compared to those of the adult sample in a future report. The BESS is used on sports fields sideline for concussion management purposes (items on a firm support only) (Harmon et al., 2013) and has been used in mTBI studies (Bell et al., 2011; Guskiewicz et al., 2001; King et al., 2014; McCrea et al., 2003).

We used the following items of the BOT-2 balance subtest: 3 (standing on one leg on a line (on the floor) – eyes open), 6 (standing on one leg on a line – eyes closed), 7 (standing on one leg on a balance beam – eyes open), 8 (standing heel-to-toe on a balance beam – eyes open), and 9 (standing on one leg on a balance beam – eyes

closed). For these items, subjects wore running shoes. Trials were stopped according to the BOT-2 administration rules.

As for the BESS, the items on foam surface (one-leg, tandem, and feet together stances) were used, as it has been shown that difficult stances (i.e., on foam surface) had better agreement with laboratory-based measures of postural control than easier ones (i.e., on firm support) (Bell et al., 2011). For these tests, subjects were barefoot. Trials were stopped if any error occurred according to the BESS administration rules. However, contrary to the BESS administration rules, subjects were not allowed to get back to their position if they failed to maintain the stance.

For all these balance tests, subjects stood on the dominant leg (defined as the preferred kicking leg) for the single-leg stance, and for the tandem stance the dominant leg was in the back, according to BOT-2 (and contrary to BESS) procedure.

For each test, we measured the time subjects were able to maintain the stance as instructed. Each test was repeated twice at each session. The mean time of each test was taken for statistical analyses.

2.6. Self-reported symptoms recording

At each testing session, participants self-reported their symptoms using the Post-Concussion Symptom Scale – Revised (PCSS-R) (Lovell & Collins, 1998; Naunheim et al., 2008). More details on the procedure as well as total score results and analysis have been reported elsewhere (Piponnier et al., 2015). In the present report, we focussed on balance-related symptoms listed in the PCSS-R, namely: “balance problems” and “dizziness.”

2.7. Statistical analysis

Statistical analyses were made on logarithmic values of the body sway computed data (BSA and body sway vRMS). As, for technical reasons (recording failure), we had data completely missing at random (63 out of 810 for BSA, and the same for body sway vRMS) we used factorial repeated linear mixed model procedures for BSA and body sway vRMS data to achieve their analyses of variance (*Condition* x *Frequency* x *Session* x *Group*). The levels of the factor *Condition* are *Eyes closed*, *Dynamic tunnel*, and *Static tunnel*. For these linear mixed model procedures, we used a first-order heterogeneous factor-analytic covariance structure.

Statistical analyses were made on the mean duration of stance for BOT-2 and BESS tests. For these measures, we used 3-way (*Condition* x *Session* x *Group*) repeated measures ANOVAs.

The level of post-concussion balance-related self-reported symptoms was analysed using a 3-way (*Symptom* x *Session* x *Group*) repeated measures ANOVA.

The Greenhouse-Geisser corrective factor was used for standard repeated measures ANOVA procedures.

Whenever justified, we made pairwise comparisons and simple effects tests based on pairwise comparisons, using the Šídák correcting method.

Finally we used two-tailed bivariate Pearson's correlations in order to investigate the relationship between the levels of symptoms and postural measures (BSA, body sway vRMS, and mean duration of stance measured with BOT-2 and BESS stance tasks). Missing values (BSA and body sway vRMS; Little's MCAR test: $\chi^2 = 0.000$, DF = 402,

p = 1.000) were replaced using multiple imputations, and correlation results from pooled estimates were used.

3. Results

3.1. Body sway antero-posterior amplitude

There was neither significant difference between groups (F(1, 29.323) = 2.397, p = 0.132), nor significant *Session* main effect (F(2, 157.731) = 2.396, p = 0.094), indicating that BSA was similar between mTBI and control participants, regardless of the session.

However, there was a significant *Condition* main effect (F(2, 69.195) = 176.675, p < 0.001). Pairwise comparisons showed that BSA was significantly greater in the *Eyes closed* than in the *Static tunnel* condition (p = 0.011), and significantly greater in the *Dynamic tunnel* than in the *Eyes closed* and *Static tunnel* conditions (p < 0.0001) (*Figure 2*).

There was also a significant *Frequency* main effect (F(2, 203.826) = 218.770, p < 0.001), where BSA was the largest at the lowest frequency (0.125 Hz) and significantly decreased with increasing frequency, regardless of the condition (*Figure 3*). Moreover, there was a significant *Frequency* x *Condition* interaction (F(4, 221.227) = 10.002, p < 0.0001) indicating that the variation of BSA as a function of frequency differed between conditions, and that the variation of BSA as a function of condition differed between frequencies. No other interaction was significant.

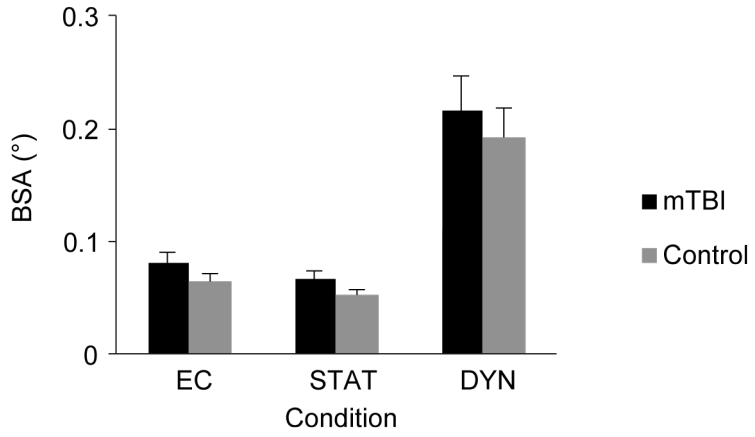

Figure 2. BSA as a function of Condition for mTBI and control group.

Marginal estimated mean ± SE across all oscillation frequencies and testing sessions.

EC: Eyes closed; STAT: Static tunnel; DYN: Dynamic tunnel.

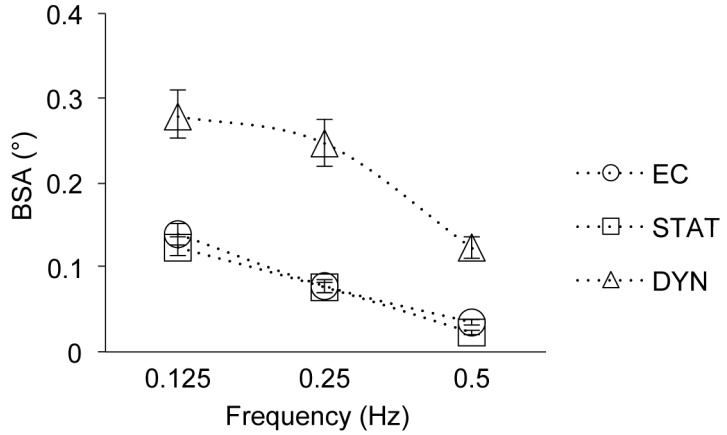

Figure 3. BSA as a function of frequency for each condition.

Marginal estimated mean ± SE across all participants and testing sessions. EC: Eyes closed; STAT: Static tunnel; DYN: Dynamic tunnel.

3.2. Body sway velocity root mean square

There was a significant *Group* main effect ($F(1, 29.660) = 4.793$, $p = 0.037$), indicating that body sway vRMS was globally significantly greater for mTBI than for control group.

There was also a significant *Session* main effect ($F(2, 68.685) = 9.943$, $p < 0.001$), and a significant *Group* x *Session* interaction ($F(2, 68.685) = 5.503$, $p = 0.006$). Pairwise comparisons revealed that (1) the body sway vRMS difference between groups was significant only at the 2 weeks and 3 months post-injury ($p = 0.002$ and $p = 0.010$, respectively); (2) the body sway vRMS was similar across sessions in the control group; (3) the decrease of body sway vRMS in the mTBI group was significant only between 3 months and one year post-injury ($p < 0.0001$) (*Figure 4*).

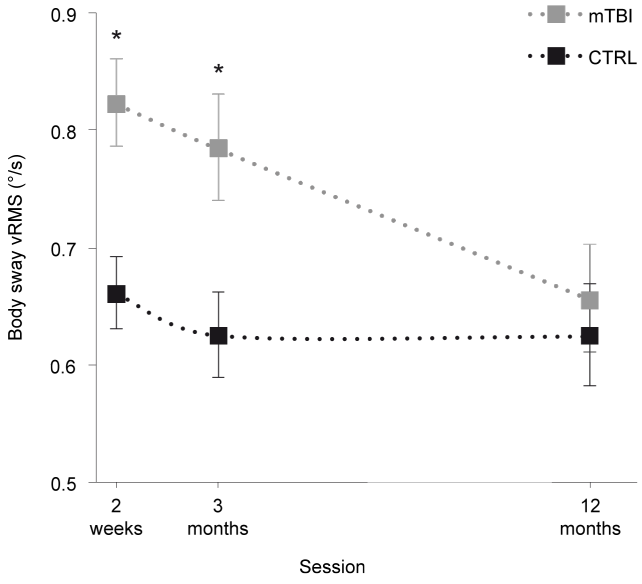

Figure 4. Body sway vRMS as a function of session time.

Marginal estimated mean ± SE across all conditions for mTBI and control (CTRL) groups. * indicates a significant difference between groups ($p \leq 0.01$).

The interaction *Group* x *Condition* x *Session* was not significant ($F(4, 99.936) = 1.532$, $p = 0.199$). However, because of the large data set, effects may have been washed out. Tests of simple effects of the factor *Group* within each level combination of *Condition* and *Session* effects, based on pairwise comparisons, revealed that body sway vRMS was significantly greater in the mTBI than in the control group in some conditions (*Figure 5*). At 2 weeks post-injury, body sway vRMS was significantly greater in the mTBI group in the *Eyes closed* ($F(1, 42.198) = 8.942$, $p = 0.005$) and *Static tunnel* ($F(1, 54.051) = 12.974$, $p = 0.001$) conditions, but not in the dynamic conditions ($F(1, 34.996) = 1.399$, $p= 0.245$)). At 3 months post-injury, body sway vRMS was significantly greater in the mTBI group in the *Static tunnel* ($F(1, 41.001) = 7.910$, $p = 0.008$) and *Dynamic tunnel* ($F(1, 37.305) = 7.651$, $p = 0.009$) conditions, but not in the *Eyes closed* ($F(1, 24.241) = 2.071$, $p= 0.163$)) condition. In the mTBI group, tests of simple effects of the factor *Session* within each level combination of *Group* and *Condition* effects, based on pairwise comparisons, also revealed that body sway vRMS significantly decreased across sessions in the *Eyes closed* ($F(2, 75.452) = 5.685$, $p = 0.005$) and *Static tunnel* ($F(2, 41.496) = 9.210$, $p < 0.001$) conditions, but not in the *Dynamic tunnel* condition ($F(4, 88.941) = 2.130$, $p = 0.125$). Else, in the control group, pairwise comparisons of the levels of the factor *Condition* showed no significant difference between conditions, regardless of the session ($p \geq 0.084$).

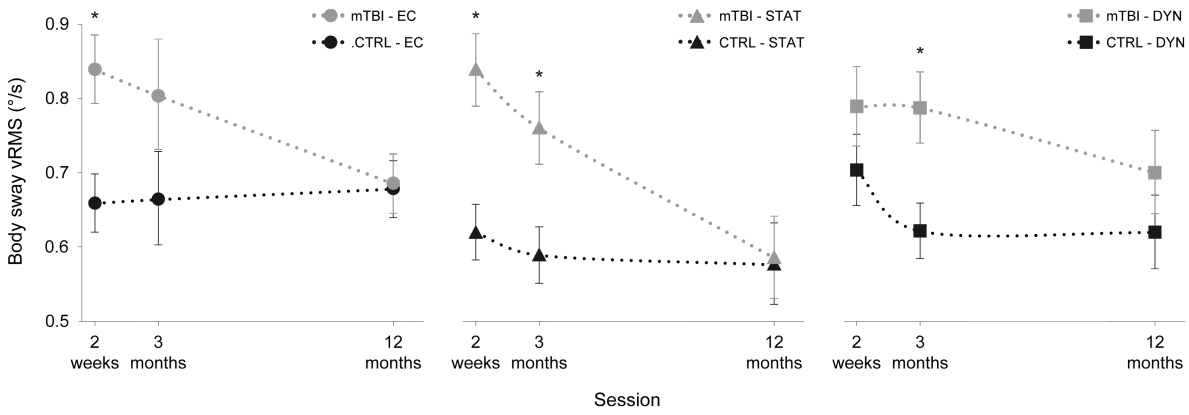

Figure 5. Body sway vRMS (marginal estimated mean ± SE) as a function of session time for each condition for mTBI and control (CTRL) groups.

EC: Eyes closed; STAT: Static tunnel; DYN: Dynamic tunnel. * indicates a significant difference between groups ($p \leq 0.009$).

3.3. BOT-2 and modified BESS measures

There was no significant *Group* main effect for modified BOT-2 ($F(1, 28) = 1.494$, $p = 0.232$), nor for modified BESS ($F(1, 28) = 1.995$, $p = 0.169$) measures (*Figures 6 & 7*, respectively). There was also no significant interaction implicating the *Group* factor for both modified BOT-2 and modified BESS data.

There was, however, a significant *Condition* main effect for both the modified BOT-2 ($F(4, 25) = 132.560$, $p < 0.0001$) and modified BESS ($F(2, 27) = 135.408$, $p < 0.0001$) measures, indicating differences among tested balance tasks. For the modified BOT-2 measures, pairwise comparisons related to the *Condition* factor revealed that (1) there was no significant difference between stances in eyes open conditions (one leg on a line, one leg on a beam, and heel-to-toe on a beam; $p \geq 0.054$); (2) stances was longer with eyes open than with eyes closed (one leg on a line and one leg on a

beam; $p < 0.0001$); (3) with eyes closed, stance was longer one leg on a line (on the floor) than one leg on a beam ($p < 0.0001$). For the modified BESS measures, pairwise comparisons related to the *Condition* factor revealed that maintenance of stance was significantly longer: (1) in the feet together than in the heel-to-toe stance ($p < 0.0001$); (2) in the feet together than in the one leg stance ($p < 0.0001$); and (3) in the heel-to-toe than in the one leg stance ($p < 0.001$). In other words, in both modified BOT-2 and modified BESS, mean duration of stance decreased as stance difficulty increased.

There was also a significant *Session* main effect for modified BOT-2 ($F(2, 27) = 9.760$, $p < 0.0001$), and for modified BESS ($F(2, 27) = 8.538$, $p = 0.001$) measures, as well as a significant *Condition* x *Session* interaction for modified BOT-2 measures only ($F(8, 21) = 4.195$, $p = 0.001$). For the modified BOT-2, pairwise comparisons related to the *Condition* x *Session* interaction revealed that stance duration increased between the first and the third session on one leg on a line with eyes closed ($p = 0.045$) and on one leg on a beam with eyes closed ($p = 0.002$). For the modified BESS, the significant *Session* main effect indicated that stance duration increased from session to session, regardless of the stance task. These results altogether suggest that there was a learning effect for all the eyes closed stance tasks.

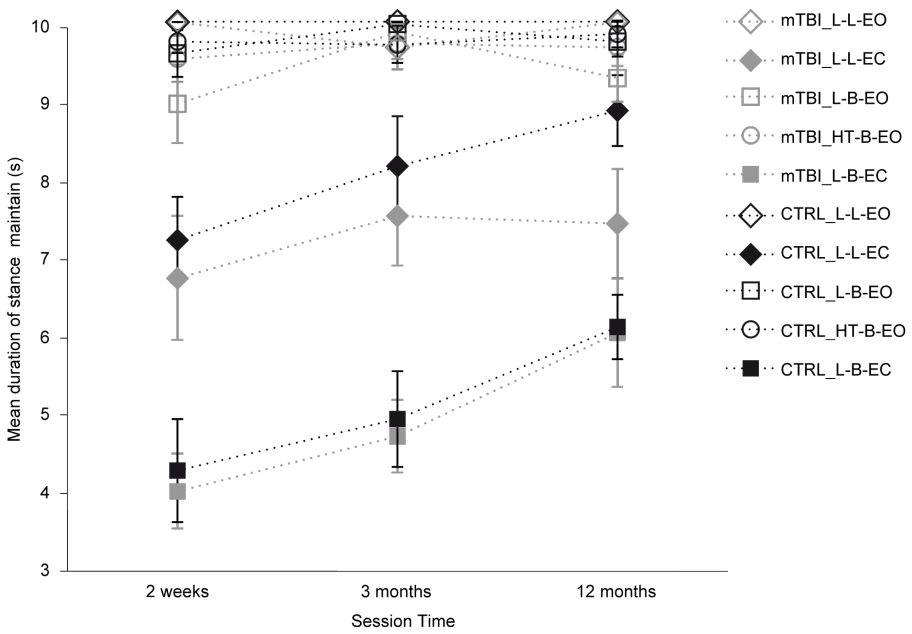

Figure 6. Modified BOT-2 duration of stance as a function of session time.

Mean ± SE for each condition for mTBI and control (CTRL) groups. L-L: one leg on a line (on floor); L-B: one leg on a beam; HT-B: heel-to-toe on a beam; EO: eyes open; EC: eyes closed. Notice that open symbols represent opened eyes tasks and filled symbols represent closed eyes tasks.

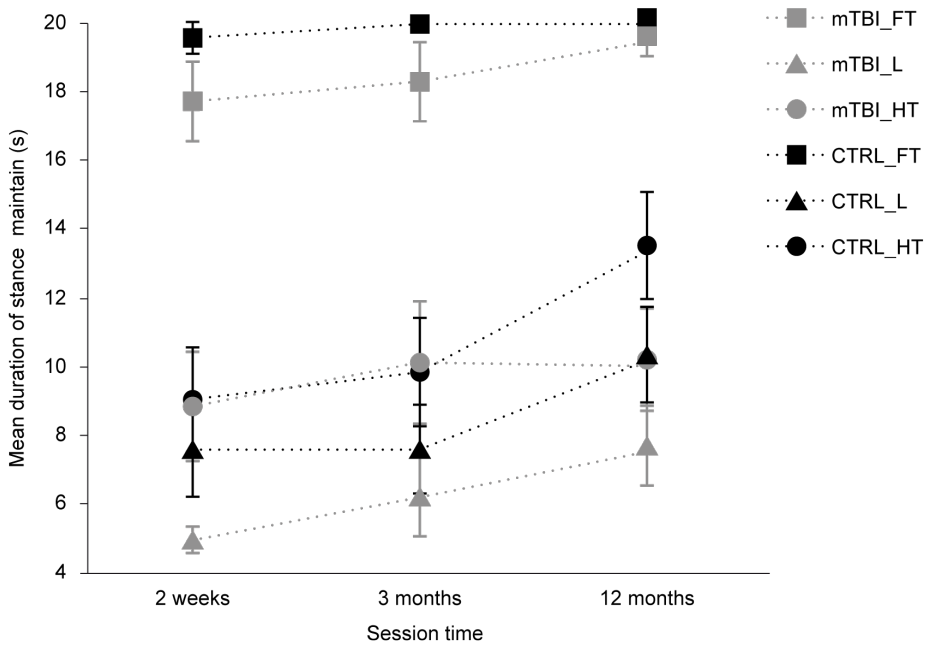

Figure 7. Modified BESS duration of stance as a function of session time.

Mean ± SE for each condition for mTBI and control (CTRL) groups.

FT: feet together; L: one leg; HT: heel-to-toe. All these balance tasks are done standing on a foam with eyes closed.

Finally, the *Group* x *Condition* x *Session* interaction was explored with pairwise comparisons of group mean stance durations for both the modified BOT-2 and modified BESS measures ($F(8, 21) = 0.453$, $p = 0.809$ and $F(4, 25) = 1.863$, $p = 0.134$, respectively). In the modified BOT-2 test, there was a trend ($F(1, 28) = 3.188$; $p = 0.085$) for poorer balance in the mTBI group in only one condition (standing on one leg on a line with eyes closed) at 12 months after the mTBI (*Figure 6*). For the modified BESS measures, there was also a trend ($F(1, 28) = 3.688$; $p = 0.065$) only for the condition standing on one leg (with eyes closed, on a foam support) to allow

discriminating between mTBI and control participants, two weeks after the mTBI (*Figure 7*).

3.4. Post-concussion balance-related self-reported symptoms

The mTBI participants reported significantly more *balance problems* and *dizziness* (i.e., balance-related symptoms listed on the PCSS-R) than control participants ($F(1, 28) = 13.772$, $p = 0.001$) (*Figure 8*). Globally, levels of *balance problems* and *dizziness* were similar one another ($F(1, 28) = 0.700$, $p = 0.410$) in mTBI participants. Neither the *Session* main effect ($F(2, 56) = 2.680$, $p = 0.092$), nor the *Group* x *Session* interaction ($F(2, 56) = 3.154$, $p = 0.064$) was significant, indicating that the level of post-concussion balance-related self-reported symptoms remained similarly higher across sessions in the mTBI than in the control group. Nevertheless, considering the scoring scale of the PCSS-R, the levels of symptoms were really mild on average in the mTBI group.

No correlation between levels of symptoms and any of the postural measures (BSA, body sway vRMS, and modified BOT-2 and modified BESS measures) was significant.

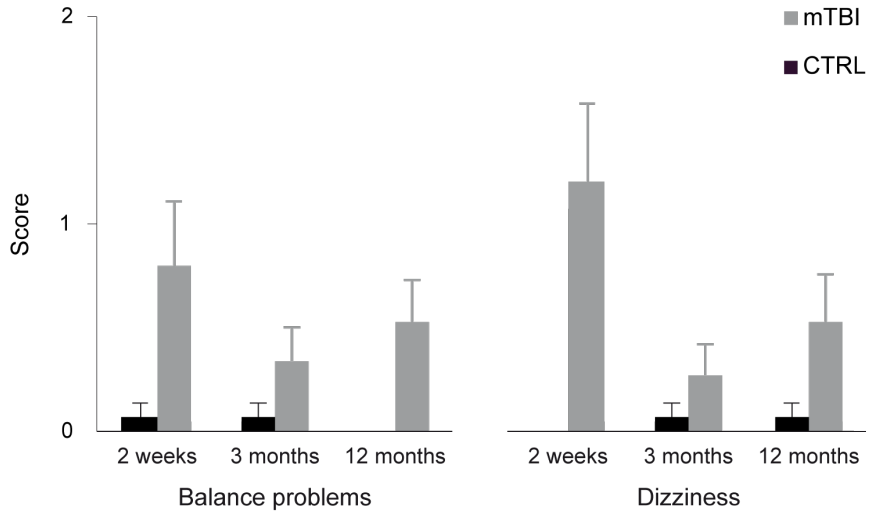

Figure 8. Post-concussion balance-related self-reported symptom scores from PCSS-R (balance problems and dizziness) as a function of session time.

Mean ± SE. Symptom scoring scale of the PCSS-R: No symptom: score = 0; Mild: score = 1; Moderate: score = 2-4; Severe: score = 5-6.

4. Discussion

4.1. Antero-posterior body sway amplitude (BSA) measures

BSA did not appear to be a measure sensitive enough to reveal subtle mTBI-related balance deficits. Indeed, it was similar between both mTBI and control groups, regardless of the session, condition, and frequency. However, there was a trend for the BSA across all conditions and sessions to be larger for the mTBI than for the control group (*Figure 2*). The fact that, on one hand, impairments left by an mTBI are subtle most of the time, and that, on the other hand, BSA focuses on a limited aspect of the postural sway during the control of quiet stance, may explain that we could not reveal differences between groups using BSA measures.

Nevertheless, what can be noticed is that, BSA-related results indicate that (1) a postural response has been visually elicited in the *Dynamic tunnel* conditions; (2) static visual cues helped controlling antero-posterior spontaneous postural sway (*Figure 2*); (3) BSA was larger at lower frequencies and decreased with increasing frequency (*Figure 3*). All these results replicate those of a previous study done on young healthy adults with similar paradigm and experimental device (Piponnier et al., 2009), demonstrating that our manipulations did induce an expected response and validates the body sway vRMS results reported below.

4.2. Mild traumatic brain injury time-course recovery measured by body sway vRMS

The only measure that allowed us to discriminate between mTBI and control groups, as well as tracking the time-course recovery after an mTBI is the body sway vRMS.

In the control group, the postural instability identified by body sway vRMS did not significantly differ between conditions and remained similar form session to session. Results of control participants for the *Static* and *Dynamic Tunnel* conditions are in agreement with the results observed in a previous study we realised on healthy young adults with similar paradigm and device (Piponnier et al., 2009). Also, Slobounov et al. (2005) found no significant center of pressure area difference between eyes closed and eyes open conditions in healthy control subjects, for static visual stimuli, even though it was slightly larger in the eyes closed condition. Further, Slobounov et al. (2012) found an increase of postural instability from eyes closed to eyes open condition, during quiet standing, not to be significant at baseline in student athletes.

At 15 days and 3 months post-injury, postural instability was significantly larger in the mTBI than in the control group, all conditions together (*Figure 4*). The body sway vRMS of the mTBI group decreased then significantly from 3 to 12 months post-injury, and the difference with the control group was, then, no longer significant. These findings are consistent with those of previous studies having found mTBI-related balance deficits to last for weeks (Slobounov et al., 2008; Slobounov et al., 2012; Slobounov et al., 2011; Slobounov, Tutwiler, et al., 2006) or months (Findling et al., 2011; Gagnon et al., 2004a; Geurts et al., 1999; Geurts et al., 1996; Kaufman et al., 2006; King et al., 2014; Thompson et al., 2005) beyond the acute stage of injury, using various balance-related measures. Also, our results are consistent with posture-related EEG findings that have demonstrated long-lasting abnormalities in balance-related cortical activity following an mTBI (Slobounov et al., 2012; Slobounov et al., 2005; Thompson et al., 2005).

Two weeks following mTBI, the higher body sway vRMS in the mTBI than in the control group in the *Eyes closed* as well as in the *Static tunnel* condition, indicates that the multisensory integration responsible for postural control (i.e., visual, vestibular and somatosensory) (Dieterich & Brandt, 2015; Guldin & Grusser, 1998; Peterka, 2002; zu Eulenburg et al., 2012), while in a situation of spontaneous body sway, was impaired in the mTBI group (*Figure 5*). The deficit in the *Eyes closed* condition, in comparison to the results obtained in the control group for this condition, indicates that vestibular and somatosensory inputs integration is affected 2 weeks after an mTBI and that these inputs are unable to fully compensate for removal of

visual inputs. However, this deficit seems to recover at 3 months contrary to the one involving visual integration (see next paragraph).

In addition, static visual cues failed, 15 days post-injury, to improve postural stability of mTBI participants, as compared to the *Eyes closed* condition. This demonstrates that visual processing contributing to the control of upright stance, was particularly affected in mTBI participants 15 days post-injury. Other researchers also reported balance-related visual processing deficits after an mTBI. Sosnoff et al. (2008) using the NeuroCom® Sensory Organization Test (SOT), showed that the overall postural control (composite balance score) and the visual information processing component of postural control (visual ratio score) were affected by mTBI, within 24 hours of injury. Findling et al. (2011) used one- and two-legged quiet stance tasks, with eyes open and eyes closed, on firm and foam support surfaces. Their results showed that postural control was affected by mTBI in all conditions, more than one year and a half since injury on average, even during the two-legged stance (hands at the sides and feet at shoulder width apart) on a firm surface with eyes open. Moreover, in a previous report with exactly the same participants, we found reaction time deficits involving visual processing in mTBI individuals (Piponnier et al., 2015), that supports and reinforce the present findings.

This study only focused on slow body sway components, which correspond to universal body sway characteristics (Yamamoto et al., 2015), and so reflect the neural control of posture. Therefore, these findings are in agreement with the hypothesis of a diffuse brain damage, such as diffuse axonal injury (Bain et al., 2001; Kirov et al., 2013; Maxwell et al., 1997; Topal et al., 2008), that may impair visual, vestibular (Fife

& Kalra, 2015), and somatosensory systems along with their connective pathways, leading to related functional deficits following mTBI.

Finally, in the *Dynamic tunnel* conditions, the body sway vRMS, although not significantly at 2 weeks and 12 months, was higher in the mTBI than in the control group. This lack of postural stability difference between mTBI and control groups may reside in the fact that vection, while increasing the magnitude and accuracy of the visually evoked response in the antero-posterior direction (i.e. tunnel direction of motion) (Thurrell & Bronstein, 2002), as reveal by BSA data, might have contributed to minimize body sway in other directions.

Three months following mTBI, the body sway vRMS of mTBI and control groups significantly differed in the *Static* and *Dynamic tunnel* conditions, while there was no longer any significant difference between mTBI and control groups in the *Eyes closed* condition (*Figure 5*). This shows that the visual processing involved in the postural control of stance was still impaired in the mTBI group 3 months post-injury.

The isolated result showing that the body sway VRMS was significantly higher for mTBI than for control group at 3 months post-injury, in the *Dynamic tunnel* conditions, could be explained as follow. In the control group, even though not significant, the body sway vRMS in this condition decreased from the first to the second session, and remained almost at the same level at the third session compared to the second-one. In the meantime, in the mTBI group, the body sway vRMS in the *Dynamic tunnel* conditions was at the same level at the first and second sessions (i.e. 2 weeks and 3 months post-injury), and decreased then from the second to the third session (i.e. from 3 to 12 months post-injury), even if not significantly. For the control group, the

decrease of body sway vRMS at the second testing session may be an effect of adaptation to the visual scene motion (Guerraz, Thilo, Bronstein, & Gresty, 2001). As visual (Piponnier et al., 2015) and balance deficits were still present 3 months after injury, moving visual scenes might have perturbed postural control of mTBI participants significantly more than for control subjects (Slobounov et al., 2011; Slobounov, Tutwiler, et al., 2006), even though mTBI participants were aware of the forthcoming visual surrounding perturbation.

4.3. Impacts of clinical measures

Although results of the clinical tests used in our study were unable to reveal significant balance deficits in mTBI subjects, they are nevertheless informative on several aspects of balance testing. They showed that duration of stance vary as a function of balance tasks difficulty. The BOT-2 items with eyes open were easy for both mTBI and control participants achieving generally the maximal score. Therefore, more elaborate measures, such as the vRMS, are better to evaluate and reveal balance problems when vision is allowed. Balance tasks with eyes closed showed, in both BOT-2 and BESS derived tasks, an effect of sessions affecting both groups, indicating that learning effects have to be considered when interpreting repeated trials across time. On the contrary, both BSA and vRMS did not vary across time in control subjects. Some tasks, such as standing on one leg on the balance beam with eyes closed (i.e. one of the BOT-2 items), where maintenance of stance last less than 5 seconds appear too difficult even for control subjects and thus might not be optimal to identify subjects with possible balance deficits. Other balance tasks of intermediate

difficulties (ex. standing on one leg, eyes closed, on the floor (a BOT-2 task) or on foam (a BESS task)) showed tendencies to discriminate between mTBI and control subjects even in this small sample size. Thus, these types of balance tasks would be preferable for clinicians to use in a clinical setting for fast screening purposes when more elaborate tests are not available. Future clinical research should also focus on these later types of tasks when designing research protocols.

4.4. Balance-related post-concussion symptoms

Levels of balance-related symptoms (*balance problems* and *dizziness* items listed on PCSS-R) of mTBI participants at 15 days post-injury are comparable with the levels reported by Kontos et al. (2012) 1 to 7 days after a sport-related concussion in student athletes. Else, the level of balance-related symptoms of control participants is comparable to the level reported in student athletes at baseline (Kontos et al., 2012). Also, it should be emphasized that, at 3 months and at 1 year post-injury, the mean level of balance-related symptoms in the mTBI group, even though higher than the one of control group, was very mild (*Figure 8*). Furthermore, it has been shown that persons having sustained an mTBI seemed to misperceive their pre-injury functioning level as better than it might have been (Heltemes, Holbrook, Macgregor, & Galarneau, 2012; Lange, Iverson, & Rose, 2010), and reported significantly more symptoms when asked to fulfill a questionnaire (Rivermead post-concussion symptoms questionnaire) as compared to when asked to do it freely (i.e. without any suggestion) (Villemure, Nolin, & Le Sage, 2011). Finally, no link could have been established between the levels of balance-related symptoms and any of the balance measures used in this study (BSA, body sway vRMS, and modified BOT-2 and

modified BESS measures). Hence, the level of symptoms, although undoubtedly informative, should be, here, considered with caution.

4.5. Limitations

The main limitation in this study is the sample size. This limitation along with others has been discussed in a previous report involving exactly the same participants (Piponnier et al., 2015).

5. Conclusion

By using postural instability measures, which measures velocity of displacement rather than amplitude, this study has demonstrated that subtle mTBI-related balance deficits may persist months after the injury. Also, the impairment of visual processing evidenced following mTBI (Piponnier et al., 2015) seemed to contribute to some extent to these balance deficits. The level of such balance deficits appeared to decrease progressively and reach a level similar to the one of healthy subjects by one year post-injury.

Measures derived from clinical tests failed to expose significant mTBI-related balance deficits even 2 weeks after injury. Antero-posterior body sway amplitude as well failed to reveal such balance deficits.

Further studies are needed to replicate the results of the present study. As results were similar between conditions, this could eventually lead to develop a fast and simple procedure adapted to the clinical reality using such a postural instability measure.

Acknowledgements

Mario Lemieux (stimuli programming)

Vadim Sutyushev (hardware installation and user interface programming)

Isabelle Roy & Ariane Demers (HSCM), Lisa Grilli (MUHC) (recruitment of participants)

Thomas Romeas (School of Optometry, Université de Montréal) (project coordinator)

Rémy Allard (stimuli programming and comments on the manuscript)

Claudine Habak (comments on the manuscript)

The Canadian Institutes of Health Research (funding of the study, MOP-18004)

All the participants in this study.

Author Disclosure Statement

No competing financial interests exist.

References

Bain, A. C., Raghupathi, R., & Meaney, D. F. (2001). Dynamic stretch correlates to both morphological abnormalities and electrophysiological impairment in a model of traumatic axonal injury. *J Neurotrauma, 18*(5), 499-511. doi:10.1089/089771501300227305

Bayly, P. V., Cohen, T. S., Leister, E. P., Ajo, D., Leuthardt, E. C., & Genin, G. M. (2005). Deformation of the human brain induced by mild acceleration. *J Neurotrauma, 22*(8), 845-856. doi:10.1089/neu.2005.22.845

Bell, D. R., Guskiewicz, K. M., Clark, M. A., & Padua, D. A. (2011). Systematic review of the balance error scoring system. *Sports Health, 3*(3), 287-295. doi:10.1177/1941738111403122

Bigler, E. D. (2007). Anterior and middle cranial fossa in traumatic brain injury: relevant neuroanatomy and neuropathology in the study of neuropsychological outcome. *Neuropsychology, 21*(5), 515-531. doi:10.1037/0894-4105.21.5.515

Bigler, E. D. (2008). Neuropsychology and clinical neuroscience of persistent post-concussive syndrome. *J Int Neuropsychol Soc, 14*(1), 1-22. doi:10.1017/S135561770808017X

Billino, J., Braun, D. I., Bremmer, F., & Gegenfurtner, K. R. (2011). Challenges to normal neural functioning provide insights into separability of motion processing mechanisms. *Neuropsychologia, 49*(12), 3151-3163. doi:10.1016/j.neuropsychologia.2011.07.009

Brown, L., Sherbenou, R. J., & Johnsen, S. K. (1997). Test of Nonverbal Intelligence: : A language-free measure of cognitive ability—Third Edition.

Bruininks, R. H., & Bruininks, B. D. (2005). Bruininks–Oseretsky Test of Motor Proficiency (2nd Edition).

Carroll, L. J., Cassidy, J. D., Holm, L., Kraus, J., Coronado, V. G., & Injury, W. H. O. C. C. T. F. o. M. T. B. (2004). Methodological issues and research recommendations for mild traumatic brain injury: the WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury. *J Rehabil Med*(43 Suppl), 113-125.

Cassidy, J. D., Carroll, L. J., Peloso, P. M., Borg, J., von Holst, H., Holm, L., . . . Injury, W. H. O. C. C. T. F. o. M. T. B. (2004). Incidence, risk factors and prevention of mild traumatic brain injury: results of the WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury. *J Rehabil Med*(43 Suppl), 28-60.

Conners, C. K. (1997). Conner's Rating Scales - Revised Technical Manual. *Toronto, Ontario, Canada: Multi-Health Systems Inc.*

Daniel, P. M., & Whitteridge, D. (1961). The representation of the visual field on the cerebral cortex in monkeys. *J Physiol, 159*, 203-221.

DeMatteo, C., Greenspoon, D., Levac, D., Harper, J. A., & Rubinoff, M. (2014). Evaluating the Nintendo Wii for assessing return to activity readiness in youth with mild traumatic brain injury. *Phys Occup Ther Pediatr, 34*(3), 229-244. doi:10.3109/01942638.2014.885103

Dieterich, M., & Brandt, T. (2015). The bilateral central vestibular system: its pathways, functions, and disorders. *Ann N Y Acad Sci, 1343*, 10-26. doi:10.1111/nyas.12585

Dumoulin, S. O., Baker, C. L., Jr., Hess, R. F., & Evans, A. C. (2003). Cortical specialization for processing first- and second-order motion. *Cereb Cortex, 13*(12), 1375-1385.

Dupont, P., Sary, G., Peuskens, H., & Orban, G. A. (2003). Cerebral regions processing first- and higher-order motion in an opposed-direction discrimination task. *Eur J Neurosci, 17*(7), 1509-1517.

Evans, R. W. (2004). Post-traumatic headaches. *Neurol Clin, 22*(1), 237-249, viii. doi:10.1016/S0733-8619(03)00097-5

Farivar, R. (2009). Dorsal-ventral integration in object recognition. *Brain Res Rev, 61*(2), 144-153. doi:10.1016/j.brainresrev.2009.05.006

Faubert, J., & Allard, R. (2004). Effect of visual distortion on postural balance in a full immersion stereoscopic environment. In A. J. Woods, Merrit, J. O., Benton, S. A. & Bolas, M. T. (Ed.), *Stereoscopic displays and virtual reality systems XI, Proceedings of SPIE IS&T Electronic Imaging, SPIE, 5291* (pp. 491–500).

Ferre, E. R., Walther, L. E., & Haggard, P. (2015). Multisensory interactions between vestibular, visual and somatosensory signals. *PLoS One, 10*(4), e0124573. doi:10.1371/journal.pone.0124573

Fife, T. D., & Kalra, D. (2015). Persistent vertigo and dizziness after mild traumatic brain injury. *Ann N Y Acad Sci, 1343*, 97-105. doi:10.1111/nyas.12678

Findling, O., Schuster, C., Sellner, J., Ettlin, T., & Allum, J. H. (2011). Trunk sway in patients with and without, mild traumatic brain injury after whiplash injury. *Gait Posture, 34*(4), 473-478. doi:10.1016/j.gaitpost.2011.06.021

Fisher, D. C., Ledbetter, M. F., Cohen, N. J., Marmor, D., & Tulsky, D. S. (2000). WAIS-III and WMS-III profiles of mildly to severely brain-injured patients. *Appl Neuropsychol, 7*(3), 126-132. doi:10.1207/S15324826AN0703_2

Gaetz, M. (2004). The neurophysiology of brain injury. *Clin Neurophysiol, 115*(1), 4-18.

Gagnon, I., Forget, R., Sullivan, S. J., & Friedman, D. (1998). Motor performance following a mild traumatic brain injury in children: an exploratory study. *Brain Inj, 12*(10), 843-853.

Gagnon, I., Swaine, B., Friedman, D., & Forget, R. (2004). Children show decreased dynamic balance after mild traumatic brain injury. *Arch Phys Med Rehabil, 85*(3), 444-452.

Geurts, A. C., Knoop, J. A., & van Limbeek, J. (1999). Is postural control associated with mental functioning in the persistent postconcussion syndrome? *Arch Phys Med Rehabil, 80*(2), 144-149.

Geurts, A. C., Ribbers, G. M., Knoop, J. A., & van Limbeek, J. (1996). Identification of static and dynamic postural instability following traumatic brain injury. *Arch Phys Med Rehabil, 77*(7), 639-644.

Gibson, J. J. (1979). *The ecological approach to visual perception*. Boston: Houghton Mifflin.

Greffou, S., Bertone, A., Hanssens, J. M., & Faubert, J. (2008). Development of visually driven postural reactivity: a fully immersive virtual reality study. *J Vis, 8*(11), 15 11-10. doi:10.1167/8.11.15

Guerraz, M., Thilo, K. V., Bronstein, A. M., & Gresty, M. A. (2001). Influence of action and expectation on visual control of posture. *Brain Res Cogn Brain Res, 11*(2), 259-266.

Guldin, W. O., & Grusser, O. J. (1998). Is there a vestibular cortex? *Trends Neurosci, 21*(6), 254-259.

Guskiewicz, K. M., Ross, S. E., & Marshall, S. W. (2001). Postural Stability and Neuropsychological Deficits After Concussion in Collegiate Athletes. *J Athl Train, 36*(3), 263-273.

Harmon, K. G., Drezner, J. A., Gammons, M., Guskiewicz, K. M., Halstead, M., Herring, S. A., . . . Roberts, W. O. (2013). American Medical Society for Sports Medicine position statement: concussion in sport. *Br J Sports Med, 47*(1), 15-26. doi:10.1136/bjsports-2012-091941

Heltemes, K. J., Holbrook, T. L., Macgregor, A. J., & Galarneau, M. R. (2012). Blast-related mild traumatic brain injury is associated with a decline in self-rated health amongst US military personnel. *Injury, 43*(12), 1990-1995. doi:10.1016/j.injury.2011.07.021

Iverson, G. (2007). Predicting slow recovery from sport-related concussion: the new simple-complex distinction. *Clin J Sport Med, 17*(1), 31-37. doi:10.1097/JSM.0b013e3180305e4d

Iverson, G. L. (2005). Outcome from mild traumatic brain injury. *Curr Opin Psychiatry, 18*(3), 301-317. doi:10.1097/01.yco.0000165601.29047.ae

Kalaycioglu, C., Nalcaci, E., Schmiedt-Fehr, C., & Basar-Eroglu, C. (2009). Corpus callosum has different channels for transmission of spatial frequency information. *Brain Res, 1296*, 85-93. doi:10.1016/j.brainres.2009.08.018

Kaufman, K. R., Brey, R. H., Chou, L. S., Rabatin, A., Brown, A. W., & Basford, J. R. (2006). Comparison of subjective and objective measurements of balance disorders following traumatic brain injury. *Med Eng Phys, 28*(3), 234-239. doi:10.1016/j.medengphy.2005.05.005

King, L. A., Horak, F. B., Mancini, M., Pierce, D., Priest, K. C., Chesnutt, J., . . . Chapman, J. C. (2014). Instrumenting the balance error scoring system for use with patients reporting persistent balance problems after mild traumatic brain injury. *Arch Phys Med Rehabil, 95*(2), 353-359. doi:10.1016/j.apmr.2013.10.015

Kirov, II, Tal, A., Babb, J. S., Reaume, J., Bushnik, T., Ashman, T. A., . . . Gonen, O. (2013). Proton MR spectroscopy correlates diffuse axonal abnormalities with post-concussive symptoms in mild traumatic brain injury. *J Neurotrauma, 30*(13), 1200-1204. doi:10.1089/neu.2012.2696

Kleffelgaard, I., Roe, C., Soberg, H. L., & Bergland, A. (2012). Associations among self-reported balance problems, post-concussion symptoms and performance-based tests: a longitudinal follow-up study. *Disabil Rehabil, 34*(9), 788-794. doi:10.3109/09638288.2011.619624

Konrad, C., Geburek, A. J., Rist, F., Blumenroth, H., Fischer, B., Husstedt, I., . . . Lohmann, H. (2011). Long-term cognitive and emotional consequences of mild

traumatic brain injury. *Psychol Med, 41*(6), 1197-1211. doi:10.1017/S0033291710001728

Kontos, A. P., Elbin, R. J., Schatz, P., Covassin, T., Henry, L., Pardini, J., & Collins, M. W. (2012). A revised factor structure for the post-concussion symptom scale: baseline and postconcussion factors. *Am J Sports Med, 40*(10), 2375-2384. doi:10.1177/0363546512455400

Lange, R. T., Iverson, G. L., & Rose, A. (2010). Post-concussion symptom reporting and the "good-old-days" bias following mild traumatic brain injury. *Arch Clin Neuropsychol, 25*(5), 442-450. doi:10.1093/arclin/acq031

Leddy, J. J., Kozlowski, K., Fung, M., Pendergast, D. R., & Willer, B. (2007). Regulatory and autoregulatory physiological dysfunction as a primary characteristic of post concussion syndrome: implications for treatment. *NeuroRehabilitation, 22*(3), 199-205.

Lee, H., Wintermark, M., Gean, A. D., Ghajar, J., Manley, G. T., & Mukherjee, P. (2008). Focal lesions in acute mild traumatic brain injury and neurocognitive outcome: CT versus 3T MRI. *J Neurotrauma, 25*(9), 1049-1056. doi:10.1089/neu.2008.0566

Lewine, J. D., Davis, J. T., Bigler, E. D., Thoma, R., Hill, D., Funke, M., . . . Orrison, W. W. (2007). Objective documentation of traumatic brain injury subsequent to mild head trauma: multimodal brain imaging with MEG, SPECT, and MRI. *J Head Trauma Rehabil, 22*(3), 141-155. doi:10.1097/01.HTR.0000271115.29954.27

Lovell, M. R., & Collins, M. W. (1998). Neuropsychological assessment of the college football player. *J Head Trauma Rehabil, 13*(2), 9-26.

Marshall, S., Bayley, M., McCullagh, S., Velikonja, D., Berrigan, L., Ouchterlony, D., & Weegar, K. (2015). Updated clinical practice guidelines for concussion/mild traumatic brain injury and persistent symptoms. *Brain Inj, 29*(6), 688-700. doi:10.3109/02699052.2015.1004755

Maxwell, W. L., Povlishock, J. T., & Graham, D. L. (1997). A mechanistic analysis of nondisruptive axonal injury: a review. *J Neurotrauma, 14*(7), 419-440.

McAllister, T. W., & Arciniegas, D. (2002). Evaluation and treatment of postconcussive symptoms. *NeuroRehabilitation, 17*(4), 265-283.

McCrea, M., Guskiewicz, K. M., Marshall, S. W., Barr, W., Randolph, C., Cantu, R. C., . . . Kelly, J. P. (2003). Acute effects and recovery time following concussion in collegiate football players: the NCAA Concussion Study. *JAMA, 290*(19), 2556-2563. doi:10.1001/jama.290.19.2556

Naunheim, R. S., Matero, D., & Fucetola, R. (2008). Assessment of patients with mild concussion in the emergency department. *J Head Trauma Rehabil, 23*(2), 116-122. doi:10.1097/01.HTR.0000314530.30401.70

Nishiike, S., Nakagawa, S., Tonoike, M., Takeda, N., & Kubo, T. (2001). Information processing of visually-induced apparent self motion in the cortex of humans: analysis with magnetoencephalography. *Acta Otolaryngol Suppl, 545*, 113-115.

Nishimoto, T., & Murakami, S. (1998). Relation between diffuse axonal injury and internal head structures on blunt impact. *J Biomech Eng, 120*(1), 140-147.

Noguchi, Y., Kaneoke, Y., Kakigi, R., Tanabe, H. C., & Sadato, N. (2005). Role of the superior temporal region in human visual motion perception. *Cereb Cortex, 15*(10), 1592-1601. doi:10.1093/cercor/bhi037

Peterka, R. J. (2002). Sensorimotor integration in human postural control. *J Neurophysiol, 88*(3), 1097-1118.

Piponnier, J. C., Forget, R., Gagnon, I., McKerral, M., Giguere, J. F., & Faubert, J. (2015). First- and second-order stimuli reaction time measures are highly sensitive to mild traumatic brain injuries. *J Neurotrauma*. doi:10.1089/neu.2014.3832

Piponnier, J. C., Hanssens, J. M., & Faubert, J. (2009). Effect of visual field locus and oscillation frequencies on posture control in an ecological environment. *J Vis, 9*(1), 13 11-10. doi:10.1167/9.1.13

Rees, P. M. (2003). Contemporary issues in mild traumatic brain injury. *Arch Phys Med Rehabil, 84*(12), 1885-1894.

Rees, R. J., & Bellon, M. L. (2007). Post concussion syndrome ebb and flow: longitudinal effects and management. *NeuroRehabilitation, 22*(3), 229-242.

Ropper, A. H., & Gorson, K. C. (2007). Clinical practice. Concussion. *N Engl J Med, 356*(2), 166-172. doi:10.1056/NEJMcp064645

Ruff, R. (2005). Two decades of advances in understanding of mild traumatic brain injury. *J Head Trauma Rehabil, 20*(1), 5-18.

Ruff, R. M. (2011). Mild traumatic brain injury and neural recovery: rethinking the debate. *NeuroRehabilitation, 28*(3), 167-180. doi:10.3233/NRE-2011-0646

Ruff, R. M., Iverson, G. L., Barth, J. T., Bush, S. S., Broshek, D. K., Policy, N. A. N., & Planning, C. (2009). Recommendations for diagnosing a mild traumatic brain injury: a National Academy of Neuropsychology education paper. *Arch Clin Neuropsychol, 24*(1), 3-10. doi:10.1093/arclin/acp006

Shaw, N. A. (2002). The neurophysiology of concussion. *Prog Neurobiol, 67*(4), 281-344.

Sheedy, J., Geffen, G., Donnelly, J., & Faux, S. (2006). Emergency department assessment of mild traumatic brain injury and prediction of post-concussion symptoms at one month post injury. *J Clin Exp Neuropsychol, 28*(5), 755-772. doi:10.1080/13803390591000864

Sheedy, J., Harvey, E., Faux, S., Geffen, G., & Shores, E. A. (2009). Emergency department assessment of mild traumatic brain injury and the prediction of postconcussive symptoms: a 3-month prospective study. *J Head Trauma Rehabil, 24*(5), 333-343. doi:10.1097/HTR.0b013e3181aea51f

Slobounov, S., Cao, C., Sebastianelli, W., Slobounov, E., & Newell, K. (2008). Residual deficits from concussion as revealed by virtual time-to-contact measures of postural stability. *Clin Neurophysiol, 119*(2), 281-289. doi:10.1016/j.clinph.2007.10.006

Slobounov, S., Sebastianelli, W., & Hallett, M. (2012). Residual brain dysfunction observed one year post-mild traumatic brain injury: combined EEG and balance study. *Clin Neurophysiol, 123*(9), 1755-1761. doi:10.1016/j.clinph.2011.12.022

Slobounov, S., Sebastianelli, W., & Moss, R. (2005). Alteration of posture-related cortical potentials in mild traumatic brain injury. *Neurosci Lett, 383*(3), 251-255. doi:10.1016/j.neulet.2005.04.039

Slobounov, S., Sebastianelli, W., & Newell, K. M. (2011). Incorporating virtual reality graphics with brain imaging for assessment of sport-related concussions. *Conf Proc IEEE Eng Med Biol Soc, 2011*, 1383-1386. doi:10.1109/IEMBS.2011.6090325

Slobounov, S., Tutwiler, R., Sebastianelli, W., & Slobounov, E. (2006). Alteration of postural responses to visual field motion in mild traumatic brain injury. *Neurosurgery, 59*(1), 134-139; discussion 134-139. doi:10.1227/01.NEU.0000219197.33182.3F

Slobounov, S., Wu, T., Hallett, M., Shibasaki, H., Slobounov, E., & Newell, K. (2006). Neural underpinning of postural responses to visual field motion. *Biol Psychol, 72*(2), 188-197. doi:10.1016/j.biopsycho.2005.10.005

Sosnoff, J. J., Broglio, S. P., & Ferrara, M. S. (2008). Cognitive and motor function are associated following mild traumatic brain injury. *Exp Brain Res, 187*(4), 563-571. doi:10.1007/s00221-008-1324-x

Sosnoff, J. J., Broglio, S. P., Shin, S., & Ferrara, M. S. (2011). Previous mild traumatic brain injury and postural-control dynamics. *J Athl Train, 46*(1), 85-91. doi:10.4085/1062-6050-46.1.85

Stoffregen, T. A. (1985). Flow structure versus retinal location in the optical control of stance. *J Exp Psychol Hum Percept Perform, 11*(5), 554-565.

Sunaert, S., Van Hecke, P., Marchal, G., & Orban, G. A. (2000). Attention to speed of motion, speed discrimination, and task difficulty: an fMRI study. *Neuroimage, 11*(6 Pt 1), 612-623. doi:10.1006/nimg.2000.0587

Thompson, J., Sebastianelli, W., & Slobounov, S. (2005). EEG and postural correlates of mild traumatic brain injury in athletes. *Neurosci Lett, 377*(3), 158-163. doi:10.1016/j.neulet.2004.11.090

Thurrell, A. E., & Bronstein, A. M. (2002). Vection increases the magnitude and accuracy of visually evoked postural responses. *Exp Brain Res, 147*(4), 558-560. doi:10.1007/s00221-002-1296-1

Topal, N. B., Hakyemez, B., Erdogan, C., Bulut, M., Koksal, O., Akkose, S., . . . Korfali, E. (2008). MR imaging in the detection of diffuse axonal injury with mild traumatic brain injury. *Neurol Res, 30*(9), 974-978. doi:10.1179/016164108X323799

Uesaki, M., & Ashida, H. (2015). Optic-flow selective cortical sensory regions associated with self-reported states of vection. *Front Psychol, 6*, 775. doi:10.3389/fpsyg.2015.00775

Vaina, L. M., & Soloviev, S. (2004). First-order and second-order motion: neurological evidence for neuroanatomically distinct systems. *Prog Brain Res, 144*, 197-212. doi:10.1016/S0079-6123(03)14414-7

Vakalopoulos, C. (2005). Neural correlates of consciousness: a definition of the dorsal and ventral streams and their relation to phenomenology. *Med Hypotheses, 65*(5), 922-931. doi:10.1016/j.mehy.2005.05.016

Viano, D. C., Casson, I. R., & Pellman, E. J. (2007). Concussion in professional football: biomechanics of the struck player--part 14. *Neurosurgery, 61*(2), 313-327; discussion 327-318. doi:10.1227/01.NEU.0000279969.02685.D0

Viano, D. C., Casson, I. R., Pellman, E. J., Zhang, L., King, A. I., & Yang, K. H. (2005). Concussion in professional football: brain responses by finite element analysis: part 9. *Neurosurgery, 57*(5), 891-916; discussion 891-916.

Villemure, R., Nolin, P., & Le Sage, N. (2011). Self-reported symptoms during post-mild traumatic brain injury in acute phase: influence of interviewing method. *Brain Inj, 25*(1), 53-64. doi:10.3109/02699052.2010.531881

Willer, B., & Leddy, J. J. (2006). Management of concussion and post-concussion syndrome. *Curr Treat Options Neurol, 8*(5), 415-426.

Winter, D. A., Patla, A. E., Prince, F., Ishac, M., & Gielo-Perczak, K. (1998). Stiffness control of balance in quiet standing. *J Neurophysiol, 80*(3), 1211-1221.

Wright, M. J., & Johnston, A. (1983). Spatiotemporal contrast sensitivity and visual field locus. *Vision Res, 23*(10), 983-989.

Yamamoto, T., Smith, C. E., Suzuki, Y., Kiyono, K., Tanahashi, T., Sakoda, S., . . . Nomura, T. (2015). Universal and individual characteristics of postural sway during quiet standing in healthy young adults. *Physiol Rep, 3*(3). doi:10.14814/phy2.12329

zu Eulenburg, P., Caspers, S., Roski, C., & Eickhoff, S. B. (2012). Meta-analytical definition and functional connectivity of the human vestibular cortex. *Neuroimage, 60*(1), 162-169. doi:10.1016/j.neuroimage.2011.12.032

Chapitre 4 : Discussion

1. Vitesse de réaction visuomotrice plus lente et plus variable suite à un TCCL

Les temps de réaction (TR) des participants du groupe TCCL étaient dans l'ensemble plus longs (moyennes et médianes) et plus variables (écarts-types et écarts interquartiles) que ceux des participants du groupe contrôle, qu'il s'agisse de TR simples ou de choix, correspondant à des stimuli de 1er ou de 2^{d} ordre, et, quelle que soit la session (c'est-à-dire à 15 jours, 3 mois et 12 mois suivants le TCCL). Autrement dit, les participants du groupe TCCL étaient significativement plus lents à répondre et moins constants que ceux du groupe contrôle, et ce jusqu'à un an après le traumatisme. Ces résultats indiquent la présence de déficits durables dès les plus bas niveaux de traitement de l'information visuelle. Ces déficits affectent des réseaux neuronaux impliqués dans les processus allant de la simple détection de l'information visuelle à la réponse motrice permettant d'y répondre, en passant, surtout pour les TR de choix, par l'intégration et l'interprétation de cette information.

Par ailleurs, en ce qui concerne plus spécifiquement les TR de choix, le fait que la discrimination de direction de mouvement, chez les participants du groupe TCCL, était plus longue pour les stimuli de 2^{d} ordre que pour ceux de 1er ordre indique que, suite à un TCCL, les étapes dédiées à la perception visuelle et à l'intégration de stimuli complexes (c'est-à-dire de 2^{d} ordre) sont davantage affectées que celles concernant les stimuli de 1er ordre. Et ce déficit a été observé jusqu'à un an après le traumatisme. Nos observations confirment ainsi celles faites par

Brosseau-Lachaine et al. (2008), qui ont mis en évidence des déficits visuels perceptifs relatifs à des stimuli de 2^{d} ordre chez des enfants ayant subi un TCCL, persistant jusqu'à 3 mois après le traumatisme.

Les perturbations neurophysiologiques (G. L. Iverson, 2005; Lee et al., 2008; Maxwell et al., 1997; Topal et al., 2008) à l'origine de ces déficits fonctionnels pourraient relever, dans un premier temps et à court terme, directement du traumatisme axonal diffus et de défauts de connexion à l'interface entre la substance blanche et la substance grise (Bain et al., 2001; Bayly et al., 2005; Bigler, 2007, 2008; Evans, 2004; Gaetz, 2004; Ivarsson et al., 2002; Nishimoto & Murakami, 1998; Ropper & Gorson, 2007; Shaw, 2002; Viano et al., 2005). Par la suite, la persistance à long terme de tels déficits pourrait être le résultat de la perte par apoptose de certains des neurones initialement affectés, comme cela a été montré chez l'humain et l'animal (Lewine et al., 2007; MacKenzie et al., 2002; Tweedie et al., 2007).

2. Déficits visuels et niveau de symptômes suite à un TCCL

Le niveau de symptômes rapporté par le biais de l'échelle des symptômes post-commotionnels révisée (Lovell & Collins, 1998) était significativement plus élevé chez les participants du groupe TCCL que chez les participants du groupe contrôle, quelle que soit la session. Cependant, cette mesure demeure cliniquement difficilement interprétable compte tenu du fait qu'il n'existe de base de données normative que chez les étudiants athlètes, et également parce que le niveau de symptômes prétraumatique n'est pas connu chez les participants du groupe TCCL. D'autre part, cette échelle a été conçue pour évaluer le niveau de symptômes dans la

phase aiguë du TCCL, c'est-à-dire dans les jours suivant le traumatisme. Les niveaux de symptômes rapportés à 3 mois et un an après le TCCL doivent donc être considérés avec prudence, d'autant plus que les symptômes listés dans le formulaire PCSS-R ne sont pas spécifiques au TCCL (Dikmen et al., 2010; Gordon et al., 2000). On peut toutefois estimer, d'après les bases de données normatives figurant dans le manuel clinique du test ImPACT® Version 2.0, que le niveau moyen de symptômes après le traumatisme dans le groupe TCCL était de léger à modéré à 15 jours, léger à 3 mois et non cliniquement significatif à un an.

Les corrélations n'ont pas permis d'établir un lien concret entre le niveau de symptômes et les variables de TR. En effet, un quart seulement des corrélations entre le niveau de symptômes et les variables de TR (moyennes et médianes, condition *Motion* 1er et 2^{d} ordres) était significatif 15 jours après le traumatisme, dans le groupe TCCL. À 3 mois et un an après le traumatisme, aucune de ces corrélations n'était significative, ce qui indique que les symptômes présents des mois après le TCCL n'ont, dans l'ensemble, pas de lien avec les déficits visuomoteurs observés.

3. Évolution des effets d'un TCCL sur l'instabilité posturale jusqu'à leur résolution

Les mesures d'instabilité posturale, comme les mesures de TR, ont permis de révéler des déficits secondaires au TCCL et durant plusieurs mois. En revanche, contrairement aux mesures de TR, les mesures d'instabilité posturale sur une année ont permis de suivre l'évolution des troubles de l'équilibre liés au TCCL jusqu'à leur résolution.

Deux semaines et 3 mois après le traumatisme, l'instabilité posturale était significativement plus grande dans le groupe TCCL que dans le groupe contrôle, toutes conditions confondues (c'est-à-dire yeux fermés, tunnels statique et dynamiques). Elle a fini par diminuer significativement entre 3 mois et un an après le TCCL, jusqu'à ce que la différence avec le groupe contrôle ne soit plus significative, et ce, bien que les participants du groupe TCCL aient eu davantage de symptômes liés à des problèmes d'équilibre que ceux du groupe contrôle.

Ces résultats sont compatibles avec ceux de travaux précédents qui ont montré, en utilisant différentes méthodes de mesure, que les troubles de l'équilibre suivant un TCCL pouvaient durer des semaines (Slobounov et al., 2008; Slobounov et al., 2012; Slobounov et al., 2011; Slobounov, Tutwiler, et al., 2006) ou des mois (Findling et al., 2011; Gagnon et al., 2004a; Geurts et al., 1999; Geurts et al., 1996; Kaufman et al., 2006; King et al., 2014; Thompson et al., 2005) après la phase aiguë du traumatisme. Nos résultats sont également en accord avec ceux des études portant sur l'activité EEG liée au contrôle postural, et qui ont mis en évidence des anomalies de l'activité corticale associée au maintien de l'équilibre qui persistaient plusieurs mois après un TCCL (Slobounov et al., 2012; Slobounov et al., 2005; Thompson et al., 2005).

Les données d'instabilité posturale des participants du groupe TCCL, prises dans leur ensemble, ont donc permis de montrer que les troubles subtils de l'équilibre postural suivant un TCCL se résorbaient entre 3 mois et un an. Cependant, il n'a pas était possible de faire de distinction claire sur l'influence des différentes conditions

(yeux fermés, tunnel statique et tunnel dynamique) sur le contrôle postural suite à un TCCL.

Il faut noter ici que cette étude sur l'instabilité posturale secondaire à un TCCL s'est intéressée aux composantes lentes de la réponse posturale, qui correspondent aux caractéristiques universelles des oscillations posturales (Yamamoto et al., 2015), et représentent donc l'aspect neurologique du contrôle postural. Aussi, les déficits révélés ici étant relativement subtils et compte tenu de l'étendue des réseaux neuronaux impliqués dans le contrôle postural, nos résultats pourraient concorder avec l'hypothèse d'un traumatisme axonal diffus (Bain et al., 2001; Kirov et al., 2013; Maxwell et al., 1997; Topal et al., 2008) qui aurait endommagé les systèmes visuel, vestibulaire (Fife & Kalra, 2015) et somatosensoriel ainsi que leurs connexions, et qui serait à l'origine de tels déficits.

4. Niveau de symptômes relatifs à l'instabilité posturale suite à un TCCL

Pour ce qui est des symptômes relatifs aux troubles de l'équilibre (c'est-à-dire les items « problèmes d'équilibre » et « étourdissement » listés dans le formulaire PCSS-R), les niveaux rapportés par les participants du groupe TCCL à 15 jours sont comparables à ceux observés par Kontos et al. (2012) entre un et 7 jours après une commotion cérébrale liée à la pratique sportive, chez des étudiants-athlètes. En outre, les niveaux des symptômes relatifs aux troubles de l'équilibre rapportés par les participants contrôles sont également comparables à ceux rapportés par des étudiants-athlètes avant le début des saisons sportives (Kontos et al., 2012).

Il faut aussi noter ici que, les niveaux moyens des symptômes relatifs aux troubles de l'équilibre rapportés par les participants du groupe TCCL à 3 mois et un an après le traumatisme sont relativement légers, même s'ils sont supérieurs à ceux des participants du groupe contrôle. De plus, il a été montré que les individus ayant subi un TCCL semblaient avoir une perception erronée de leur niveau de fonctionnement prétraumatique, en le considérant meilleur que ce qu'il avait dû être (Heltemes et al., 2012; Lange et al., 2010), et rapportaient davantage de symptômes lorsqu'on leur demandait de remplir un formulaire (comme le formulaire de symptômes post-commotionnels PCSS-R), que lorsqu'on leur laissait la possibilité de les exprimer librement (Villemure et al., 2011). De ce fait, bien que les niveaux des symptômes relatifs aux troubles de l'équilibre rapportés par les participants du groupe TCCL présentent un certain intérêt clinique, ils doivent être interprétés avec prudence.

Finalement, aucun lien n'a pu être établi par le biais de corrélations entre les niveaux des symptômes relatifs aux troubles de l'équilibre et les mesures posturales, quel que soit le groupe et quelle que soit la session.

5. Différence d'évolution de l'instabilité posturale et des déficits visuomoteurs relatifs à la perception du mouvement, suite à un TCCL

Les systèmes visuel, vestibulaire et somatosensoriel contribuent au contrôle postural (Peterka, 2002). Des mécanismes d'interaction corticale inhibitrice réciproque entre ces différents systèmes ont été mis en évidence (Dieterich & Brandt,

2015). Ces mécanismes permettraient notamment, dans des situations de conflit intra- ou intersensoriel, de privilégier l'information la plus fiable pour le contrôle de l'équilibre. Cette interaction corticale inhibitrice réciproque est à la fois inter- et intrahémisphérique. Or, on sait que le système vestibulaire est caractérisé par la dominance de l'hémisphère non dominant (c'est-à-dire situé du côté de la main qui écrit). Aussi, si le système vestibulaire d'un hémisphère est défaillant, il sera inhibé par le système vestibulaire de l'autre hémisphère (Dieterich & Brandt, 2015). C'est ce qui explique, notamment, le fait que les dysfonctions vestibulaires secondaires à des lésions unilatérales du réseau cortical vestibulaire ou de ses voies afférentes soient transitoires.

Par ailleurs, un processus complexe de compensation vestibulaire, impliquant des changements neurophysiologiques moléculaires et structurels au niveau du système nerveux central, a été mis en évidence chez l'animal ayant subi des lésions unilatérales des organes récepteurs vestibulaires (Giardino et al., 2002). Ce processus se traduit par la résolution rapide des déficits fonctionnels relatifs à l'équilibre et à la locomotion. À notre connaissance, de tels processus de plasticité n'ont pas été mis en évidence au niveau du système visuel. Tout cela pourrait donc expliquer que, suite à un TCCL, les déficits de stabilité posturale durent moins longtemps que les déficits visuomoteurs liés à la perception du mouvement.

En effet, il y a d'abord le fait que le contrôle postural est basé sur l'association de systèmes qui fonctionnent initialement en parallèle, et de façon complémentaire lors de l'intégration multisensorielle, alors que la réaction visuomotrice, elle, résulte d'un ensemble de processus en série qui dépendent d'une seule et unique entrée

sensorielle. Ensuite, l'interaction corticale inhibitrice réciproque des réseaux corticaux du système vestibulaire permet de sélectionner les systèmes ayant le fonctionnement le plus fiable pour le contrôle postural (Mergner, 2010). Dans le cas de la réaction visuomotrice, en revanche, chaque étape est nécessaire, et tout déficit affectant une étape a des répercussions sur les étapes suivantes. Enfin, les processus neurophysiologiques de compensation vestibulaire ne semblent pas avoir leur équivalent au niveau de la réponse visuomotrice.

6. Limites

Une des principales limites de ce projet est liée la taille de l'échantillon. En effet, le nombre de participants recrutés était insuffisant pour pouvoir établir des sous-catégories, concernant, par exemple, le degré de sévérité du TCCL, le mécanisme traumatique ou le niveau de symptômes. Cependant, le respect strict des critères de sélection, qui étaient relativement restrictifs, notamment pour ce qui a trait à l'absence de consommation de drogue ou d'alcool, a fait que le recrutement a été assez laborieux. D'autre part, la volonté de participer à des projets de recherche étant généralement moindre chez les individus TCCL qui récupèrent complètement, cela a pu amener à sous-estimer le niveau de récupération suivant un TCCL, pour ce qui a trait aux déficits visuomoteurs révélés par les mesures de TR (Lingsma et al., 2015).

Ensuite, pour ce qui relève des déficits observés relativement au contrôle postural, la grande quantité de données par sujet a pu contribuer à atténuer les effets de certaines conditions (Carroll et al., 2004), notamment celles qui utilisaient le tunnel dynamique.

Il faut noter également que deux individus du groupe TCCL avaient un antécédent de TCCL. Cependant, conformément aux critères de recrutement, le TCCL le plus ancien avait eu lieu un an ou plus avant le second, qui les amenait à participer à ce projet de recherche. D'autre part, cela ne concernant que deux personnes sur quinze, les déficits mis en évidence dans le groupe TCCL ne peuvent raisonnablement être attribués à cela.

Finalement, en raison des périodes relativement longues entre chaque session d'expériences, il fallait s'attendre à ce que des participants puissent subir un TCCL dans ces intervalles. Cela a donc été vérifié systématiquement avant les deuxième et troisième sessions. Aucun des participants du groupe contrôle n'a eu de TCCL durant toute la période du projet. Dans le groupe TCCL, en revanche, un des participants a déclaré, à la dernière session, avoir eu un TCCL en jouant au soccer 6 semaines après la deuxième session (c'est-à-dire 4 mois et demi après le TCCL l'ayant amené à participer à ce projet de recherche). Il a affirmé n'avoir pas perdu connaissance, ni avoir eu d'amnésie post-traumatique, suivant ce traumatisme. Ses symptômes (nausée, étourdissement, confusion et fatigue) ont duré environ deux mois. Enfin, il a dit avoir interrompu toute activité sportive après cet accident (c'est-à-dire pendant une période de 7 mois et demi). À la dernière session d'expériences, il a affirmé n'avoir plus aucun symptôme. Aucune aberration n'a été trouvée dans les résultats de cet individu à la dernière session. Il a donc été décidé de les inclure dans l'étude.

7. Le TCCL est-il comparable au vieillissement ?

Il est maintenant bien établi que des déficits perceptifs visuels (Faubert, 2002; Owsley, 2011) et des déficits du contrôle postural (Eikema, Hatzitaki, Tzovaras, & Papaxanthis, 2012; Iwasaki & Yamasoba, 2015), entre autres, apparaissent avec les processus de vieillissement normal du cerveau. Certains de ces déficits semblent ressembler à ceux observés suite à un TCCL. Nous nous proposons donc ici d'examiner le rapprochement possible entre TCCL et vieillissement normal, du point de vue des déficits visuels perceptifs et posturaux auxquels ils sont associés.

7.1. Déficits perceptifs visuels

Comme nos résultats l'indiquent, et en accord avec les conclusions d'autres chercheurs (Brosseau-Lachaine et al., 2008; Lachapelle et al., 2008), il existe des déficits perceptifs visuels suite à un TCCL. Nos résultats montrent que ces déficits concernent non seulement le traitement de l'information de haut niveau (discrimination de direction de mouvement de 2^{d} ordre, perception de flux optique), comme l'avaient observé Brosseau-Lachaine et al. (2008) et Lachapelle et al. (2008), mais aussi l'information de bas niveau (détection simple, et discrimination de direction de mouvement de 1er ordre). Parallèlement, des études portant sur la perception visuelle au cours du vieillissement normal ont montré que les déficits perceptifs visuels liés à l'âge affectaient le traitement des stimuli de 1er (Adams, Bullimore, Wall, Fingeret, & Johnson, 1999; Raghuram, Lakshminarayanan, & Khanna, 2005) et/ou de 2^{d} ordre (Allard, Lagace-Nadon, & Faubert, 2013; Billino et al., 2011; Habak & Faubert, 2000; Tang & Zhou, 2009).

Les mesures de TR des sujets TCCL effectuées dans notre étude indiquent que la perception du mouvement est davantage affectée, suite à un TCCL, pour les stimuli de 2^{d} ordre que pour ceux de 1er ordre. Les mesures de seuil de sensibilité au contraste chez des sujets jeunes et des sujets âgés, effectuées par Habak and Faubert (2000), indiquent que la perception du mouvement est également davantage affectée, au cours du vieillissement normal, pour les stimuli de 2^{d} ordre que pour ceux de 1er ordre.

7.2. Déficits de l'équilibre postural

En ce qui concerne le contrôle postural, les participants du groupe TCCL présentaient globalement plus d'instabilité dans le maintien de la station debout, au moins jusqu'à 3 mois après le traumatisme. Or, il a été montré qu'au cours du vieillissement normal la variabilité des oscillations posturales lors de la station debout augmentait dans un environnement statique et dans un environnement dépourvu d'indices visuels (Eikema et al., 2012). Il a également été montré que, dans un environnement visuel virtuel tridimensionnel dynamique, les personnes âgées en santé présentaient plus d'oscillations posturales orientées selon le mouvement de la scène visuelle que des adultes jeunes (Haibach, Slobounov, & Newell, 2008). Par ailleurs, relativement au contrôle postural, Pedalini, Cruz, Bittar, Lorenzi, and Grasel (2009), ont montré à l'aide de la posturographie dynamique assistée par ordinateur (test d'organisation sensorielle), qu'il y avait, au cours du vieillissement normal, d'une part, globalement plus d'instabilité posturale, et que, d'autre part, les déficits fonctionnels sous-jacents affectaient alors davantage les systèmes vestibulaire et visuel que le système somatosensoriel.

Les effets produits par un TCCL sur la stabilité posturale paraissent donc semblables à ceux du vieillissement. Cependant, il faut remarquer ici que, contrairement aux mesures de temps de réaction, les données posturales des participants du groupe TCCL ont montré une amélioration avec le temps, au point qu'il n'y avait plus de différence entre les groupes TCCL et contrôle un an après le traumatisme. Ainsi, on peut penser que les structures cérébrales impliquées lors des mesures de temps de réaction et lors des mesures de stabilité posturale ont été différemment affectées (Bigler, 2008) ou qu'elles ont fait l'objet de processus de récupération différents (Giardino et al., 2002).

7.3. Changements cérébraux

Des changements physiques cérébraux semblables à ceux observés suite à un TCCL ont également été observés au cours du vieillissement normal. Ces changements microstructuraux du cerveau semblent pouvoir expliquer, du moins en partie, les déficits perceptifs visuels et posturaux observés suite à un TCCL, comme dans le cas du vieillissement normal.

Des études utilisant l'imagerie cérébrale ont permis de montrer et d'identifier les lésions cérébrales secondaires à un TCCL, comme le traumatisme axonal diffus (Lee et al., 2008; Topal et al., 2008). En outre, des chercheurs ont mis en évidence des signes d'atrophie de tout le parenchyme cérébral suite à un TCCL, onze mois en moyenne après le traumatisme (MacKenzie et al., 2002). D'autres chercheurs ont également trouvé des signes d'atrophie cérébrale suite à un TCCL chez certains sujets (Lewine et al., 2007). Cette atrophie n'était cependant pas étendue à tout le parenchyme, mais restreinte à certaines zones qui variaient suivant les sujets.

D’autres chercheurs encore ont mis en évidence des signes de traumatisme axonal diffus, de microhémorragies (Topal et al., 2008) et de contusions corticales suite à un TCCL (Lee et al., 2008). Aussi, un modèle animal de TCCL reproduisant le traumatisme axonal diffus a montré que les perturbations physiologiques dues à un TCCL étaient suivies d’un phénomène d’apoptose (Tweedie et al., 2007). De la même manière, l’imagerie cérébrale a permis de mettre en évidence une atrophie étendue affectant les substances blanche et grise (Draganski et al., 2011; Giorgio et al., 2010) ainsi que des défauts des petits vaisseaux associés à la substance blanche (Salat, 2013), au cours du vieillissement normal.

L’histologie et les modèles animaux ont permis de montrer que le traumatisme axonal entraîne des perturbations physiologiques et de conduction de l’influx nerveux (Bain et al., 2001; Maxwell et al., 1997). Chez l’homme, l’électrophysiologie a permis de mettre en évidence, suite à un TCCL, des déficits de connectivité fonctionnelle inter- et intrahémisphérique (Sukumar & Waugh, 2007) et un ralentissement de la conduction nerveuse lors du traitement de l’information visuelle (Lachapelle et al., 2008).

Au cours du vieillissement normal, l’électrophysiologie a également permis de révéler des ralentissements de la conduction nerveuse lors du traitement de l’information visuelle (Jiang, Luo, & Parasuraman, 2009; Langrova, Kuba, Kremlacek, Kubova, & Vit, 2006). Chez le singe vieillissant, l’enregistrement par microélectrodes de signaux extracellulaires a montré une dégradation de la sensibilité spatiale et temporelle des neurones du cortex visuel primaire (Zhang et al., 2008), ainsi qu’une plus grande variabilité des réponses cellulaires et une diminution du ratio signal-bruit

au niveau du cortex visuel primaire (V1) et de l'aire temporale médiale (MT) (Yang, Liang, Li, Wang, & Zhou, 2009). Yang et al. (2009) ont suggéré que cette variabilité de la réponse neuronale associée à une diminution du ratio signal-bruit chez le singe vieillissant était compatible avec l'hypothèse d'une dégradation liée à l'âge des circuits inhibiteurs intracorticaux. Toujours chez le singe vieillissant, d'autres chercheurs ont mis en évidence un ralentissement du traitement de l'information au niveau du cortex visuel primaire et du cortex extrastrié (aire V2) (Wang, Zhou, Ma, & Leventhal, 2005). Enfin, d'autres chercheurs encore ont montré, chez le singe vieillissant, que la diminution de la sensibilité au contraste des cellules de l'aire MT était plus affectée que celle des cellules de l'aire V1 sélectives pour la direction du mouvement, avec également une diminution du ratio-signal-bruit (Yang et al., 2008). Ils ont ainsi suggéré que la diminution de sensibilité au contraste de ces cellules pouvait résulter d'une dégénérescence des circuits inhibiteurs intracorticaux liée à l'âge.

Nos mesures de TR présentaient à la fois des valeurs centrales et une variabilité plus grandes chez les participants ayant subi un TCCL que chez les participants contrôles. Les TR plus longs indiquent possiblement une conduction nerveuse plus lente, et leur plus grande variabilité découle probablement d'une diminution du ratio signal-bruit dans les processus d'intégration visuomotrice. Nos observations concernant les déficits perceptifs visuels chez les sujets adultes TCCL semblent donc également compatibles avec un défaut des réseaux inhibiteurs intracorticaux. La plus grande dispersion des TR pour le mouvement de 1er ordre que pour celui de 2^{d} ordre suggère que ces réseaux inhibiteurs auraient une fonction plus

importante dans le traitement du mouvement de premier ordre que dans celui du 2^{d} ordre. Cette fonction consisterait notamment, à basses fréquences spatiale et temporelle, à sélectionner l'un ou l'autre des mécanismes disponibles (simple détection ou pistage de motif (« *feature tracking* ») de traitement du mouvement de 1er ordre.

Comme indiqué plus haut, des déficits de connectivité fonctionnelle inter- et intrahémisphérique (Sukumar & Waugh, 2007) ont été mis en évidence chez l'humain suite à un TCCL. Or on sait que le corps calleux et les réseaux sous-corticaux du système vestibulaire jouent un rôle essentiel dans l'intégration sensorimotrice intervenant notamment dans le contrôle postural (Dieterich & Brandt, 2015). Ces connexions inter- et intrahémisphériques permettraient au cerveau de résoudre aussi bien des conflits intersensoriels entre les systèmes visuel et vestibulaire, que d'éventuels conflits intrasensoriels entre les deux hémisphères, afin d'avoir une expérience unique de la façon dont nous percevons notre environnement visuel et nous préparons nos actions. Ainsi, certains experts estiment que les troubles de l'équilibre secondaires à un TCCL relèveraient principalement du traumatisme axonal diffus (Fife & Kalra, 2015) qui affecterait les connections inter- et intrahémisphériques du système vestibulaire.

D'autre part, l'imagerie cérébrale fonctionnelle a permis de démontrer, chez l'humain, que l'induction visuelle d'une sensation de vection entraîne l'activation des aires visuelles pariétales et occipitales et une désactivation simultanée du cortex vestibulaire multisensoriel (cortex vestibulaire pariéto-insulaire (*parieto-insular vestibular cortex*, PIVC)) (Dieterich & Brandt, 2015). D'autre part, l'activation

bilatérale (c'est-à-dire dans les deux hémisphères) des neurones du réseau vestibulaire temporo-pariétal entraîne une désactivation bilatérale des cortex visuel et somatosensoriel (Dieterich & Brandt, 2015). Il a donc été suggéré qu'il y avait, entre les systèmes visuel et vestibulaire, une interaction corticale inhibitrice réciproque. Cette interaction contribuerait au fonctionnement automatique du contrôle postural (Zwergal et al., 2012). Elle représenterait aussi un moyen de sélectionner l'information sensorielle la plus fiable dans le cas de conflits intersensoriels (Dieterich & Brandt, 2015). Par ailleurs, Zwergal et al. (2012) ont montré, au moyen de l'imagerie cérébrale fonctionnelle, que ces mécanismes d'interaction corticale inhibitrice réciproque entre les systèmes sensoriels impliqués dans le contrôle postural étaient affectés au cours du vieillissement normal. Cela suggèrerait que le maintien de l'équilibre soit basé sur des stratégies plus conscientes (moins automatiques) chez les personnes âgées.

Ainsi, la plus grande instabilité posturale observée suite à un TCCL pourrait être due à une perturbation des mécanismes d'interaction corticale inhibitrice réciproque entre les systèmes sensoriels impliqués dans le contrôle postural, semblable à celle retrouvée au cours du vieillissement normal. La présence de symptômes relatifs à l'équilibre suite à un TCCL qui ne peuvent être objectivés cliniquement (Fife & Kalra, 2015; McCrea et al., 2003) suggère également que les individus concernés s'adapteraient en mettant en place des stratégies de contrôle postural plus conscientes, comme cela serait le cas chez les personnes âgées en santé.

Chapitre 5 : Conclusion

Les résultats de nos expériences indiquent clairement la présence de déficits perceptivo-moteurs subtils après un TCCL, et qui persistent au-delà de la période supposée de récupération complète, c'est-à-dire au-delà de 3 mois.

L'étude portant sur les temps de réaction liée à la perception de stimuli de premier et de second ordre a permis de mettre en évidence des déficits perceptifs visuels affectant les processus de haut niveau comme ceux de bas niveau, après un TCCL. De plus, les résultats relatifs aux temps de réaction liée à la discrimination de direction de mouvement ont démontré que les processus de haut niveau étaient davantage affectés par ces déficits visuomoteurs que ceux de bas niveau. Enfin, les déficits ainsi identifiés et les symptômes des participants TCCL n'étaient toujours pas résolus un an après le traumatisme, et ce, malgré une tendance à la diminution dans les deux cas. Cela montre bien que, quoique le TCCL soit suivi d'une diminution de ce type de déficits visuomoteurs et des symptômes, le niveau de récupération fonctionnelle observé un an après un tel traumatisme n'est toujours pas comparable à celui d'individus n'ayant pas d'antécédent de TCCL.

Les mesures d'instabilité posturale, quant à elles, ont permis de mettre en évidence la présence de perturbations de l'équilibre postural de la station debout persistant plusieurs mois après le TCCL. Les mesures prises dans les situations d'oscillation posturale spontanée (avec les yeux fermés et dans un environnement visuel statique) ont notamment montré des déficits au niveau des processus d'intégration multisensorielle permettant le contrôle postural (c'est-à-dire concernant

les voies afférentes visuelle, vestibulaire et proprioceptive), 2 semaines après le traumatisme. D'autre part, les déficits affectant les processus visuels participant au contrôle postural, que la scène visuelle soit statique ou dynamique, étaient toujours présents chez les participants ayant subi un TCCL, 3 mois après leur traumatisme. Aussi, les déficits des processus de traitement de l'information visuelle secondaires à un TCCL révélés au cours de la première expérience semblent avoir contribué, au moins en partie, aux troubles de l'équilibre postural observés ici. Toutefois, ces déficits relatifs à l'équilibre ont fini par se résorber, permettant aux sujets TCCL de retrouver un niveau de stabilité posturale comparable à celui d'individus n'ayant pas d'antécédent de TCCL, un an après le traumatisme.

D'une part, des tâches basées sur l'analyse de la perception du mouvement de stimuli de premier et de second ordre se sont avérées suffisamment sensibles pour détecter des déficits de la perception visuelle secondaire à un TCCL. D'autre part, l'analyse de la vitesse quadratique moyenne des oscillations posturales (*body sway vRMS*) a permis de détecter des déficits au niveau des processus d'intégration multisensorielle impliqués dans le contrôle postural. Le développement de tests de perception visuelle utilisant des stimuli de premier et de second ordre, comme celui de tests d'instabilité posturale basés sur l'analyse de la vitesse quadratique moyenne des oscillations posturales, et destinés à l'évaluation des TCCL suivant leur phase aiguë, présente donc un intérêt certain.

Bibliographie

Adams, C. W., Bullimore, M. A., Wall, M., Fingeret, M., & Johnson, C. A. (1999). Normal aging effects for frequency doubling technology perimetry. *Optom Vis Sci, 76*(8), 582-587.

Allard, R., & Faubert, J. (2006). Same calculation efficiency but different internal noise for luminance- and contrast-modulated stimuli detection. *J Vis, 6*(4), 322-334. doi:10.1167/6.4.3

Allard, R., & Faubert, J. (2013a). No dedicated second-order motion system. *J Vis, 13*(11). doi:10.1167/13.11.2

Allard, R., & Faubert, J. (2013b). No second-order motion system sensitive to high temporal frequencies. *J Vis, 13*(5). doi:10.1167/13.5.4

Allard, R., Lagace-Nadon, S., & Faubert, J. (2013). Feature tracking and aging. *Front Psychol, 4*, 427. doi:10.3389/fpsyg.2013.00427

Allen, H. A., & Ledgeway, T. (2003). Attentional modulation of threshold sensitivity to first-order motion and second-order motion patterns. *Vision Res, 43*(27), 2927-2936.

Armstrong, V., Maurer, D., & Lewis, T. L. (2009). Sensitivity to first- and second-order motion and form in children and adults. *Vision Res, 49*(23), 2774-2781. doi:10.1016/j.visres.2009.08.016

Ashida, H., Lingnau, A., Wall, M. B., & Smith, A. T. (2007). FMRI adaptation reveals separate mechanisms for first-order and second-order motion. *J Neurophysiol, 97*(2), 1319-1325. doi:10.1152/jn.00723.2006

Bain, A. C., Raghupathi, R., & Meaney, D. F. (2001). Dynamic stretch correlates to both morphological abnormalities and electrophysiological impairment in a model of traumatic axonal injury. *J Neurotrauma, 18*(5), 499-511. doi:10.1089/089771501300227305

Bayly, P. V., Cohen, T. S., Leister, E. P., Ajo, D., Leuthardt, E. C., & Genin, G. M. (2005). Deformation of the human brain induced by mild acceleration. *J Neurotrauma, 22*(8), 845-856. doi:10.1089/neu.2005.22.845

Beaupre, M., De Guise, E., & McKerral, M. (2012). The Association between Pain-Related Variables, Emotional Factors, and Attentional Functioning following Mild Traumatic Brain Injury. *Rehabil Res Pract, 2012*, 924692. doi:10.1155/2012/924692

Bell, D. R., Guskiewicz, K. M., Clark, M. A., & Padua, D. A. (2011). Systematic review of the balance error scoring system. *Sports Health, 3*(3), 287-295. doi:10.1177/1941738111403122

Bertone, A., & Faubert, J. (2003). How is complex second-order motion processed? *Vision Res, 43*(25), 2591-2601.

Bertone, A., Hanck, J., Cornish, K. M., & Faubert, J. (2008). Development of static and dynamic perception for luminance-defined and texture-defined information. *Neuroreport, 19*(2), 225-228. doi:10.1097/WNR.0b013e3282f48401

Bigler, E. D. (2007). Anterior and middle cranial fossa in traumatic brain injury: relevant neuroanatomy and neuropathology in the study of neuropsychological outcome. *Neuropsychology, 21*(5), 515-531. doi:10.1037/0894-4105.21.5.515

Bigler, E. D. (2008). Neuropsychology and clinical neuroscience of persistent post-concussive syndrome. *J Int Neuropsychol Soc, 14*(1), 1-22. doi:10.1017/S135561770808017X

Billino, J., Braun, D. I., Bremmer, F., & Gegenfurtner, K. R. (2011). Challenges to normal neural functioning provide insights into separability of motion processing mechanisms. *Neuropsychologia, 49*(12), 3151-3163. doi:10.1016/j.neuropsychologia.2011.07.009

Borg, J., Holm, L., Cassidy, J. D., Peloso, P. M., Carroll, L. J., von Holst, H., . . . Injury, W. H. O. C. C. T. F. o. M. T. B. (2004). Diagnostic procedures in mild traumatic brain injury: results of the WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury. *J Rehabil Med*(43 Suppl), 61-75.

Brosseau-Lachaine, O., Gagnon, I., Forget, R., & Faubert, J. (2008). Mild traumatic brain injury induces prolonged visual processing deficits in children. *Brain Inj, 22*(9), 657-668. doi:10.1080/02699050802203353

Brown, L., Sherbenou, R. J., & Johnsen, S. K. (1997). Test of Nonverbal Intelligence: : A language-free measure of cognitive ability—Third Edition.

Bruininks, R. H., & Bruininks, B. D. (2005). Bruininks–Oseretsky Test of Motor Proficiency (2nd Edition).

Bryan, C. J., & Hernandez, A. M. (2011). Predictors of post-traumatic headache severity among deployed military personnel. *Headache, 51*(6), 945-953. doi:10.1111/j.1526-4610.2011.01887.x

Carroll, L. J., Cassidy, J. D., Holm, L., Kraus, J., Coronado, V. G., & Injury, W. H. O. C. C. T. F. o. M. T. B. (2004). Methodological issues and research recommendations for mild traumatic brain injury: the WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury. *J Rehabil Med*(43 Suppl), 113-125.

Cassidy, J. D., Carroll, L. J., Peloso, P. M., Borg, J., von Holst, H., Holm, L., . . . Injury, W. H. O. C. C. T. F. o. M. T. B. (2004). Incidence, risk factors and prevention of mild traumatic brain injury: results of the WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury. *J Rehabil Med*(43 Suppl), 28-60.

Cavanagh, P. (1992). Attention-based motion perception. *Science, 257*(5076), 1563-1565.

Cavanagh, P., & Mather, G. (1989). Motion: the long and short of it. *Spat Vis, 4*(2-3), 103-129.

Chakor, H., Bertone, A., McKerral, M., Faubert, J., & Lachapelle, P. (2005). Visual evoked potentials and reaction time measurements to motion-reversal luminance- and texture-defined stimuli. *Doc Ophthalmol, 110*(2-3), 163-172. doi:10.1007/s10633-005-3694-8

Chubb, C., & Sperling, G. (1988). Drift-balanced random stimuli: a general basis for studying non-Fourier motion perception. *J Opt Soc Am A, 5*(11), 1986-2007.

Cicerone, K. D., & Azulay, J. (2002). Diagnostic utility of attention measures in postconcussion syndrome. *Clin Neuropsychol, 16*(3), 280-289. doi:10.1076/clin.16.3.280.13849

Conners, C. K. (1997). Conner's Rating Scales - Revised Technical Manual. *Toronto, Ontario, Canada: Multi-Health Systems Inc.*

Daniel, P. M., & Whitteridge, D. (1961). The representation of the visual field on the cerebral cortex in monkeys. *J Physiol, 159*, 203-221.

Datta, S. G., Pillai, S. V., Rao, S. L., Kovoor, J. M., & Chandramouli, B. A. (2009). Post-concussion syndrome: Correlation of neuropsychological deficits, structural lesions on magnetic resonance imaging and symptoms. *Neurol India, 57*(5), 594-598. doi:10.4103/0028-3886.57810

de Guise, E., Lepage, J. F., Tinawi, S., LeBlanc, J., Dagher, J., Lamoureux, J., & Feyz, M. (2010). Comprehensive clinical picture of patients with complicated vs uncomplicated mild traumatic brain injury. *Clin Neuropsychol, 24*(7), 1113-1130. doi:10.1080/13854046.2010.506199

De Moraes, C. G. (2013). Anatomy of the visual pathways. *J Glaucoma, 22 Suppl 5*, S2-7. doi:10.1097/IJG.0b013e3182934978

Delorme, A. (2006). Statistical methods. *Encyclopedia of Medical Device and Instrumentation* (Vol. 6, pp. 240-264): Wiley Interscience.

DeMatteo, C., Greenspoon, D., Levac, D., Harper, J. A., & Rubinoff, M. (2014). Evaluating the Nintendo Wii for assessing return to activity readiness in youth with mild traumatic brain injury. *Phys Occup Ther Pediatr, 34*(3), 229-244. doi:10.3109/01942638.2014.885103

Dieterich, M., & Brandt, T. (2015). The bilateral central vestibular system: its pathways, functions, and disorders. *Ann N Y Acad Sci, 1343*, 10-26. doi:10.1111/nyas.12585

Dikmen, S., Machamer, J., Fann, J. R., & Temkin, N. R. (2010). Rates of symptom reporting following traumatic brain injury. *J Int Neuropsychol Soc, 16*(3), 401-411. doi:10.1017/S1355617710000196

Draganski, B., Ashburner, J., Hutton, C., Kherif, F., Frackowiak, R. S., Helms, G., & Weiskopf, N. (2011). Regional specificity of MRI contrast parameter changes in

normal ageing revealed by voxel-based quantification (VBQ). *Neuroimage, 55*(4), 1423-1434. doi:10.1016/j.neuroimage.2011.01.052

Dumoulin, S. O., Baker, C. L., Jr., Hess, R. F., & Evans, A. C. (2003). Cortical specialization for processing first- and second-order motion. *Cereb Cortex, 13*(12), 1375-1385.

Dupont, P., Sary, G., Peuskens, H., & Orban, G. A. (2003). Cerebral regions processing first- and higher-order motion in an opposed-direction discrimination task. *Eur J Neurosci, 17*(7), 1509-1517.

Eikema, D. J., Hatzitaki, V., Tzovaras, D., & Papaxanthis, C. (2012). Age-dependent modulation of sensory reweighting for controlling posture in a dynamic virtual environment. *Age (Dordr), 34*(6), 1381-1392. doi:10.1007/s11357-011-9310-9

Ellemberg, D., Lavoie, K., Lewis, T. L., Maurer, D., Lepore, F., & Guillemot, J. P. (2003). Longer VEP latencies and slower reaction times to the onset of second-order motion than to the onset of first-order motion. *Vision Res, 43*(6), 651-658.

Evans, R. W. (2004). Post-traumatic headaches. *Neurol Clin, 22*(1), 237-249, viii. doi:10.1016/S0733-8619(03)00097-5

Farivar, R. (2009). Dorsal-ventral integration in object recognition. *Brain Res Rev, 61*(2), 144-153. doi:10.1016/j.brainresrev.2009.05.006

Faubert, J. (2002). Visual perception and aging. *Can J Exp Psychol, 56*(3), 164-176.

Faubert, J., & Allard, R. (2004). Effect of visual distortion on postural balance in a full immersion stereoscopic environment. In A. J. Woods, Merrit, J. O., Benton, S. A. & Bolas, M. T. (Ed.), *Stereoscopic displays and virtual reality systems XI, Proceedings of SPIE IS&T Electronic Imaging, SPIE, 5291* (pp. 491–500).

Fayol, P., Carriere, H., Habonimana, D., & Dumond, J. J. (2009). Preliminary questions before studying mild traumatic brain injury outcome. *Ann Phys Rehabil Med, 52*(6), 497-509.

Ferre, E. R., Walther, L. E., & Haggard, P. (2015). Multisensory interactions between vestibular, visual and somatosensory signals. *PLoS One, 10*(4), e0124573. doi:10.1371/journal.pone.0124573

Fife, T. D., & Kalra, D. (2015). Persistent vertigo and dizziness after mild traumatic brain injury. *Ann N Y Acad Sci, 1343*, 97-105. doi:10.1111/nyas.12678

Findling, O., Schuster, C., Sellner, J., Ettlin, T., & Allum, J. H. (2011). Trunk sway in patients with and without, mild traumatic brain injury after whiplash injury. *Gait Posture, 34*(4), 473-478. doi:10.1016/j.gaitpost.2011.06.021

Fisher, D. C., Ledbetter, M. F., Cohen, N. J., Marmor, D., & Tulsky, D. S. (2000). WAIS-III and WMS-III profiles of mildly to severely brain-injured patients. *Appl Neuropsychol, 7*(3), 126-132. doi:10.1207/S15324826AN0703_2

Gaetz, M. (2004). The neurophysiology of brain injury. *Clin Neurophysiol, 115*(1), 4-18.

Gagnon, I., Forget, R., Sullivan, S. J., & Friedman, D. (1998). Motor performance following a mild traumatic brain injury in children: an exploratory study. *Brain Inj, 12*(10), 843-853.

Gagnon, I., Friedman, D., Swaine, B., & Forget, R. (2001). Balance findings in a child before and after a mild head injury. *J Head Trauma Rehabil, 16*(6), 595-602.

Gagnon, I., Swaine, B., Friedman, D., & Forget, R. (2004a). Children show decreased dynamic balance after mild traumatic brain injury. *Arch Phys Med Rehabil, 85*(3), 444-452.

Gagnon, I., Swaine, B., Friedman, D., & Forget, R. (2004b). Visuomotor response time in children with a mild traumatic brain injury. *J Head Trauma Rehabil, 19*(5), 391-404.

Gegenfurtner, K. R., & Hawken, M. J. (1996). Perceived velocity of luminance, chromatic and non-fourier stimuli: influence of contrast and temporal frequency. *Vision Res, 36*(9), 1281-1290.

Geurts, A. C., Knoop, J. A., & van Limbeek, J. (1999). Is postural control associated with mental functioning in the persistent postconcussion syndrome? *Arch Phys Med Rehabil, 80*(2), 144-149.

Geurts, A. C., Ribbers, G. M., Knoop, J. A., & van Limbeek, J. (1996). Identification of static and dynamic postural instability following traumatic brain injury. *Arch Phys Med Rehabil, 77*(7), 639-644.

Giardino, L., Zanni, M., Fernandez, M., Battaglia, A., Pignataro, O., & Calza, L. (2002). Plasticity of GABA(a) system during ageing: focus on vestibular compensation and possible pharmacological intervention. *Brain Res, 929*(1), 76-86.

Gibson, J. J. (1979). *The ecological approach to visual perception*. Boston: Houghton Mifflin.

Giorgio, A., Santelli, L., Tomassini, V., Bosnell, R., Smith, S., De Stefano, N., & Johansen-Berg, H. (2010). Age-related changes in grey and white matter structure throughout adulthood. *Neuroimage, 51*(3), 943-951. doi:10.1016/j.neuroimage.2010.03.004

Gordon, W. A., Haddad, L., Brown, M., Hibbard, M. R., & Sliwinski, M. (2000). The sensitivity and specificity of self-reported symptoms in individuals with traumatic brain injury. *Brain Inj, 14*(1), 21-33.

Greffou, S., Bertone, A., Hanssens, J. M., & Faubert, J. (2008). Development of visually driven postural reactivity: a fully immersive virtual reality study. *J Vis, 8*(11), 15 11-10. doi:10.1167/8.11.15

Guerraz, M., Thilo, K. V., Bronstein, A. M., & Gresty, M. A. (2001). Influence of action and expectation on visual control of posture. *Brain Res Cogn Brain Res, 11*(2), 259-266.

Guldin, W. O., & Grusser, O. J. (1998). Is there a vestibular cortex? *Trends Neurosci, 21*(6), 254-259.

Guskiewicz, K. M., Ross, S. E., & Marshall, S. W. (2001). Postural Stability and Neuropsychological Deficits After Concussion in Collegiate Athletes. *J Athl Train, 36*(3), 263-273.

Habak, C., & Faubert, J. (2000). Larger effect of aging on the perception of higher-order stimuli. *Vision Res, 40*(8), 943-950.

Haibach, P. S., Slobounov, S. M., & Newell, K. M. (2008). The potential applications of a virtual moving environment for assessing falls in elderly adults. *Gait Posture, 27*(2), 303-308. doi:10.1016/j.gaitpost.2007.04.004

Halterman, C. I., Langan, J., Drew, A., Rodriguez, E., Osternig, L. R., Chou, L. S., & van Donkelaar, P. (2006). Tracking the recovery of visuospatial attention deficits in mild traumatic brain injury. *Brain, 129*(Pt 3), 747-753. doi:10.1093/brain/awh705

Harmon, K. G., Drezner, J. A., Gammons, M., Guskiewicz, K. M., Halstead, M., Herring, S. A., . . . Roberts, W. O. (2013). American Medical Society for Sports Medicine position statement: concussion in sport. *Br J Sports Med, 47*(1), 15-26. doi:10.1136/bjsports-2012-091941

Heltemes, K. J., Holbrook, T. L., Macgregor, A. J., & Galarneau, M. R. (2012). Blast-related mild traumatic brain injury is associated with a decline in self-rated

health amongst US military personnel. *Injury, 43*(12), 1990-1995. doi:10.1016/j.injury.2011.07.021

Hugenholtz, H., Stuss, D. T., Stethem, L. L., & Richard, M. T. (1988). How long does it take to recover from a mild concussion? *Neurosurgery, 22*(5), 853-858.

Hutchinson, C. V., & Ledgeway, T. (2006). Sensitivity to spatial and temporal modulations of first-order and second-order motion. *Vision Res, 46*(3), 324-335. doi:10.1016/j.visres.2005.03.002

Ivarsson, J., Viano, D. C., & Lovsund, P. (2002). Influence of the lateral ventricles and irregular skull base on brain kinematics due to sagittal plane head rotation. *J Biomech Eng, 124*(4), 422-431.

Iverson, G. (2007). Predicting slow recovery from sport-related concussion: the new simple-complex distinction. *Clin J Sport Med, 17*(1), 31-37. doi:10.1097/JSM.0b013e3180305e4d

Iverson, G. L. (2005). Outcome from mild traumatic brain injury. *Curr Opin Psychiatry, 18*(3), 301-317. doi:10.1097/01.yco.0000165601.29047.ae

Iwasaki, S., & Yamasoba, T. (2015). Dizziness and Imbalance in the Elderly: Age-related Decline in the Vestibular System. *Aging Dis, 6*(1), 38-47. doi:10.14336/AD.2014.0128

Jiang, Y., Luo, Y. J., & Parasuraman, R. (2009). Neural correlates of age-related reduction in visual motion priming. *Neuropsychol Dev Cogn B Aging Neuropsychol Cogn, 16*(2), 164-182. doi:10.1080/13825580802348588

Kalaycioglu, C., Nalcaci, E., Schmiedt-Fehr, C., & Basar-Eroglu, C. (2009). Corpus callosum has different channels for transmission of spatial frequency information. *Brain Res, 1296*, 85-93. doi:10.1016/j.brainres.2009.08.018

Kaufman, K. R., Brey, R. H., Chou, L. S., Rabatin, A., Brown, A. W., & Basford, J. R. (2006). Comparison of subjective and objective measurements of balance disorders following traumatic brain injury. *Med Eng Phys, 28*(3), 234-239. doi:10.1016/j.medengphy.2005.05.005

King, L. A., Horak, F. B., Mancini, M., Pierce, D., Priest, K. C., Chesnutt, J., . . . Chapman, J. C. (2014). Instrumenting the balance error scoring system for use with patients reporting persistent balance problems after mild traumatic brain injury. *Arch Phys Med Rehabil, 95*(2), 353-359. doi:10.1016/j.apmr.2013.10.015

Kirov, II, Tal, A., Babb, J. S., Reaume, J., Bushnik, T., Ashman, T. A., . . . Gonen, O. (2013). Proton MR spectroscopy correlates diffuse axonal abnormalities with post-concussive symptoms in mild traumatic brain injury. *J Neurotrauma, 30*(13), 1200-1204. doi:10.1089/neu.2012.2696

Kleffelgaard, I., Roe, C., Soberg, H. L., & Bergland, A. (2012). Associations among self-reported balance problems, post-concussion symptoms and performance-

based tests: a longitudinal follow-up study. *Disabil Rehabil, 34*(9), 788-794. doi:10.3109/09638288.2011.619624

Konrad, C., Geburek, A. J., Rist, F., Blumenroth, H., Fischer, B., Husstedt, I., . . . Lohmann, H. (2011). Long-term cognitive and emotional consequences of mild traumatic brain injury. *Psychol Med, 41*(6), 1197-1211. doi:10.1017/S0033291710001728

Kontos, A. P., Elbin, R. J., Schatz, P., Covassin, T., Henry, L., Pardini, J., & Collins, M. W. (2012). A revised factor structure for the post-concussion symptom scale: baseline and postconcussion factors. *Am J Sports Med, 40*(10), 2375-2384. doi:10.1177/0363546512455400

Korth, M., Rix, R., & Sembritzki, O. (2000). The sequential processing of visual motion in the human electroretinogram and visual evoked potential. *Vis Neurosci, 17*(4), 631-646.

Krainik, A., Feydy, A., Colombani, J. M., Helias, A., & Menu, Y. (2003). [Functional anatomy of the central nervous system]. *J Radiol, 84*(3), 285-297.

Kuba, M., & Kubova, Z. (1992). Visual evoked potentials specific for motion onset. *Doc Ophthalmol, 80*(1), 83-89.

Kumar, S., Rao, S. L., Chandramouli, B. A., & Pillai, S. V. (2009). Reduction of functional brain connectivity in mild traumatic brain injury during working memory. *J Neurotrauma, 26*(5), 665-675. doi:10.1089/neu.2008-0644

Lachapelle, J., Bolduc-Teasdale, J., Ptito, A., & McKerral, M. (2008). Deficits in complex visual information processing after mild TBI: electrophysiological markers and vocational outcome prognosis. *Brain Inj, 22*(3), 265-274. doi:10.1080/02699050801938983

Lachapelle, J., Ouimet, C., Bach, M., Ptito, A., & McKerral, M. (2004). Texture segregation in traumatic brain injury--a VEP study. *Vision Res, 44*(24), 2835-2842. doi:10.1016/j.visres.2004.06.007

Lange, R. T., Iverson, G. L., & Rose, A. (2010). Post-concussion symptom reporting and the "good-old-days" bias following mild traumatic brain injury. *Arch Clin Neuropsychol, 25*(5), 442-450. doi:10.1093/arclin/acq031

Langrova, J., Kuba, M., Kremlacek, J., Kubova, Z., & Vit, F. (2006). Motion-onset VEPs reflect long maturation and early aging of visual motion-processing system. *Vision Res, 46*(4), 536-544. doi:10.1016/j.visres.2005.06.024

Larson, M. J., Clayson, P. E., & Farrer, T. J. (2012). Performance monitoring and cognitive control in individuals with mild traumatic brain injury. *J Int Neuropsychol Soc, 18*(2), 323-333. doi:10.1017/S1355617711001779

Leddy, J. J., Kozlowski, K., Fung, M., Pendergast, D. R., & Willer, B. (2007). Regulatory and autoregulatory physiological dysfunction as a primary characteristic of post concussion syndrome: implications for treatment. *NeuroRehabilitation, 22*(3), 199-205.

Ledgeway, T., & Hutchinson, C. V. (2005). The influence of spatial and temporal noise on the detection of first-order and second-order orientation and motion direction. *Vision Res, 45*(16), 2081-2094. doi:10.1016/j.visres.2005.02.005

Ledgeway, T., & Hutchinson, C. V. (2008). Choice reaction times for identifying the direction of first-order motion and different varieties of second-order motion. *Vision Res, 48*(2), 208-222. doi:10.1016/j.visres.2007.11.008

Lee, H., Wintermark, M., Gean, A. D., Ghajar, J., Manley, G. T., & Mukherjee, P. (2008). Focal lesions in acute mild traumatic brain injury and neurocognitive outcome: CT versus 3T MRI. *J Neurotrauma, 25*(9), 1049-1056. doi:10.1089/neu.2008.0566

Levin, H. S., Mattis, S., Ruff, R. M., Eisenberg, H. M., Marshall, L. F., Tabaddor, K., . . . Frankowski, R. F. (1987). Neurobehavioral outcome following minor head injury: a three-center study. *J Neurosurg, 66*(2), 234-243. doi:10.3171/jns.1987.66.2.0234

Lewine, J. D., Davis, J. T., Bigler, E. D., Thoma, R., Hill, D., Funke, M., . . . Orrison, W. W. (2007). Objective documentation of traumatic brain injury subsequent to mild head trauma: multimodal brain imaging with MEG, SPECT, and MRI. *J Head Trauma Rehabil, 22*(3), 141-155. doi:10.1097/01.HTR.0000271115.29954.27

Lingsma, H. F., Yue, J. K., Maas, A. I., Steyerberg, E. W., Manley, G. T., Cooper, S. R., . . . Yuh, E. L. (2015). Outcome Prediction after Mild and Complicated Mild

Traumatic Brain Injury: External Validation of Existing Models and Identification of New Predictors Using the TRACK-TBI Pilot Study. *J Neurotrauma, 32*(2), 83-94. doi:10.1089/neu.2014.3384

Lovell, M. R., & Collins, M. W. (1998). Neuropsychological assessment of the college football player. *J Head Trauma Rehabil, 13*(2), 9-26.

Lu, Z. L., & Sperling, G. (2001). Three-systems theory of human visual motion perception: review and update. *J Opt Soc Am A Opt Image Sci Vis, 18*(9), 2331-2370.

MacKenzie, J. D., Siddiqi, F., Babb, J. S., Bagley, L. J., Mannon, L. J., Sinson, G. P., & Grossman, R. I. (2002). Brain atrophy in mild or moderate traumatic brain injury: a longitudinal quantitative analysis. *AJNR Am J Neuroradiol, 23*(9), 1509-1515.

Malojcic, B., Mubrin, Z., Coric, B., Susnic, M., & Spilich, G. J. (2008). Consequences of mild traumatic brain injury on information processing assessed with attention and short-term memory tasks. *J Neurotrauma, 25*(1), 30-37. doi:10.1089/neu.2007.0384

Marion, D. W. (1998). Head and spinal cord injury. *Neurol Clin, 16*(2), 485-502.

Marshall, S., Bayley, M., McCullagh, S., Velikonja, D., & Berrigan, L. (2012). Clinical practice guidelines for mild traumatic brain injury and persistent symptoms. *Can Fam Physician, 58*(3), 257-267, e128-240.

Marshall, S., Bayley, M., McCullagh, S., Velikonja, D., Berrigan, L., Ouchterlony, D., & Weegar, K. (2015). Updated clinical practice guidelines for concussion/mild traumatic brain injury and persistent symptoms. *Brain Inj, 29*(6), 688-700. doi:10.3109/02699052.2015.1004755

Maxwell, W. L., Povlishock, J. T., & Graham, D. L. (1997). A mechanistic analysis of nondisruptive axonal injury: a review. *J Neurotrauma, 14*(7), 419-440.

McAllister, T. W., & Arciniegas, D. (2002). Evaluation and treatment of postconcussive symptoms. *NeuroRehabilitation, 17*(4), 265-283.

McCrea, M., Guskiewicz, K. M., Marshall, S. W., Barr, W., Randolph, C., Cantu, R. C., . . . Kelly, J. P. (2003). Acute effects and recovery time following concussion in collegiate football players: the NCAA Concussion Study. *JAMA, 290*(19), 2556-2563. doi:10.1001/jama.290.19.2556

McKerral, M., Lepore, F., & Lachapelle, P. (2001). Response characteristics of the normal retino-cortical pathways as determined with simultaneous recordings of pattern visual evoked potentials and simple motor reaction times. *Vision Res, 41*(8), 1085-1090.

Mergner, T. (2010). A neurological view on reactive human stance control. *Annual Reviews in Control, 34*(2), 177-198. doi:10.1016/j.arcontrol.2010.08.001

Naunheim, R. S., Matero, D., & Fucetola, R. (2008). Assessment of patients with mild concussion in the emergency department. *J Head Trauma Rehabil, 23*(2), 116-122. doi:10.1097/01.HTR.0000314530.30401.70

Nishiike, S., Nakagawa, S., Tonoike, M., Takeda, N., & Kubo, T. (2001). Information processing of visually-induced apparent self motion in the cortex of humans: analysis with magnetoencephalography. *Acta Otolaryngol Suppl, 545*, 113-115.

Nishimoto, T., & Murakami, S. (1998). Relation between diffuse axonal injury and internal head structures on blunt impact. *J Biomech Eng, 120*(1), 140-147.

Noguchi, Y., Kaneoke, Y., Kakigi, R., Tanabe, H. C., & Sadato, N. (2005). Role of the superior temporal region in human visual motion perception. *Cereb Cortex, 15*(10), 1592-1601. doi:10.1093/cercor/bhi037

Owsley, C. (2011). Aging and vision. *Vision Res, 51*(13), 1610-1622. doi:10.1016/j.visres.2010.10.020

Pedalini, M. E., Cruz, O. L., Bittar, R. S., Lorenzi, M. C., & Grasel, S. S. (2009). Sensory organization test in elderly patients with and without vestibular dysfunction. *Acta Otolaryngol, 129*(9), 962-965. doi:10.1080/00016480802468930

Peterka, R. J. (2002). Sensorimotor integration in human postural control. *J Neurophysiol, 88*(3), 1097-1118.

Piponnier, J. C., Forget, R., Gagnon, I., McKerral, M., Giguere, J. F., & Faubert, J. (2015). First- and second-order stimuli reaction time measures are highly sensitive to mild traumatic brain injuries. *J Neurotrauma*. doi:10.1089/neu.2014.3832

Piponnier, J. C., Hanssens, J. M., & Faubert, J. (2009). Effect of visual field locus and oscillation frequencies on posture control in an ecological environment. *J Vis, 9*(1), 13 11-10. doi:10.1167/9.1.13

Pontifex, M. B., Broglio, S. P., Drollette, E. S., Scudder, M. R., Johnson, C. R., O'Connor, P. M., & Hillman, C. H. (2012). The relation of mild traumatic brain injury to chronic lapses of attention. *Res Q Exerc Sport, 83*(4), 553-559.

Pontifex, M. B., O'Connor, P. M., Broglio, S. P., & Hillman, C. H. (2009). The association between mild traumatic brain injury history and cognitive control. *Neuropsychologia, 47*(14), 3210-3216. doi:10.1016/j.neuropsychologia.2009.07.021

Prieto, E. A., Barnikol, U. B., Soler, E. P., Dolan, K., Hesselmann, G., Mohlberg, H., . . . Tass, P. A. (2007). Timing of V1/V2 and V5+ activations during coherent motion of dots: an MEG study. *Neuroimage, 37*(4), 1384-1395. doi:10.1016/j.neuroimage.2007.03.080

Raghuram, A., Lakshminarayanan, V., & Khanna, R. (2005). Psychophysical estimation of speed discrimination. II. Aging effects. *J Opt Soc Am A Opt Image Sci Vis, 22*(10), 2269-2280.

Rees, P. M. (2003). Contemporary issues in mild traumatic brain injury. *Arch Phys Med Rehabil, 84*(12), 1885-1894.

Rees, R. J., & Bellon, M. L. (2007). Post concussion syndrome ebb and flow: longitudinal effects and management. *NeuroRehabilitation, 22*(3), 229-242.

Ropper, A. H., & Gorson, K. C. (2007). Clinical practice. Concussion. *N Engl J Med, 356*(2), 166-172. doi:10.1056/NEJMcp064645

Ruff, R. (2005). Two decades of advances in understanding of mild traumatic brain injury. *J Head Trauma Rehabil, 20*(1), 5-18.

Ruff, R. M. (2011). Mild traumatic brain injury and neural recovery: rethinking the debate. *NeuroRehabilitation, 28*(3), 167-180. doi:10.3233/NRE-2011-0646

Ruff, R. M., Iverson, G. L., Barth, J. T., Bush, S. S., Broshek, D. K., Policy, N. A. N., & Planning, C. (2009). Recommendations for diagnosing a mild traumatic brain injury: a National Academy of Neuropsychology education paper. *Arch Clin Neuropsychol, 24*(1), 3-10. doi:10.1093/arclin/acp006

Ruffolo, C. F., Friedland, J. F., Dawson, D. R., Colantonio, A., & Lindsay, P. H. (1999). Mild traumatic brain injury from motor vehicle accidents: factors associated with return to work. *Arch Phys Med Rehabil, 80*(4), 392-398.

Salat, D. H. (2013). Imaging small vessel-associated white matter changes in aging. *Neuroscience*. doi:10.1016/j.neuroscience.2013.11.041

Schofield, A. J., & Georgeson, M. A. (2000). The temporal properties of first- and second-order vision. *Vision Res, 40*(18), 2475-2487.

Shaw, N. A. (2002). The neurophysiology of concussion. *Prog Neurobiol, 67*(4), 281-344.

Sheedy, J., Geffen, G., Donnelly, J., & Faux, S. (2006). Emergency department assessment of mild traumatic brain injury and prediction of post-concussion symptoms at one month post injury. *J Clin Exp Neuropsychol, 28*(5), 755-772. doi:10.1080/13803390591000864

Sheedy, J., Harvey, E., Faux, S., Geffen, G., & Shores, E. A. (2009). Emergency department assessment of mild traumatic brain injury and the prediction of postconcussive symptoms: a 3-month prospective study. *J Head Trauma Rehabil, 24*(5), 333-343. doi:10.1097/HTR.0b013e3181aea51f

Slobounov, S., Cao, C., Sebastianelli, W., Slobounov, E., & Newell, K. (2008). Residual deficits from concussion as revealed by virtual time-to-contact measures of postural stability. *Clin Neurophysiol, 119*(2), 281-289. doi:10.1016/j.clinph.2007.10.006

Slobounov, S., Sebastianelli, W., & Hallett, M. (2012). Residual brain dysfunction observed one year post-mild traumatic brain injury: combined EEG and balance study. *Clin Neurophysiol, 123*(9), 1755-1761. doi:10.1016/j.clinph.2011.12.022

Slobounov, S., Sebastianelli, W., & Moss, R. (2005). Alteration of posture-related cortical potentials in mild traumatic brain injury. *Neurosci Lett, 383*(3), 251-255. doi:10.1016/j.neulet.2005.04.039

Slobounov, S., Sebastianelli, W., & Newell, K. M. (2011). Incorporating virtual reality graphics with brain imaging for assessment of sport-related concussions. *Conf Proc IEEE Eng Med Biol Soc, 2011*, 1383-1386. doi:10.1109/IEMBS.2011.6090325

Slobounov, S., Tutwiler, R., Sebastianelli, W., & Slobounov, E. (2006). Alteration of postural responses to visual field motion in mild traumatic brain injury. *Neurosurgery, 59*(1), 134-139; discussion 134-139. doi:10.1227/01.NEU.0000219197.33182.3F

Slobounov, S., Wu, T., Hallett, M., Shibasaki, H., Slobounov, E., & Newell, K. (2006). Neural underpinning of postural responses to visual field motion. *Biol Psychol, 72*(2), 188-197. doi:10.1016/j.biopsycho.2005.10.005

Smith, A. T., Greenlee, M. W., Singh, K. D., Kraemer, F. M., & Hennig, J. (1998). The processing of first- and second-order motion in human visual cortex assessed by functional magnetic resonance imaging (fMRI). *J Neurosci, 18*(10), 3816-3830.

Smith, A. T., & Ledgeway, T. (1997). Separate detection of moving luminance and contrast modulations: fact or artifact? *Vision Res, 37*(1), 45-62.

Sosnoff, J. J., Broglio, S. P., & Ferrara, M. S. (2008). Cognitive and motor function are associated following mild traumatic brain injury. *Exp Brain Res, 187*(4), 563-571. doi:10.1007/s00221-008-1324-x

Sosnoff, J. J., Broglio, S. P., Shin, S., & Ferrara, M. S. (2011). Previous mild traumatic brain injury and postural-control dynamics. *J Athl Train, 46*(1), 85-91. doi:10.4085/1062-6050-46.1.85

Stoffregen, T. A. (1985). Flow structure versus retinal location in the optical control of stance. *J Exp Psychol Hum Percept Perform, 11*(5), 554-565.

Stuss, D. T., Stethem, L. L., Hugenholtz, H., Picton, T., Pivik, J., & Richard, M. T. (1989). Reaction time after head injury: fatigue, divided and focused attention, and consistency of performance. *J Neurol Neurosurg Psychiatry, 52*(6), 742-748.

Sukumar, S., & Waugh, S. J. (2007). Separate first- and second-order processing is supported by spatial summation estimates at the fovea and eccentrically. *Vision Res, 47*(5), 581-596. doi:10.1016/j.visres.2006.10.004

Sunaert, S., Van Hecke, P., Marchal, G., & Orban, G. A. (2000). Attention to speed of motion, speed discrimination, and task difficulty: an fMRI study. *Neuroimage, 11*(6 Pt 1), 612-623. doi:10.1006/nimg.2000.0587

Swaine, B. R., & Friedman, D. S. (2001). Activity restrictions as part of the discharge management for children with a traumatic head injury. *J Head Trauma Rehabil, 16*(3), 292-301.

Tang, Y., & Zhou, Y. (2009). Age-related decline of contrast sensitivity for second-order stimuli: earlier onset, but slower progression, than for first-order stimuli. *J Vis, 9*(7), 18. doi:10.1167/9.7.18

Thompson, J., Sebastianelli, W., & Slobounov, S. (2005). EEG and postural correlates of mild traumatic brain injury in athletes. *Neurosci Lett, 377*(3), 158-163. doi:10.1016/j.neulet.2004.11.090

Thurrell, A. E., & Bronstein, A. M. (2002). Vection increases the magnitude and accuracy of visually evoked postural responses. *Exp Brain Res, 147*(4), 558-560. doi:10.1007/s00221-002-1296-1

Tinius, T. P. (2003). The intermediate visual and auditory continuous performance test as a neuropsychological measure. *Arch Clin Neuropsychol, 18*(2), 199-214.

Topal, N. B., Hakyemez, B., Erdogan, C., Bulut, M., Koksal, O., Akkose, S., . . . Korfali, E. (2008). MR imaging in the detection of diffuse axonal injury with mild traumatic brain injury. *Neurol Res, 30*(9), 974-978. doi:10.1179/016164108X323799

Tweedie, D., Milman, A., Holloway, H. W., Li, Y., Harvey, B. K., Shen, H., . . . Greig, N. H. (2007). Apoptotic and behavioral sequelae of mild brain trauma in mice. *J Neurosci Res, 85*(4), 805-815. doi:10.1002/jnr.21160

Uesaki, M., & Ashida, H. (2015). Optic-flow selective cortical sensory regions associated with self-reported states of vection. *Front Psychol, 6*, 775. doi:10.3389/fpsyg.2015.00775

Ulrich, R., & Miller, J. (1994). Effects of truncation on reaction time analysis. *J Exp Psychol Gen, 123*(1), 34-80.

Vaina, L. M., & Soloviev, S. (2004). First-order and second-order motion: neurological evidence for neuroanatomically distinct systems. *Prog Brain Res, 144*, 197-212. doi:10.1016/S0079-6123(03)14414-7

Vakalopoulos, C. (2005). Neural correlates of consciousness: a definition of the dorsal and ventral streams and their relation to phenomenology. *Med Hypotheses, 65*(5), 922-931. doi:10.1016/j.mehy.2005.05.016

Vanderploeg, R. D., Curtiss, G., & Belanger, H. G. (2005). Long-term neuropsychological outcomes following mild traumatic brain injury. *J Int Neuropsychol Soc, 11*(3), 228-236. doi:10.1017/S1355617705050289

Viano, D. C., Casson, I. R., & Pellman, E. J. (2007). Concussion in professional football: biomechanics of the struck player--part 14. *Neurosurgery, 61*(2), 313-327; discussion 327-318. doi:10.1227/01.NEU.0000279969.02685.D0

Viano, D. C., Casson, I. R., Pellman, E. J., Zhang, L., King, A. I., & Yang, K. H. (2005). Concussion in professional football: brain responses by finite element analysis: part 9. *Neurosurgery, 57*(5), 891-916; discussion 891-916.

Villemure, R., Nolin, P., & Le Sage, N. (2011). Self-reported symptoms during post-mild traumatic brain injury in acute phase: influence of interviewing method. *Brain Inj, 25*(1), 53-64. doi:10.3109/02699052.2010.531881

Wadood, A. C., Azuara-Blanco, A., Aspinall, P., Taguri, A., & King, A. J. (2002). Sensitivity and specificity of frequency-doubling technology, tendency-oriented perimetry, and Humphrey Swedish interactive threshold algorithm-fast perimetry in a glaucoma practice. *Am J Ophthalmol, 133*(3), 327-332.

Wang, Y., Zhou, Y., Ma, Y., & Leventhal, A. G. (2005). Degradation of signal timing in cortical areas V1 and V2 of senescent monkeys. *Cereb Cortex, 15*(4), 403-408. doi:10.1093/cercor/bhh143

Willer, B., & Leddy, J. J. (2006). Management of concussion and post-concussion syndrome. *Curr Treat Options Neurol, 8*(5), 415-426.

Winter, D. A., Patla, A. E., Prince, F., Ishac, M., & Gielo-Perczak, K. (1998). Stiffness control of balance in quiet standing. *J Neurophysiol, 80*(3), 1211-1221.

Wright, M. J., & Johnston, A. (1983). Spatiotemporal contrast sensitivity and visual field locus. *Vision Res, 23*(10), 983-989.

Yamamoto, T., Smith, C. E., Suzuki, Y., Kiyono, K., Tanahashi, T., Sakoda, S., . . . Nomura, T. (2015). Universal and individual characteristics of postural sway during quiet standing in healthy young adults. *Physiol Rep, 3*(3). doi:10.14814/phy2.12329

Yang, Y., Liang, Z., Li, G., Wang, Y., & Zhou, Y. (2009). Aging affects response variability of V1 and MT neurons in rhesus monkeys. *Brain Res, 1274*, 21-27. doi:10.1016/j.brainres.2009.04.015

Yang, Y., Liang, Z., Li, G., Wang, Y., Zhou, Y., & Leventhal, A. G. (2008). Aging affects contrast response functions and adaptation of middle temporal visual area neurons in rhesus monkeys. *Neuroscience, 156*(3), 748-757. doi:10.1016/j.neuroscience.2008.08.007

Yeates, K. O., Taylor, H. G., Rusin, J., Bangert, B., Dietrich, A., Nuss, K., . . . Jones, B. L. (2009). Longitudinal trajectories of postconcussive symptoms in children with mild traumatic brain injuries and their relationship to acute clinical status. *Pediatrics, 123*(3), 735-743. doi:10.1542/peds.2008-1056

Zhang, J., Wang, X., Wang, Y., Fu, Y., Liang, Z., Ma, Y., & Leventhal, A. G. (2008). Spatial and temporal sensitivity degradation of primary visual cortical cells in senescent rhesus monkeys. *Eur J Neurosci, 28*(1), 201-207. doi:10.1111/j.1460-9568.2008.06300.x

zu Eulenburg, P., Caspers, S., Roski, C., & Eickhoff, S. B. (2012). Meta-analytical definition and functional connectivity of the human vestibular cortex. *Neuroimage, 60*(1), 162-169. doi:10.1016/j.neuroimage.2011.12.032

Zwergal, A., Linn, J., Xiong, G., Brandt, T., Strupp, M., & Jahn, K. (2012). Aging of human supraspinal locomotor and postural control in fMRI. *Neurobiol Aging, 33*(6), 1073-1084. doi:10.1016/j.neurobiolaging.2010.09.022