Université de Montréal

Caractérisation des fonctions exécutives et prédiction de la participation sociale après un traumatisme craniocérébral

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Table des matières

Résumé

L'objectif principal de la thèse est d'outiller les cliniciens œuvrant auprès d'une population atteinte d'un traumatisme craniocérébral (TCC) dans l'établissement d'un profil compréhensif et un pronostic des fonctions exécutives (FE), ainsi que dans leur capacité à cibler les patients qui développeront des difficultés d'intégration sociale, sur la base des troubles cognitifs objectivés et plus précisément des troubles des FE. Afin de répondre à cet objectif, la présente thèse contient deux articles qui se basent sur le modèle théorique de Miyake (Miyake, Friedman, et al., 2000) afin de définir les FE. Le premier article s'intéresse à caractériser les associations entre des variables sociodémographiques, liées au TCC léger et des symptômes post TCC léger d'une part, et les performances des FE d'autre part. Le deuxième article vise à (1) mesurer la récupération des FE entre la phase aiguë et six mois post-TCC et (2) explorer la relation entre les FE et la participation sociale après un TCC.

Les résultats des articles suggèrent principalement que les personnes ayant subi un TCC léger qui sont les plus éduquées et dont le QI estimé prémobide est plus élevé (réserve cognitive plus grande), sont susceptibles de présenter de meilleures performances aux mesures des FE à la suite de leur accident. Les résultats suggèrent aussi que la performance des patients sur certaines mesures des FE s'améliore significativement dans les six mois suivant leur accident et qu'elle peut être associée, notamment pour la fluence verbale alternée, avec le niveau de participation sociale des patients après leur accident.

Globalement, les résultats de cette thèse nous permettent de statuer que certains facteurs sont importants à prendre en compte lorsque l'on évalue les FE chez des personnes atteintes d’un TCC, et ce, afin de mieux comprendre les différences inter-individuelles chez cette population. Ainsi, la thèse suggère qu’il est crucial de considérer la notion de réserve cognitive avec une population atteinte d’un TCC. Puisqu’il est postulé que la réserve cognitive permet de compenser les déficits cognitifs, les déficits des FE chez des patients présentant une haute réserve cognitive pourraient apparaitre comme plus préoccupant que chez des patients présentant un faible niveau de réserve cognitive. De surcroît, les résultats de la thèse mettent de l’avant l’importance du test de fluence verbale alternée qui s’avère suffisamment sensible auprès de cette population pour mesurer la récupération des FE dans le temps, mais également pour donner un portrait de l’atteinte exécutive qui pourrait aussi se manifester et être associée à certaines difficultés de participation sociale dans la vie de tous les jours.

Mots clés : Traumatisme craniocérébral, fonctions exécutives, prédiction, réserve cognitive, participation sociale, récupération.

Abstract

The main objective of this thesis is to provide clinicians working with a population suffering from traumatic brain injury (TBI) in establishing an accurate comprehensive profile and prediction of executive functions (EF), as well as in their ability to target patients who will develop difficulties in social integration, based on objectified cognitive disorders and more specifically on EF disorders. In order to meet this objective, this thesis contains two articles that will use Miyake's theoretical model (Miyake, Friedman, et al., 2000) to define EF. The first paper is interested in characterizing the associations between sociodemographic variables, related to mild TBI and post- mild TBI symptoms on the one hand, and EF performance on the other. The second article aims to (1) measure the recovery of EF between the acute phase and six months post-TBI and (2) explore the relationship between EF and social participation after TBI.

The results of the articles primarily suggest that individuals with mild TBI who are more educated and have higher premorbid estimated IQ (cognitive reserve), are likely to show better performance on EF measures following their accident. The results also suggest that patients' performance on some EF measures improves significantly in the six months following their accident and may be associated, particularly for alternating verbal fluency, with patients' level of social participation following their accident.

Overall, the results of this thesis allow us to state that certain factors are important to consider when assessing cognitive functions, especially EF in people with TBI. Thus, the thesis suggests that it is crucial to consider the notion of cognitive reserve with a TBI population. Since cognitive reserve is postulated to compensate for cognitive deficits, EF deficits in patients with high cognitive reserve might appear to be of greater concern than in patients with low cognitive reserve. Furthermore, the results of the thesis highlight the importance of the alternate verbal fluency test, which is sufficiently sensitive in this population to measure the recovery of EFs over time, but also to give a picture of the executive impairment that could also occur and be association with some difficulties in social participation in everyday life.

Keywords : Traumatic brain injury, executive function, prediction, cognitive reserve, social participation, recovery.

Liste des tableaux

Contexte théorique

Article 1

Article 2

Liste des figures

Article 1

Liste des abréviations

Traumatisme craniocérébral (TCC)

Fonctions exécutives (FE)

Traumatic brain injury (TBI)

Executive functions (EF)

Amnésie post-traumatique (APT)

Glasgow Coma Scale (GCS)

Quotient intellectuel (QI)

Symptômes post-commotionnels (PCS)

Mayo-Portland Adaptability Inventory (MPAI)

Temps 1 (T1)

Temps 2 (T2)

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Introduction

À ce jour, il est bien connu que le TCC engendre des conséquences cognitives (Azouvi, 2009; Karr et al., 2014), affectives (Mel B. Glenn, 2001) et socio-fonctionnelles (Andelic et al., 2009; Jourdan et al., 2013; Kashluba et al., 2008). Parmi les conséquences cognitives, les FE seraient davantage vulnérables à la suite d'un TCC puisque le mécanisme même de la pathologie implique un mouvement du cerveau vers l'avant, soit vers les régions frontales, qui sont considérés comme le siège des FE (McAllister, 2011; McDonald et al., 2002). Or, la nature exacte et l'intensité des difficultés liées aux FE après le TCC sont particulièrement hétérogènes à travers les différentes études (Karr et al., 2014). Ceci s'explique notamment par une définition peu spécifique et variable des FE à travers les études ou de l'absence de groupes de comparaison appropriés. De surcroît, en plus de la lésion cérébrale traumatique subie, plusieurs variables socio-démographiques, médicales ou liées à l'accident influent également sur les FE à la suite du TCC. Ces diverses associations complexifient le tableau neuropsychologique pour les cliniciens qui doivent statuer sur la présence de types de déficits à la suite d'un TCC. Un autre défi pour les cliniciens est d'établir clairement les trajectoires de récupération des FE dans le temps. De fait, les études ayant tenté d'établir ces trajectoires comportent souvent des faiblesses méthodologiques importantes, dont l'absence de contrôle pour les effets de pratique (Mollayeva et al., 2019). Ceci est particulièrement important puisque les FE sont associées au devenir du patient après le TCC (Allanson et al., 2017). Toutefois, malgré cette association existante entre FE et le devenir, très peu d'études se sont intéressées plus spécifiquement à l'association entre les FE et la participation sociale à la suite d'un TCC.

Dans ce contexte, un des objectifs de la thèse sera d’explorer les relations entre les FE et diverses variables sociodémographiques, médicales ou liées à l’accident afin de mieux en comprendre ce qui est susceptible d’influencer les FE à la suite d’un TCC léger (Étude 1). Cette thèse portera également sur l’étude longitudinale de deux groupes de patients, l’un de toute sévérité de TCC confondue et un autre ayant subi des blessures traumatiques sans TCC et ce, sur une période de six mois. Le but de ce suivi étant de mieux comprendre la récupération des FE spécifique au TCC entre la phase aiguë et la phase chronique de récupération (Étude 2). Enfin, cette thèse portera également sur l’étude pronostique des associations entre les FE et la participation sociale des patients et ce, en phase chronique de réadaptation du TCC (Étude 2).

Chapitre 1 : Contexte théorique

1.1. Le traumatisme craniocérébral (TCC)

1.1.1. Prévalence

Il est difficile d'obtenir l'incidence précise du TCC, notamment, parce que les définitions et les méthodes de collecte de données varient grandement à travers les études (Ponsford et al., 2012). De fait, la prévalence mondiale du TCC n'est pas documentée de manière fiable (Roozenbeek et al., 2013). De plus, le TCC léger a longtemps été considéré comme une « épidémie silencieuse » (Banville & Nolin, 2008; Langlois et al., 2005) parce que les intervenants de la santé et le public étaient alors peu sensibilisés aux conséquences du TCC et à l'ampleur du problème. Le TCC représente aujourd'hui une préoccupation croissante pour les intervenants de la santé mais également pour la communauté et le public (de Souza et al., 2015).

De surcroît, il est reconnu que le TCC engendre des coûts importants pour le système de santé (de Souza et al., 2015). Au Canada, un taux d'occurrence annuelle du TCC de 500 sur 100 000 individus est rapporté, ce qui équivaut à environ 165 000 individus (chiffres extrapolés de données des États-Unis) (Langlois et al., 2006 cité dans le site Web Statistics on brain Injury). Le taux de mortalité des patients atteints d'un TCC est plus élevé que celui de la population générale (Baguley et al., 2000), mais demeure plutôt faible puisqu'il s'applique davantage dans les cas de TCC plus sévères (de Souza et al., 2015).

1.1.2. Définition

Le traumatisme craniocérébral est définit comme étant : « une altération dans le fonctionnement cérébral ou tout autre évidence de pathologie cérébrale causée par une force externe » (Menon et al., 2010). Concernant son étiologie, sans considérer le niveau de sévérité, les mécanismes de blessure les plus fréquents sont, les chutes, le fait d'être frappé par un objet, les accidents de véhicule à moteur, les assauts, les mécanismes autres ou non spécifiés et le fait de se faire du mal intentionnellement (Peterson et al., 2019). Le TCC comporte trois niveaux de sévérité, soit le TCC léger, modéré et sévère (Voir table 1).

Table 1.

Les indicateurs des différents niveaux de sévérité du TCC.

Indicateurs	TCC léger	TCC modéré	TCC sévère
Durée de la perte de conscience	0 à 30 min	30 min à 24 h (souvent inférieur à 6 heures)	Au-delà de 6 heures (souvent supérieur à 24 heures)
Résultat au GCS	13 à 15	9 à 12	3 à 8
Lésion cérébrale objective	Positif ou négatif	Souvent positif	Positif
Examen neurologique	Possiblement positif	Positif	Positif
APT	Inférieur à 24 heures	Entre 1 et 14 jours	Plusieurs semaines

*Adapté de INESSS (2018) GCS : Score à l'Échelle de Coma de Glasgow; APT : amnésie post-traumatique

Notons que le TCC léger est largement le niveau de sévérité le plus fréquent puisqu'il représente 80% des cas de TCC alors que 10% des cas sont des TCC modérés et 10% des TCC sévères (classification basée sur le l'Échelle de Coma de Glasgow uniquement) (de Souza et al., 2015). Le niveau de sévérité est déterminé en se fiant aux indicateurs suivants : la durée de la perte de conscience ou de l'altération de la conscience, le résultat obtenu à l'Échelle de Coma de Glasgow (GCS), la présence de lésions cérébrales objectives, un examen neurologique (positif ou négatif) et/ou la présence d'une amnésie post-traumatique (APT) (INESSS, 2018).

1.1.3. Physiopathologie

Le coup à la tête ou la force externe (Menon et al., 2010) évoqué plus haut, peut engendrer des atteintes cérébrales diffuses ou focales (Ponsford et al., 2012; Povlishock & Katz, 2005). Étant donné que le cerveau et le crâne ne sont pas attachés l'un à l'autre, ils bougent à des rythmes différents. Ainsi, la force d'impact du TCC est transmise en premier au crâne, puis au cerveau et c'est cela qui étire les vaisseaux sanguins et les rompt. On peut parler d'une accélération translationelle (la tête bouge dans une ligne droite avec le cerveau comme centre de gravité), d'une accélération rotationnelle (le cerveau tourne autour de son centre de gravité et de son axe central – le tronc cérébral) ou d'une accélération angulaire (combine les accélérations rotationelle et translationelle) (Lezak, Howieson, Bigler, & Tranel, 2012; Ponsford et al., 2012). On note principalement deux types d'atteintes après le TCC, soit les atteintes primaires (les atteintes immédiates aux structures extra et intra crâniennes) et les atteintes secondaires (les changements pathophysiologiques résultants des atteintes primaires et de complications systémiques) (Ponsford et al., 2012; Roth & Farls, 2000). Le type d'atteintes dépend également des mouvements engendrés par le TCC. Ainsi, on sait que les mouvements dans l'axe antérieur-postérieur (sagittal) sont plus susceptibles de provoquer des hématomes sous-duraux et que les impacts latéraux occasionnent davantage de blessures axonales/de la matière blanche (Lezak et al., 2012).

De manière non-exhaustive, les mécanismes primaires incluent principalement des atteintes intra et extra crâniennes (Lezak et al., 2012; Ponsford et al., 2012; Roth & Farls, 2000). Premièrement, sur le plan extra crânien, il peut s'agir de fractures du crâne résultant d'une force ou d'une pression sur celui-ci. Cela peut, à son tour, occasionner des hématomes ou des dommages des tissues (Roth & Farls, 2000). De fait, les fractures du crâne sont une source commune d'hématome extradural ou épidural (une accumulation de sang entre le crâne et la dure-mère). On peut aussi retrouver l'hématome sous dural (entre la dure-mère et l'arachnoïde) (Lezak et al., 2012). Deuxièmement, les atteintes intra crâniennes incluent les contusions (qui peuvent résulter en des œdèmes cérébraux), les blessures axonales diffuses (dommages microscopiques/déchirements axonaux), les traumas aux nerfs crâniens (conséquence d'un étirement ou d'une compression du nerf), et les hémorragies intracrâniennes (une hémorragie dans le tissu cérébral) (Roth & Farls, 2000). Les hémorragies intracrâniennes peuvent être sous-arachnoïdienne ou pial (sur la surface corticale) ou encore intraventriculaire (dans le système ventriculaire) (Lezak et al., 2012).

Les mécanismes secondaires sont des réponses biochimiques et cellulaires hautement complexes et, encore aujourd'hui, peu compris par les scientifiques (Ladak et al., 2019; Roth & Farls, 2000). Ce faisant, nous n'entrerons pas dans les détails concernant ces mécanismes, et ce, d'autant plus que cela s'éloigne du sujet principal de la présente thèse. De manière non-exhaustive, notons tout de même que ces mécanismes peuvent inclure une augmentation du volume cérébral (Marmarou, 1994; Marmarou et al., 2006), une cascade chimique qui altère le fonctionnement des axones et peut mener à la mort cellulaire (Giza & Hovda, 2001), une altération de la capacité cérébrale d'autorégulation du volume sanguin qui peut engendrer des difficultés sur le plan du fonctionnement des cellules qui dépendent de l'apport en oxygène que fournit le sang (Roth & Farls, 2000), enfin, une cascade neurochimique cause la mort neuronale (apoptose) (Werner & Engelhard, 2007). Immédiatement après l'atteinte biomécanique du TCC, il se produit un relâchement de neurotransmetteurs, ainsi qu'un flux d'ions (Giza & Hovda, 2001). On note une augmentation de la dépolarisation de neurones (Giza & Hovda, 2001). Ce faisant, les pompes sodium-potassium au niveau de la membrane cellulaire travaillent davantage ce qui cause une augmentation du glucose (Giza & Hovda, 2001). Ceci prend place dans un contexte dans lequel l'afflux en sang est réduit, alors que les demandes en énergie cellulaire sont augmentées, ce qui fragilise le cerveau (Giza & Hovda, 2001). Cette série d'évènements chimiques finit par réduire le niveau de production d'énergie de la cellule et engendre la mort neuronale (Giza & Hovda, 2001).

Certains auteurs observent que la pathologie du TCC est très hétérogène, non seulement sur le plan des facteurs qui la causent, mais également sur le plan des conséquences physiologiques qu'elle engendre (Ponsford et al., 2012). On note toutefois que certaines régions sont plus communément touchées que d'autres, notamment, les lobes frontaux (Lezak et al., 2012; Ponsford et al., 2012). Les atteintes frontales, en particulier, sont hautement prévalentes, suite au TCC car les mécanismes d'accélération/décélération rendent ces régions plus vulnérables que les autres, et ce, peu importe la pathophysiologie du TCC (Brooks et al., 1999; McAllister, 2011; McDonald et al., 2002; Stuss, 2011). Or, nous savons que les régions frontales sont le siège des FE (McAllister, 2011).

1.2. Les fonctions exécutives (FE) à la suite du TCC

1.2.1. Le modèle théorique de Miyake : Le concept des FE

Le modèle de Miyake et collègues (Miyake, Friedman, et al., 2000) définit les FE comme un ensemble de trois fonctions cognitives, soit : (1) la flexibilité cognitive, qui est la capacité à se désengager d'une tâche moins importante pour créer un engagement actif envers une tâche plus importante; (2) la mise à jour, qui se caractérise par la capacité de mettre à jour et monitorer les représentations en mémoire de travail, nécessitant d'activement manipuler l'information en mémoire de travail, plutôt que de simplement stocker passivement l'information et enfin (3) l'inhibition, qui est la capacité à inhiber de manière délibérée une réponse dominante, automatique et prépondérante. Le modèle de Miyake se base sur ces trois fonctions, car elles sont « relativement circonscrites et basiques », elles sont aussi très spécifiques et peuvent être décrites de manière précise (Miyake, Emerson, et al., 2000). Malgré sa forte valeur scientifique et reconnaissance dans le domaine, très peu d'études ont appliqué le modèle de Miyake à l'étude des FE après un TCC (Allanson et al., 2017; de Guise et al., 2020).

1.2.2 Les impacts du TCC sur les FE : Variabilité

Il est globalement reconnu que les déficits des FE sont communs après un TCC, même lorsque la sévérité est légère (Rabinowitz & Levin, 2014). Toutefois, tel qu'il sera démontré ci-dessous, la nature exacte et la sévérité de ces déficits varie à travers les études.

D'abord, des études s'intéressant au TCC léger rapportent que ces groupes de participants performent de manière significativement plus faible dans des tâches de flexibilité (parfois appelée *shifting*) (Brooks et al., 1999; Erez et al., 2009). Dans les études s'intéressant aux participants atteints d'un TCC modéré-sévère, une revue de littérature rapporte des résultats contradictoires à travers les études en ce qui concerne la flexibilité mentale. De fait, certaines études rapportent des déficits de lenteur mais non de flexibilité alors que d'autres observent des résultats différents (Azouvi et al., 2017). Les résultats semblent toutefois un peu plus cohérents sur le plan de la mémoire de travail. De fait, une revue de littérature portant sur les données empiriques et cliniques concernant les atteintes exécutives suivant un TCC de toutes sévérités confondues rapporte des déficits communs de mémoire de travail (Azouvi et al., 2017). Sur le plan de l'inhibition, des revues de littérature rapportent une plus grande sensibilité à l'interférences suite au TCC (Azouvi et al., 2017), ainsi que des difficultés quant à la prise de risque (un type d'impulsivité) (Ozga et al., 2018).

Néanmoins, on rapporte une pléthore de résultats et de concepts disparates concernant l'impact du TCC sur les FE. Des études se définissant comme mesurant les FE vont rapporter des déficits dans des tâches de planification et d'utilisation de stratégies (Erez et al., 2009), une perte de conceptualisation et une plus grande lenteur de planification (Azouvi et al., 2017), des déficits de fluence catégorielle (Kumar et al., 2013) ou encore des problèmes de planification et de contrôle exécutif mesuré à l'aide d'une tâche de fluence verbale (Rakers et al., 2018).

Finalement, une intéressante étude rapporte des différences de groupe (TCC vs contrôles) très variables en fonction de la mesure de FE utilisée. Dans cette étude où plusieurs mesures des FE sont administrées, les auteurs rapportent que parfois ce sont les participants contrôles qui performent le mieux (Alpha Span et Brown-Peterson (mesures de mémoire de travail et de contrôle de l'interférence) et parfois ce sont les participants atteints d'un TCC (léger et modéré-sévère) (Stroop Test Word Naming (mesure de l'inhibition et de la flexibilité cognitive). Enfin, dans cette étude, certaines mesures ne permettent pas de dissocier les groupes (WOC-R (mesure de l'utilisation de stratégie)) (Krpan et al., 2007). Afin d'expliquer ces résultats contradictoires et non cohérents, les auteurs mentionnent la présence de grandes variabilités inter-individuelles des performances à l'intérieur même de chacun des groupes (Krpan et al., 2007). En somme, la littérature n'est pas encore claire sur les FE spécifiquement atteintes après le TCC, c'est dans ce sens qu'on retrouve une inconsistance et une hétérogénéité à travers les études. Pour compliquer le tout, ces inconsistances se constatent également dans la littérature portant sur la récupération des FE à la suite d'un TCC.

1.2.3 La récupération des FE à la suite d'un TCC

Sur le plan de la récupération des déficits et à la suite d'un TCC léger, la majorité des patients présenteraient une récupération généralement trois mois après l'accident (INESSS, 2018; Mel B. Glenn, 2001). De fait, on rapporte globalement des déficits dans les 48 heures à deux semaines suivant le TCC léger (L. J. Carroll et al., 2014). Concernant le TCC modéré-sévère, certains auteurs suggèrent une amélioration de la cognition entre un et cinq ans post-accident, mais certains patients, particulièrement ceux développant des symptômes dépressifs, pourraient montrer un déclin dans les mesures nécessitant de la vitesse et de la flexibilité cognitive (Millis et al., 2001). Tel que citée dans la dernière étude, cette amélioration ou récupération graduelle à travers le temps ne semble, toutefois, pas entièrement et systématiquement appuyée par une récente revue systématique et méta-analyse (Mollayeva et al., 2019). Cette dernière suggère des changements à travers le temps qui sont positifs, donc que les patients TCC récupèreraient graduellement. Toutefois, cette méta-analyse permet parallèlement d'observer que pour d'autres fonctions cognitives (dont les FE), il y aurait des changements négatifs, donc une détérioration ou encore aucun changement et ce, dans plusieurs domaines cognitifs (ex. la mémoire, les habiletés visuospatiales, les FE et la vitesse de traitement de l'information) (Mollayeva et al., 2019). Les auteurs de cette méta-analyse expliquent ces inconsistances de la littérature par la possible présence d'effets de pratique non-contrôlés dans certaines études faisant en sorte que l'amélioration observée ne serait dû qu'à un effet de pratique plutôt qu'à une réelle récupération de la fonction et ce, particulièrement chez les patients dont les TCC sont plus sévères (Mollayeva et al., 2019). Ces inconsistances relèvent de faiblesses méthodologiques liées notamment au fait que des groupes contrôles ne sont pas toujours employés dans les designs expérimentaux. En outre, il est également important que le groupe contrôle utilisé soit approprié (L. Carroll et al., 2004) et permette de contrôler pour la douleur lors de l'hospitalisation, cette dernière étant reconnue pour affecter la cognition (Moriarty et al., 2011), ainsi que les effets psychologiques de l'hospitalisation (Curran et al., 2000). En somme, un manque important d'études longitudinales prospectives avec un groupe contrôle apparié s'intéressant particulièrement aux FE est mis à jour dans la littérature actuelle.

1.2.4 Hypothèses explicatives des incohérences de la littérature : Le concept et la mesure

Tel que déjà bien démontré précédemment, quoique les atteintes des FE soient dites généralement fréquentes (Rabinowitz & Levin, 2014), elles demeureraient tout de même particulièrement inconsistantes et hétérogènes à travers les études (Karr et al., 2014). Quelques pistes d'explication ont été émises dans la section précédente mais d'autres critiques à ces études peuvent être soulevées, telles que les définitions des concepts des FE ou encore les outils de mesures utilisés pour évaluer ces dits concepts.

Plusieurs hypothèses explicatives ont été émises quant à ce phénomène d'incohérences des résultats. D'abord, les définitions des FE varient grandement (Keil & Kaszniak, 2002; Mueller & Dollaghan, 2013). De fait, tel que bien démontré dans une section précédente, une pluralité de concepts sont inclus dans le construit global des FE qui fait office de « fourre-tout ». Par exemple, organisation-utilisation de stratégies, fluence-générativité-initiation, suppression-alternance, abstraction-formation de concepts, attention contrôlée et inhibition des distracteurs sont toutes des fonctions considérées comme FE dans certaines études (Keil & Kaszniak, 2002; Wood & Worthington, 2017). Cela pose un problème car les concepts peuvent se superposer ou être fondamentalement différents (Miyake, Emerson, et al., 2000). De plus, certains auteurs postulent que les FE sont un processus unitaire, alors que d'autres parlent de processus dissociables (Miyake, Emerson, et al., 2000).

Ce faisant, les FE sont évalués de différentes manières en clinique (Keil & Kaszniak, 2002; Miyake, Emerson, et al., 2000) et les tests utilisés diffèrent dans leur format et dans les types de processus des FE visés par la mesure (Mueller & Dollaghan, 2013). De surcroît, les mesures de FE sont souvent considérées comme des mesures sensibles, mais peu spécifiques (Keil & Kaszniak, 2002; Miyake, Emerson, et al., 2000). En ce sens, les patients semblent avoir des déficits des FE puisqu'ils performent moins bien dans les mesures dites des FE administrées. Toutefois, on ne sait pas si c'est le processus des FE visé qui est touché ou bien les processus sous-jacents qui le supportent (par exemple, l'attention ou la vitesse de traitement) (Keil & Kaszniak, 2002; Miyake, Emerson, et al., 2000). Un des exemples les plus flagrants de cette limite s'illustre avec le Trail Making test B. Un déficit dans ce test, s'il n'est pas analysé en tenant compte des résultats du tracé A, peut être considéré comme un déficit de vitesse de traitement ou d'attention sélective, plutôt qu'un déficit de flexibilité mentale en tant que tel. De fait, étant donné que le construit des FE est mal définit, on retrouve une hétérogénéité dans la manière donc ce construit est mesuré à travers les études citées de la littérature (Mueller & Dollaghan, 2013). Les tâches manquent donc de pureté, et on ne sait pas exactement quelle FE est mesurée (Miyake, Emerson, et al., 2000).

Tout ceci suggère que l'utilité clinique du concept empirique des FE n'est pas encore clairement établie (Mueller & Dollaghan, 2013), et ce, en raison des nombreux problèmes conceptuels et théoriques entourant l'étude de ces mêmes fonctions. Face à ces nombreuses problématiques conceptuelles et théoriques, une revue de littérature (Miyake, Emerson, et al., 2000) propose plusieurs recommandations pour les recherches futures et pour la pratique clinique. Entre autres, on mentionne de choisir des tâches qui ciblent les composantes unitaires des FE (par exemple, l'inhibition ou la mise à jour) et non pas les FE en général, d'utiliser plusieurs mesures pour chaque composante des FE et de les combiner si possible, pour en faire des scores composites (Miyake, Emerson, et al., 2000). Quoiqu'il en soit, il reste primordial d'améliorer la précision de la mesure des FE (Mueller & Dollaghan, 2013) en se basant sur une définition opérationnelle et celle de Miyake a souvent été suggérée (Allanson et al., 2017; Karr et al., 2014). En somme, lorsque l'on s'intéresse aux FE, il est donc important d'utiliser un modèle théorique solide afin de pouvoir appréhender au mieux la variabilité et la complexité intrinsèque à ces fonctions. De surcroît, il est important de considérer que les FE et la cognition en général sont affectées par de multiples variables inhérentes au patient.

1.3. Les variables associées à la cognition et aux FE

1.3.1. La sévérité du TCC : Amnésie post-traumatique, Perte de conscience et *Glasgow Coma Scale*

Deux mesures principales sont communément utilisées afin de mesurer la sévérité d'un TCC. L'une est la durée de l'amnésie post-traumatique (APT) et l'autre le score au *Glasgow Coma Scale* (GCS). D'abord, le manuel de Ponsford et collègues (Ponsford et al., 2012) offre une description détaillée et complète de la notion d'APT. Selon ces auteurs, l'APT correspond à la phase de désorientation après la blessure cérébrale. Principalement, l'APT est caractérisée par une incapacité à emmagasiner ou récupérer de nouvelles informations. Les patients atteints d'un TCC ne se souviennent pas de l'événement accidentel, sont généralement confus et désorientés et absorbent peu d'information provenant des stimuli environnementaux. Le contenu du discours peut être confus, il peut y avoir de l'agitation et des agressions physiques ou verbales, ainsi que des hallucinations et des délires. Le patient ne se souvient généralement pas de cette période après coup. Des méthodes très variables ont été utilisées dans la littérature pour mesurer la présence et la durée de l'APT (questionner la personne, les dossiers médicaux, des outils standardisés), ce qui diminue notre capacité à comparer équitablement les études, les unes avec les autres (Ponsford et al., 2012). On sait toutefois que l'APT est un prédicteur important du devenir, car elle a été associée à de nombreuses variables, dont la présence d'atteintes comportementales, mnésiques et des FE (rigidité mentale, se sentir submergé par les stimuli environnants et difficulté à s'adapter à de nouvelles situations), ainsi que des problèmes de régulation de l'humeur et une réduction de la fréquence de pratique d'une activité sociale (de Guise et al., 2017; Rassovsky et al., 2015; Skilbeck et al., 2020).

La durée de la perte de conscience, quant à elle, a aussi été corrélée aux performances des FE. Plus spécifiquement, une durée plus longue de la perte de conscience, représentant ainsi un TCC plus grave, a été associée à davantage de déficits des FE (Rassovsky et al., 2015; Sorg et al., 2014). De manière similaire, le résultat à la GCS est un prédicteur reconnu dans la littérature du devenir après le TCC, ainsi que de la mortalité. Un score plus bas obtenu à la GCS, représentant un TCC plus grave, a été associé à un devenir moins favorable et dans certains cas à risque plus élevé de mortalité (McNett et al., 2014). Plus spécifiquement au point de vue des FE et du comportement, une étude effectuée par notre équipe de recherche a mis en évidence que les patients ayant obtenus un score GCS plus bas (TCC plus sévère) présentant également davantage de comportements de labilité émotive, d'irritabilité et de désinhibition. Ceci suggère ainsi des capacités d'inhibition davantage atteintes que chez des patients ayant obtenu un score GCS plus élevé, donc un TCC moins sévère (de Guise et al., 2017). Dans la littérature, on retrouve certaines alternatives à la mesure de GCS. Le FOUR (*full outline of unresponsiveness score*) est un outil alternatif considéré comme équivalent au GCS. Le FOUR contient 4 sous-échelles, soit les réponses des yeux, les réponses motrices, les réflexes du tronc cérébral et la respiration (Nair et al., 2017). De fait, l'élaboration de cette nouvelle mesure vise à combler le manque de mesure des réflexes du tronc cérébral qui est manquante, alors que c'est un important indicateur du niveau d'éveil et de conscience, et donc une critique du GCS (Nair et al., 2017). Le FOUR ajoute également la taille et la réactivité des pupilles à la lumière (Nair et al., 2017). Plus anciennement, la Reaction Level Scale (RLS85) avait été rapportée dans la littérature (Starmark et al., 1988), mais semble peu utilisée aujourd'hui.

1.3.2 La réserve cognitive

La réserve cognitive est « la capacité qu'ont les individus à résister aux dommages cérébraux » (Villeneuve & Belleville, 2010). Elle est différente pour chaque individu et représente la capacité à surmonter les effets d'un maladie ou d'une atteinte (Bigler & Stern, 2015; Mathias & Wheaton, 2015). De manière générale, plus la réserve cognitive de la personne est estimée comme étant élevée, et plus cette personne serait en mesure de compenser et s'adapter à la suite d'un événement, comme par exemple un TCC (Bigler & Stern, 2015; Mathias & Wheaton, 2015). Deux principales mesures sont utilisées dans la littérature pour l'estimer, soit le niveau d'éducation et un estimé du quotient intellectuel (QI) prémorbide du patient (Mathias & Wheaton, 2015). Même si plusieurs mesures estimées de QI prémorbide sont utilisées dans la littérature, ce qui crée une certaine variabilité dans les résultats (Mathias & Wheaton, 2015), la majorité des celles-ci rapporte globalement des relations positives entre l'éducation et le QI prémorbide et le devenir du patient (Mathias & Wheaton, 2015; Schneider et al., 2014). Ainsi, une réserve cognitive plus élevée serait associée à une récupération et un devenir fonctionnel plus favorable à la suite d'un TCC. En outre, cette relation se retrouverait également entre le QI prémorbide et le devenir cognitif du patient mesuré notamment par le test du Trail Making B qui est reconnu pour mesurer la flexibilité mentale, une composante des FE (Fraser et al., 2019). Une étude plus récente effectuée par notre équipe de recherche et s'intéressant aux FE suggère aussi des associations entre la mémoire de travail et la réserve cognitive (l'éducation) chez des participants âgés atteints d'un TCC (léger ou modéré). Dans cette étude, les patients plus éduqués présentaient des scores plus élevés aux tâches d'empan de chiffre à rebours (de Guise et al., 2020). Enfin, une étude auprès de participants atteints d'un TCC léger rapporte que l'intelligence estimée (la réserve cognitive) modère les différences de fonctionnement cognitif (score composite de vitesse de traitement de l'information, mémoire et fluence verbale) entre les participants atteints d'un TCC léger et le groupe contrôle (Stenberg et al., 2020).

1.3.3 L'âge

L'âge a été longuement étudié chez la population atteinte d'un TCC mais beaucoup moins d'études se sont intéressées aux liens entre cette variable et les FE. Néanmoins, une méta-analyse rapporte des relations positives entre l'âge et les performances à des mesures des FE et de temps de réaction, les plus jeunes auraient de meilleures performances dans ces épreuves (Mathias & Wheaton, 2015). Il est également reconnu que le fait d'être plus âgé serait associé à une moins bonne récupération de plusieurs fonctions cognitives, dont les FE (mesures de flexibilité cognitive, d'inhibition, et de mémoire de travail) (Fraser et al., 2019; Senathi-Raja et al., 2010). Certains auteurs suggèrent que le fait que les personnes plus âgées aient une moins bonne récupération des fonctions cognitives, notamment les FE, s'expliquerait par une moins bonne capacité de plasticité cérébrale et de compensation des déficits (Senathi-Raja et al., 2010). De fait, il est connu qu'avec l'âge, une perte des cellules nerveuses (dendrites et axones) et une démyélinisation seraient observables (Pannese, 2011), expliquant du même coup l'efficacité diminuée du cerveau à compenser et à se réorganiser à la suite d'une lésion cérébrale.

1.3.4 Les symptômes post-commotionnels

Les symptômes post-commotionnels (PCS) correspondent à ensemble des symptômes rapportés à la suite d'un TCC (Broshek et al., 2015). Les PCS se regroupent en symptômes physiques (ex. : fatigue et maux de tête), cognitifs (ex. : problèmes de mémoire et de concentration) et émotionnels (ex. : dépression et anxiété) (Broshek et al., 2015; Ryan & Warden, 2003). Malgré l'importance de cette symptomatologie à la suite d'un TCC, il est étonnant de constater que très peu d'études se sont intéressées aux liens entre la sévérité des PCS et le fonctionnement cognitif et encore moins aux liens avec les FE. Il est intuitif de penser que les patients qui présentent davantage de céphalées, d'étourdissements et de nausées seront ceux qui auront davantage de troubles cognitifs et des FE objectivés. Une rare revue de la littérature suggère que les PCS seraient liés à des atteintes objectives du fonctionnement cognitif et donc ne serait pas que des plaintes subjectives (Ryan & Warden, 2003). Dans cette revue de littérature, on ne retrouve toutefois aucune mention des FE (Ryan & Warden, 2003). Les résultats d'une autre étude suggèrent que les patients atteints d'un TCC légers et modérés avec des plaintes post-commotionnelles cognitives subjectives auraient de moins bons scores à des tests cognitifs objectifs, comparé à des patients sans plaintes cognitives, notamment lors d'épreuves mesurant la mémoire de travail et les comportements de persévérations (scores total et réponses de persévérations au WCST) (Chamelian & Feinstein, 2006).

1.3.5 Les affects anxio-dépressifs

Plusieurs groupes de recherche se sont intéressés aux conséquences psychologiques à la suite d'un TCC, particulièrement les affects anxio-dépressifs. Les symptômes dépressifs sont souvent secondaires à la présence de multiples PCS ainsi qu'aux impacts psychosociaux ou comportementaux que ceux-ci entraînent, tels que des pertes d'emploi, des séparations ou l'abus de substances (Busch & Alpern, 1998; Rapoport et al., 2003). La présence d'affects dépressifs post-TCC a été démontré comme ayant un effet sur les plaintes cognitives subjectives du patient (Chamelian & Feinstein, 2006), ainsi que sur les performances cognitives objectives (Donders et al., 2015; Gould et al., 2014; Jorge et al., 2004; Schiehser et al., 2011). Plus spécifiquement en liens avec les FE, des associations entre la présence d'affects dépressifs post-TCC et les performances des participants à des tests mesurant les FE (Jorge et al., 2004; Schiehser et al., 2011) ont été établies dans la littérature. Les patients avec une dépression majeure suivant leur TCC ont significativement démontré plus de difficultés avec la résolution de problèmes et la flexibilité cognitive que les patients sans affects dépressifs (Jorge et al., 2004). D'autres évidences suggèrent des associations positives entre les FE comportementales mesurées par le biais du questionnaire *Frontal Systems Behavior Scale* qui mesure l'apathie, la désinhibition et les dysfonctions exécutives, et un questionnaires de symptômes dépressifs (Schiehser et al., 2011). Pour expliquer cette association, certains auteurs mentionnent que la dépression majeure et les dysfonctions exécutives seraient reliées aux mêmes mécanismes pathophysiologiques, soit les circuits fronto-striataux-thalamiques (Jorge et al., 2004).

Contrairement aux affects dépressifs, beaucoup moins d'études se sont intéressées aux liens entre l'anxiété et les FE. Une étude pertinente à la présente thèse effectuée par Gould et collaborateurs (Gould et al., 2014) a comparé plusieurs fonctions cognitives d'un groupe de patients atteint d'un TCC présentant des troubles anxieux avec un groupe sans trouble anxieux. Leurs résultats suggèrent que, parmi plusieurs types de processus cognitifs, ce sont les FE qui ont permis de différencier les deux groupes, ces types de fonctions démontrant donc davantage de sensibilité pronostique. Ainsi, les performances obtenues aux mesures des FE ont permis de classifier correctement 47.1% des patients avec anxiété et 93.3% des patients sans anxiété dans le bon groupe.

En somme, pour la grande majorité de ces prédicteurs ou variables, leurs associations avec les différentes composantes des FE établies par Miyake et collègues (2000) n'ont pas encore été clairement démontrées dans la littérature. Or, la compréhension de ces associations ou interactions de même que l'évaluation ciblée des FE à la suite d'un TCC sont cruciales en contexte clinique, et ce, afin d'être en mesure d'identifier rapidement et avec précision les patients à risque de présenter des difficultés du fonctionnement exécutif et d'intégration à plus long-terme. De fait, il semble établit que les FE jouent un rôle capital dans le succès du devenir et de la réintégration aux activités des patients ayant subi un TCC (Cristofori & Grafman, 2017; Fortin et al., 2003; Hanks et al., 1999).

1.4. Associations entre les FE et le devenir à la suite d'un TCC

Le devenir après le TCC se définit globalement comme étant la capacité à réintégrer les activités fonctionnelles de la vie de tous les jours. Les études portant sur le devenir sont particulièrement hétéroclites mais il est tout de même possible de la conceptualiser en trois phases suivant un TCC. Lors de la première phase, c'est-à-dire la phase de traumatologie ou précoce de réadaptation, le devenir cible surtout la survie du patient et est surtout médical. Lors de la phase de réadaptation fonctionnelle intensive, le devenir porte sur l'autonomie fonctionnelle dans les activités de la vie quotidienne (se nourrir, se laver, etc). À la suite de cette phase débute la phase de réadaptation axée sur l'intégration sociale où les activités sont participatives et axées sur la réintégration socio-professionnelle. C'est cette dernière phase qui nous intéresse davantage dans le cadre de cette thèse, car c'est celle qui requière une plus grande implication des FE pour la réalisation de diverses activités. À titre d'exemple, il est reconnu que la flexibilité mentale est cruciale pour mettre en application les habiletés sociales qui sont nécessaires à la participation sociale (Frazier, 2018). Néanmoins, une étude a démontré que les professionnels de la santé, quoiqu'au fait que les FE sont à risque d'affecter la réintégration aux activités du patient, éprouvent malgré tout de la difficulté à identifier les patients qui sont à risque de développer des problèmes dans la vie de tous les jours et dans leur communauté, en lien avec ces lacunes des FE (Baum et al., 2017). Les cliniciens sont d'ailleurs confrontés à un manque important de littérature sur les associations entre le devenir et les FE, ce qui explique cet obstacle à la prédiction. Parmi cette littérature, une méta-analyse réalisée par Allanson et collègues (Allanson et al., 2017) fait état d'associations entre la flexibilité cognitive et l'autonomie fonctionnelle. En outre, ils concluent leur méta-analyse en suggérant d'utiliser la Mayo-Portland Adaptability Inventory (MPAI), notamment si la participation sociale est visée comme facteur de prédiction.

1.4.1 La Mayo-Portland Adaptability Inventory

La MPAI est l'un des outils les plus utilisés dans la littérature sur le TCC pour mesurer l'intégration à la communauté (Sander et al., 2010). Sa sensibilité aux effets du TCC et son utilité ont été démontrées (Testa et al., 2005). La MPAI est une mesure d'intégration plus inclusive que d'autres mesures connues dans la littérature telles que la *Disability Rating Scale* et le *Community Integration Questionnaire* et donc moins susceptible à des effets plafonds (Malec et al., 2000). De fait, étant donné qu'elle couvre davantage d'habiletés, les patients sont plus susceptibles de présenter des difficultés sur l'une des habiletés présentées. La MPAI permet de représenter les indicateurs clés de limitations dans trois domaines : capacité (*ability*) (ex. : la mobilité ou les capacités de communication verbale), adaptation (*adjustment*) (ex. : l'anxiété ou la dépression) et participation (ex. : la capacité à initier des activités) en plus d'un score total combinant les trois (Kreutzer et al., 2011;

Malec et al., 2000). Chez les patients qui ont des atteintes plus subtiles et moins sévères, notamment ceux se retrouvant dans la phase de réadaptation axée sur l'intégration sociale (plusieurs mois post accident), celles-ci seront mieux évaluées et davantage représentées dans les mesures de participation (Kreutzer et al., 2011). Néanmoins, les domaines de capacité et d'adaptation sont des facteurs explicatifs du domaine de participation (Kreutzer et al., 2011; Malec et al., 2000). En lien avec la prédiction du devenir, une étude a montré que l'indice de participation corrélait modérément à fortement au score total et était donc un indice assez représentatif du devenir global de la personne (Malec, 2004). Basé sur cette analyse, il a été conclu que les chercheurs ou les gestionnaires de programmes cliniques pouvaient se fier uniquement à l'indice de participation comme mesure représentative du devenir après le TCC (Malec, 2004). De fait, les propriétés psychométriques de cette échelle sont bonnes (consistance interne et fiabilité des items) (Malec, 2004).

Pour faire le lien avec la thématique des FE de cette thèse, il est pertinent de mentionner que même si cet instrument semble un très bon outil de mesure du devenir et de la participation sociale à la suite d'un TCC, il est tout de même important de souligner que les études sur les liens MPAI-FE rapportent des résultats mitigés et assez disparates. Dans un premier temps, des associations positives ont été démontrées entre le score total de la MPAI et des performances aux tests mesurant les FE, où les patients démontrant un meilleur devenir mesuré par la MPAI avaient aussi de meilleures performances des FE mesurées par des épreuves telles que le Zoo map, le Trail Making test B et l'échelle de mémoire de travail du *Wechsler Memory Scale-III* (Spitz et al., 2012). D'autres associations positives ont été montrées entre l'échelle cognitive et l'indice spatial du *Neuropsychological Assessment Battery* et l'échelle de participation sociale et d'habileté de la MPAI (Zgaljardic et al., 2011) ou entre des mesures comportementales des FE et des items comme la gestion de l'argent et l'employabilité de la MPAI (Erez et al., 2009). Toutefois, dans un second temps, d'autres résultats ne témoignent d'aucune associations entre des performances des FE mesurées par les sous-tests de la *Behavioral Assessment of the Dysexecutive Syndrome* et du Trail Making test B et le score de participation sociale de la MPAI (Erez et al., 2009; Scott et al., 2016).

En somme, très peu d'études se sont intéressées aux liens entre les FE et le devenir des patients atteints d'un TCC et encore moins se sont intéressées à la participation sociale mesurée avec un outil pourtant valide et pertinent comme la MPAI. Les quelques études existantes à notre connaissance proposent des résultats hétérogènes. Tel que souligné dans les sections précédentes sur l'étude des FE à la suite d'un TCC, plusieurs problèmes méthodologiques sont susceptibles d'expliquer ces divergences de résultats, notamment des échantillons restreints, l'absence de groupe comparatif, des délais variables entre la collecte des mesures et l'accident et bien entendu le concept des FE qui est souvent mal défini. Basés sur ces constats de la littérature actuelle, la pertinence des objectifs de cette thèse demeure actuelle.

1.5. Position du problème et objectifs de la thèse

Tel qu'il a été démontré précédemment, les FE sont particulièrement vulnérables à la suite d'un TCC mais la littérature scientifique ne s'entend pas encore sur la nature spécifique de ces déficits, notamment en raison d'une définition peu opérationnelle des FE et également parce que les différences individuelles et les nombreuses variables affectant la cognition ne sont pas prises en compte. Ainsi et pour toutes ces raisons, il est encore à ce jour difficile pour les cliniciens de déterminer un pronostic précis des FE. Il est aussi difficile de cibler quels patients développeront des difficultés d'intégration sociale, sur la base des troubles cognitifs objectivées et plus précisément des troubles des FE. La présente thèse tentera donc de présenter des solutions à ces défis.

1.5.1 Première étude de la thèse

L'objectif global de la première étude est de caractériser à l'aide d'un devis rétrospectif les associations entre des variables sociodémographiques, liées au TCC léger et des symptômes post TCC léger d'une part, et les performances des FE d'autre part. Il est visé de : (1) Caractériser les associations entre les facteurs de vulnérabilité prémorbide et les FE. Nous émettons l'hypothèse que plus la réserve cognitive sera élevée chez les patients TCC léger (plus éduqués, QI prémorbide estimé plus élevé) et plus les patients seront jeunes, plus ceux-ci auront de bonnes performances aux mesures des FE; (2) Caractériser les associations entre les facteurs liés à l'accident et les FE. Nous émettons l'hypothèse que la présence d'une perte de conscience, d'une amnésie post-traumatique, de lésions frontales et d'un délai plus court entre l'accident et l'évaluation des FE seront associés à de moins bonnes performances lors d'épreuves mesurant les FE; (3) Caractériser les associations entre la sévérité des symptômes post-commotionnels et anxio-dépressifs et les FE. Nous émettons l'hypothèse que plus les symptômes post-commotionnels et anxio-dépressifs seront sévères, moins bonnes seront les performances aux épreuves des FE.

1.5.2 Seconde étude de la thèse

La seconde étude de la thèse comporte deux objectifs : (1) Mesurer la récupération entre la phase aiguë (le temps 1 : T1) et six mois post-TCC (le temps 2 : T2) des trois sous-composantes des FE du modèle de Miyake (2000) et (2) Explorer la relation entre les FE et la participation sociale après un TCC. Les hypothèses suivantes sont émises : (1)

Contrairement au groupe contrôle, les deux groupes de patients (léger et modéré/sévère) montreront une amélioration de la flexibilité, de la mise à jour et de l'inhibition entre T1 et T2. De plus, à T2, on s'attend à ce que les patients souffrant d'un TCC léger aient une performance des FE équivalente à celle du groupe contrôle mais supérieure à celle du groupe de patients souffrant d'un TCC modéré/sévère et (2) Une meilleure performance des FE aux T1 et T2 sera significativement associée à une meilleure participation sociale à T2.

Chapitre 2: Article 1

Relationships between predisposing, precipitating, and perpetuating factors and executive functioning following mild traumatic brain injury

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Concernant cet article, l'étudiante a procédé aux analyses statistiques, à la recension de littérature, à l'élaboration du projet de recherche (objectifs et hypothèses) et à la rédaction de l'article. Le Dr Tinawi, ainsi que Monsieur Michel Abouassaly ont été des partenaires à la collecte des données médicales et neuropsychologique à l'Hôpital général de Montréal. Lucie C. Frenette a contribué à la collecte de données et a fourni son aide pour les analyses statistiques. Dre de Guise a chapeauté le projet.

Abstract

Introduction. The aim of this study was to determine the sociodemographic and MTBI-related variables associated with executive functioning (EF). **Methods.** Based on the theoretical model of Hou and colleagues (Hou et al., 2012), data on predisposing (age, education, premorbid IQ), precipitating (post-traumatic amnesia, loss of consciousness, presence of frontal lesions, post-accident time to evaluation) and perpetuating (anxious and depressive affects and post-concussive symptoms) factors were retrospectively collected from the medical records of 172 patients with MTBI. EF data based on the 3 processes included in Miyake's prediction model (2000) (*updating, cognitive flexibility and inhibition*) were collected using respectively the Digit span task of the Weschler – 4th edition, the Trails A and B (Reitan, 1955) as well as the initiation time on the Tower of London- Drexel University. **Results.** *Updating* was significantly associated with education, premorbid IQ, age, anxiety, and depressive affect. *Inhibition* was associated with education and age. No variable was associated with *cognitive flexibility*. **Conclusions.** Following a MTBI, clinicians should consider that level of education and pre-morbid IQ may "predispose" patients to higher EF performances. They should also measure level of anxiety and depressive affect knowing that these may "perpetuate" some EF impairments (specifically the *updating* process).

Word count: 194

Key words: Traumatic brain injury; executive function; cognitive reserve; anxio-depressive; age.

Introduction

Mild traumatic brain injury (MTBI) is an "extremely common" condition (Gardner & Yaffe, 2015), affecting approximately 600 people in 100,000 per year (Cassidy et al., 2004). MTBI results in cognitive, psychological, and functional impairment (Karr et al., 2014; Kashluba et al., 2008; Ponsford et al., 2000). More specifically, executive functions (EF) are frequently affected as a result of MTBI (Ponsford, 2013), which is particularly disabling since they are intrinsically linked to functional independence (Hanks et al., 1999), return to work, and social autonomy (Bar-Haim Erez et al., 2009).

Despite being frequently affected following MTBI, the literature reports variability in EF performance in this group. Thus, according to a systematic review, the effect sizes of EF measuring the magnitude of difference between a MTBI group and controls stand out as being particularly inconsistent and heterogeneous across studies (Karr et al., 2014). In order to improve the accuracy of EF measurements, Karr et al. (2014) suggested using well-established operational definitions, such as Miyake's model (Miyake et al., 2000). According to this model, EF consist of (1) cognitive flexibility (the ability to alternate between tasks or mental states), (2) updating (the ability to monitor representations in working memory), and (3) inhibition (inhibiting a dominant response in a controlled and deliberate manner).

Although having an empirical model to operationalize EF is an important consideration for investigations in this area, the lack of a model is not sufficient to explain the heterogeneity of performance (Karr et al., 2014). In fact, previous studies have shown that several types of factors are recognized as predictors of good and poor prognosis after MTBI (Belanger et al., 2018; Iverson & Lange, 2011; Karr et al., 2014; Mathias &

Wheaton, 2015; Ponsford et al., 2000) and the variability in these factors would explain the inconsistencies observed in outcome after MTBI (Belanger et al., 2018). In addition, in order to better understand the mechanisms explaining the persistence of symptoms following MTBI, Hou et al. (2012) developed a model identifying the types of predictors. It consists of three components (three p): (1) predisposing factors (premorbid vulnerability), (2) precipitating factors (the MTBI) and (3) perpetuating factors (cognitive, emotional and behavioural responses to brain injury). This model is useful for predicting the risk of developing persistent post-concussive symptoms but has not yet been used to our knowledge to predict cognitive functioning, specifically the status of EF after MTBI. However, several pieces of evidence suggest that the variables raised by Hou et al. (2012) could apply to cognitive and executive functioning. In fact, a recent literature review suggested that the three-p model could be applied to the prediction of several domains, whether physical, psychological, or neurological (Rickards et al., 2020).

As predisposing factors, studies agree that younger, more educated patients generally have better cognitive and functional outcomes (de Guise et al., 2005; Green et al., 2008; Karr et al., 2014; Mathias & Wheaton, 2015) after TBI. As well, premorbid IQ has also been linked to better cognitive or functional outcomes (Mathias & Wheaton, 2015; Nunnari et al., 2014). When considered together, education and premorbid IQ constitute cognitive reserve (Nunnari et al., 2014). This concept postulates that each individual benefits from their own level of reserve and that the higher the level of reserve, the better the outcome after TBI (Bigler & Stern, 2015; Mathias & Wheaton, 2015). However, given the relatively recent nature of the study of cognitive reserve in TBI, studies have not yet related the variables of education and premorbid IQ to EF.

In the category of precipitating factors, characteristics of the neurological impairment related to the MTBI need to be considered. One of these characteristics, the duration of post-traumatic amnesia (PTA) is known to significantly predict short-term outcome (de Guise et al., 2006), behavioural, memory and EF impairment after TBI (de Guise et al., 2017). Another, the occurrence of loss of consciousness (LOC), is associated with greater EF deficits (Sorg et al., 2014), and the presence of post-concussive symptoms after TBI (Roy et al., 2019). The severity of MTBI should also be considered as a precipitating factor that may influence outcome (Kaufman et al., 2019). In this regard, a differentiation between uncomplicated MTBI and complicated MTBI (i.e., visible presence of intracranial injury observed on CT or MRI) should be taken into account as an inter-individual difference. For example, studies have shown that a group with complicated MTBI showed a greater decrease in information processing speed and visuomotor coordination compared to an uncomplicated MTBI group (Comerford et al., 2002) as well as poorer cognitive performances such as EF measured with the Trail Making Test-B (Iverson, 2006). The presence of frontal lobe lesions is another important factor. The frontal regions are often considered to house the neural substrates of EF, which are believed to be highly dysfunctional in TBI (Azouvi, 2000; McDonald et al., 2002). The presence of frontal lesions has been linked to irritability (McAllister, 2011), psychosocial integration difficulties (Wallesch et al., 2001) and EF difficulties (Lehtonen et al., 2005). Finally, post-accident time to evaluation also seems to be an important consideration in this model since a more severe disorder is found when assessment is carried out early compared to later when some spontaneous recovery could have occurred (Karr et al., 2014).

As perpetuating factors, the presence of anxiety and depressive affect as well as post-concussive symptoms seem important to consider. Unfortunately, these factors have been less studied in relation to EF, and few investigations have been published on this topic to date. However, in a study of participants with moderate to severe TBI, individuals with anxiety disorders performed significantly worse on tests measuring EF (Gould et al., 2014). In another study, the presence of major depression after TBI was associated with poorer scores on cognitive tests, including EF tests (Rapoport et al., 2005). Additionally, it is known that depressive symptoms following TBI are predictive of performance on EF tests (Schiehser et al., 2011). It has also been found that patients with post-concussive symptoms of a cognitive or physical nature tend to score lower on formal tests measuring cognitive function, including EF (Chamelian & Feinstein, 2006). Finally, the presence of pain is associated with poorer EF scores after TBI (Anderson, 2020).

Given this information regarding EF following MTBI, the overall objective of this study was to characterize the associations between EF and predisposing, precipitating and perpetuating factors after MTBI. Application of the three-p model to the Miyake model of EF will allow, for the first time, a comprehensive study of the most relevant predictors of EF in order to better understand what underlies the high variability of EF performance in the MTBI population. In regard to each subset of the three-p model, the goals and hypotheses are: (1) *Predisposing factors*: Characterize the associations between pre-morbid vulnerability factors and EF. We hypothesize that the higher the cognitive reserve in patients with MTBI (more educated, higher premorbid IQ) and the younger the patients are, the better will be their performance on EF measures. (2) *Precipitating factors*: Characterize the associations between injury-related factors and EF. We hypothesize that the presence of loss of consciousness, post-traumatic amnesia, frontal lesions and a shorter time period between the accident and the EF assessment will be associated with poorer performance on EF tests. (3) *Perpetuating factors*: Characterize the associations between the severity of post-concussive symptoms, anxiety and depression and EF. We hypothesize that more severe post-concussive symptoms and anxiety and depression will be associated with more EF difficulties.

Materials and methods

Most of the recommendations made by Bauman and colleagues in their recent publication on retrospectively designed studies (Bauman et al., 2019) were followed for this retrospective study.

Participants

Calculation of the sample size. According to statistical power calculations using G*Powers 3.1.9.6, the minimum sample size for a 10-predictor multiple regression model should be at least 107 participants in order to obtain a power of 99% (effect size f2 = 0.15; a err prob = 0.05).

Data collection. In this study, the medical records of 172 patients from the Montreal General Hospital-McGill University Health Center (MGH-MUHC), admitted between July 2014 and January 2017, were retrospectively accessed (data entry between May and August 2017). The MGH-MUHC is an urban tertiary trauma center and receives approximately 10,000 trauma victims annually, according to their website. The sample consisted of patients from the MGH-MUHC outpatient MTBI clinic who had all been diagnosed with MTBI by a physician. This clinic follows 411 patients per year, as per the annual report of the Trauma Program, between 2014 and 2019. These patients all have post-concussive complaints and are assessed by a neuropsychologist at the clinic. The data was collected by a student research assistant who was blinded to the study and trained in the data collection process. Ethical approval was obtained (MUHC).

Inclusion and exclusion criteria. Two inclusion criteria were applied: (1) age 16 years and older and (2) a diagnosis of MTBI: loss of consciousness between 0 and 30 minutes; Glasgow Coma Scale between 13 and 15; and ≤24-hour PTA. Participants were excluded if they had (1) an active substance use disorder, (2) a declaration of incapacity, (3) a significant neurological disorder other than TBI based on the information obtained in a semi-structured interview conducted by a physician, or (4) were not fluent in English or French. The participant inclusion and exclusion flow chart is presented in Figure 1.

Measures

Demographic, previous medical history (antecedents) and accident related characteristics. Demographic information (age, gender, education), medical antecedents (psychological, learning disability, neurological disorder, and attention deficit disorder (ADHD)) and accident-related characteristics (post-accident time to evaluation, PTA, LOC, mechanism of the accident, and presence of cerebral lesion) were collected retrospectively from participants' medical records. The presence of cerebral lesions (lesion site) was assessed by a neurosurgeon blinded to the neuropsychological test results. The neurosurgeon read the computed-tomography (CT scan) imaging (brain CT scan) that had been carried out during the emergency room visit based on the criteria of the Canadian CT Head Rules (Stiell et al., 2001). Regarding the distribution between uncomplicated and complicated MTBI, a total of 94 patients were diagnosed with uncomplicated MTBI and 15 were diagnosed with complicated MTBI. A total of 62 patients did not undergo a CT scan. The absence of a CT scan in this group is not surprising since the Canadian CT head rule is used in the emergency department (Stiell et al., 2001). Thus, if there are not sufficient evidentiary signs, according to this rule, there is no need for brain imaging. This data was also collected retrospectively.

Executive functions (EF). (1) Cognitive flexibility. Trails A and B (Reitan, 1955) was used. The following formula was calculated to create a composite score for cognitive flexibility: total completion time score B/ total completion time score A. (2) Updating. The number sequence of the Weschler Intelligence Scale - 4th Edition (WAIS-IV) (Wechsler et al., 2008) was administered. The following formula was used to calculate a composite updating score: raw direct span score + raw inverse span score. (3) Inhibition. The Tower of London-Drexel University (TDLDX) 2nd Edition (Culbertson & Zillmer, 2005) was presented. The raw initiation time score was taken as a measure of inhibition. In fact, the Tower of London (TOL) has demonstrated sensitivity to EF deficits following TBI, and the initiation time measure has demonstrated sensitivity to EF deficits following TBI or the presence of cerebral lesion (Donders & Larsen, 2012; Krishnan et al., 2012; Sullivan et al., 2009) and factor analysis suggests that time to initiation can be considered a valid measure of inhibition (Levin et al., 1996).

Premorbid IQ. IQ was estimated using the vocabulary subtest of the Wechsler Abbreviated Scale of Intelligence - Second Edition (WASI-II), a recognized measure of crystallized intelligence, thus resistant to neurological impairment (Weschler, 2011). The total raw score of the test was obtained.

Post-concussive symptoms. The total score on the Post-Concussion Symptom Scale-Revised (PCSR) questionnaire (Lovell et al., 1999; Lovell & Collins, 1998) was used.

Anxiety and depression. The Beck Anxiety Inventory (BAI) (Beck & Steer, 1988) and the Beck Depression Inventory (BDI) (Beck et al., 1996) were used to measure anxiety and depressive affect. The total raw score was calculated for both measures.

Statistical analysis

Exploratory analyses. Exploratory analyses were conducted to determine the influence of the presence of antecedents (psychological, learning disability, neurological disorder, accident related orthopedic injuries, and attention deficit disorder (ADHD) on EF. It should be noted that five participants with neurological disorders deemed significant by the researchers were excluded (see Figure 1), but that five other participants with neurological disorders deemed less serious by the researchers were included in the study to form the "with neurological disorder" group. To determine whether a difference existed between patients with negative CT (uncomplicated MTBI; n=94) and positive CT (complicated MTBI; n=15) confirmed on imaging, independent-samples t-tests and effect sizes were calculated on EF and on variables such as premorbid IQ, depression, and anxiety. Furthermore, considering the unequal groups and the number of missing data, it was decided to consider all these patients in a single group for the regression analyses.

The analyses included: (1) First, group differences (student t-test) for each antecedent group (yes/no dichotomized variable) were calculated on each of the EF components (cognitive flexibility, updating and inhibition). The following formula was used to calculate the partial squares: $t2/t2 +(n1+n2-2)$. (2) Second, in the case of variables showing significant differences, linear regressions were performed on these variables (independent variables) with the different EF components (dependent variables), controlling for age and education in order to explore whether these differences persist beyond the effect of age and education.

The statistical analyses by objectives were the following:

Objective 1: Predisposing factors. In order to test associations between cognitive reserve and EF, linear regressions were performed between several independent variables including cognitive reserve (education and premorbid IQ) and age and each of the EF components (inhibition, updating and flexibility) (dependent variables), controlling for age and/or education when necessary.

Objective 2: precipitating factors. To test associations between accident-related factors and EF, linear regressions were performed between several independent variables representing accident-related factors (PTA, LOC, frontal injury and post-accident time to evaluation) and each of the EF components (inhibition, updating and flexibility) (dependent variables), controlling for age and education when necessary. For the variable "post-accident time to evaluation", age and education were not controlled since there is no reason to believe that these variables share a common variance.

Objective 3: Perpetuating factors. In order to verify the association between the presence of post-concussive and anxiety and depressive symptoms and EF, linear regressions were performed between these independent variables (anxiety and depressive affect, post-concussive symptoms) and each of the EF components (inhibition, updating and flexibility) (dependent variables), controlling for age and education.

Results

Participants

Demographic and accident-related characteristics are described in Table 1. Table 2 shows performance on neuropsychological tests and questionnaires. Note that the percentage of missing data ranged from 0% to 38.4%.

As established in previous studies, performance was considered impaired with a Z score cut-off of –1.5 SD (Barr, 2003; Kavé et al., 2011). Deficit performance was therefore below a Z score of -1.5 for the subtests Trail A and B, a scaled score of 6 or less for the subtests direct and indirect span and an equivalence score of 69 or less for the TOL initiation time. Patients with MTBI in our cohort had an average Z score of -0.67 (SD: 2.39) on Trail A and an average of -1.00 (SD: 2.05) for Trail B. The direct span average scaled score was 8.32 (SD: 2.95) and the average scaled score for the indirect span was 8.95 (SD: 2.65). The average equivalence score of the TOL initiation time was 102.07 (SD: 16.41). Thus, our patients' average scores were not in the deficit zone but, a total of 18.8% of them had a performance considered impaired on the Trail A subtest and 29.4% on the Trail B task. A total of 26.5% of the cohort had a score considered as a deficit performance on the direct span task and this was the case for 17.9% of the participants in the indirect span condition. Only 0.9% of patients had a performance considered as a deficit for the initiation time of the TOL.

Normality and extreme data

To validate the normality of the continuous variables, skewness and kurtosis were calculated. A kurtosis between -7 and 7 was considered acceptable and the skewness had to be between -2 and 2 to be considered acceptable (Curran et al., 1996). Normality data for the continuous variables are found in Tables 1 and 2. Note that the inhibition variable did not meet the normality assumption. To overcome this problem, this variable underwent log transformation (log10), which solved the normality problem.

Exploratory analyses

Initially, t-tests to compare uncomplicated and complicated MTBI were performed on EF and on variables such as premorbid IQ, depression, and anxiety. The group differences for these analyses are presented in Table 3. Only one difference was found to be significant for the measure of updating t(107) = 2.16, p = .02, η^2=4.01

In addition, t-tests were performed on all antecedent categories (psychological problems, learning disability, neurological diagnoses, orthopedic injuries, and attention deficit disorder (ADHD). The significant result for these analyses are presented in Table 4. Only one difference was found to be significant. The difference between the group with a psychological history compared to the group without these problems was significant for the measure of updating, *t*(153;147.379)=-2.111, *p*<.05, *d*=-1.37, 95% CI [-2.66,-0.09]. Patients without a psychological history performed better on the updating task (digit span). The partial eta-square (*η2*) was small (Cohen, 1988).

In a second step, a linear regression controlling for age and education did not show a significant relationship between the presence of psychological antecedents and updating. Thus, when the effect of age and education was extracted from the group difference observed with the t-test, this difference disappeared. For this regression analysis, the tolerance statistic for the presence of multicollinearity between the multiple predictors is 0.957, which seems acceptable (over 0.10 according to Bowerman & O'Connell (1990) and Myers (1990) in Field (2018)).

Analyses on EFs

The regression results for the predisposing factors are reported in Table 5. First, significant relationships were found between updating scores and education (*F*(2,155) = 10.380, *p* = 0.000, variation *R2* = 0.119) when the effect of age was controlled and between updating scores and premorbid IQ (*F*(3,148) = 8.367, *p* = 0.005, variation *R2* = 0.047), when age and education were controlled. Thus, education explained 11.9% of the variance of score on the updating task and premorbid IQ explained 4.7%. More specifically, the results indicate that patients with MTBI with a higher level of education and those with higher premorbid IQ scores tended to show better performance on digit span tasks (updating). In a second step, significant relationships were found between inhibition (log10) and the following two predictors: age (*F*(2,108) = 8.864, *p* = 0.000, variation *R2* = 0.033) and education (*F*(2,108) = 8.864, *p* = 0.000, variation *R2* = 0.067). Age explained 3.3% of the variance of the inhibition score and education explained 6.67%. These results indicate that older patients and those who were more educated took more time to plan their movements on the TOL task, therefore were more inhibited or less impulsive, taking more time to plan their first move.

The regression results for the precipitating factors are reported in Table 6. No significant relationship was found for this objective.

The regression results for the perpetuating factors are reported in Table 7. Significant relationships were found between performance on the updating task and BDI scores (*F*(3.146) = 10.688, *p* = 0.016, *R2* variation = 0.034) and BAI results (*F*(3.145) = 10.363, *p* = 0.020, *R2* variation = 0.032), when the effect of age and education was controlled. Thus, BDI performance explained 3.4% of the variance of the updating results and BAI explained 3.2%. These results indicate that the more patients reported depressive and anxious symptoms, the less well they performed on the updating task (digit span).

Discussion

The aim of this study was to characterize the associations between predisposing, precipitating and perpetuating factors and EF after MTBI. A summary of the main significant results of this study is shown in Figure 2.

Predisposing factors

According to the model proposed in this study, predisposing factors are cognitive reserve (education and estimated premorbid IQ) and age. We found that the most educated of the patients with MTBI in terms of years of schooling showed better performance in working memory (better digit span scores) and better inhibition skills (higher initiation times). These associations are not surprising since education correlates positively with cognition in general in healthy individuals (Beck & Steer, 1988). In addition, education has been shown to be positively associated with cognitive outcome (de Guise et al., 2017) and functional outcome (de Guise et al., 2006; Mathias & Wheaton, 2015; Schneider et al., 2014) in patients with TBI. More specifically, a study of patients with MTBI showed a positive association between education and working memory, a task related to updating (de Guise et al., 2017), which is consistent with the results of this study. To explain this, some authors postulate that people with more education could be more intellectually active, allowing them to develop stronger and more numerous cortical connections which in turn would support a more efficient reorganization/compensation after TBI (Stern, 2002) or would permit a better adaptation to brain impairment (Bigler & Stern, 2015; Fortune et al., 2016). In the context of this study, this premorbid intellectual stimulation would therefore help maintain better executive abilities, i.e., the ability to retain or actively manipulate information in immediate memory or to plan actions to be taken while inhibiting behaviour. As for premorbid IQ, it is associated with updating (positive relationship), according to the results of the current study. In a consistent manner, a study by Friedman and colleagues (Friedman & Miyake, 2004) suggests relationships between IQ and updating, but not with the other EF. In fact, we know that general intelligence factor "g" is related to several neuropsychological measures, because this crystallized intelligence (unaffected by TBI) allows patients to adapt and overcome cognitive deficits or difficulties through effective problem-solving strategies (Leary et al., 2018; Nunnari et al., 2014).

Regarding the influence of age on EF, the results of the present study suggest that older patients are more inhibited on the TOL task than younger ones, i.e. the older the patients are, the longer it takes them to perform the first movement of the task, which contradicts our initial hypothesis. This hypothesis stated that with age, patients would have more difficulty inhibiting their behaviour and therefore would take less time to plan their first movement. The delay that was found in the current study may not have been due to increased inhibition but may reflect increased information processing time. Thus, our measure may not have been indicative of the degree of impulsivity linked to the process of inhibition but could be related to the time required to process the information. This delay could therefore be explained, at least in part, by the presence of a certain slowness in planning with advanced age, particularly since it is known that age is associated with a decrease in information processing speed in general (Bors & Forrin, 1995). In fact, we know that the inhibition construct is very difficult to differentiate from information processing speed (Miyake et al., 2000), particularly in an older population (Adrover-Roig et al., 2012). Another possibility to explain this result is related to the common presence of apathy after TBI (Starkstein & Pahissa, 2014) which leads to a decrease in goal-oriented behaviours (Starkstein & Leentjens, 2008). Some authors suggest that apathy and disinhibition are opposite expressions of the same cognitive domain (Mann, 1990 in Starkstein & Leentjens, 2008). Thus, it is possible that the higher inhibition time with older age observed in our sample may in fact be a manifestation of apathy the older the patients are. It will be important to try to dissociate these three concepts (inhibition, apathy, speed of information processing) in future studies.

Precipitating factors

Precipitating factors are those associated with the severity of brain injury, i.e. PTA, LOC, the presence of frontal lesions and post-accident time to evaluation. First, for the presence of PTA or LOC where no association was observed, it is possible that the dichotomous categorization used in the analyses (presence or absence), instead of considering length of PTA or LOC, masked some variability within these variables. In addition, since all our patients had MTBI, there may be less variability in these indicators than if we had included patients with different levels of severity of TBI. Thus, we know that in patients with moderate and severe TBI, the predictors most strongly associated with outcome are severity factors (GCS, PTA, LOC). However, when we look at patients with MTBI only, the notion of injury severity could play a role in explaining deficits in the very short term, but in the long term, psychological factors have a more significant role in understanding deficits (Belanger et al., 2018). It is interesting to note that better performances were found in the uncomplicated group only for the updating component while inhibition, flexibility and other variables showed no group differences. However, as indicated in our results, it would have been relevant to dichotomize the regression analyses between the complicated MTBI and uncomplicated MTBI groups specifically for the updating variable of the EF since the latter differed between the groups where the group with intracranial injury showed poorer performance in working memory. The presence of unequal groups and a group of only 15 participants in the complicated MTBI group in this study limits the power needed to perform regression analyses. Future studies should consider separating the groups according to this severity criterion. Although our interpretation needs to be cautious because of the small group size, this study thus suggests that the updating process is more sensitive to the presence of a brain lesion after sustaining a MTBI but that it is not the presence of a frontal lesion that seems to explain this result. In that sense, in contrast to our hypothesis, no association could be established between the presence of frontal lesions and EFs. Several explanations are possible. It is known that it can be difficult to establish a relationship between the site of a brain lesion and neuropsychological performance, since the presence of diffuse lesions can lead to general and non-focal disorganization in patients with TBI (Povlishock & Katz, 2005). In addition, a lack of sensitivity of neuropsychological tests or even the lack of sensitivity of the CT-Scan to detect small non-hemorrhagic lesions (Balzano et al., 2020; Povlishock & Katz, 2005) unlike magnetic resonance imaging may have also played a role in masking the relationship between EF and frontal lesions following MTBI in the present study. It should also be noted that the majority of our patients with MTBI did not undergo a CT scan at the time of admission to the emergency room. In fact, there was missing data rate of 32.56% and very few patients in our total sample had frontal damage (13/172). This low number of CT scans performed on admission is not surprising and is clinically justified since it is based on the Canadian CT head rule, which recommends that a CT scan be performed following the MTBI only if the patient presents certain specific characteristics, such as vomiting, headaches, being over 60-65 years of age, etc. (Jagoda et al., 2009; Stiell et al., 2001). Thus, the number of patients in our sample presenting with a frontal injury may have been underestimated. Finally, post-accident time to evaluation did not appear to be an influential variable in EF performance. As such, it was unnecessary to control for its effect in other analyses.

Perpetuating factors

In this study, the presence and extent of anxiety, depressive affect and post-concussive symptoms were explored as perpetuating factors of EF weakness following MTBI. The results indicate that anxiety and depressive affect were associated with *updating,* and this is beyond the effect of age and education on this variable, since these two factors were controlled. Thus, the more anxious or depressed the patients with MTBI were, the more *updating* test performance was affected. A study by Gould and colleagues (Gould et al., 2014) found similar results. In their study, performance in working memory tasks correctly classified two groups of patients, one group with an anxiety disorder (lower performance) and one group without an anxiety disorder (higher performance). In fact, it is known that anxiety has, in the general population, a facilitating effect on less cognitively demanding tasks, but a disabling effect on more difficult and demanding tasks (Humphreys & Revelle, 1984), a phenomenon that is also found in patients with TBI (Perlstein et al., 2004). Thus, in more difficult tasks, anxious thoughts act as a "distractor", focusing the patient's cognitive capacity on their worries and thereby reducing the cognitive resources allocated to the task (Humphreys & Revelle, 1984) or to cognitive functioning in everyday life (Boals & Banks, 2012). Here, the *updating* task is the only EF that is not timed, and therefore allows patients a certain leeway to think (Visu-Petra et al., 2013). It is possibly the only task, among the three EF, that allows anxious thoughts to infiltrate information processing, which explains the lack of relationship with *cognitive flexibility* and *inhibition.*

In regard to depressive affect, results also indicated that the higher this measure, the poorer the updating performance. This is consistent with previous literature, since the presence of depression diagnosed after TBI is associated with more deficits in EF (Jorge et al., 2004) and working memory (Rapoport et al., 2005). This result can be based on the hypothesis that the mental processes associated with depression and those involved in EF have more or less the same pathophysiological substrates (involving the frontal regions, particularly the fronto-striato-thalamic circuit) (Jorge et al., 2004).

Finally, the present study did not demonstrate any relationship between the presence of psychological antecedents and performance on EF tests, when the variances of age and education were excluded from the analysis (controlled). Thus, it can be assumed that anxiety or depression experienced prior to the TBI (psychological history) did not have a significant impact, but that it is anxiety and depression experienced following the TBI (as assessed by the BDI and BAI) that had an impact on EF (*updating*). In fact, this is entirely consistent with the consideration that the presence of anxiety and depressive affect are perpetuating factors in executive deficits and not predisposing factors. Regarding our last perpetuating factor, the presence of post-concussive symptoms (i.e., nausea, dizziness, headaches, etc.) did not appear to affect performance on EF tests. However, we found a significant amount of missing data (38.4%) for the PCSR total score variable, in addition to the fact that a higher percentage of patients did not report a significant level of post-concussive symptoms (18.9%) (PCSR<21) (Bottari et al., 2012). That said, it is possible that some lack of variability may have limited the scope of the results for this variable.

Limitations

This study has some limitations. First, it would have been preferable to use a greater number of neuropsychological tests to calculate EF ratios, especially for *cognitive flexibility* and *inhibition*. In addition, the variable defined as presence of a frontal lesion lacked precision, particularly due to the use of a CT-scan to identify this since it can lead to a high rate of false negatives (De Rosa et al., 1995) and has limited resolution when the lesion is less than 5 mm (Bigler & Maxwell, 2011). In addition, measures of depressive and anxiety affect, and post-concussive symptoms were self-reported and therefore subjective and not medically diagnosed. There may therefore have been a bias related to the patient's perceived condition at the time the questionnaires were completed (e.g., "good old days" theory (Iverson et al., 2010)). Finally, many other variables could have been included within the proposed three-p model, in terms of predisposing (e.g. personality, perceptions, social support, socio-economic level, etc.), precipitating (e.g. presence of post-traumatic stress) and perpetuating (e.g. chronic pain, erroneous thoughts) factors (Rickards et al., 2020). It should be noted that the use of a retrospective design by definition limits the choice of measures but favours the generalisation of results to real clinical contexts (Bauman et al., 2019).

Conclusion

To conclude, this study brings two innovative aspects to the scientific literature: (1) it fills a gap in the study of EF sub-components following MTBI by adopting a well-supported empirical theoretical model to conceptualize them (Miyake et al., 2000) and (2) it provides a better understanding of the inherent variability of EF by targeting predictive factors through the application of the three-p model (Hou et al., 2012; Rickards et al., 2020) and the cognitive reserve model (premorbid IQ and education) (Nunnari et al., 2014). Our main objective was to allow clinicians to further understand the effect of various demographic and injury related factors on EF post MTBI. More specifically, clinicians should initially consider that the lower the premorbid IQ and education level of patients, the more "predisposed" they are to have lower EF skills post MTBI. Second, the higher the anxiety and depressive affect, the poorer the EF results could be. Taken together, the novelty of the present study lies not only in associating cognitive reserve and anxio-depressive affects with EF, but in comparing the variables with each other. Thus, the results suggest that of all the variables that play a role in cognitive (executive) status after TBI, level of education holds a particularly important place since it is the only variable associated with two subcomponents of EF.

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Declaration of interest statement

No potential conflict of interest was reported by the authors.

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Figures captions

Figure 1.

Flow-chart of the participant recruitment

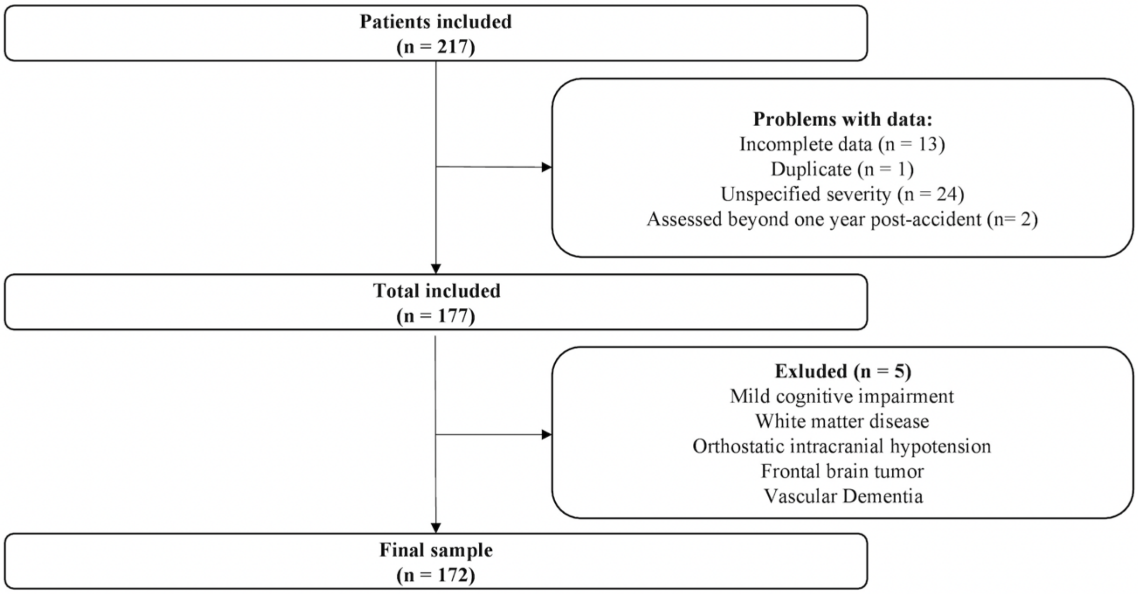
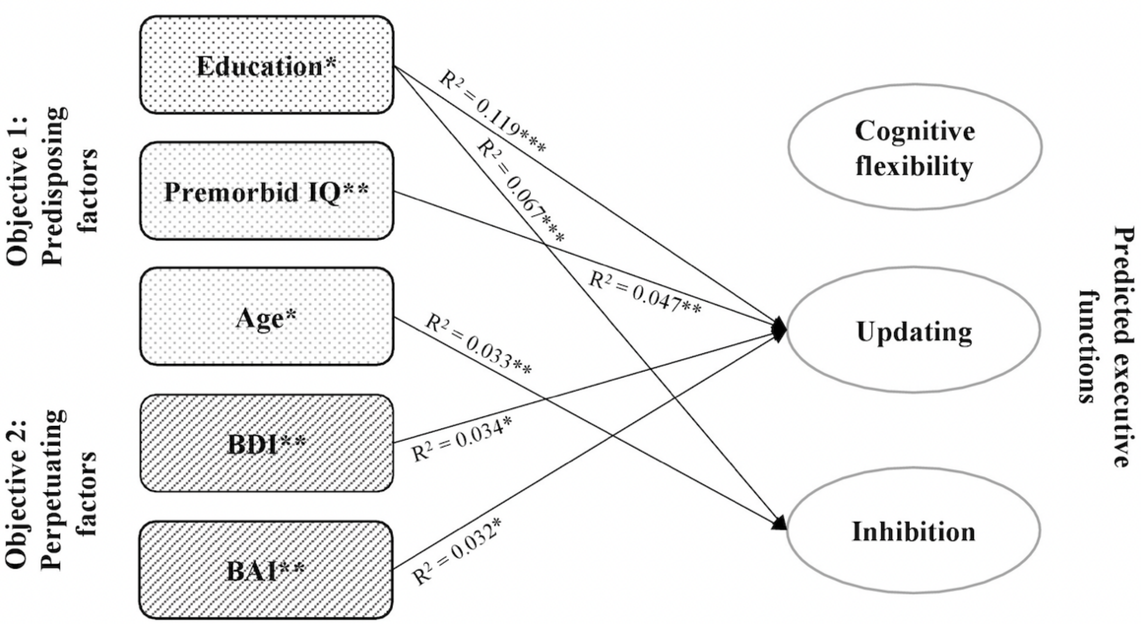


Figure 2.

Prediction model: significant results



Note. This model brings together all significant predictors of executive functions. Since the predictors in the precipitating factors were not significant, they are not included in this figure. Variables with two asterisks (**) were controlled for age AND education and those with one asterisk were controlled for age OR education.
*p<.05. **p<.01. ***p <.001.

Table 1. *Demographic and accident related variables*

	Mean (%)	SD	Range	Missing data (%)	Normality
Demographics					
Age (years)	35.74	13.99	16-72	1 (0.58%)	0.42; -1.03
Gender (female (%))	106 (60.2%)			0 (0%)	
Education (years)	14.49	2.94	6-24	2 (1.16%)	0.16; 0.58
Accident related variables					
Post-accident time (days)	79.26	52.40	10-359	1 (0.58%)	2.14; 7.54
PTA (yes (%))	86 (48.9%)			34 (19.3%)	
LOC (yes (%))	55 (31.3%)			38 (21,6%)	
Mechanism of injury					
Fall	50 (28.4%)			1 (0.58%)	
MVA	60 (34.1%)				
Assault	9 (5.1%)				
Sports	32 (18.2%)				
Others	20 (11.4%)				
Presence of brain lesion					
Frontal	13 (7.4%)			56 (32.56%)	
Temporal	11 (6.3%)				
Parietal	8 (4.5%)				
Occipital	1 (0.6%)				

Note. Normality = skewness; kurtosis; PTA = Post-traumatic amnesia; LOC = Loss of consciousness; MVA = Motor vehicle accident.

Table 2. *Neuropsychological and questionnaire performances*

	Mean	SD	Range	Missing data (%)	Normality
Neuropsychological Performances					
Cognitive flexibility	2.31	0.69	0.52-5.10	28 (16.3%)	0.83; 2.18
Inhibition	61.55	46.12	12-328	63 (36.63%)	3.70; 18,96
Updating	18.03	4.06	7-28	16 (9.30%)	-0.11; -0.30
Premorbid IQ (vocabulary)	52.51	11.38	25-76	20 (11.63%)	-0.09; -0.70
Questionnaire performances					
PCSR (total score)	44.41	25.17	5-106	66 (38,4%)	0.26; -0.73
BDI	19.48	10.48	3-50	16 (9.30%)	0.90; 0.42
BAI	17.26	11.75	1-49	17 (9.88%)	0.82; -0.11

Note. Normality = skewness; kurtosis; PCSR = Post-Concussion Symptom Scale-Revised; BDI = Beck depression inventory; BAI = Beck anxiety inventory.

Table 3. *Differences between uncomplicated and complicated MTBI*

	Uncomplicated MTBI (n=94		Complicated MTBI (n=15)			
	M (n)	*SD*	*M (n)*	*SD*	*p value*	η^2
Cognitive Flexibility	2.33(125)	.87	2.48(19)	.72	.47	.85
Updating	18.34(131)	3.99	16.40(25)	4.14	**.02**	**4.01**
Inhibition (log10)	1.71(94)	.25	1.73(15)	.18	.75	.25
Premorbid IQ	52.67(131)	11.52	51.48(21)	10.66	.66	11.41
BDI	19.78(132)	10.51	17.85(24)	10.42	.41	10.49
BAI	17.90(132)	12.04	13.61(23)	9.32	.11	11.69

Note. η^2 *= cohen's d.*

Table 4. *Exploratory Analyses t-test: Psychological antecedents*

	Present		Absent			
	M (n)	SD	M (n)	SD	p value	η^2
Cognitive flexibility	0.36 (61)	0.12	0.34 (82)	0.16	0.427	0.00
Updating	17.29 (70)	4.03	18.66 (85)	4.03	**0.036**	**-0.03**
Inhibition (log10)	1.74 (43)	0.22	1.70 (66)	0.26	0.430	0.01

Note. η^2 = partial eta-square.

Table 5. *Predisposing factors: Linear regression on each executive function*

	B	Standard error	Bêta	t	*p* value	R^2
Cognitive flexibility						
Age*	0.001	0.004	0.020	0.226	0.822	0.000
Education*	-0,028	0.021	-0.114	-1.313	0.191	0.012
Premorbid IQ**	0.001	0.005	0.013	0.148	0.883	0.018
Updating						
Age*	-0.033	0.023	-0.115	-1.463	0.146	0.012
Education*	0.485	0.107	0.356	4.543	**0.000**	**0.119**
Premorbid IQ**	0.078	0.27	0.225	2.842	**0.005**	**0.047**
Inhibition (log10)						
Age*	0.003	0.002	0.192	2.026	**0.045**	**0.033**
Education*	0.022	0.008	0.272	2.872	**0.005**	**0.067**
Premorbid IQ**	0.001	0.002	0.048	0.505	0.615	0.002

Note. *Controlled for age OR education via a multiple regression. Tolerance statistics to verify the presence of multicolinearity are all acceptable (>0.10). **Controlled for age AND education via a multiple regression. Tolerance statistics to verify the presence of multicolinearity are all acceptable (>0.10).

Table 6. *Precipitating factors: Linear regression on each executive function*

	B	Standard error	Bêta	t	*p* value	R^2
Cognitive flexibility						
PTA*	-0.049	0.144	-0.033	-0.341	0.734	0.001
LOC*	-0.017	0.146	-0.011	-0.115	0.908	0.000
Frontal lesions*	0.062	0.275	0.024	0.225	0.823	0.001
Post-accident time (days)	-0.001	0.001	-0.062	-0.735	0.464	0.004
Updating						
PTA*	0.673	0.736	0.079	0.915	0.362	0.006
LOC*	-0.327	0.738	-0.040	-0.443	0.658	0.002
Frontal lesions*	0.186	1.168	0.019	0.159	0.874	0.000
Post-accident time (days)	0.009	0.006	0.124	1.545	0.124	0.009
Inhibition (log10)						
PTA*	-0.015	0.049	-0.030	-0.308	0.759	0.001
LOC*	0.057	0.051	0.112	1.128	0.263	0.012
Frontal lesions*	0.017	0.093	0.021	0.183	0.855	0.000
Post-accident time (days)	-4.094	0.000	-0.010	-0.099	0.922	0.000

Note. *Controlled for age and education via a multiple regression. Tolerance statistics to verify the presence of multicolinearity are all acceptable (>0.10). PTA = Post-traumatic amnesia; LOC = Loss of consciousness.

Table 7. *Perpetuating factors: Linear regression on each executive function*

	B	Standard Error	Bêta	t	*p* value	R^2
Cognitive flexibility						
PCSR total score*	0.002	0.003	0.066	0.591	0.556	0.004
BDI*	0.004	0.006	0.057	0.644	0.520	0.003
BAI*	0.007	0.005	0.112	1.277	0.204	0.012
Updating						
PCSR total score*	-0.026	0.015	-0.168	-1.745	0.084	0.027
BDI*	-0.078	0.032	-0.188	-2,442	**0.016**	**0.034**
BAI*	-0.064	0.027	-0.180	-2.352	**0.020**	**0.032**
Inhibition (log10)						
PCSR total score*	0.001	0.001	0.100	0.982	0.329	0.009
BDI*	0.003	0.002	0.120	1.321	0.190	0.014
BAI*	0.002	0.002	0.081	0.877	0.383	0.006

Note. *Controlled for age and education via a multiple regression. Tolerance statistics to verify the presence of multicolinearity are all acceptable (>0.10). PCSR = Post-Concussion Symptom Scale-Revised; BDI = Beck depression inventory; BAI = Beck anxiety inventory.

Chapitre 3: Article 2

Longitudinal recovery of executive functions and social participation prediction following traumatic brain injury

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Concernant cet article, l'étudiante a contribué à la collecte des données (au temps 1 et au temps 2). Concernant le temps 2, elle a organisé la collecte (en présentiel et par zoom) et chapeauté des étudiants engagés pour faire les évaluations, en plus de compléter des évaluations elle-même. L'étudiante a procédé aux analyses statistiques, à la recension de la littérature, à l'élaboration du projet de recherche (objectifs et hypothèses) et à la rédaction de l'article. Les docteurs Lague-Beauvais, Marcoux et Dagher, ainsi que Monsieur Michel Abouassaly ont permis l'accès aux participants à l'Hôpital général de Montréal. Audrey Sheehan et Coralie Francoeur ont également participé à la collecte des données en temps 1. Emma Colucci et Adriana Ursulet ont participé à la collecte des données en temps 2. Dre de Guise a chapeauté le projet.

Abstract

There is heterogeneity across studies and a lack of knowledge about recovery of EFs over time following traumatic brain injury (TBI). Also, EFs are associated with functional outcome, but there is still a gap in knowledge concerning the association between EFs and social participation following TBI. For this reason, we aim to (1) measure the recovery of the three executive function subcomponents of Miyake's (2000) model, namely flexibility, updating and inhibition between the acute phase (T1) and 6 months post TBI (T2) and (2) measure the relationship between EFs and social participation after TBI. Thus, a prospective longitudinal study that included 75 patients with TBI (mild and moderate-severe) and 50 patients with orthopedic injuries (controls) without brain damage was carried out. An extensive EFs test battery was administered at T1 and T2 whereas the Mayo-Portland Adaptability Inventory-4 (MPAI-4) was administered only at T2. In contrast with the controls, both TBI groups improved significantly between T1 and T2 on WMS-III Mental Control test (MC) and the D-KEFS Category Switching Condition of the Verbal Fluency task (SVF). Results also showed a simple time effect for the WAIS-IV Digit span and the Hayling tests. Moreover, there was an association between the SVF test and social participation (MPAI-4) at T2. In conclusion, the MC and SVF tests were found to be the best tools for measuring recovery of EFs following TBI. The SVF test was the most likely measure of EFs to give the neuropsychologist an idea of the patient's social participation.

Key words: Traumatic brain injury, recovery, executive function, social participation.

Introduction

Executive functions (EFs) are a set of general-purpose control processes that regulate one's thoughts and behavior (Miyake et al., 2000). According to the Miyake and colleagues' model (2000), EFs consists of three major components. *Flexibility* allows one to redirect thoughts in order to perceive, process and respond to situations in different ways and to switch from one cognitive task to another. *Updating* allows for the constant monitoring of information in working memory and allows for its removal or addition. Finally, *inhibition* is the ability to control one's attention, behavior, thoughts, and emotions by intentionally preventing the production of a dominant response (Miyake et al., 2000).

EFs are mainly supported by the prefrontal cortex and associated circuits (Rabinowitz & Levin, 2014). These regions are often the most vulnerable following a TBI (McDonald et al., 2002) (McAllister et al., 2006). Thus, TBI can lead to deficits in cognitive functioning, including difficulties with EFs (Belanger et al., 2005; Kumar et al., 2013; Podell et al., 2010; Rabinowitz & Levin, 2014; Stuss, 2011). In fact, some studies have highlighted the presence of executive function (EF) disorders following a TBI, both in the acute recovery phase (Ghawami et al., 2017; McDonald et al., 2002; Rojas, 2017) and in the longer term following a TBI, i.e., several months (Ruttan et al., 2008) or even a few years following the injury (Ruttan et al., 2008). However, there is significant heterogeneity across studies regarding the severity of such EF deficits and highly variable effect sizes across studies (Karr et al., 2014). This heterogeneity is observed due to the fact that EFs are a broad and often ill-defined concept (Karr et al., 2014) which makes it sometimes difficult to compare performance associated with EFs that is measured by various tools. In addition, authors have proposed various time frames for post-TBI evaluation or did not use an appropriate control group (L. Carroll et al., 2004). Indeed, in studies that are interested in the evaluation of a TBI population and particularly when these patients are evaluated in the acute phase of trauma, a matched control group is minimally needed to determine the specific impact of TBI on EFs. One of the reasons for this involves the impact of the presence of pain and medication use on EFs. Previous studies have shown the negative impact of acute pain from musculoskeletal injuries on EFs (Morogiello et al. 2018; Buk et al., 2019). In this context, the matched control group can help to control for the confounding variables of pain and medication effect. A further point explaining the heterogeneity of prior research is that studies frequently included patients with TBI of all severities in the same group. According to a meta-analysis by Mathias et al (2007), variables related to TBI such as its severity induce variability in performance on different tests. For example, performance on mental flexibility function assessed with the Trail Making Test was found to be negatively affected by injury severity (Lange et al., 2005). Likewise, studies have shown that the recovery of cognitive functions over time occurs at different rates depending on the severity of the TBI, but generally within a few months after a mild TBI (L. J. Carroll et al., 2014; Mel B. Glenn, 2001). In moderate-severe TBI, improvements in EFs are significant in the first months (Christensen et al., 2008) and the first year (Rabinowitz et al., 2018; Sigurdardottir et al., 2020), but they reach a plateau and start to stagnate after a few years (Sigurdardottir et al., 2020) with residual and persistent deficits over time (Millis et al., 2001). Currently, little is still known about the evolution of EFs between the acute phase (up to a few weeks post-TBI) and the chronic phase of recovery for patients with TBI of different severity levels. To our knowledge, no study using a prospective longitudinal design has looked at the recovery of Miyake's EFs between the acute phase and at six months post-accident. Understanding the recovery pattern of EFs according to TBI severity is important, in fact, since these skills greatly impact everyday functioning.

EFs allow the individual to perform many complex cognitive tasks and perform daily activities independently (Wood & Worthington, 2017) (Cicerone et al., 2000; Liu-Ambrose et al., 2008). They are indeed highly correlated with various skills such as taking care of oneself, engaging in pleasurable activities or interacting socially (Lewis et Horn, 2013). Thus, the extent of cognitive deficits observed immediately after TBI are among the best predictors of patient outcome and recovery after TBI (Rassovsky et al., 2015; Senathi-Raja et al., 2010; Spitz et al., 2012) (Ponsford et al., 2008; Boake et al. 2001; Sherer et al., 2002). Of the investigations that specifically looked at EFs, Rojas' study found a relationship between EFs measured by the Fontal Assessment Battery (FAB) and patient outcome in areas such as dependence on others and productivity, assessed by the Disability Rating Scale (DRS) in the acute recovery phase (Rojas, 2017). Another study conducted in our laboratory found a relationship between EFs measures and short-term functional outcome (see Francoeur, 2020). However, a gap still exists in the literature on the predictive role of acute deficits in EFs on the longer-term outcome after TBI, such as in social participation. Yet, understanding more about this relationship would allow for better targeting of rehabilitation goals (Allanson et al., 2017). In sum, it is currently difficult to identify acutely those patients who are at risk of developing social participation problems in everyday life related to these executive problems (Baum et al., 2017).

Given this context, the aim of the study was to measure recovery between the acute phase (T1) and 6 months post TBI (T2) of the three EF subcomponents of Miyake's (2000) model, namely *flexibility, updating and inhibition*. This study also aimed to explore the relationship between EFs and social participation after TBI. We hypothesized for our first objective that unlike the control group, both groups of patients (mild and moderate/severe) would show improvement in *flexibility, updating and inhibition* between T1 and T2. Furthermore, at T2, it was expected that patients with mild TBI would be equivalent in EF performance to the control group and superior to the group with moderate/severe TBI. As for our second objective, we expected that better EF performance at T1 and T2 would be significantly associated with better social participation at T2.

Materials and methods

Participants

In this study, 75 patients with TBI and 50 control participants with orthopedic injuries but no brain damage were recruited at the Montreal General Hospital - McGill University Health Centre (MUHC-MGH), between March, 2018 and March, 2020. For the TBI group, the medical diagnosis and TBI severity were established by a physician. TBI severity was determined using the Glasgow Coma Scale (GCS) score, the duration of alteration or loss of consciousness, and the duration of post-traumatic amnesia (PTA). Mild TBI most often results in a PTA of less than 24 hours, a loss of consciousness of 30 minutes or less, and an GCS score between 13 and 15 (Marshall et al., 2012). Neurological damage is often less than in moderate or severe TBI. The latter have altered consciousness of more than 30 minutes, PTAs of more than 24 hours or more than 7 days for severe TBI, and GCS scores of 9 to 12 and 3 to 8, respectively (Lezak, Howieson, Bigler, & Tranel, 2012). Patients in the TBI group who also had other traumatic injuries were invited to participate as well. Except for TBI, the control group patients' injuries in the study were similar to those of the TBI group. Patients within the experimental and control group may suffered the following injuries: chest trauma, pulmonary contusion, intra-abdominal injuries and orthopedic injuries such as fracture of the pelvis, upper and lower extremities, sternum, and rib fracture including flail chest.

For both groups, exclusion criteria were previously diagnosed major neurological or psychiatric disorder, previously diagnosed TBI, chronic substance abuse disorder, acute medical conditions (e.g., pneumonia), intravenous narcotic use and a general inability to participate in or consent to the assessment. Patients with spinal cord injuries and cardiac injuries were excluded as well as those with complex pelvic fractures.

Procedure

At T1, all participants were seen at the bedside by a trained doctoral neuropsychology student or a neuropsychologist who administered neuropsychological tests as part of this assessment. Approximately 6 months after the accident (T2), patients were called back to take part in the second phase of the research project. Three evaluation locations were proposed to the participants: testing done in their home, testing done in a university or hospital room, and the possibility of simply completing a questionnaire by mail. Following the beginning of the COVID-19 pandemic in March 2020, the last participants also had the option of completing the evaluation by teleconference via Zoom. Ethics approval was obtained (McGill University Heath Center - Research Ethics Board (MUHC-REB))

Measures

Demographic and accident related characteristics

Demographic (sex, age, education) and accident-related variables (TBI severity, exclusion criteria, mechanism of the accident) were collected at T1 from the patients' medical files.

Executive functions (EF)

Updating

In the *WMS-III Mental Control test* (Wechsler, 1997), the participant was asked to manipulate over-learned information in short-term memory for which the raw score of the first seven items was calculated. In addition, the backward span of the *Digit span subtest of the WAIS-IV* (Wechsler et al., 2008) was administered where the participant was asked to recall and repeat a sequence of numbers presented orally in reverse order (Backward) for which the total raw score was computed.

Inhibition

The *Hayling Test* (Burgess & Shallice, 1997) was administered. In this task, the participant was first asked to complete a sentence with the most logical word (Condition 1) and then inhibit a word at the end of a sentence and produce one that makes no sense with the beginning of the sentence (Condition 2). A ratio was computed by using the time of completion for the first condition divided by the time of completion in the second condition and then multiplied by 100, which gave an inhibition score. Finally, the *D-KEFS Color-Word Interference Test* (Condition 3) (Delis et al., 2001) was done by the participants. In the first condition, the participant was asked to name, line by line, as quickly as possible and without making mistakes, the colours of rectangles on the board. In the second condition, the participant was asked to read a list of words representing colours written in black ink as quickly and accurately as possible. In this third condition, a list of colour words was presented, but these were printed in colours that differed from those they identify (e.g., the word "blue" printed in red) and the participant named the colour of the ink, preventing him/herself from reading the word. An inhibition ratio was calculated by dividing the average completion time for condition 1 and 2 by the completion time for condition 3 and then multiplying by 100.

Cognitive flexibility

The *Delis-Kaplan Executive Function System (D-KEFS) Category Switching Condition of the Verbal Fluency task* (Delis et al., 2001) was administered. In this task, the participant had to name as most words as possible while alternate between two categories. The number of correct switching between categories was collected. The *Parts A and B of the Trail Making Test* (Reitan, 1955) was also administered. In Part A, the participant is asked to connect a series of numbers that are randomly distributed on a page in increasing order as quickly as possible. The principle remains the same for part B, but the idea is to alternate between a number, in ascending order, and a letter, in alphabetical order (e.g., 1-A-2-B-3-C...). A ratio was calculated by dividing the completion time of Trail A by the completion time of Trail B, multiplied by 100. Finally, the participant has to complete the *D-KEFS Color-Word Interference Test (Condition 4)* where the last and fourth condition of the test was identical to the third, except that the framed words must be read and for which a ratio was calculated by dividing the average completion time of condition 1 and 2 by the completion time of condition 4 and multiplying by 100 (Delis et al., 2001).

Social participation

The social participation scale of the *Mayo-Portland Adaptability Inventory-4* (Malec, 2004) was administered to participants at follow-up (T2). The participant had to read and complete the questionnaire. The social participation scale of the *Mayo-Portland Adaptability Inventory-4* is used as a global outcome measure in a clinical or research context (Malec, 2004). It contains an item concerning the initiation of social participation which has been shown to be sensitive to EF deficits (Malec, 2004). It is one of the most widely used tools in the literature to measure the impact of TBI on daily life (Sander et al., 2010). The T-score was used in the analyses where a lower score corresponds to better social participation (i.e., fewer difficulties reported).

Statistical analysis

Normality was checked for continuous variables such as age, education as well as EF and social participation scores. Skewness between -2 and 2 and kurtosis between -7 and 7 were accepted (P. J. Curran et al., 1996). For variables that did not meet normality, the extreme data were reduced to the mean. If this did not restore normality, these variables were log-transformed.

To measure the impact of participant *attrition* from follow-up (T2) on the measures, EF scores on tests administered at T1 were compared between patients who were seen at T2 and those who were not assessed at T2. In addition, a chi-square was performed to measure the percentage of attendance at T2 versus T1 (mild, moderate, or severe TBI and controls) to determine if attrition at T2 of one group was greater than the other groups. In addition, to measure the effect of assessment *administration modality* at T2 (zoom, university/hospital, or home) as a function of group (control, mild, moderate, and severe TBI), mixed ANOVAs (administration modality X group) were performed on EF performance at T2 to determine whether EF performance was influenced differently by administration modality as a function of group. Finally, mixed ANOVAs (pandemic setting X group) on EF performance at T2 were performed to measure whether the *pandemic context* (pre-COVID-19 or post-COVID-19) had a different influence between groups (control, mild, moderate, and severe TBI) and to measure whether this effect was greater in one group than the other. If an interaction was found for either attrition, administration modality or the pandemic context, this variable was integrated as a co-variable in the ANOVAs.

Analyses (one-way ANOVA) were performed to determine whether the groups were comparable for age, education, and time to assessment post-injury. If differences were observed, these variables were controlled and included as co-variables in the analyses (ANCOVAs). In addition, correlations were performed between each EF (at T1 and T2) and age, education, and time to assessment post-injury. If significant, the associated variables were included as covariates in the analyses. The previously selected covariates were applied for analyses measuring both study objectives.

To address the first study objective, Mixed design repeated measures ANOVA analyses (within-subject factor/dependent variable: measurement time (2 levels); between-subject factor: group (4 levels) were performed on each EF performance. To address the second objective, exploratory linear regression analyses were performed between the different tests of the EFs at T1 and T2 and the social participation score, incorporating the appropriate co-variates. Only MPAI-4 social participation scores of the TBI groups were included in this analysis.

Results

Preliminary analyses

Demographic and accident-related variables are presented in Table 1. Normality in terms of skewness and kurtosis was not respected for two variables, namely the composite score of *condition 3 of the D-KEFS Color-Word Interference Test* in T1 and the *Hayling test* composite score in T2. For these two variables, an extreme data value was found and reduced to a Z-score of 3.29. Since normality was not restored after performing this transformation, a log transformation was applied to both variables. For the repeated measures analyses (objective 1), the score at both measurement times for these variables underwent logarithmic transformations. Finally, as illustrated in Table 2, it should be noted that a significant level of missing data was found for the neuropsychological outcomes at T1, due to the hospitalization context. At T1, the percentage of missing data ranged from 6.4% to 28.8%, while at T2, it ranged from 1.6% to 5.6%.

Regarding the *attrition* analyses, the t-tests performed on each EF performance at T1 between the group that was assessed at T2 and the group of participants who were not tested at T2 were all non-significant. Thus, participants who were not assessed at T2 did not perform significantly higher or lower at T1 on the EF tasks compared to those who were assessed at follow-up (T2). However, the chi-square result measuring the percentage of attendance at T2 versus T1 between groups was significant 2(2) = 6.47. *p* = .04. *Cramer's V* = .23. In fact, we noted a small sample size at T2, which varied according to the group (mild TBI, moderate-severe TBI and control). We noted that the moderate-severe TBI group tended to return for follow-up (T2) to a greater extent than the other two groups (see Table 2).

Concerning the analyses of the *evaluation modality* at T2, the results are significant only for an interaction effect between the group and the modality (F(4,48) = 2.62, p = .05), *partial* h^2 = .18 for the *Category Switching Condition of the Verbal Fluency task*.

Regarding the *pandemic context* analyses, the results are significant only for an interaction effect between group and COVID-19 context (F(2,49) = 3.45, p = .04), *partial* h^2 = .12 for the *D-KEFS Color-Word Interference Test (Condition 3)* score.

Differences in EF performances between T1 and T2 among groups

The results for this objective are shown in detail in Table 3 and only significant results will be described in this section.

For the *updating measures*, there was a significant simple effect of time for the backward condition of the Digit span subtest (p = .02; η^2 =.10). Thus, regardless of the group, all participants improved between the two measurement times. There was a significant group X time interaction for the Mental Control test (p = .00; η^2 =.18). Post-hoc analyses showed that the mild TBI (p = .038; η^2 =.08) and moderate-severe TBI (p = .020; η^2 =.10) groups improved significantly between T1 and T2, but the control group did not experience a significant change in performance across both measurement times. In addition, the moderate-severe TBI group performed significantly worse than the control group (p= .004) at T1 but no significant differences between the groups were found at T2.

For the *inhibition measures*, there was a significant simple effect of time for the *Hayling test* (p=.00; η^2 =.37). Thus, all patients improved regardless of group between T1 and T2.

For the *cognitive flexibility measures*, there was a significant group X time interaction (p = .029; η^2 =.15) for the *Category Switching condition of the verbal fluency task*. Post-hoc analyses showed that only the moderate-severe TBI group had significant improvement between T1 and T2 (p = .024; η^2 =.11). In addition, there were significant differences in performance between the moderate-severe TBI group and the control group (p = .000) at T1. For this measure at T2, no significant difference was found between any of the groups.

Social participation prediction analyses

The results are presented in Table 4. No significant relationships were observed between the various potential covariates (age, education, and group) and the MPAI-4 social participation score at T2. Thus, no covariates were included in the regressions. No significant relationship between the MPAI-4 social participation score at T2 (mean: 29.52; SD: 17.93) and EFs at T1 was found. Thus, no measure of EFs collected during hospitalization (T1) predicted social participation in patients with TBI at six months post injury. There was, however, a significant negative relationship (p= .04) between the *Category Switching condition of the verbal fluency task* and the social participation score of the MPAI-4 at T2. Thus, the higher the *Category Switching condition of the verbal fluency task score* at T2, better was social participation.

Discussion

Recovery of EFs between the acute (T1) and chronic (T2) phases

The first objective was to measure recovery of the three EFs described by Miyake between the acute and chronic phases. The hypothesis was partially confirmed since we observed a significant improvement of both TBI groups (mild and moderate-severe) compared to controls on the *Mental Control task* (updating) and an improvement of the moderate-severe TBI group on the *Category Switching condition of the verbal fluency test* (cognitive flexibility). These two measures thus appear to be more sensitive to recovery in our TBI groups. These results are partially consistent with the scientific literature that suggests improvement in EFs generally within the first year after TBI (Christensen et al., 2008; Rabinowitz et al., 2018; Sigurdardottir et al., 2020).

On the *Mental Control* measure, only the TBI groups (mild and moderate-severe) improved significantly over time, unlike the control group. This improvement is consistent with the findings in a similar study by Sanchez-C and colleagues (2008) (Sanchez-Carrion et al., 2008) that suggested amelioration (six months post-accident) in patients with TBI compared to stability in controls on several measures of working memory (updating) (digit span, n-back, letter-number sequencing). Also, in the present study, similar results were reported on the *Category Switching condition of the verbal fluency task* (Miyake's cognitive flexibility's measure) where the moderate-severe TBI group showed significant improvement over time. To explain these improvements, the hypothesis of brain plasticity is proposed. In this regard, a previous study with the mild TBI population reported a significant improvement in brain activation patterns of working memory in the six months following the accident, i.e. more extensive and efficient activations in the working memory circuit (Chen et al., 2012). This could explain why we observe improvements in this function in our TBI patient groups.

As demonstrated, the present study showed a significant recovery effect only on two types of EFs (updating and flexibility) and on two tasks (*Mental Control test and Category Switching condition of the verbal fluency task*). Given these results, it is relevant to question what is common to these two tasks, unlike the other tasks in our study, and how they are more sensitive to recovery from TBI between the acute phase and at 6-month post-accident follow-up. According to a recent review of the literature, neuroimaging studies suggest that the three components of EFs (updating, flexibility, and inhibition) overlap greatly in terms of brain activation (Uddin, 2021). The concept of cognitive flexibility would therefore be difficult to isolate from the others, particularly updating, because the regions that govern EFs and flexibility are extensive (Uddin, 2021). Thus, following TBI and based on the results of the current study, attempting to isolate the three cognitive functions in Miyake's model (Miyake et al., 2000) may not be the best conceptual approach for this clinical population. It may, in fact, be more relevant to attempt to isolate the mechanism that is common to these two tasks. In this respect, the "set-task shifting" deficit hypothesis could be proposed.

In regard to this hypothesis, some authors suggest a subdivision of cognitive flexibility into two categories, namely "set-shifting" (using different rules within a task in order to succeed in the task) and "task-shifting" (switching between two types of instruction), the latter being more complex as it would require better working memory skills (Dajani & Uddin, 2015). In fact, in the paradigm of "task-shifting", participants would have to constantly update the task representation (Derrfuss et al., 2005). It can be postulated, in line with the results of our study, that the *Category Switching condition* acts as a measure of "set-shifting", as the patient can use different rules within the task to generate their responses (they can decide to implement a phonological strategy or use contextual cues, etc.) and the *Mental Control test* could be considered a measure of "task-shifting", as the working memory load is higher and the manipulation of different content or instructions is required within the same task. Ultimately, both of these mechanisms would be representations of the patient's mental flexibility at different levels and would be more sensitive to TBI and to damage to the frontolateral cortex regions (Derrfuss et al., 2005), which are also vulnerable to TBI (Rabinowitz & Levin, 2014).

Even though no significant differences in cognitive functions assessed in the current study were noted between T1 and T2, the results still suggest that all patients, both with TBI and without TBI but with other traumatic injuries, improve between the two measurement times, especially for the *Backward digit span task* and the *Hayling task*. Furthermore, no differences between the three groups were observed at T2. This differs from the results of the study by Sanchez-C and colleagues (Sanchez-Carrion et al., 2008) who reported persistence of group differences (severe TBI vs. controls) at T2 in two updating measures (*Digit span and N-Back*). In their study, the control group were healthy participants, thus this design did not control for context and the possible presence of traumatic confounding factors such as pain (Moriarty et al., 2011) or accident-related psychological coping factors (C. A. Curran et al., 2000). In fact, if these factors are not considered, the performance gap between a healthy control group and a group of patients with trauma and with TBI could possibly be heightened while the actual impact of TBI lessened. This comparison leads to a methodological limitation since it complicates the observation of the effects of brain damage by not considering other factors related to the accident and its context (Satz, 1998). This weakness can be overcome by using an appropriate control group, such as a group with orthopedic injuries but without brain damage, as was done in the current investigation. Thus, the use of a more appropriate control group in the current investigation could explain the difference in the findings. In addition, it is also possible to consider that the *Backward digit span* and the *Hayling tasks* are not sufficiently sensitive to the effects of a TBI, thus explaining a non-specific improvement in performance in all groups, including the group of control patients. One final consideration is that at T2, all patients were then in a context more conducive to being tested as they were no longer hospitalized or being assessed at the bedside, nor under conditions where pain and other factors related to traumatic injury and hospitalisation might interfere with cognitive performance, thereby limiting the differences in performance between groups.

In addition to the relevance of comparing the performance of TBI groups to a control group within the same assessment context in trauma studies, the results of the present study also highlight the importance of distinguishing TBI groups by severity (mild and moderate-severe) since they behave differently in terms of recovery over time, but also in terms of performance at the two measurement times. In fact, it is recognized that the greater the severity of the TBI, the greater the cognitive impairment (Ord et al., 2010) and the longer it persists over time (Dikmen et al., 2009; Schretlen & Shapiro, 2003). It is therefore possible that the lack of distinction between different levels of TBI severity combined with the lack of an appropriate control group may explain the inconsistencies found in the literature on EF recovery following TBI.

Prediction of social participation based on EFs in the acute (T1) and chronic (T2) phases

The second objective was to explore the predictive effect of EFs (acute and then chronic) on social participation after TBI. A positive association between EF status and social participation was expected. In the present study, there was only a significant positive association between the *Category Switching condition of the verbal fluency test* (a measure of cognitive flexibility) at T2 and the social participation score in participants with TBI (mild and moderate-severe). The hypothesis is therefore only partially confirmed.

Our findings showed that the *Category Switching condition of the verbal fluency task* still appears to be the most sensitive to predict social participation in the chronic phase of TBI, six months post-accident. In fact, it is suggested in the literature that mental flexibility, as assessed by the *Category Switching* condition, is crucial for applying social and daily living skills (Frazier, 2018; García-Molina et al., 2012). In addition to the "set-shifting" mechanism (Dajani & Uddin, 2015), this task could also involve the concept of "generativity". "Generativity" is an addition to Miyake's model and is defined as the ease of accessing information stored in long-term memory and is measured by word generation (verbal fluency) tests (Adrover-Roig et al., 2012; Fisk & Sharp, 2004). Thus, it may be the "generativity" or communicative aspect of the fluency test that is more important than its flexibility aspect when predicting social participation following TBI. Indeed, a recent meta-analysis reports an association between "generativity" and patient outcome following TBI that is of greater magnitude than that for cognitive flexibility (Allanson et al., 2017). Furthermore, this would be consistent with the literature as several studies have reported associations between word generation (fluency) tasks and functional outcome and employability (Williams et al., 2013), social communication (Struchen et al., 2008), interpersonal behavior (García-Molina et al., 2012), and social disinhibition (Honan et al., 2017) following TBI.

Finally, it should be noted that verbal fluency has been shown to be sensitive to frontal lesions (Lehtonen et al., 2005). Moreover, joint deficits in "generativity" and cognitive flexibility correspond in the literature to dysfunction of the lateral prefrontal and dorsal basal ganglia (Lane-Brown & Tate, 2011; Ord et al., 2010). These types of impairments lead to the "cognitive" subtype of apathy following TBI, thus the cognitive manifestation of difficulties in implementing goal-directed behavior (Lane-Brown & Tate, 2011; Levy & Dubois, 2006). Therefore, it is possible that apathy related to a generativity deficit is the most important factor to consider in understanding difficulties in social participation following TBI. However, future studies are needed to confirm this conceptual hypothesis.

Study limitations

Although this study has strengths such as the use of an orthopedic control group, which controls for the effect of hospitalization and pain, the distinction of patients according to the severity of the TBI (mild vs moderate to severe), and the application of a longitudinal and prospective design, it does have some limitations. Importantly, there is a lack of statistical power due to high level of missing data, particularly at T1 (hospitalisation context), and the high attrition rate. Multi-site recruitment should be considered to increase the number of participants in the groups. Moreover, with more participants, it would have been possible to use additional EF measures and other measures of social participation and activity integration and to construct regression models including sociodemographic and medical variables as well as EF results to create predictive models and thus, be able to predict social participation more accurately at T2. Another limitation has to do with the fact that our patients recruited in the acute care setting were out of the post-traumatic amnesia phase. We can therefore consider that we recruited less severe types of TBI, which represents a recruitment bias. Still related to the context of hospitalization and regarding the musculoskeletal injuries that the patients may have suffered, these were not documented in this study, nor were the medications that these patients may have received prior to or during the assessments. In addition, no pain assessment tool was administered. Future studies evaluating EFs could add better controls for the effects of medication or pain. Finally, a systematic longer-range longitudinal study beyond six months would have better documented the recovery of EFs observed in the longer term.

Conclusion

This prospective and longitudinal study with a control group adapted to the acute care context demonstrated that the Mental Control test and the Category Switching condition of the verbal fluency test appear to be the best tools to measure the recovery of EFs following a TBI, of any severity, from the acute phase to six months post-accident. The Category Switching condition was also associated with social participation six months post-accident. The “set-task shifting” (Dajani & Uddin, 2015) and “generativity” (Adrover-Roig et al., 2012; Fisk & Sharp, 2004) hypotheses post TBI are proposed to explain the results. Future studies with large groups are suggested, however, to support the findings of the present study and to better understand EF recovery and prediction of social participation in patients following TBI.

Disclosure statement

No potential conflict of interest was reported by the authors.

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Table 1. *Demographic and accident-related variables*

	Mild TBI (n=44)	Moderate-severe TBI (n=31)	Orthopedic controls (n=50)	Total (n=125)
Demographics				
Age, M (SD) (years)	46.61 (19.86)	52.29 (19.39)	49.74 (16.70)	49.27 (18.52)
Gender (female (%)	16 (36.36%)	9 (29.03%)	15 (30%)	40 (32)
Education, M (SD) (years)	13.07 (2.99)	13.25 (2.99)	14.52 (2.83)	13.69 (2.98)
Accident related variables				
Post-accident time, M (SD) (days)*	9.02 (12.35)	27.26 (36.45)	5.45 (4.52)	12.28 (21.70)
Mechanism of injury				
Fall	21	21	25	67
MVA	19	5	15	39
Assault	1	1	1	3
Other	3	3	7	13

Note. *Time between injury and first evaluation; a= n at T1; MVA = Motor vehicle accident.

Table 2. *Sample size at both measurement times*

	Mild TBI	**Moderate-severe TBI**	**Controls**	**Total**
T1	44	31	50	125
T2				
Unreachable/refused/other	24	9	28	61
university/hospital	11	10	10	31
Home	5	6	3	14
Questionnaires by mail	2	1	2	5
Videoconference	2	5	7	14
Attrition rate	54.54%	29.03%	56%	48.8%

Table 3. *Variance analysis for recovery of EFs between T1 and T2*

	Mild TBI (M (SD))		Moderate-severe TBI (M (SD))		Orthopedic controls (M (SD))		Time effect			Group effect			Time X Group		
	T1	T2	T1	T2	T1	T2	*F*	*P*	η^2	*F*	*P*	η^2	*F*	*P*	η^2
Updating															
Digit span	7.76 (1.89)	.65 (1.93)	6.74 (2.60)	8.47 (2.99)	8.89 (2.62)	8.60 (2.51)	5.56	.02*	.10	1.46	.243	.05	2.85	.06	.10
Mental Control test[a]	23.17 (6.25)	25.28 (7.22)	20.76 (5.94)	23.18 (7.08)	28.00 (6.32)	26.37 (5.79)	1.59	.21	.03	2.97	.061	.18	5.49	.007**	.18
Inhibition															
Hayling test (LOG10) (ratio)	1.25 (.38)	1.45 (.25)	1.23 (.36)	1.52 (.22)	1.43 (.21)	1.63 (.33)	23.70	.00**	.37	2.23	.120	.10	.31	.73	.01
Color-Word (Cond. 3) (LOG10)[b] (ratio)	1.66 (.13)	1.68 (.10)	1.64 (.11)	1.68 (.09)	1.67 (.10)	1.68 (.08)	.69	.41	.02	.08	.927	.00	.43	.64	.02
Cognitive Flexibility															
Trail Making Test (ratio)	2.71 (1.05)	2.41 (.79)	3.07 (1.37)	2.57 (.67)	2.50 (.58)	2.52 (.71)	2.33	.13	.06	.60	.552	.03	1.18	.31	.06
Category switching task[c]	13.15 (2.58)	13.61 (3.97)	10.40 (3.62)	12.47 (3.46)	14.89 (2.73)	13.63(3. 11)	.50	.48	.02	4.39	.018*	.17	3.85	.02*	.15
Color-Word Cond. 4[d] (ratio)	44.24 (8.00)	45.27 (7.95)	44.77 (10.45)	43.66 (6.71)	44.38 (9.50)	46.80 (9.07)	1.84	.18	.05	.12	.890	.01	.69	.50	.04

Notes.
*p<0.05; **p<0.01; a=controlled for education; b= controlled for COVID-19; c= controlled for modality T2; d=controlled for age.

Table 4. *Social participation (T2) prediction based on EFs (T1)*

Variables	Bêta*	SE	t	R	p
Updating					
Digit span T1	.11	1.43	.55	.11	.59
Digit span T2	.07	1.34	.38	.07	.70
Mental Control test T1	-.20	.58	-1.00	1.00	.32
Mental Control test T2	-.13	.50	-.65	.13	.52
Inhibition					
Hayling test T1	.27	.18	1.14	.27	.27
Hayling test (LOG) T2	-.06	9.73	-.33	.07	.74
Color-Word Interference Test Cond. 3 (LOG) T1	.17	28,69	.72	.17	.48
Color-Word Interference Test Cond. 3 T2	-.09	.41	-.43	.09	.67
Cognitive Flexibility					
Trail Making test T1	.02	3.32	.10	.02	.92
Trail Making test T2	-.26	4.74	-1.35	.26	.19
Category switching task T1	-.37	.95	-1.76	.37	.09
Category switching task T2	-.40	.04	-2.18	.40	.04**
Color-Word Interference Test Cond. 4 T1	-.065	.40	-.26	.07	.80
Color-Word Interference Test Cond. 4 T2	-.12	.09	-.59	.12	.56

Note.

Analyses were carried out only with TBI group.

*Standardized coefficient (beta) corresponds to the Pearson correlation coefficient since the regression does not include any co-variables.

**p<.05.

Chapitre 4 : Discussion

4.1 Retour sur l'article 1

L'un des objectifs de cette thèse était de caractériser la présence d'associations entre divers prédicteurs ou variables individuelles et liées au TCC léger avec les différentes composantes des FE établies par Miyake et collègues (Miyake, Emerson, et al., 2000). De fait, il nous apparaissait essentiel de fournir aux cliniciens une meilleure compréhension des variables inter-individuelles pouvant affecter les performances aux épreuves mesurant les FE de leurs patients ayant subi un TCC léger. Dans cet article, les trois objectifs spécifiques étaient de caractériser les associations entre les FE et (1) les facteurs de vulnérabilité prémorbide, (2) les facteurs liés à l'accident et (3) les facteurs pouvant se présenter à la suite du TCC. Les hypothèse proposées étaient que (1) plus la réserve cognitive est élevée chez les patients atteints d'un TCC léger (plus éduqué, QI prémorbide estimé plus élevé) et plus les patients sont jeunes, plus ceux-ci auront de bonnes performances aux mesures des FE; (2) la présence d'une perte de conscience, d'une amnésie post-traumatique, de lésions frontales et d'un délai plus court entre l'accident et l'évaluation des FE seront associés à de moins bonnes performances lors d'épreuves mesurant les FE; (3) des symptômes post-commotionnels et anxio-dépressifs plus sévères seront associés à de moins bonnes performances des FE.

L'analyse des conclusions de la présente thèse et l'intégration des résultats ne permettent pas de conclure à des relations fortes et systématiques entre toutes les variables proposées de cette étude et les trois composantes des FE de Miyake et collègues (Miyake, Emerson, et al., 2000), soit la flexibilité cognitive, la mise à jour et l'inhibition. En somme, il est possible de conclure que nos hypothèses ont été partiellement confirmées. La Figure

2 (voir plus haut, au sein de l'article) illustre bien les relations significatives obtenues à l'aide de flèches entre les variables. Les conclusions de cette étude permettent de mettre en évidence que les facteurs de vulnérabilité prémorbide semblent représenter d'importants prédicteurs des FE. En outre, une vulnérabilité plus grande (moins éduqué et QI estimé prémorbide plus bas) chez la personne atteinte d'un TCC léger était associée à de moins bonnes performances des FE. De plus, les résultats de cette étude permettent de conclure que plus les participants présentent de symptômes anxio-dépressifs, moins bonnes sont leurs performances dans les tâches de mise à jour des FE. De manière intéressante, aucun des prédicteurs sélectionnés dans cette étude n'ont permis d'établir un lien significatif avec la flexibilité cognitive. Les prochaines sections tenteront de proposer des explications à la présence de ces associations.

4.1.2 La réserve cognitive : l'éducation et l'intelligence

Concernant les facteurs de vulnérabilité prémorbide, l'éducation semble être un facteur de prédiction particulièrement important dans cette thèse puisqu'il est lié à deux FE du modèle de Miyake et collègues (Miyake, Emerson, et al., 2000), soit la mise à jour et l'inhibition. Le rôle crucial de l'éducation dans le fonctionnement cognitif est connu dans la littérature (Mathias & Wheaton, 2015) et nos résultats permettent de statuer que ce facteur aurait sans doute un rôle de protection lorsque survient une atteinte cérébrale. De surcroît, le QI prémorbide s'avère aussi jouer un rôle important dans la mise à jour. Encore une fois, le rôle de cette variable dans le fonctionnement cognitif des patients est connu dans la littérature (Mathias & Wheaton, 2015) et plusieurs hypothèses ont été émises, notamment celle sur la notion d'intelligence cristallisée qui serait moins sensible et affectée par des lésions cérébrales (Leary et al., 2018). La notion de réserve cognitive qui a été développée dans l'introduction de la thèse demeure un concept relativement récent dans la littérature du TCC alors qu'il existe une prolifération d'études sur ce sujet en lien avec le vieillissement cognitif depuis déjà plusieurs années (Kim et al., 2017; Villeneuve & Belleville, 2010).

Étant donné l'importance de ces deux variables (éducation et QI prémorbide) comme facteurs d'influence des FE après le TCC, il convient de se demander si ces deux variables sont liées et laquelle de ces deux variables jouerait le rôle le plus important ou affecterait davantage les FE. De fait, certains auteurs suggèrent que les personnes « plus intelligentes » auraient tendance à acquérir davantage d'éducation et qu'une éducation plus longue rendrait « plus intelligent » (Deary & Johnson, 2010). On souligne toutefois que toutes les personnes n'ont pas accès aux mêmes opportunités d'éducation (Deary & Johnson, 2010), ce qui rend l'interaction entre ces deux variables biaisée par le facteur socio-économique. Notons que ces recherches ont été effectuées aux États-Unis, contexte qui est très différent de celui du Québec qui offre une éducation plus accessible à tous. Quoiqu'il en soit, il apparait important de distinguer les notions d'éducation et d'intelligence et de considérer que ces deux variables seraient possiblement médiées par des facteurs biogénétiques et environnementaux. De fait, selon une récente revue de littérature sur la notion de réserve cognitive après un TCC, l'éducation et les expériences de vie (acquis) influenceraient davantage le niveau de réserve cognitive que l'intelligence (inné) (Bigler & Stern, 2015). En outre, les auteurs de cette revue ajoutent que la réserve cognitive n'aurait pas un caractère fixe, mais serait évolutive tout au long de la vie et à travers les expériences acquises (Bigler & Stern, 2015). Malgré ces réflexions intéressantes, il semble impossible dans le cadre de la présente thèse de dissocier entièrement ces deux concepts et d'identifier celui qui affecte davantage les FE, ce qui nécessiterait la mise en place de devis de recherche beaucoup plus complexe (Deary & Johnson, 2010). Par exemple, une manière de dissocier l'intelligence (en terme de QI) de l'éducation serait d'étudier les parcours de jumeaux monozygotes avec un QI similaire, mais un niveau d'éducation différent, comme cela est souvent fait lorsque l'on souhaite départager l'inné de l'acquis.

4.1.3 Le vieillissement et l'inhibition à la suite du TCC

Une autre association intéressante a été mise en évidence dans cette étude sur les liens entre les variables socio-démographiques et les FE, soit celle entre l'inhibition et l'âge. À première vue, les résultats de l'étude 1 de cette thèse suggèrent que plus les patients sont âgés et plus ils sont inhibés et peu impulsifs, c'est-à-dire qu'ils prennent un temps plus long pour planifier le premier mouvement ou pour réagir (au test de Tour de Londres). Ces résultats sont contre-intuitifs et portent à réfléchir davantage et au-delà de ces conclusions statistiques. De fait, si nous adoptons l'hypothèse de la perte cérébrale plus importante avec l'âge, notamment dans les régions frontales (Calso et al., 2016), il aurait été plus logique d'observer davantage de déficits des processus d'inhibition avec l'âge avec des temps de réaction plus courts (plus impulsifs) pour planifier le premier mouvement. C'est pourtant le contraire que nous avons observé chez nos patients, ce résultat nous ayant obligé à mieux réfléchir au processus impliqué dans la condition « temps pour effectuer le premier mouvement » de cette tâche. Ainsi, un temps de réaction plus long pour effectuer le premier mouvement à la Tour de Londres n'est peut-être pas indicatif de bonnes capacités à s'inhiber (pas d'impulsivité), il est peut-être aussi indicatif d'une lenteur psychomotrice pour effectuer ce premier mouvement (c-à-d. une légère bradykinésie) ou une lenteur de traitement de l'information (c-à-d. une légère bradyphrénie). Basé sur ce constat, nous expliquons davantage ce résultat par la possibilité d'une lenteur plus importante chez les personnes plus âgées, ce qui est d'ailleurs cohérent avec la littérature (Bors & Forrin, 1995). La vitesse de traitement de l'information serait affectée par le vieillissement normal et aurait également été mise en relation avec les FE (Madigan et al., 2000). En somme, cette hypothèse contribue à nuancer l'interprétation que les cliniciens doivent apporter à des résultats obtenus dans une condition telle que « le temps pour effectuer le premier mouvement » dans des tâches comme la Tour de Londres ou celle de la D-KEFS. Un temps plus court peut être expliqué par un trouble de l'inhibition (impulsivité) ou par un ralentissement au niveau dans le traitement de l'information. D'autres études que celle de la présente thèse impliquant également des tâches de temps de réaction qui allient les processus d'inhibition, comme le Stroop (Delis et al., 2001) par exemple, seront toutefois nécessaires afin de confirmer cette hypothèse chez la population atteinte d'un TCC léger.

4.1.4 Les affects anxio-dépressifs à la suite d'un TCC léger

Outre les variables sociodémographiques comme facteurs d'influence des FE à la suite d'un TCC léger, la présente thèse suggère également que les réactions psychologiques post accident, tels que les affects anxio-dépressifs sont aussi contributifs aux FE et plus précisément à la composante de la mise à jour du modèle de Miyake et collègues (2000). Ainsi, l'augmentation des niveaux d'affects anxio-dépressifs concorde avec une augmentation des difficultés de manipulation de l'information en mémoire à court terme, soit de mémoire de travail. Ces résultats sont compatibles avec la littérature existante portant sur le TCC et l'anxiété (Gould et al., 2014) ainsi qu'avec celle sur l'impact de l'anxiété sur le fonctionnement cognitif (Humphreys & Revelle, 1984). Quant à la relation entre les FE et les affects dépressifs, les résultats de l'étude 1 de cette thèse sont également cohérents avec la littérature qui suggère que les patients ayant des symptômes dépressifs auraient davantage de troubles de mémoire de travail que les patients qui ont une humeur moins ou peu dépressive (Jorge et al., 2004; Rapoport et al., 2005). En outre, notons qu'il est connu que la dépression est aussi liée à une baisse de la vitesse de traitement de l'information (Himanen et al., 2009; Nuño et al., 2021; Tsourtos et al., 2002). Ce fonctionnement cognitif plus lent chez des patients plus déprimés auraient aussi sans doute un effet délétère supplémentaire pour la manipulation active de l'information en mémoire et plus spécifiquement sur la boucle phonologique, ce qui pourrait expliquer en partie le processus sous-jacent à la relation positive entre la présence d'affects dépressifs et la performance de mise à jour. Ces affects dépressifs ont une symptomatologie similaire à la présence de comportements apathiques après le TCC (Lane-Brown & Tate, 2011). De fait, l'apathie et la dépression sont liées et impliquent tous deux une altération dans les processus émotionnels, notamment, une certaine anhédonie, soit une réduction de la sensibilité au plaisir (Levy & Dubois, 2006).

4.2 Retour sur l'article 2

La seconde étude de la thèse comportait deux objectifs, soit (1) mesurer la récupération entre la phase aiguë et six mois post-TCC des trois sous-composantes des FE du modèle de Miyake (Miyake, Friedman, et al., 2000) et (2) explorer la relation entre les FE (phase aiguë et 6 mois post-TCC) et la participation sociale après un TCC (tous niveaux de sévérité confondus). Les hypothèses suivantes avaient alors été émises (1) les patients atteints d'un TCC (léger et modéré/sévère) s'amélioreraient sur les mesures des FE entre le T1 et T2, mais pas le groupe contrôle composé de patients sans TCC mais atteints de blessures orthopédiques. De plus, il était attendu que (1) les patients atteints d'un TCC léger aient des performances équivalentes des composantes des FE au groupe contrôle au T2, mais des performances supérieures que le groupe TCC modéré/sévère et enfin que (2) la performance des composantes des FE au T1 soit significativement associée à la participation sociale en T2.

Concernant l'objectif 1, les principaux résultats suggèrent que les tâches de Contrôle mental et de Fluence verbale alternée seraient les plus sensibles pour mesurer la récupération des FE dans le temps. Concernant l'objectif 2, on retrouve une association entre les performances au test de Fluence verbale alternée (6 mois post-TCC) et le score de Participation sociale de la MPAI-IV, chez les patients atteints d'un TCC (tous les niveaux de sévérité). Afin d'expliquer ces résultats, les concepts de plasticité cérébrale et de récupération spontanée seront abordés de même que les concepts tels que la générativité et l'apathie comportementale.

4.2.1. La plasticité cérébrale et la récupération spontanée

D'abord, pour ce qui est des résultats de l'objectif 1, une hypothèse portant sur la plasticité cérébrale ou le concept de récupération spontanée à la suite d'un TCC a été mise de l'avant dans la littérature afin d'expliquer l'amélioration des processus cognitifs requis lors des performances aux tâches de Contrôle mental et de Fluidité alternée. Nudo et collègues (2011) recensent trois principaux mécanismes permettant d'expliquer la récupération spontanée. (1) D'abord, la théorie de la « diaschisis », mise de l'avant il y a plusieurs décennies, est postulée (Feeney & Baron, 1986). Cette hypothèse suggère que des régions intactes, mais connectées (ou adjacentes) au site de la lésion, pourraient également subir un « choc » fonctionnel en raison d'une « perte d'excitation » secondaire à la lésion de la zone adjacente. Ce processus serait réversible, ce qui permettrait à cette zone intacte et adjacente de réactiver la zone atteinte par la lésion primaire et donc de lui permettre de récupérer de cette lésion. On mentionne qu'il s'agirait d'un processus adaptatif darwinien utilisé par le cerveau pour « s'adapter » aux déficits et ainsi compenser en cas de lésions. Toutefois, les auteurs soulignent qu'il y aurait de grandes différences individuelles dans ce processus de compensation et de récupération par « diaschisis ». (2) La seconde hypothèse suggère la présence d'une amélioration sur le plan fonctionnel (ou comportemental), sans que celle-ci ne soit nécessairement attribuable à une réorganisation cérébrale (Krakauer, 2006). Ainsi, cette hypothèse suggère que même si la zone lésée demeure cérébralement non-fonctionnelle, il y aurait une réorganisation ou une compensation sur le plan fonctionnel attribuable à des comportements qui prendraient le relai afin d'assurer le fonctionnement de l'individu. Enfin, le dernier mécanisme explicatif (3) suggère une récupération directe sur le plan pathophysiologique de la zone lésée, plus spécifiquement la « guérison » de la zone lésée permettant d'observer une récupération ou amélioration de la fonction médiée par cette aire cérébrale. Pour ce faire, une série de mécanismes physiologiques complexes, notamment étudiés au niveau du cortex moteur (Nudo, 2006), assureraient le rétablissement du cortex par différents types de processus, telle que la plasticité cérébrale. Un processus de neurogénèse ou de « jouvence cérébrale » se mettrait en place afin d'agir directement sur les neurotransmetteurs excitateurs et inhibiteurs altérés dans le but de rétablir les changements anatomiques au niveau des dendrites, des axones et des synapses. De manière intéressante et en liens avec les résultats de la thèse, certains auteurs suggèrent que le cortex préfrontal présenterait une plasticité différente et bonifiée par rapport aux autres régions cérébrales (Kolb et al., 2011), ce qui nous amène à émettre l'hypothèse que les tâches comme le Contrôle mental ou la Fluidité alternée seraient possiblement des processus cognitifs médiés par ces régions qui auraient bénéficiés en quelque sorte de cette plasticité cérébrale. Toutefois, ces mécanismes explicatifs de la récupération spontanée doivent être nuancés puisqu'ils sont toujours au stade de la conjecture et qu'ils n'ont pas nécessairement été appliqués directement à l'être humain cérébrolésé (Kolb et al., 2011). En fait, selon cette revue de la littérature citée, les résultats qu'on retrouve dans les études s'intéressant à la plasticité cérébrale dans le cortex préfrontal sont mitigés. Certaines études suggèrent que les modifications au niveau de la plasticité cérébrale sont différentes en fonction des individus. Cette plasticité semble alors plus complexe que la plasticité agissant dans les autres régions cérébrales. Quoique ce champ de recherche ne soit pas entièrement consensuel à ce sujet, à l'heure actuelle, une revue de littérature publiée dans la revue Nature apporte certains éléments de réflexion intéressants. De fait, ceci s'explique possiblement parce qu'une étude intégrée de l'entièreté du cortex préfrontal peut être superficielle et manquer de finesse. Selon la revue de littérature de Moghaddam et collègues (2008), le cortex préfrontal médial et orbitofrontal ont des « patterns » de plasticité opposés, car les « patterns » de connexions anatomiques seraient différents dans ces deux régions (simplement dit, ces deux régions seraient connectées à des régions cérébrales différentes) et elles auraient des « patterns » d'activation différents. De fait, ces deux régions ont des « patterns » d'activations qui alternent pendant l'apprentissage et donc pendant la plasticité. On parle donc d'une relation dynamique entre les deux régions.

Des auteurs ont tenté d'appliquer ces mécanismes de plasticité cérébrale ou de récupération spontanée spécifiquement chez les patients ayant subi un TCC dont plusieurs mécanismes cérébraux complexes ont été proposés dans une importante revue de littérature

(Kou & Iraji, 2014). Dans cette revue, il est proposé que chez les patients ayant subi un TCC, il y aurait deux processus impliqués dans la récupération, soit la réorganisation structurelle directe qui fait référence à la guérison de la zone lésée ainsi que la compensation fonctionnelle par le biais du recrutement d'autres régions cérébrales. Cette seconde hypothèse fait référence à la plasticité synaptique qui serait basée sur le recrutement de nouvelles régions cérébrales (Munoz-Cespedes et al., 2005). Néanmoins, les liens entre cette plasticité cérébrale et ce qui se passe réellement lors de la réadaptation de la fonction demeurent peu compris à ce jour et encore moins les techniques à mettre en place pour promouvoir cette plasticité cérébrale à la suite d'un TCC (Kou & Iraji, 2014). Des hypothèses intéressantes émises par les auteurs de la revue de littérature proposent qu'une plus grande stimulation intellectuelle serait bénéfique à une réorganisation cérébrale optimale, ce qui favoriserait le retour plus rapide au travail et un meilleur devenir (Kou & Iraji, 2014). Les résultats de cette thèse et plus spécifiquement de notre étude 1 sur l'importance de la réserve cognitive, exprimée par le niveau d'éducation et le fonctionnement intellectuel prémorbide, semblent alors rejoindre ces postulats. Enfin, quoique très intéressantes, ces hypothèses demeurent spéculatives puisque nous ne comprenons pas encore les mécanismes de plasticité cérébrale mis de l'avant dans ce phénomène de récupération spontanée (Kou & Iraji, 2014). De surcroît et tel que proposé par les auteurs de la revue de littérature, il est difficile d'étudier le phénomène de plasticité cérébrale auprès de la population atteinte d'un TCC en raison de la grande hétérogénéité inhérente à cette condition clinique (Kou & Iraji, 2014). Enfin, tel qu'étudié dans cette thèse, ce ne sont pas tous les processus cognitifs qui peuvent bénéficier de cette récupération, voire cette plasticité cérébrale dans le temps, à la suite du TCC. Cependant, il semble malgré tout qu'un processus spécifique lié à la tâche de Fluence verbale alternée ait été démontré comme étant sensible à cette plasticité. La prochaine section s'intéressera aux processus sous-jacents à cette tâche, notamment le concept de générativité.

4.2.2. La fluence verbale alternée

Tout comme les résultats de la présente thèse, la littérature portant sur les trajectoires de récupération des fonctions cognitives à la suite d'un TCC semble suggérer que le concept ou la mesure de fluence verbale tient une importance particulière. De fait, une toute récente étude (Schultz et al., 2021) ayant mesuré au cours d'une année post TCC l'évolution de sept domaines cognitifs (orientation, attention, vitesse de traitement de l'information, FE, mémoire, langage et fonctions visuospatiales) indique que la mesure de fluence verbale (mesure des FE) serait celle qui aurait la trajectoire de récupération et l'amélioration dans le temps la plus importante. Une autre étude employant un design similaire à la présente thèse a démontré que la mesure de fluence verbale serait susceptible de capturer avec plus de précisions et de sensibilité les changements dans le temps chez un groupe de patients atteints d'un TCC (léger complexe et modéré-sévère), alors qu'aucun changement sur cette mesure n'aurait été observé chez un groupe contrôle (Steward et al., 2018). Pour expliquer la spécificité de ce résultat, l'auteur suggère que la mesure de fluence verbale alternée solliciterait simultanément le langage expressif, la vitesse de traitement de l'information et les FE, ce qui la rendrait particulièrement sensible aux effets neuropathologiques d'une atteinte cérébrale. De fait, cette mesure (fluence verbale) semble solliciter des aires cérébrales plutôt diffuses et est donc très sensibles aux effets d'une atteinte cérébrale, même si cette dernière est circonscrite. Enfin, notons que la tâche de fluence verbale apparaît comme une mesure sensible pour capter des déficits des processus sous-jacents à cette tâche et suivant le TCC, mais qu'elle peut aussi être très affectée par un ralentissement plus généralisé du traitement de l'information (Henry & Crawford, 2004). Les liens entre la fluence verbale et la vitesse sont pertinents dans un contexte tel que le TCC puisque ces deux fonctions sont souvent affectées à la suite de ce trouble acquis (Dikmen et al., 2009; Steward et al., 2018). De surcroît, des concepts comme la générativité et l'apathie comportementale sont aussi fortement liés et partagent des processus communs avec la fluence verbale.

Comme exemple dans le quotidien, on peut penser à la capacité du patient à initier les activités sociales, donc carrément prendre l'initiative de contacter ses proches pour engendrer un contact social. Bref, il s'agit presque d'une mesure de vivacité ou d'activation. La tâche de fluence verbale permet de donner une idée de ce processus. On la considère comme une mesure relativement fiable de ce processus. Toutefois, étant donné que cette notion est relativement nouvelle, on utilise cette mesure en étant conscient qu'elle n'a pas été initialement été élaborée dans l'optique de mesurer la générativité. Pour le moment, c'est la meilleure tâche que nous avons et qui permet de mesurer la capacité du patient d'initier la recherche en mémoire à long terme. On la considère comme une fonction exécutive parce qu'elle est intrinsèquement liée à la notion de comportement orienté vers un but. En lien avec les pages 124-125, on pourrait penser, par exemple, qu'un patient qui a un niveau de générativité plus élevé aura un meilleur devenir d'employabilité parce qu'il sera plus réactif et plus rapide au travail, il sera en mesure de commencer les tâches par sa propre initiative plus rapidement. Si nous voulons un exemple très précis, nous pouvons penser qu'un employé de bureau sera plus autonome et aura moins besoin de rappels de ses employeurs pour proposer des rencontres d'équipe afin de trouver une solution à un problème potentiel. Enfin, la fluence verbale est fréquemment utilisée comme mesure de générativité, mais on retrouve aussi des mesures de générativité idéationnelle (générer le plus d'utilisations possibles pour un objet) ou la fluence graphique (dessiner le plus de « patterns » possibles dans une série de grilles) (Dichter et al., 2009). Personnellement, nous pensons que les mesures de fluence verbale et de générativité idéationnelle sont les plus intéressantes parce qu'elles font appel à la mémoire à long terme.

4.2.3. Le concept de générativité et l'apathie comportementale

Certains auteurs suggèrent que la fluence verbale serait une mesure de générativité qui est définie comme le processus facilitant l'accès à l'information stockée en mémoire à long terme (Adrover-Roig et al., 2012; Fisk & Sharp, 2004). Le concept de générativité soulève de plus en plus d'intérêt et a été associé à plusieurs mesures de devenir après le TCC, notamment l'employabilité, la communication sociale, le comportement interpersonnel et la désinhibition sociale (Honan et al., 2017; Struchen et al., 2008; Villalobos et al., 2021; Williams et al., 2013). Nous pouvons en comprendre que plus le patient est capable de réussir des tâches de générativité, donc d'initier les processus et d'aller chercher en mémoire à long terme les informations nécessaires et requises, plus il est en mesure dans la vie de tous les jours et surtout dans des contextes sociaux, d'initier et mener à bien les tâches du quotidien.

En plus du processus d'initiation de la recherche en mémoire (c-à-d. générer ou récupérer), le concept de générativité semble aussi avoir été lié aux processus des FE, sujet d'intérêt de cette thèse. Une étude suggère notamment que la désinhibition sociale serait corrélée avec la générativité (Honan et al., 2017) dans la mesure où cette dernière serait responsable du processus de sollicitation des capacités attentionnelles pour maintenir le comportement adéquat tout en inhibant des distracteurs non pertinents. La générativité permettrait à la personne d'aller rechercher ou solliciter sa capacité à rester « focusé » ou concentré sur un comportement approprié et ne pas se laisser distraire par les distractions de ses propres pensées ou de l'environnement. Également, la générativité semble jouer un rôle important dans la conscience de soi, et ce même à la suite d'un TCC (Villalobos et al., 2021). Plus précisément, la générativité serait responsable de la capacité de la personne à se canaliser pour rechercher en soi et rapatrier à la conscience les caractéristiques pertinentes de sa personne. La conscience de soi est un processus complexe et difficile à définir et encore plus à mesurer. Il semble alors que la tâche de fluence verbale serait une mesure acceptée mais indirecte de la conscience globale, et ce, puisqu'elle est complexe et reflète plusieurs sous-capacités exécutives (Villalobos et al., 2021). Ainsi, cette mesure pourrait agir comme une sorte d'indicateur global de l'état cognitif du patient et notamment du niveau de conscience de soi. En somme, la générativité est considérée comme une FE de haut niveau qui est soutenue par plusieurs sous-composantes des FE, telles l'initiation de réponses ou le monitoring des réponses inappropriées (Fischer-Baum et al., 2016; Villalobos et al., 2021). C'est possiblement pour ces raisons que la fluence verbale s'avère être une mesure si sensible.

De manière plus concrète et plus observable au plan clinique à la suite d'un TCC, il est possible de faire un parallèle entre la générativité et l'apathie comportementale (Lane-Brown & Tate, 2011; Levy & Dubois, 2006). De fait, l'apathie après le TCC a été mise en relation avec de nombreuses problématiques pour le patient et pour ses proches (Arnould et al., 2013). Les patients apathiques participent peu à leur réadaptation, ils prennent peu d'initiatives ou de décisions et sont peu impliqués dans leur vie sociale ou communautaire. Ce manque d'implication peut devenir un fardeau pour la famille et les proches. Ainsi, il est important de se questionner et d'identifier les processus psychologiques sous-jacents à l'apathie. En outre, plusieurs mécanismes psychologiques (cognitif, affectif, motivationnel) seraient impliqués dans l'apathie (Arnould et al., 2013). Il est possible de se questionner quant aux associations théoriques entre les notions d'apathie et de générativité. La générativité a parfois été considérée comme une manifestation neuropsychologique de la créativité (Peters, 2005). Une personne présentant un trouble de générativité serait par le fait même apathique et cette apathie inhiberait la créativité, soit la capacité à générer des idées nouvelles. Or, la créativité serait vu comme un processus adaptatif sur le plan évolutionniste (Simonton, 1999), mais aussi psychologique (Peterson & Seligman, 2004 cité dans Peters, 2005). Plus précisément, certains modèles suggèrent des associations significatives entre la pensée créative et la résilience, les gens créatifs seraient résilients (Metzl & Morrell, 2008). À la suite d'un TCC, les personnes ayant démontrées de bonnes capacités en fluence verbale, dont le mécanisme sous-jacent serait une générativité efficace, seraient aussi plus créatifs et donc plus résilients. Par conséquent, il est possible de se demander si la générativité ne représenterait pas un élément de réserve cognitive, afin de lutter ou de compenser les effets néfastes du TCC sur les habiletés ou le fonctionnement social. Bien entendu, cette théorie, quoique très intéressante, est tout à fait spéculative à l'heure actuelle et devra être explorée dans des études futures.

4.2.4 La fluence verbale alternée et les habiletés sociales

Concernant l'objectif 2 de la thèse, nos résultats suggèrent une association entre la tâche de fluence verbale alternée et la participation sociale évaluée à l'aide de la MPAI-IV. Quelques études antérieures publiées dans la littérature ont mis en évidence une relation similaire entre la flexibilité mentale, telle que mesurée par une tâche comme la fluence verbale alternée, et les habiletés sociales. De fait, les habiletés sociales requièrent une bonne flexibilité mentale puisque les contextes sociaux sont souvent complexes et nécessitent de s'adapter et de modifier fréquemment son comportement (Frazier, 2018). À la suite d'un TCC, des recommandations telles que la reprise des activités socio-professionnelles ou vocationnelles sont suggérées, ce qui est bénéfique au mécanisme de récupération d'une fonction comme la flexibilité mentale puisqu'elle est sollicitée dans les activités sociales. Le fait de ne pas retourner au travail très rapidement ou réduire les activités de loisirs et être moins actifs et socialement impliqué à la suite d'un TCC limitent ainsi l'impact de effets bénéfiques de réadaptation et de stimulation de la flexibilité cognitive (Frazier, 2018). En ce sens, la reprise du travail après l'accident a été postulée comme un facteur bonifiant la plasticité cérébrale (Kou & Iraji, 2014). En somme, les résultats de l'étude 2 de la thèse appuie indirectement le fait que la flexibilité cognitive serait nécessaire pour ajuster son comportement dans les activités de la vie quotidienne en fonction des demandes constamment changeantes du monde réel (García-Molina et al., 2012). Ainsi, les relations sociales et la participation sociale telle que mesurée dans cette thèse par la MPAI-IV, requièrent des capacités d'adaptation et d'ajustement rapides qui sont médiées par la flexibilité mentale et qui pourrait être concrètement mesurée avec une tâche comme la fluence alternée. La tâche de fluence verbale s'avère donc être une mesure de prédilection afin de comprendre les déficits et les difficultés de participation sociale vécues par les patients suite au TCC.

Le concept de participation sociale est intrinsèquement lié aux relations interpersonnelles puisque la participation sociale correspond au niveau d'intégration sociale et donc de participation à des activités relationnelles. La participation sociale peut être considérée comme une mesure d'intégration à la communauté. Ainsi, on peut dire qu'un patient qui a un niveau de participation sociale plus faible est plus isolé. Par exemple, ce patient pourrait, après son accident, ne plus avoir l'initiative de prendre part à ses anciennes activités de loisir, telle qu'un club de lecture ou de bridge.

Quant aux troubles du comportement après un TCC, une revue de littérature (Stéfan et al., 2016) en a recensé les plus prévalents. Ainsi, on note des troubles primaires (agitation, agressivité, irritabilité et abus d'alcool/drogues), ce que les auteurs considèrent comme des troubles primaires par défaut (soit l'apathie), des désordres affectifs (dépression, anxiété, stress post-traumatique, trouble obsessionnel compulsif et même psychose) et le suicide. Il est effectivement logique de croire que la présence de tels comportements puisse isoler le patient et impacter sa participation sociale.

Pour conclure cette section, les constats cliniques issus de cette thèse, tels que ceux portant sur la générativité ou la participation sociale, sont intéressants mais se doivent d'être transférés à la pratique clinique pour permettre un réel échange de connaissances ainsi qu'un impact au point de vue de la pratique clinique actuelle et future.

4.3 Considérations cliniques et directions futures

Sur le plan clinique, les trouvailles de l'étude 1 de cette thèse mettent de l'avant l'importance d'évaluer et de considérer la réserve cognitive dans l'interprétation des résultats liés aux FE, chez des patients présentant un TCC léger. De fait, il semblerait que ce soit un des facteurs les plus importants permettant de comprendre la présence ou non de déficits des FE. À titre d'exemple, il est possible que certains patients réussissent à bien performer ou obtenir des résultats dans la norme ou la moyenne dans les tests des FE, mais que leur réussite s'explique par un QI prémorbide élevé et non pas par une réelle préservation de ces fonctions à la suite du traumatisme. Ceci implique qu'il est possible que ces patients passent « sous le radar » et donc que les cliniciens ne jugent pas utile de leur fournir les interventions nécessaires. Plus spécifiquement, il se peut que leurs performances qui étaient au-dessus de la norme avant le TCC aient été malgré tout affectées à la suite du TCC, ces performances étant alors moyennes et compensées par un QI prémorbide élevé. Ces patients voient donc leurs performances affectées lors de l'accomplissement de leurs tâches plus complexes du quotidien (ex. : retour au travail). En somme, il ne faut pas négliger l'effet « confondant » du QI prémorbide et du niveau de scolarité dans l'évaluation clinique des patients atteints d'un TCC léger. Ainsi, face aux résultats de cette thèse, nous recommandons aux cliniciens œuvrant auprès d'une population atteinte d'un TCC léger de se munir systématiquement d'un test de mesure estimé du QI prémorbide, tel que le test de vocabulaire de la WAIS-IV, afin de nuancer leurs résultats.

Par ailleurs, bien que des facteurs comme la réserve cognitive évaluée par des proxys tels que l'éducation et le QI estimé soient importants à considérer comme variable de prédiction du fonctionnement des FE à la suite d'un TCC léger, l'étude 1 de cette thèse n'a permis d'explorer qu'un nombre restreint de variables de prédiction et ce, en raison de la puissance statistique limitée par notre échantillon. Par exemple et plus spécifiquement en lien avec le modèle de Hou (Hou et al., 2012), il serait pertinent de comprendre l'association entre les cognitions et les comportements d'un part (ex. : la perception du TCC par le patient, les croyances, le sentiment de contrôle, la pensée du tout ou rien, la tendance au perfectionnisme, l'optimisme vs le pessimisme, etc) et l'état des FE après le TCC d'autre part. Pour aller, plus loin, il serait aussi intéressant de bien mesurer les associations entre les autres facteurs prédisposants (ex. : la personnalité) ou encore les modulateurs (ex. : dynamique familiale, litige, milieu de travail, etc.) et leurs impacts sur les FE à la suite d'un TCC. En somme, les études futures permettront aux cliniciens de mieux comprendre les enjeux et les interactions qui sont à la source des différences inter-individuelles si manifestes auprès de cette clientèle clinique.

Également sur le plan clinique, les trouvailles de l'étude 2 de cette thèse mettent de l'avant l'importance d'utiliser une mesure de fluence verbale alternée permettant de mesurer la flexibilité cognitive et, de manière indirecte, la générativité. De fait, il semblerait qu'il s'agisse d'un facteur possiblement contributif et explicatif du niveau de participation sociale du patient après le TCC. Ceci implique qu'il est possible d'estimer ou de monitorer les chances que le patient puisse jouir d'une bonne participation sociale avec une mesure neuropsychologique de fluence verbale alternée et, si affecté le cas échéant, agir d'une manière précoce et offrir des interventions cognitives ciblées pour bonifier la plasticité cérébrale liée à la flexibilité mentale. Quand on parle d'interventions cognitives « ciblées », on veut suggérer que la tâche de générativité permet de cibler les patients qui vont bénéficier d'interventions parce qu'ils sont plus à risque de développer des problèmes de participation sociale (donc de vivre de l'isolement) 6 mois après l'accident. De plus, «

bonifier la plasticité cérébrale » signifie stimuler le patient pour le pousser à contrecarrer une potentielle apathie qui pourrait entraver plus tard son niveau de participation sociale.

Sur le plan empirique et théorique, les résultats de l'étude 2 de cette thèse mettent l'accent sur l'importance d'ajouter le facteur de générativité au sein du modèle de Miyake (Miyake, Friedman, et al., 2000), tel que précédemment proposé (Adrover-Roig et al., 2012; Fisk & Sharp, 2004). Le présent travail de recherche permet de surenchérir cette proposition en mettant de l'avant l'importance de prendre en compte ce mécanisme cognitif lors des évaluations cliniques d'une population atteinte d'un TCC. De fait, la mesure de générativité semble particulièrement utile afin de prédire le devenir et notamment la participation sociale. Ainsi, à des fins cliniques et dans le cadre d'évaluations neuropsychologiques en contexte de traumatologie ou de soins aigus, l'utilisation d'une mesure de générativité, telle que la fluence verbale, semble recommandable pour les neuropsychologues. Cette mesure, en plus d'être sensible aux changements liés à la plasticité ou la récupération spontanée à la suite d'un TCC, semble également utile pour la prédiction des personnes susceptibles de présenter des défis au plan de la participation sociale et donc de l'intégration à la vie sociale et communautaire.

La littérature actuelle présentée dans cette thèse permet de statuer que peu d'études s'intéressent au facteur de générativité en général et encore moins au sein du modèle de Miyake. De surcroît, peu d'études se basent sur une définition opérationnelle des FE, telle que celle proposée par le modèle de Miyake, et l'appliquent à la population atteinte d'un TCC. Pour les directions futures, nous recommandons aux chercheurs de baser leurs études des FE sur un modèle théorique solide et valide afin de permettre l'appropriation d'un langage commun. Ce langage commun favorisera l'utilisation d'outils similaires pour évaluer un seul et même concept et donc permettra alors de comparer les résultats, d'effectuer des méta-analyses et ainsi d'en dégager des recommandations pour la pratique clinique spécifiquement pour la population atteinte d'un TCC. Enfin, les sous-composantes bien définies des FE pourront alors être mise en relation avec une multitudes de mesures du devenir après le TCC (ex. : devenir fonctionnel, intégration sociale, devenir psychologique) et de modèles de prédiction de plus en plus précis pourront émerger de cette recherche.

4.4 Forces et limitations

La thèse présente plusieurs forces. D'abord, l'utilisation d'une définition opérationnelle des FE est une force importante. Dans la littérature, plusieurs études incluent des concepts disparates sous le chapeau des FE et la présente thèse permet d'étudier de manière distincte chaque FE sans les mélanger. Ceci permet une étude des FE plus rigoureuse et de comprendre plus précisément les mécanismes exécutifs qui tiennent une place importante auprès des patients atteints d'un TCC. De surcroît, l'étude de la réserve cognitive auprès d'un population atteinte d'un TCC par le biais des FE est novatrice. De fait, l'exploration de la réserve cognitive et ses liens avec les FE à la suite d'un TCC a été que très peu étudiée dans la littérature et davantage appliquée à la population vieillissante et à risque de développer un trouble neurocognitif majeur (Villeneuve & Belleville, 2010). Or ici, l'application du concept de réserve cognitive aux patients atteints d'un TCC léger s'avère particulièrement utile étant donnée la grande hétérogénéité inhérente à cette population (Karr et al., 2014) et apporte des éclairages considérables dans l'orientation des patients vers les étapes de réadaptation subséquentes. En outre, l'utilisation d'un devis prospectif/longitudinal est novateur. De plus, l'inclusion d'un groupe contrôle atteint de blessures orthopédiques permet de contrôler de manière rigoureuse l'effet de l'hospitalisation et de la médication en temps 1 de l'étude 2, ce qui constitue une force majeure. En effet, l'importance de l'utilisation d'un groupe contrôle approprié permettant d'isoler au maximum les variables confondantes est mise de l'avant dans la littérature (L. Carroll et al., 2004). De fait, le TCC est souvent associé à des blessures extra-crâniennes qui peuvent causer des dysfonctionnements et atteindre la qualité de vie, et ce, indépendamment de l'atteinte cérébrale (Stocchetti & Zanier, 2016), d'où l'importance de tenter de contrôler leur effet par le biais d'un groupe contrôle approprié.

La présente thèse présente toutefois certaines limitations. Dans la première étude, les mesures manquent généralement de sensibilité et de spécificité. Par exemple, il aurait été pertinent d'utiliser une mesure plus « pure » de l'inhibition, comme dans celle retrouvée dans les tests de Stroop (Delis et al., 2001) ou encore du Hayling test (Burgess & Shallice, 1997). Il aurait aussi été pertinent d'utiliser davantage de mesures des FE pour chacune des composantes et créer des scores composites ou des facteurs. Ceci aurait permis d'acquérir une plus grande puissance statistique. Notons, toutefois, que l'utilisation d'un devis rétrospectif limite par définition le choix des mesures. Par contre, au sein de la deuxième étude, des mesures plus sensibles et plus spécifiques ont été utilisées pour chaque FE, notamment, pour la mesure d'inhibition. Enfin, la puissance statistique demeure limitée dans les deux études, le nombre de participants est assez restreint et le nombre de données manquantes est important, notamment, pour le temps 1 de la deuxième étude. Les prochaines études devront considérer la possibilité d'effectuer des études multicentriques afin de bonifier le recrutement et augmenter le nombre de patients par groupe et contrer l'attrition. Notons également que l'échantillon de la première étude contient un vaste étendu d'âge. Ceci a donc pu avoir comme effet de générer davantage de variabilité dans l'échantillon. De plus, les études futures devraient prendre en considération dans les analyses l'effet des médications, notamment, sur les affects anxio-dépressifs. De fait, une étude de Yue et collègues (2017) suggère que certaines médications (ex. : Fluoxetine) peuvent avoir un effet bénéfique sur les fonctions exécutives, d'autres n'ont pas d'effets notables (ex. : sertraline). Ils rapportent aussi des études qui ont trouvé des améliorations des fonctions exécutives avec la Setraline. Quoiqu'il en soit, il s'agit effectivement d'une variable d'importance qui n'a pas été prise en compte dans le cadre de cette thèse. Toutefois, pour pouvoir vraiment explorer cette aspect, il faudrait avoir accès à des données précises sur le type de molécule que le patient prend, la dose et faire un suivi serré de l'adhérence au traitement pendant une longue période de temps puisque souvent les médicaments antidépresseurs sont à longue action.

Par ailleurs, quant à l'amnésie post-traumatique, on relève dans la littérature un manque de définition consistante (Marshman et al., 2013). La PTA réfère généralement à la phase de récupération immédiatement après la période d'inconscience, mais sa pathophysiologie est mal connue (Ahmed et al., 2000). Elle repose sur un ensemble d'observations comportementales, ce qui peut poser certains problèmes. Notamment, il peut y avoir des « îles de mémoire » pendant la PTA, ce qui peut pousser les cliniciens à sous-estimer la PTA (Symonds et Russel, 1943 dans Ahmed et al., 2000). De plus, on manque de mesures standardisées pour mesurer la PTA (Levin et al., 1979 dans Ahmed et al., 2000). Il y aurait effectivement le GOAT comme mesure standardisé, mais celle-ci est peu utilisée en clinique, car elle doit être effectuée tous les jours (Vanier, 1991). Si cet outil était utilisé dans la réalité clinique, nous aurions une meilleure idée de la durée de l'APT et donc de la sévérité du TCC.

Également, le CT-scan possède plusieurs limitations. On l'utilise généralement dans la phase aiguë du TCC pour identifier la présence de larges lésions extra ou intra cérébrales (ex. : hématome sous-dural ou intracrânien) et pour lesquelles il faut agir de manière urgente (Jain, 2019). On peut comprendre qu'il ne s'agit pas d'un outil diagnostic très précis, mais qu'il est davantage utilisé pour les urgences. Le CT-scan est sujet à une certaine variabilité en fonction de l'observateur (Jain, 2019) et a une sensibilité moindre que l'IRM (Spikman, 2010).

4.5 Conclusion

Dans le cadre de la présente thèse, plusieurs facteurs sociodémographiques et liés à l'accident influençant l'état des FE ont été étudiés (étude 1 rétrospective), mais également leur évolution dans le temps et comment ils sont associés au devenir du patient TCC (étude 2 prospective/longitudinale). Deux grands constats semblent se dégager de cette thèse. Le premier suggère que l'application du concept de réserve cognitive à la population TCC léger demeure une notion relativement récente mais cruciale à prendre en compte dans l'interprétation nuancée des résultats neuropsychologiques des FE mais aussi pour l'atteinte d'une meilleure compréhension des différences inter-individuelles inhérente à cette population clinique. Le second constat nous pousse à considérer que dans un contexte d'application théorique à une population de patients TCC, le modèle de Miyake (Miyake, Friedman, et al., 2000) serait incomplet sans l'ajout du facteur de générativité. Ce dernier semble être le mécanisme cognitif sous-jacent et intrinsèque aux difficultés cognitives caractéristiques à la suite d'un TCC et constitue une représentation neuropsychologique de la participation sociale du patient. Par le fait même, une évaluation neuropsychologique dans le cadre d'un TCC et qui vise à orienter la réadaptation du patient, devrait comporter une mesure de flexibilité cognitive ou de générativité, comme la tâche de Fluidité alternée. En conclusion, nous croyons que les résultats de la présente thèse ont un impact clinique notable et que ces derniers sont directement transférables aux neuropsychologues qui doivent notamment poser des pronostics neuropsychologiques et identifier de manière précoce les patients les plus à risque de développer des difficultés sur le plan de l'intégration sociale après le TCC.

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Annexe

Early Reading Comprehension and Speed of Reading Impairments in Individuals with Uncomplicated and Complicated Mild Traumatic Brain Injury

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ABSTRACT

Purpose: Several studies have investigated cognitive-communication disorders affecting oral expression skills following TBI but very few have dealt with reading comprehension abilities. The current study aims to measure reading comprehension and speed of reading in adults with uncomplicated and complicated mild traumatic brain injury (TBI) and to determine which demographic and TBI-related variables are predictive of their performance. **Method:** The performances of three groups of participants were compared on the Chapman-Cook Speed of Reading Test (CCSRT). The CCSRT was administered in an acute care setting to 85 hospitalized participants with mild TBI showing traumatic cerebral lesions (complicated mild TBI), to 15 hospitalized participants with uncomplicated mild TBI (no cerebral lesions) and to 68 adults without TBI. Linear regression analyses were performed to determine which variables among sex, age, education, TBI severity (measured by the Glasgow Coma Scale score), speed of processing skills, and site of cerebral lesions significantly predicted CCSRT performances. **Results**: The control group showed a lower percentage of errors than both TBI groups. On the total score of the CCSRT, the uncomplicated and complicated TBI groups performed worse than the control group. Moreover, as age and speed of processing skills increased, and education decreased, the odds of having a lower score on the CCSRT increased. **Conclusion:** These findings suggest that reading abilities are compromised after mild TBI. Furthermore, the CCSRT may be a useful bedside tool for clinicians who work with individuals with mild TBI.

Keywords: Traumatic brain injury, concussion, reading, comprehension, speed of information processing

Highlights

- Complicated (visible cerebral lesion on CT Scan) and uncomplicated mild traumatic brain injury (no cerebral lesion on CT Scan) have a significant impact on reading comprehension and speed of reading.
- No significant difference was found between the complicated mild and the uncomplicated mild traumatic brain injury groups which suggests that sustaining a cerebral lesion visible on imaging did not have an impact on acute reading comprehension and reading abilities.
- A younger age and higher level of schooling was associated with better performances on reading comprehension and speed of reading.
- In the acute care setting, support should be provided to patients with mild traumatic brain injury when they are required to read, complete and sign documents.

Introduction

Reading is a complex cognitive activity that is vulnerable to neurological injury. According to one theory of reading, Dual-Route Cascaded hypothesis of reading model, reading requires lexical and phonological processes, as well as general cognitive functions (Coltheart, Curtis, Atkins, & Haller, 1993; Coltheart, Rastle, Perry, Langdon, & Ziegler, 2001). Specifically, lexical processing (direct pathway) allows for sequential processing of word elements: when a subject reads, visual processing of the word activates a spelling representation within the lexicon and allows the subject to access the phonological form of the word and then its meaning. The phonological procedure (indirect pathway) consists of sequential processing of the word and is based on grapho-phonemic matching. The reader decomposes the word into its constituent graphemes and attributes each grapheme to the corresponding phoneme to finally construct a unified word.

In addition to lexical and phonological processes, reading as a complex ability requires the integration of other diverse cognitive and perceptual processes (Christopher et al. 2012; Johansson, Berglund, & Rönnbäck, 2009). Based on the theory developed by Hecker and colleagues (2002), reading comprehension also involves attentional, memory and inhibition processes. Knowing that many cognitive functions such as attention, memory, speed of information processing, mental endurance and inhibition (Karr, Areshenkoff, & Garcia-Barrera, 2014; Finnanger et al., 2015) are also compromised in individuals who suffer from mild traumatic brain injury (mild TBI), especially in the acute recovery period, it appears relevant to investigate reading abilities in this population. Mild TBI is defined as a cerebral physiological disturbance caused by an abrupt shock to the head (Marshall, Bayley, McCullagh, Velikonja & Berrigan, 2012). It can result in physical, cognitive, behavioural and/or emotional symptoms (Harmon et al., 2013). The most common symptoms are headaches, sleep difficulties, disturbance of balance, fatigue, irritability, mental slowness as well as attention and memory difficulties, anxiety and depression (Carroll et al., 2004; Dikmen et al., 2010; Marshall et al., 2012). In general, these symptoms gradually disappear within 2 to 12 weeks after the accident (Hiploylee et al., 2017; Levin and Diaz-Arrastia, 2015). However, 10% to 20% of individuals will have symptoms that persist beyond the three-month period (Carroll et al., 2004), sometimes worsening and becoming chronic if interventions are not implemented early (Centers for Disease Control and Prevention, 2015). In order to avoid chronicity, it is essential to assess persons with mild TBI as soon as possible to counter the possible persistence of symptoms and offer intervention, including speech-language pathology services for cognitive-communication disorders.

In the literature, several studies looking at cognitive-communication disorders affecting oral expression skills following TBI can be found (Coelho, 1995; Gauthier et al. 2018, Hagen, 1981; Hartley & Jensen, 1991; Levin, Grossman, & Kelly, 1976; McKinlay, Brooks, Bond, Martinage, & Marshall, 1981; Raskin, & Rearick, 1996; Snow, Douglas, & Ponsford,1998), but very few have dealt with reading comprehension abilities (Gauthier et al. 2018; Sohlberg, Griffiths, & Fickas, 2014). Most investigations in this domain have nevertheless highlighted the presence of reading deficits in silent reading vocabulary and comprehension tasks such as on the *Nelson-Denny Reading Test* (NDRT). For example, Sohlberg, et al., found that individuals with mild to moderate TBI had impairments in reading speed and comprehension, measured by performance on the NDRT more than 8 years post-injury (Sohlberg, Griffiths, & Fickas, 2014). Reading comprehension impairments were also found in a group of persons with severe TBI on the NDRT and the *Wide Range Achievement Test-3* (WRAT-3) from two to 24 months post accident (Harvey & Hux*,* 2015; Catroppa & Anderson, 1999). Further, Harvey and Hux (2015) suggested that individuals with severe TBI have better comprehension capacities for factual rather than inferential texts. Also, Schmitter-Edgecombe and Bales (2005) showed that persons with severe TBI assessed over six months post-TBI had more difficulties than control subjects reading and integrating information from narrative texts, which led to poorer understanding of stories.

While most studies that explored reading comprehension were carried out several months or years post accident and with a more severe TBI population, investigations looking at the effect of TBI severity have shown inconsistent results. Some have found a positive relationship between TBI severity and comprehension of written information abilities, with the individuals with the most severe TBI showing the greatest reading impairments on a test which screened achievement using reading recognition, spelling, and arithmetic tasks like the WRAT-3 (Catroppa et al., 1999). Others have found no significant differences in oral word-reading accuracy and speed of reading assessed with different tools such as the *Test of Word Reading Efficiency* (TOWRE), the *Gray Oral Reading Test (*GORT-4) and the *DLS reading speed test* between a group of individuals with mild TBI and a group with severe TBI, although the mild group obtained slightly higher scores compared to normal controls (Johnson, Juranek, Swank, Kramer, Cox Jr, & Ewing-Cobbs*,* 2015; Johansson et al., 2009). More recently, participants with TBI show the greatest reading impairments than a group of healthy controls on a test of reading comprehension and speed of reading (Chapman-Cook Speed of Reading Test) but no difference was noted between mild, moderate and severe TBI groups assessed at one month post accident (Gauthier at al. 2018). The lack of variability in TBI severity and the GCS scores of participants included in the study by Gauthier and colleagues (2018) could explain this absence of difference in comprehension and speed of reading among mild, moderate and severe TBI. Moreover, this study did not specify the number of errors or the number of correct answers. This result contrasts with other studies which have shown a relationship between TBI severity and outcome where more severe TBI was associated with poorer functional outcome (Lannoo et al., 2000; Toschlog et al., 2003; Sobuwa, Hartzenberg, Geduld & Uys, 2014). Some previous investigations found that individuals having suffered TBI of different severities had more impaired language and communication skills when

GCS scores were lower (more severe TBI) than when they were higher (Chabok et al. 2012; LeBlanc et al. 2014). However, to our knowledge, few studies have explored the relationship between the GCS score as a measure of mild TBI severity (i.e. scores between 13 and 15) and reading abilities.

As described, although some studies have highlighted the presence of reading deficits following TBI of all severities, very few have explored reading skills specifically post mild TBI. In fact, to our knowledge, only one focused on the mild TBI population. In this study, the *ADR iNet Dynamic Reader* was used to measure reading comprehension and speed of reading in a mild TBI group and in a healthy control group. Results indicated an alteration in speed of reading among individuals with 65% of the mild TBI group failing the reading task, while 15% of the control group did not pass it (Capo-Aponte, Urosevich, Temme, Tarbett, & Sanghera, 2012). Interestingly, this study was done in a relatively acute recovery period, from 15 to 45 days post trauma and was conducted with mild TBI participants who sustained a blast-injury. Blast induced mild TBI was caused by improvised explosive devices (IEDs), rocket propelled grenades and mortars. Blast and non-blast mild TBI are qualitatively different in their mechanism of injury and may carry different consequences for the structural and functional connectivity of the brain (Davenport, Lim, Armonstrong & Sponheim, 2012). Thus, in our knowledge, this is the first time that reading comprehension was assessed in mild TBI participants from the community and in the acute phase of recovery.

Thus, there is still a gap in the literature regarding the influence of TBI severity and more particularly level of reading impairment following mild TBI in the acute period of recovery and following mechanism of injuries such as fall, vehicle accident, work or sport accident. Moreover, little is known about these impairments regarding different severity of mild TBI. In fact, within the mild TBI population, different levels of severity may be defined based on the presence or absence of cerebral lesions observed in imaging. A positive finding on imaging is defined as a complicated mild TBI and the absence of cerebral lesions is considered an uncomplicated mild TBI (Iverson, 2006). There is evidence in a few studies of poorer cognitive performances for individuals with complicated mild TBI compared to those with uncomplicated mild TBI (Iversen, 2006; Lange, Iverson, Zakrzewski, Ethel-King, & Franzen, 2005). To our knowledge, no study to date has explored the difference in reading comprehension and reading speed between a group of persons with uncomplicated mild TBI and a group with complicated mild TBI.

Another area which has not been investigated is the determination of where cortical damage occurs in relation to reading difficulties in individuals with mild TBI. Borowsky and colleagues (2006) examined the independence of the different brain pathways involved in the dual route cascaded reading model. According to these authors, phonological processing is governed by a dorsal system (occipito-parieto-frontal pathway) which is activated when reading pseudowords. In contrast, lexical processing is governed by the ventral system (occipito-temporal pathway), which is activated when reading irregular familiar words. In the healthy population, functional imaging of skilled adult readers has revealed involvement of the occipitotemporal junction, middle and superior temporal gyri, and the inferior frontal gyrus in sentence comprehension (Constable, Pugh, Berroya, Mencl, Westerveld, Ni, & Shankweiler, 2004) but the lesions associated with reading impairment have not been examined in people with mild TBI. In a study done by our group (Gauthier et al. 2018), lesion location was not associated with reading performance in a

TBI population of all severities confounded but information regarding the mild group was not analysed separately.

In addition to TBI severity and cerebral lesion sites, other factors are likely to influence reading performance after mild TBI such as age, level of education and sex. Previous studies have clearly demonstrated the impact of age on reading in the healthy population (Bob, 2002; Ramig, 1983). For example, lower performances on reading comprehension tasks have been observed in healthy older adults compared to their younger counterparts, especially regarding language processes such as the time needed to process the context. The older adults seemed to have more difficulty than the younger individuals relying on the context and the richness of detailed information in the text read to guide semantic processing (Federmeier, & Kutas, 2005; Federmeier, Van Petten, Schwartz, & Kutas, 2003). Moreover, previous studies have shown age-related decline in reading speed (McGowan, White, Jordan, & Paterson, 2014). It is also logical to suggest that reading speed would be affected by age since it has been shown that older people have slower information processing (Catts, Gillispie, Leonard, Kail, & Miller, 2002). Age was recently found to be a significant predictor of reading performances in a group of TBI participants of all severities (Gauthier et al. 2018). Regarding level of education, one investigation showed that a higher level of education was associated with better reading comprehension in healthy adults (Silagi, Romero, Mansur, & Radanovic, 2014). This relationship has also been reported in other previous studies done with a healthy population that looked at the association between vocabulary knowledge (Keuleers, Stevens, Mandera, & Brysbaert, 2015) and verbal phonemic fluency (Mathuranath, George, Cherian, Alexander, Sarma, & Sarma, 2003; Ratcliff, & Rouder, 1998) and naming (Albert, Heller, & Milberg, 1988).

Our previous study (Gauthier, et al., 2018) also showed that more educated participants with TBI of all severities performed better on a comprehension and speed of reading test but again this variable was not analysed separately for the mild TBI group. Thus, for both age and level of education, it is not known if these variables would be significant in a group consisting only of participants with mild TBI. Another demographic variable to consider is sex but very few studies previously explored the effect of this variable on communication skills post mild TBI. One study done by Bai et al. (2019) showed impairments in verbal fluency in male participants with mild TBI compared to a healthy control group whereas this difference with a control group was not found in a group of female participants with mild TBI.

It has been shown that a reading disability leads to a restriction in social and professional activities resulting in a reduced quality of life (Balazs, Miklosi, Toro & Nagy-Varga, 2016; Karande, Bhosrekar, Kulkarni, & Thakker, 2008). It is therefore essential to assess reading at a very early stage following a mild TBI (i.e. first days or weeks) before discharge from acute care. In fact, a comprehensive evaluation by a rehabilitation team should be carried out to determine the participant's safety for discharge home. This evaluation should also include a speech-language pathology assessment to determine the participant's degree of autonomy and independence for the oral and written communication skills necessary for adequate interaction with their family, their social network, their work colleagues and community members and their need for rehabilitation services to optimize social and vocational reintegration following hospital discharge.

The first aim of this study was therefore to explore reading comprehension and speed of reading using the Chapman-Cook Speed of Reading Test (CCSRT) in adults who have sustained a mild TBI and to do so in the first two weeks following their injury while still hospitalized in the acute care setting. The CCSRT performances were compared between three groups of participants: (1) participants with mild TBI and with traumatic cerebral lesions (complicated mild TBI), (2) participants with uncomplicated mild TBI (no cerebral injuries on CT scan) and (3) a control group composed of healthy adults, without TBI. We hypothesized that participants in the complicated mild TBI group would have more errors as well as a lower total score (number of items read) than the uncomplicated mild TBI group and that the control group would have fewer errors as well as a higher score (more items read) than both TBI groups. The second aim of this study, which is exploratory, was to determine which variables among sex, age, education, TBI severity based on the GCS score, speed of processing skills and site of cerebral lesions significantly predict reading comprehension and speed of reading performances as measured with the CCSRT in participants with mild TBI. We hypothesized that older and less educated male participants with a lower GCS score (more severe mild TBI) and lower speed of processing skills and with a frontal or temporal lesion would have a lower total CCSRT score (fewer items read).

Methods

Participants

Only participants with mild TBI admitted to our hospital were part of the sample; participants only seen in the emergency room, those who died during hospitalisation and those with moderate or severe TBI were not included. Identification of a mild TBI was based on the presence of one or more of the following symptoms: the participant was confused or disoriented, the participant lost consciousness for 30 minutes or less, a post-traumatic amnesia of less than 24 hours was present or the participant showed other transient neurological abnormalities such as focal signs, seizures, and intracranial lesions not requiring surgery. In addition, Glasgow Coma Scale score (GCS) was between 13 and 15 within the first thirty minutes post injury, or on arrival to the ER. The diagnosis of mild TBI was confirmed by a physician and was based on the Centers for Disease Control and prevention (2015). According to the Canadian CT head rule (Stiell et al., 2001), participants had a first CT scan done soon after their arrival in the ER. A complicated mild TBI was identified when a cranial or intracranial injury was seen on radiological imaging.

Moreover, participants who presented with agitation (no collaboration) were excluded as well as those with aphasia since linguistically based impairments in reading were not the focus of this study. Participants with post-traumatic visual impairments (i.e. double or blurred vision) were also excluded to avoid any difficulty accurately seeing the characters in the material presented. The evaluators did not carry out any cognitive assessment when participants were under intravenous narcotic medication or while they were still in the intensive care unit. These participants were not excluded but were tested later, when they were transferred to a regular ward or when they were no longer using intravenous narcotic medication.

For both TBI and control groups, a semi-structured interview was carried out to determine if potential participants presented with any of the following exclusion criteria. These included pre-morbid history of alcohol or drug abuse, a diagnosed psychiatric disorder, history of a previous TBI or pre-existing neurological deficits (i.e.

neurodevelopmental or degenerative disorders, stroke, epilepsy, tumor). Participants in both groups (TBI and controls) who were not fluent speakers of English or French were also not included because the language barrier could have biased our measures. All participants were evaluated in their preferred language (English or French) by examiners fluent in these languages.

A total of 168 individuals aged between 18 and 89 years participated in the study. The cohort included 100 participants with a diagnosis of mild TBI composed of 15 with a diagnosis of uncomplicated mild TBI and 85 participants with a diagnosis of complicated mild TBI (participants with mild TBI and with traumatic cerebral lesions) as well as 68 healthy controls recruited from the community. The participants with mild TBI (with or without orthopedic injuries) were admitted to the TBI program of the McGill University Health Centre - Montreal General Hospital (MUHC-MGH), a level 1 trauma centre, between November 2014 and March 2016. The research ethics board of the MUHC-MGH approved this study.

Demographic characteristics. Gender (male or female), age and education were collected from the medical charts.

Medical and accident related characteristics. The Glasgow Coma Scale score (GCS) upon arrival to the tertiary trauma center, as assessed by the emergency physician before resuscitation, intubation, or administration of narcotics was collected as well as the occurrence of a loss of consciousness and the trauma mechanism. Concerning the mechanism of the accident, a total of 46,6% had a fall, 46,3% was involved in a vehicle accident, 7,3% sustained a work accident and 9,8% was involved in a sport accident. A GCS score of 13-15 indicates a mild TBI. A neurosurgeon blinded to the CCSRT data reviewed the CT scans of our participants to determine sites of intracerebral lesions. The results were in the following categories: (1) Left-frontal, (2) Right-frontal, (3) Left-parietal, (4) Right-parietal, (5) Left-temporal (6) Right-temporal, (7) Occipital. Participants may have had injuries in more than one location.

Instruments

In order to measure comprehension and speed of reading, the Chapman-Cook Speed of Reading Test (CCSRT) was administered. First introduced in an article by Chapman and Cook (1923), this test allows for a quick screening of reading abilities and generates similar scores to other validated but longer to administer reading tests (Holtzer, Mcguire, Burright, & Donovick, 1998). According to Holtzer, and colleagues (1998), the CCSRT scores correlate to measures of intellectual functioning (such as the *Shipley Institute of Living Scale* and the *Kaufman Brief Intelligence Test (*KBIT*)*) and to other scales of reading abilities (such as the *Gray Oral Reading Test* (GORT) and the *National Adult Reading Test Revised (*NAART-R*)*). This test was also validated in French by Goize and colleagues (2018). The French or the English version was administered according to the native language of the participant.

In this task, participants were asked to read silently and identify and cross out as fast as possible the word that was incongruent with the meaning of a short paragraph. Six examples were read by the participant and their responses were corrected as needed by the evaluator. The entire task included 30 paragraphs (texts of different stories) and participants were instructed to cross out the incongruent word as many as they could in 2 minutes and 30 seconds. The 30 paragraphs of the test were spread over six pages (5 paragraphs per page). A total of 30 words (SD=2.7) made up a paragraph and the word to be crossed out was a subject complement for 9 paragraphs, was in the main clause for 2 paragraphs, in a secondary clause for 4 paragraphs and in a subordinate clause for 15 paragraphs. The data analyzed were: (1) the total score (number of items completed within the time limit, scores between 0 and 30) which is a measure of reading speed and (2) the percentage of mistakes (number of mistakes divided by the number of items completed multiplied by one hundred) within the time limit. To measure speed of information processing, the *Digit-Symbol-Coding subtest* of the WAIS-III (Wechsler, 1997) was performed in the TBI groups. In this test, the participant must copy symbols corresponding to numbers as quickly as possible in a time limited to 120 seconds. The total number of correct answers was collected.

Procedure

Experienced speech-language pathologists evaluated the participants with the CCSRT and experienced neuropsychologists administered the WAIS-III. Both tests were presented at bedside in the acute care setting within the first two weeks following the trauma.

Statistics

Descriptive data are presented (mean, percentage and standard deviation). For categorical variables, counts and percentages are reported. Separate oneway ANOVAs *were first performed* on age and education as dependent variables to measure if the three groups (independent variable) were equivalent in terms of these demographic variables.

Regarding the first objective of this study which was to compare the CCSRT performances in the three groups (complicated mild, uncomplicated mild and healthy controls), separated one-way ANOVAs followed by *Bonferroni's post-hoc* comparisons *tests were performed* on computed CCSRT scores (total score and percentage of mistakes). With respect to the second hypothesis, which is exploratory, multiple linear regressions were performed on the CCSRT total score (dependent variable) obtained by the participants with mild TBI only (uncomplicated and complicated). The independent variables included were gender, age, years of education, GCS score, results on the *Digit-Symbol-Coding* task of the WAIS-III and sites of cerebral lesions (frontal, parietal, temporal, occipital). All statistical tests of hypotheses were carried out at a level of significance of 0.05 and effect sizes were also provided (Cohen, 1988). All analyses were performed using IBM SPSS statistics 24.0 (United States).

Results

Participants

The demographic (age, education, gender) and medical characteristics (GCS and lesion sites) are presented in Table 1. The ANOVAs showed no significant differences between the three groups for age (*F*(2,167) = 2.71 *p* =.07) or education (*F*(2,167) = 2.97 *p* =.06). Even though these differences are not significant, they are close to significant, and the numerical differences favor the control group. For this reason, we included age and education in our linear regressions to assess the impact of these variables.

Insert table 1 about here

In our cohort of mild TBI participants, 33.9% were involved in a motor vehicle accident, a total of 47.9% had a fall, 9.7% were victims of an assault, 4.3 % were involved in a work accident and 4.2% had a sports accident. A loss of consciousness was documented for 61.5% of the TBI participants whereas 22.5% did not lose consciousness at the time of the trauma. For 16% of the cohort, this information was unavailable.

Regarding language background, 46.9% of the participants with uncomplicated mild TBI were bilingual (25.6% with English as their first language and 74.4% with French as their first language), 51.2% of those with complicated mild TBI were bilingual (31.9% with English as their first language and 68.1% with French as their first language) and bilingualism was reported in a total of 41.4% of the control group (100% with French as the first language). The speech-language pathologist administered the CCSRT to the mild TBI group 10.3 days on average (SD=3.6) post accident and the neuropsychologist administered the Digit-Symbol-Coding subtest of the WAIS within 9.7 days on average (SD=4.1) after injury.

Chapman-Cook Speed of Reading Test performances (CCSRT)

On the total score of the CCSRT (speed of reading), an analysis of variance (ANOVA) showed a significant difference among groups ($F(2,167) = 54.93$, $p = .001$; $R^2=0.40$). Bonferroni post-hoc tests showed that the total score of the control group was significantly higher than the groups with uncomplicated mild TBI ($p=.01$) and complicated mild TBI ($p = .001$) but no difference between both mild TBI groups was found ($p=.96$). Figure 1 shows the group difference on the total score of the CCRST for both mild TBI groups in comparison to controls.

In regard to the percentage of errors, an analysis of variance (ANOVA) showed a significant difference among groups in the percentage of errors on the CCRST ($F(2,167) = 9.30$, $p =.003$; $R^2=.10$). *Bonferroni's post-hoc* analysis revealed a significant difference between control participants and both mild TBI groups. The control group had a significantly lower percentage of mistakes than the complicated mild TBI group ($p=.02$) and the uncomplicated mild TBI group ($p=.005$).However, no differences were found between both TBI groups (*p*=.07). Figure 2 shows the group difference on performances obtained on the CCSRT for the percentage of errors where both mild TBI groups performed worse than the group of healthy participants.

Predictive Variables

The multiple regression model with all predictors produced $R^2 = .361$, F(12, 68) = 2.63, p= .007 meaning that all those variables explained 36.1% of the variance of the total CCSRT score. As can be seen in Table 2, the individual predictors were examined further and indicated that age (t = -.46, p = .04), education (t = 1.60, p = .01) and *Digit-Symbol-Coding subtest* (t=3.53, p = .001), were significant predictors in the model. This result suggests that older participants had lower total scores on the CCSRT than their younger counterparts. Moreover, as the number of years of education increased, the likelihood of having a better score on the CCSRT also increased. The most significant predictive variable for the CCSRT total score was the total score on the *Digit-Symbol-Coding* test of the WAIS-III. As the total score obtained on the *Digit-Symbol-Coding* task of the WAIS-III increased, the likelihood of having a better score on the CCSRT also increased. However, sex, TBI severity (GCS score) and cerebral lesion site were not related to CCSRT performance. Figure 3 illustrates the CCSRT total score based on the presence or absence of a traumatic cerebral lesion site.

Discussion

The goal of this study was to add to the knowledge regarding acute reading abilities following mild TBI. Some interesting studies have already been published showing impairments in reading following TBI of all severities (Catroppa et al., 1999; Gauthier et al. 2018; Johnson et al. 2015; Johansson et al., 2009; Sohlberg et al. 2014; Harvey & Hux, 2015; Schmitter-Edgecombe, & Bales, 2005; Holliday et al., 2005). However, to our knowledge, there is no study that specifically looked at reading comprehension and speed of reading performances of individuals from community with complicated and uncomplicated mild TBI in the acute phase assessed at bedside. To accomplish this goal, CCRST performances of participants with complicated mild TBI, uncomplicated mild TBI and those of healthy controls were compared. The results suggest that participants with mild TBI (uncomplicated and complicated) have significantly more impairments in reading comprehension and speed of reading evaluated in the early days post injury with the CCSRT than the matched-healthy participants. Thus, in addition to the fact that participants were slower than controls in the reading task, they also demonstrated a lower reading proficiency, expressed by a higher percentage of errors. It is important however to consider that the effect sizes were small. A previous study carried out with military with mild TBI from blast-injury showed comparable results (Capo-Aponte et al. 2012). This finding is now relevant for the individuals from the community who sustained different mechanism of injury, such as fall, vehicle accident or work and sport accident. In addition, other researchers have shown the same pattern of results where impairments on a reading task were observed in mild, moderate and severe TBI groups compared to a control group (Gauthier et al. 2018; Harvey et al., 2015; Johansson et al., 2009). However, no difference between the uncomplicated and complicated mild TBI groups was shown which does not support our hypothesis. This result has been previously reported in other studies that showed no difference in outcomes based on the presence of acute intracranial abnormalities (Hellstrøm et al., 2017; Holthe, Hellstrom, Andelic, Server, & Sigurdardottir, 2019). This finding may be explained by the unequal number of participants per group, with a very low number in the uncomplicated group and a large standard deviation for this group, especially for the number of mistakes. In addition, our results demonstrate that the presence of a cerebral lesion does not have a real impact on reading speed and comprehension. These localized lesions may not be sufficient to impair reading. In fact, more diffuse lesions affecting the reading network may be required to sufficiently influence reading. It is therefore possible that microlesions, not observable on CT Scan, especially in the white matter, may have affected the process in both groups of mild TBI participants, but not in one group more than the other.

Previous research has identified speed of processing as the impaired cognitive process causing reading difficulties in the TBI population for all severities (Perbal, Couillet, Azouvi, & Pouthas, 2003; Harvey et al., 2015; Christopher et al., 2012). Thus, it seems plausible to state that impairment in speed of processing assessed with the *Digit-Symbol-Coding* task of the WAIS-III may be at play in causing poorer reading performances observed in both groups of participants with mild TBI in the present study. In fact, analyses carried out in this study on speed of information processing allowed us to clarify, in part, its impact on the total score of the CCRST. As shown, speed of information processing was a good predictor of the total CCRST score, suggesting that participants with mild TBI who have higher speed of information processing also have faster reading skills.

Regarding the percentage of errors as well as the total CCSRT score, no significant difference was found between the complicated mild and the uncomplicated mild TBI groups which suggests that sustaining a cerebral lesion visible on imaging did not have a significant impact on acute reading comprehension and reading abilities. These findings are in keeping with previous studies addressing the difference between complicated and uncomplicated mild TBI. Iverson and colleagues (2012) compared two groups of individuals with mild TBI (complicated and uncomplicated) and found no difference on the neuropsychological measures administered (Trail Making Test (TMT; Reitan, 1992); California Verbal Learning Test—2nd Edition (Delis, Kramer, Kaplan, & Ober, 2000); Conners' Continuous Performance Test—2nd Edition (CPT-II; Conners, 2002); subtests from the Wechsler Adult Intelligence Scale—Third Edition (Wechsler, 1997): Similarities, Letter-Number Sequencing, Digit Symbol-Coding, Block Design, and Matrix Reasoning). Another study done by our group comparing clinical outcomes of a complicated and an uncomplicated group at 2 weeks post injury found similar results where no significant difference was observed on the neuropsychological scores between both groups (de Guise et al., 2010). Interestingly, the study by Iverson et al. (2012) was carried out longer post mild TBI, that is at three to four weeks post, suggesting that an absence of difference among these two groups persists even as time progresses.

As in the 2018 study with a TBI population of all severities (Gauthier et al. 2018), the current findings also suggest that age and level of education influenced performance on the CCRST when only participants with mild TBI were included, with the odds of having a better score on the CCSRT decreasing (slower reading) as age increased and as the number of years of education decreased. The relationship between age and language and communication following a TBI is supported by our previous studies (de Guise et al., 2016; LeBlanc et al., 2014). The finding that age correlated with speed of processing is consistent with a large aging literature, going back to Salthouse (1996). Other studies in the TBI population also showed that age is related to speed of processing (Rassovsky, Levi, Agranov, Sela-Kaufman, Sverdlik, & Vakil, 2015; Spitz, Ponsford, Rudzki, & Maller, 2012). Interestingly, in the present study, age was also found to be associated with speed of processing (*Digit-Symbol-Coding*). One hypothesis about the effect of ageing on cognitive functioning suggests that synaptic connections are weaker and there are fewer alternative neural networks to rely on as we age. This could explain the relationship between age and speed of reading. Another possible explanation could lie in the reduction of functional and cortical plasticity as the brain ages leading to greater limits to the compensation system when the brain is injured (Spitz, Bigler, Abildskov, Maller, O'Sullivan, & Ponsford, 2013).

Regarding education, a higher level of schooling was associated with better performances on speed of reading. Previous studies also support the positive relationship between level of education and short-term cognitive and functional outcome in the TBI population. These studies revealed that participants with a higher level of education had a better acute outcome in the cognitive and functional domains (de Guise, LeBlanc, Feyz & Lamoureux, 2005; Spitz, Ponsford, Rudzki, & Maller, 2012) and better long-term outcome (Kesler, Adams, Blasey, & Bigler, 2003) post TBI. The results regarding education may be explained by the cognitive reserve theory developed by Stern (2002). This theory suggests that following damage to the brain, it actively tries to utilize alternate mechanisms and brain systems to compensate for those areas affected. More specifically, Kesler and colleagues (2003) suggested that cerebral vulnerability and the prevalence of cognitive impairment post TBI would be offset by a higher premorbid cerebral volume secondary to a higher level of education. To support this hypothesis, a meta-analysis done by Mathias and Wheaton (2015) that consolidated data from 90 studies in order to compare the outcomes of groups with high and low cognitive reserve demonstrated that a higher education level was associated with better outcome. The authors concluded that education provides a source of cognitive reserve, which leads to better outcomes after a TBI. Moreover, relative to cognitive reserve, it is interesting to note that tests such as the QI KBIT, and the NART-R as well as the GORT, which are used as proxies for pre-morbid IQ, are correlated with CCSRT performance (Holtzer et al. 1998). Finally, as in the case of age, it is possible that compensatory mechanisms become less efficient when education level is lower. However, it is interesting to note that education was not related to the speed of processing test (*Digit-Symbol-Coding*) in the present study which leads us to believe that education could play a role in the process of word detection and comprehension but not in the process of speed. Again, further studies will have to be carried out to confirm this hypothesis.

Despite the innovative results of this study, there are some limitations. First, the numbers in the two mild TBI groups were unequal with a larger number of participants with complicated mild TBI (n = 85) and a lower number of those with uncomplicated mild TBI (n= 15). Also, even though age and education were included in the multiple linear regressions, the groups were not well matched on these variables. Moreover, generalization of these results to the global population of persons with mild TBI or concussion would be unfounded. The participants included in our study were admitted to a tertiary trauma center which means that their injury was significant enough that they could not be immediately discharged home. Also, since participants with a premorbid history of alcohol and drug abuse were excluded this may have created a selection bias which would again not allow generalization of the results to all other individuals with mild

TBI. Regarding time to assessment, despite the very short time frame post injury (i.e. two weeks), the difference in the delay between the onset of the accident and the day of evaluation may have influenced the results of both the reading test and the speed of processing test. This should be taken into consideration in future research. In addition, only one reading test was administered (CCSRT), which limits the conclusions about reading ability. In this regard, other tools that could examine the lexical and phonological processes of reading would be important to administer with this clientele. One last limitation to mention is in regard to the imaging technique that was part of this investigation. In an acute hospital setting, CT is widely used for clinical diagnostic purposes. It is not however the imaging technique of choice to observe diffuse microscopic cerebral injuries and so these may have been missed in our investigation. Along the same line, because of the limited number participants with complicated mild TBI, the effect of lesion size and cerebral lesion pathways were not explored. The data gathered in this study (i.e. presence of absence of lesion) limits the interpretation regarding any effect related to the extent of cerebral damage sustained and this should be explored in the future.

In conclusion, these findings suggest that speed of reading and reading comprehension are compromised after mild TBI and that the CCSRT can be a useful tool in the acute phase for clinicians who work with these individuals. The test seems to be sensitive enough to measure reading disorders and to discriminate a mild TBI group from a healthy group but not to differentiate persons with uncomplicated mild TBI from those with complicated mild TBI. Moreover, the test seems appropriate to the specific needs of the acute TBI population in terms of length and accessibility for bedside administration. However, even if the CCSRT is widely used among clinicians, the literature on its sensitivity with individuals who have suffered TBI is poor and still needs to be addressed in future studies. Our results also indicated that the ability to read material quickly did not ensure accurate comprehension of what was read. Given these findings, we recommend that speech-language pathologists working in the acute care setting verify reading comprehension and speed of reading for participants with mild TBI and that support be provided to them when they are required to read, complete and sign documents such as those related to their medical care or insurance coverage. Moreover, written material should be short, easy to read and written in simple language as to optimize their understanding of the information provided.

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Disclosure

The authors report no conflicts of interest

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Table 1. *Demographic and accident related variables*

Variables\Groups	Uncomplicated mTBI	Complicated mTBI	Control
Number of participants	15	85	68
Age (Mean and SD)	56.73 ± 23.04	57.29 ± 19.93	50.93 ± 1.32
Education (Mean and SD)	11.80 ± 2.51	13.08 ± 2.86	13.56 ± 0.26
Gender (number)	10M/5F	62M/23F	19M/49F
GCS (Mean and SD)	14.87 ± 0.35	14.45 ± 0.93	
Presence of cerebral lesions (Number and %)			
Frontal left		50 (58.8)	
Frontal right		48 (56.5)	
Parietal left		31 (36.4)	
Parietal right		16 (18.8)	
Temporal left		31 (36.4)	
Temporal right		21 (24.7)	
Occipital		21 (24.7)	

Note. SD = Standard deviation; GCS = Glasgow Coma Scale; M = Male; F = Female.

Table 2. *Multiple regression analyses on the Chapman-Cook Speed of Reading Test (Total score)*

Variable	Unstandardized Coefficient B	Standard Error	Standardized coefficient Bêta	t	p	Tol.	VIF
Intercept	-15.42	13.12		-1.17	.24		
Gender (vs Male)	.25	1.06	.02	.23	.81	.83	1.19
Age	.01	.02	.06	.46	.04	.62	1.61
Years of Education	.27	.16	.19	1.60	.01	.81	1.22
Glasgow Coma Scale	.48	.84	.06	.57	.57	.77	1.28
Digit symbol-Coding	.22	.06	.48	3.53	.001	.60	1.65
Cerebral lesion							
Frontal							
Left	-1.26	1.04	-.15	-1.21	.23	.67	1.48
Right	1.13	.98	.14	1.15	.25	.75	1.32
Parietal							
Left	-.19	1.49	-.02	-.13	.89	.45	2.17
Right	.27	2.02	.01	.13	.89	.66	1.50
Temporal							
Left	-.74	1.15	-.08	-.63	.52	.64	1.54
Right	-1.55	1.22	-.15	-1.27	.20	.76	1.31
Occipital	.51	1.70	.04	.30	.76	.61	1.62

*$p<0.05$ ($r=0.601$, $r^2=0.36$, $Adjr^2=0.22$)

Figure 1. *Chapman-Cook Speed of Reading Test: Total scores (Maximum=30)*

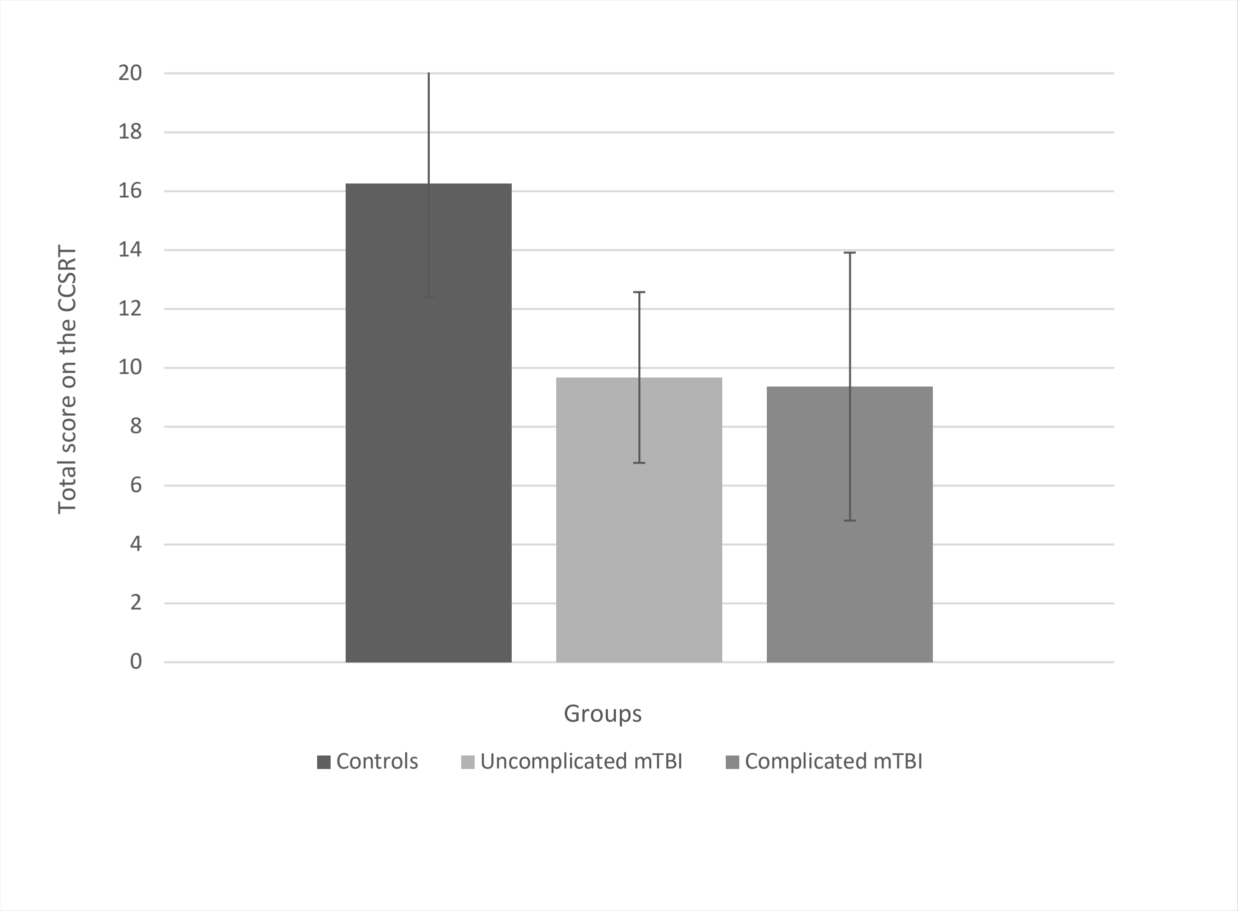

Figure 2. *Chapman-Cook Speed of Reading Test: Percentage of errors*

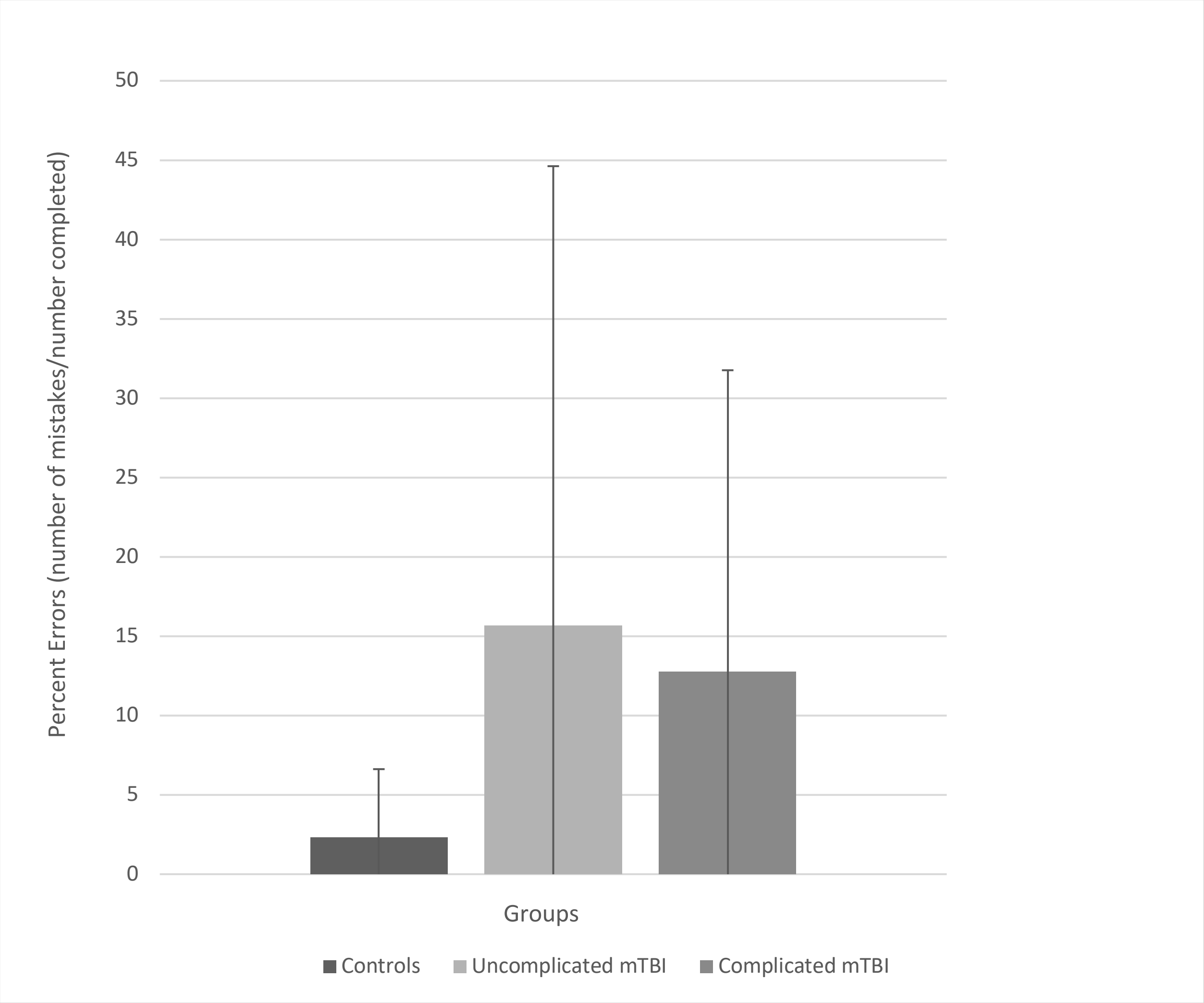

Figure 3. *Total score on the CCSRT based on the presence or absence of a traumatic cerebral lesion site.*