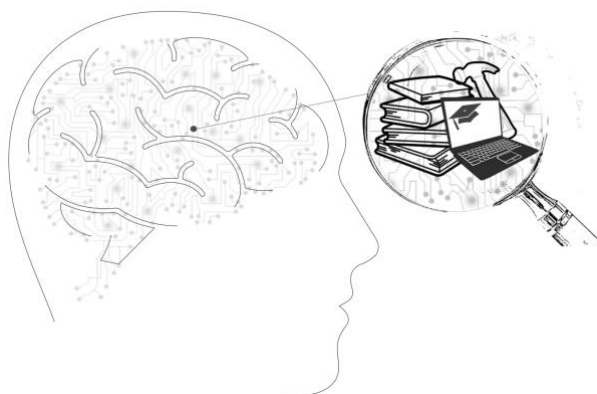


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IMPACT DES FACTEURS COGNITIFS ET COMPORTEMENTAUX SUR LA REHABILITATION SOCIO-PROFESSIONNELLE DES PERSONNES CEREBROLESEES



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Résumé

L'objectif général de ce travail de recherche était d'identifier des profils cognitivo-comportementaux compatibles ou incompatibles avec un retour en formation au stade séquellaire d'une lésion cérébrale acquise (LCA). Ainsi, l'intérêt était porté sur les aspects fonctionnels consécutifs à une LCA qui permettraient ou non un retour efficient en formation. D'abord, en menant une revue systématique de la littérature, nous avons voulu identifier les facteurs cognitivo-comportementaux impliqués dans la réinsertion professionnelle des personnes souffrant d'une LCA d'origine traumatique en phase post-aigüe. Ensuite, nous avons testé la spécificité de deux outils dédiés à l'évaluation des troubles cognitifs et comportementaux des personnes victimes d'une LCA, avant de tester leur pouvoir prédictif. Enfin, en adoptant une méthodologie rétrospective et une méthodologie prospective et en s'appuyant sur l'apprentissage automatique (*machine learning*), nous avons étudié, chez ces personnes, le lien entre les performances cognitives et comportementales et la réussite / l'échec d'une formation qualifiante. Ces travaux nous ont permis d'identifier, sur le plan théorique, des modèles cognitifs explicatifs de la réussite et de l'échec en formation professionnelle de personnes souffrant d'une LCA. Sur le plan clinique, ils permettront aux professionnels chargés de la prise en charge de ces personnes de les guider vers la réinsertion socio-professionnelle en s'appuyant sur des indices objectifs.

Mots-clefs : lésion cérébrale acquise, modèle cognitif, apprentissage automatique, formation, réhabilitation socio-professionnelle, UEROS.

Abstract

The aim of this dissertation was to identify cognitive and behavioral patterns enabling or hindering the return to vocational training of patients in post-acute stages of an acquired brain injury (ABI). Thus, the focus was on the functional aspects due to the ABI that would or would not allow an effective return to vocational training. First, we conducted a systematic review in order to identify, in the post-acute stages of an ABI, cognitive and behavioral factors involved in the vocational rehabilitation of patients suffering from a traumatic ABI. Then, we tested the specificity of two neuropsychological tools to assess cognitive and behavioral sequelae in patients with ABI, before testing their predictive power. Finally, we adopted a retrospective and a prospective methodology, relying on machine learning algorithms, to study the link between cognitive and behavioral performance evaluated at the beginning of a vocational rehabilitation program and the probability to succeed or fail a vocational training after an ABI. These studies allowed us to identify, from a theoretical perspective, cognitive models explaining the success and failure of a vocational training in patients with ABI. From a clinical perspective, these models would enable clinicians to adapt neuropsychological practice to this specific population relying on objective factors that would improve their vocational guidance.

Key-words: *acquired brain injury, cognitive model, machine learning, vocational training, vocational rehabilitation.*

PARTIE I :

LESION CEREBRALE ET REINSERTION

PROFESSIONNELLE

1. Les lésions cérébrales acquises

1.1. Définition et étiologies

Une lésion cérébrale acquise (LCA) est définie comme toute atteinte du cerveau, survenant après la naissance (King & Dean, 2009) ; elle n'a donc, par définition, pas de caractère héréditaire, congénital ou dégénératif et n'est pas due à un traumatisme lié à l'accouchement (Byrne, Coetzer, & Addy, 2017). Cette atteinte entraîne un changement de l'activité neuronale, ayant des conséquences sur la constitution et l'activité métabolique et/ou fonctionnelle des neurones (Pekna & Pekny, 2012). Elle survient le plus fréquemment par l'intermédiaire de deux processus, à savoir, l'intervention d'une force mécanique ou l'interruption de l'apport en oxygène (Dimancescu, 2007). Dans le premier cas, la force mécanique peut provenir de l'extérieur, il en est ainsi d'un coup porté à la tête (Meaney & Smith, 2011), ou de l'intérieur, à l'instar des hémorragies spontanées au sein du cerveau ou des membranes qui l'entourent (Leonardo, Robbins, & Doré, 2012). Dans le second cas, l'apport en oxygène peut être interrompu, ce qui correspond à une anoxie, ou cet apport peut être réduit sans être totalement interrompu, ce qui correspond à une hypoxie (Stuart, Farrer, & Heintzelman, 2017). L'anoxie et l'hypoxie peuvent survenir en dehors de chocs extérieurs, mais sont souvent associées à l'intervention de forces mécaniques sur ou dans le cerveau (Dimancescu, 2007).

La classification des LCA repose sur la présence ou l'absence d'un traumatisme (Curran, Dorstyn, Polychronis, & Denson, 2015; Donker-Cools, Wind, & Frings-Dresen, 2016; van Velzen, van Bennekom, Edelaar, Sluiter, & Frings-Dresen, 2009).

Une LCA d'origine traumatique, appelée traumatisme crânien (TC), est le résultat d'une force extérieure exercée sur la tête entraînant une perturbation cérébrale (Albert-Weissenberger et al., 2019; Wang & Han, 2018). Cette force extérieure peut éventuellement se traduire par une pénétration de la boîte crânienne, raison pour laquelle le TC est défini comme pénétrant ou non-

pénétrant ; le TC pénétrant suppose qu'un objet extérieur entre en contact avec le tissu cérébral (Prasad & Bondy, 2015; Walker et al., 2015). Qu'elle conduise ou non à un TC pénétrant, cette force peut être exercée dans différentes situations, comme les chutes, les agressions, les accidents de la voie publique, les blessures par balle et militaires (Bigler & Maxwell, 2013), les blessures sportives (Ivancevic, 2009) ou au travail (H. Kim, Colantonio, & Chipman, 2006; Paci, Infante-Rivard, & Marcoux, 2017), les violences familiales (Hunnicutt, Lundgren, Murray, & Olson, 2017; Valera & Kucyi, 2017; Valera et al., 2018), le syndrome du bébé secoué (Ashton, 2010; Runyan, 2008) ou les mauvais traitements infligés aux enfants (Foster, Recker, Lee, Bell, & Tyler-Kabara, 2014). Ces différentes causes provoquent des lésions cérébrales selon trois mécanismes différents : par impact avec un objet, par un mouvement d'accélération / décélération de la tête, qu'elle heurte ou non un objet, et par diffusion d'ondes de choc à travers la boîte crânienne (Hanlon, Demery, Martinovich, & Kelly, 1999) (voir **Figure I**).

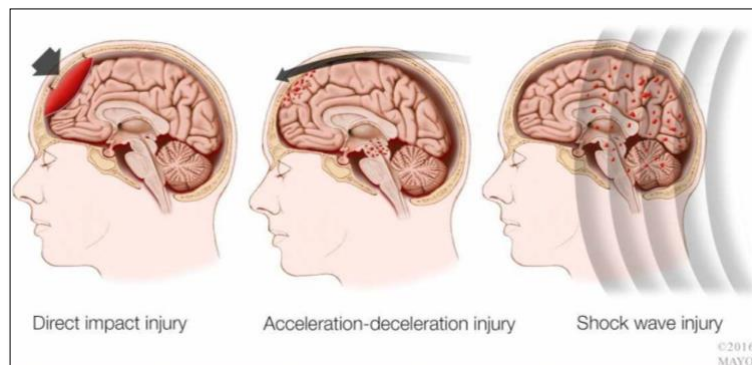


Figure I. Les mécanismes physiques mis en jeu lors d'un traumatisme crânien.

Impact direct de la tête avec un objet (*gauche*), accélération/décélération avec ou sans contact avec un objet (*centre*) et ondes de choc (*droite*) (d'après Torborg, 2016).

Ces mécanismes physiques ont, de par leur diversité, des conséquences lésionnelles spécifiques (Hammeke & Gennarelli, 2003). En effet, dans le cas d'un impact direct de la tête avec un objet, les lésions cérébrales sont généralement focalisées au niveau de l'impact et sont provoquées par des contusions corticales, lésions vasculaires, hémorragies et ischémies. Les lésions cérébrales correspondent davantage à des lésions axonales diffuses dans le cas d'un TC par accélération/décélération avec ou sans contact avec un objet (Albert-Weissenberger & Sirén, 2010; Blennow, Hardy, & Zetterberg, 2012) et dans le cas d'un TC par ondes de choc (Fievisohn, Bailey, Guettler, & VandeVord, 2018).

Une LCA d'origine non-traumatique est le résultat d'une force intérieure exercée sur le tissu cérébral entraînant une perturbation cérébrale (Eagan-Johnson & Grandinette, 2018). Cette force se manifeste notamment lors d'un accident vasculaire cérébral (AVC) (Dimancescu, 2007), défini par l'Organisation Mondiale de la Santé (OMS) comme « le développement rapide de signes localisés ou globaux de dysfonction cérébrale avec des symptômes durant plus de 24 heures, pouvant conduire à la mort, sans autre cause apparente qu'une origine vasculaire » (Hatano, 1976, p.541; National Collaborating Centre for Chronic Conditions, 2008, p.4). On dénombre deux types d'AVC, l'AVC hémorragique et l'AVC ischémique, le dernier représentant une proportion de 87% des AVC (Chen, Thakkar, Robinson, & Doré, 2018; Ovbiagele & Nguyen-Huynh, 2011). L'AVC hémorragique est dû à une rupture des vaisseaux sanguins entraînant un épanchement de sang dans le parenchyme intracrânien (Caplan, 2013; Pritchard & Alloway, 2002). L'AVC ischémique est dû à une interruption de l'apport sanguin au cerveau à cause d'une obstruction de vaisseaux sanguins par des agrégats, et ce type d'AVC peut être précédé d'un accident ischémique transitoire (AIT), qui présente tous les signes d'un AVC mais qui dure moins de 24 heures (Pritchard & Alloway, 2002) (voir **Figure II**).

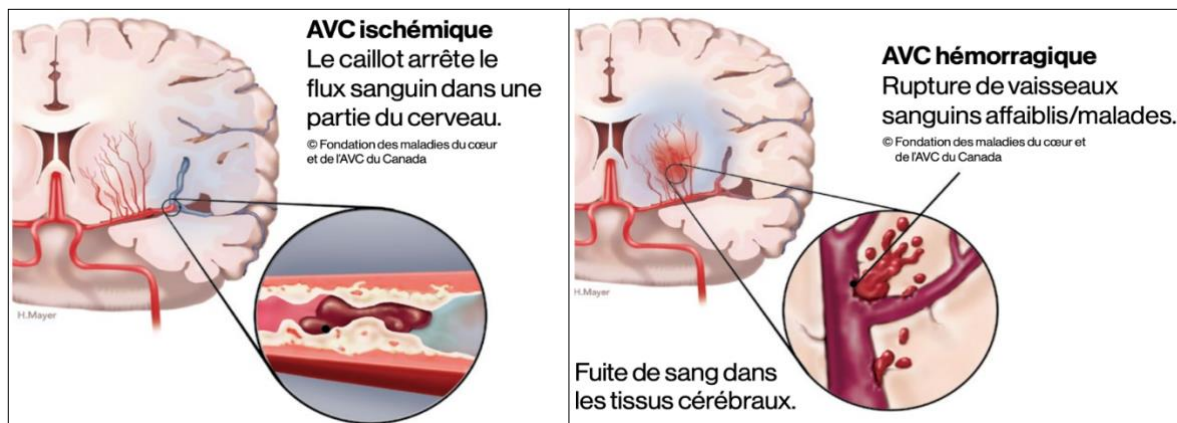


Figure II. Les deux types d'accident vasculaire cérébral (AVC)

(d'après la Fondation des maladies du cœur et de l'AVC du Canada, 2017).

Une LCA d'origine non-traumatique peut également survenir lors d'une tumeur cérébrale, d'une maladie infectieuse, d'une hémorragie sous-arachnoïdienne non-traumatique (Kutsuna et al., 2018), d'une encéphalopathie, (Tibæk, Kammergaard, Johnsen, Dehlendorff, & Forchhammer, 2019), mais aussi en cas de manque d'oxygène comme lors de blessures hypoxiques, en cas de troubles métaboliques et d'exposition toxique (Khuu, Chan, & Colantonio, 2017).

1.2. Épidémiologie

1.2.1. Traumatisme crânien (TC)

Dans le monde, 10 millions de personnes seraient atteintes d'un TC chaque année (Hyder, Wunderlich, Puvanachandra, Gururaj, & Kobusingye, 2007).

Aux États-Unis, 12% de la population générale serait atteinte d'un TC (Frost, Farrer, Primosch, & Hedges, 2013), celui-ci survenant chaque année chez 1,7 millions de personnes (Faul, Xu, Wald, Coronado, & Dellinger, 2010). Ces chiffres sont souvent calculés sur la base de personnes ayant bénéficié d'un suivi médical, c'est pourquoi une nouvelle estimation a été

réalisée à partir d'un registre national de civils ; celle-ci serait plus représentative de la population des Etats-Unis : 0,52% des citoyens américains aurait subi un TC entre avril 2012 et juin 2013. Ces derniers chiffres résultent cependant d'informations auto-rapportées, qui peuvent notamment faire l'objet d'un biais de rappel (Hale, Bohnert, Grekin, & Sripada, 2019). Les personnes les plus touchées seraient les enfants en bas âge (0-4 ans), les adolescents (15-24 ans), et les personnes âgées de plus de 65 ans (Brown, Elovic, Kothari, Flanagan, & Kwasnica, 2008; Kohnen, Gerritsen, Smals, Lavrijsen, & Koopmans, 2018).

En Europe, la prévalence de personnes hospitalisées ou décédées à la suite d'un TC est de 235 pour 100 000 (Tagliaferri, Compagnone, Korsic, Servadei, & Kraus, 2006). En France, 150 000 personnes auraient un TC chaque année (Mathé, Richard, & Rome, 2005). La seule enquête épidémiologique française portant sur les TC, quelle que soit leur sévérité, a été réalisée dans la région d'Aquitaine en 1986 (Mathé et al., 2005) et l'incidence des TC était estimée à 280 pour 100 000 habitants, la région comptant à l'époque 4,9% de la population française totale (Tiret et al., 1990).

Des estimations à partir de données internationales soulignent que 50 à 60 millions d'individus souffriraient d'un TC chaque année et une proportion de 50% de la population mondiale en subirait un au cours de leur vie (Maas et al., 2017; Mollayeva, Mollayeva, & Colantonio, 2018; Quaglio, Gallucci, Brand, Dawood, & Cobello, 2017).

1.2.2. Accident vasculaire cérébral (AVC)

Selon une revue d'articles parus entre 2013 et 2016, et en se rapportant à la population mondiale standard calculée par l'OMS, l'incidence de l'AVC la plus faible était de 76 pour 100 000 habitants par an en Australie entre 2009 et 2010, et la plus élevée était de 119 pour 100 000 habitants par an en Nouvelle-Zélande entre 2011 et 2012 (Thrift et al., 2017). Chaque année

aux Etats-Unis, 610 000 d'individus subiraient un premier AVC, sa prévalence ayant été estimée en 2014 à 2,7% de la population américaine (Benjamin et al., 2017).

A partir de l'enquête SHARE (*Survey of Health, Aging, and Retirement in Europe* ; en français, « Enquête sur la santé, le vieillissement et la retraite en Europe ») réalisée en 2004-2005 et 2006-2007 à laquelle ont participé plusieurs pays d'Europe, les taux d'incidence des AVC étaient compris entre 2,17% (Espagne) et 4,46% (Danemark), avec une incidence de 2,95% en France (Tsendsuren, Li, & Liu, 2016). Une étude menée à Dijon (France) entre 1985 et 2011 a recensé 4506 patients ayant subi un premier AVC correspondant à près de 3% d'habitants dijonnais, l'incidence de l'AVC ayant fortement augmenté chez les patients de moins de 55 ans entre 1994-2002 et 2003-2011 (Béjot et al., 2014).

1.2.3. Tumeurs cérébrales

L'incidence des tumeurs cérébrales varie d'une étude à l'autre entre 2,0 et 7,1 pour 100 000 habitants par an (Crocetti et al., 2012; Ostrom et al., 2014; Sehmer et al., 2014) avec une mortalité qui décline, notamment grâce aux nouvelles prises en charge chirurgicales (Crocetti et al., 2012; Sitas et al., 2013; Tibæk, Forchhammer, Dehlendorff, Johnsen, & Kammergaard, 2017). Une étude épidémiologique française menée dans le département de la Gironde entre 2000 et 2012 a mis en évidence une incidence des tumeurs affectant le système nerveux central de 19 pour 100 000 habitants par an ; au cours de cette période, l'incidence a augmenté de 2,7%, ce qui pourrait être expliqué par une amélioration du diagnostic mais aussi par un changement des facteurs de risque potentiels, comme l'exposition accrue aux pesticides ou aux champs électromagnétiques (Miranda-Filho, Piñeros, Soerjomataram, Deltour, & Bray, 2017; Philips, Henshaw, Lamburn, & O'Carroll, 2018; Pouchieu et al., 2018).

1.2.4. Maladies infectieuses

Dans les rapports sur les maladies infectieuses du système nerveux central, leur épidémiologie est étudiée selon chaque type de maladie (Tibæk et al., 2017). En effet, concernant la méningite d'origine bactérienne, son incidence était de 0,94 pour 100 000 adultes par an aux Pays-Bas entre 2006 et 2014 (Bijlsma et al., 2016) et de 1,44 pour 100 000 adultes par an en Angleterre et au Pays de Galles entre 2004 et 2011 (Okike et al., 2014). En France métropolitaine, son incidence était de 2,23 pour 100 000 en 2006 (Varon, 2009). Concernant l'encéphalite, une revue de littérature a mis en évidence une incidence de 2,2 pour 100 000 adultes par an dans les pays industrialisés et les pays tropicaux (Jmor, Emsley, Fischer, Solomon, & Lewthwaite, 2008). En France métropolitaine, l'incidence mesurée sur la base du nombre de patients enregistrés entre 2000 et 2002 était de 1,9 pour 100 000 habitants et par an (Mailles, Vaillant, & Stahl, 2007).

1.3. Manifestations cliniques des lésions cérébrales acquises et troubles associés

Les LCA sont à l'origine de plusieurs manifestations cliniques. Au niveau neurologique, on décrit une altération des fonctions vitales (Godbolt et al., 2015), pupillaires (Dimancescu, 2007; Ventura, Balcer, & Galetta, 2014), motrices et sensorielles (Hegde, 2014) et une dégradation de la conscience pouvant aller jusqu'au coma (Giacino, Fins, Laureys, & Schiff, 2014). Dans les cas les plus graves, la sortie du coma évolue vers un état végétatif, chronique (EVC) à partir de 3 mois dans le cas de LCA d'origine non-traumatique et à partir de 12 mois en cas de TC (Multi-Society Task Force on PVS, 1994a, 1994b). L'EVC se caractérise par une réaction d'ordre purement végétatif aux stimulations environnementales, en l'absence de toutes interventions conscientes (Baricich et al., 2017; Giacino et al., 2014; Laureys et al., 2010). Un

autre état neurologique consécutif aux LCA est l'état pauci-relationnel (EPR) ou état minimal de conscience caractérisé par des comportements simples d'adaptation à l'environnement (Georgiopoulos et al., 2010; Giacino et al., 2002; Lancioni et al., 2010).

La diversité des troubles suite à une LCA résulte de sa neuropathologie, des manifestations cliniques et de son épidémiologie (March, Salzberg, & Hopwood, 2013). Cette diversité est également fonction de la sévérité, de la présence de crises de nature épileptique, et notamment de la localisation de la LCA (Rosenberg, Simantov, & Patel, 2007; Whyte, Hart, Laborde, & Rosenthal, 1998). Le niveau de sévérité initial est communément évalué par le niveau de conscience de l'individu (Jain & Iverson, 2018; Teasdale et al., 2014), mesuré grâce à l'échelle de Glasgow (*Glasgow Coma Scale*) (Teasdale & Jennett, 1974). Des déficits typiques apparaissent lorsque la LCA touche une région et/ou un réseau neuronal sous-tendant certaines habiletés de manière spécifique (Rosenberg et al., 2007; Roth & Harvey, 2000), comme le soulignent les modèles anatomo-fonctionnels de la neuropsychologie (Batrancourt et al., 2002; Seron, Baron, & Jeannerod, 1998). Ces troubles peuvent également être modulés par d'autres facteurs, tels que l'âge, la présence de comorbidités et la prise de substances addictives (Dimancescu, 2007).

Les troubles suite à une LCA touchent à la fois le fonctionnement cognitif (Holmqvist, Ivarsson, & Holmefur, 2014; Simblett, Ring, & Bateman, 2017; Watter, Copley, & Finch, 2017) et physique (Biajar, Mollayeva, Sokoloff, & Colantonio, 2017; Mills, McDonnell, Thewlis, & Mackintosh, 2017; Parker et al., 2018), mais aussi le comportement (Beni et al., 2017; Jackson, Turner-Stokes, Murray, & Leese, 2007; Kelly, Brown, Todd, & Kremer, 2008; Martínez-Pernía et al., 2016; Mumford & Wilson, 2009) et l'humeur (Byrne et al., 2017; Spitz, Alway, Gould, & Ponsford, 2017; Yutsis et al., 2012), ce qui contribue à un changement de la personnalité

(Basagni et al., 2015; Beck, Franks, & Hall, 2010; Jacobs, 2014; Owen, Freyenhagen, Martin, & David, 2017; Prigatano, 1992).

Au niveau cognitif, quelle que soit leur étiologie et en fonction de la localisation cérébrale, les LCA sont à l'origine de déficits exécutifs (Clark, Anderson, Nalder, Arshad, & Dawson, 2017; Krasny-Pacini, Chevignard, & Evans, 2014; Lannin et al., 2014), mnésiques (Leśniak, Mazurkiewicz, Iwański, Szutkowska-Hoser, & Seniów, 2018; McDonald et al., 2011; Spreij, Visser-Meily, van Heugten, & Nijboer, 2014), attentionnels (Ricker et al., 2002; Sivan, Neumann, Kent, Stroud, & Bhakta, 2010; Virk, Williams, Brunsdon, Suh, & Morrow, 2015), langagiers et communicationnels (Anderson, Anzalone, Holland, & Tracey, 2011; Lancioni et al., 2010; Thiele, Quinting, & Stenneken, 2016).

Au niveau comportemental, les LCA peuvent être à l'origine d'achats excessifs (Rochat, Beni, Billieux, Annoni, & Linden, 2011), de troubles liés à l'usage de l'alcool (Bombardier, Temkin, Machamer, & Dikmen, 2003; Dikmen, Machamer, Donovan, Winn, & Temkin, 1995; Ponsford, Whelan-Goodinson, & Bahar-Fuchs, 2007; Rist et al., 2010) ou au jeu d'argent (jeu pathologique) (Guercio, Johnson, & Dixon, 2012; Regard, Knoch, Gütling, & Landis, 2003), de modifications du comportement alimentaire (Ciurli, Formisano, Bivona, Cantagallo, & Angelelli, 2011; Rowell & Faruqui, 2010) et du comportement sexuel (Clay, Bloom, & Lambert, 2018; Kelly & Simpson, 2011; Turner, Schöttle, Krueger, & Briken, 2015).

Au niveau thymique, les LCA sont à l'origine de troubles fréquents tels que les troubles anxieux/dépressifs (Hackett, Yapa, Parag, & Anderson, 2005; Longworth, Deakins, Rose, & Gracey, 2018; Whelan-Goodinson, Ponsford, & Schönberger, 2009), ou de troubles bipolaires (Kim & Humaran, 2002; Zwi, McAllister, & Raimo, 1992) et psychotiques (Ardila, 2018; Liao, Wei, & Chen, 2018), moins fréquents.

L'ensemble de ces troubles ont un réel impact sur les activités de la vie quotidienne (Erikson, Karlsson, Borell, & Tham, 2007; Farmer & Eakman, 1995; Lannin et al., 2014; Longworth et al., 2018; Simpson, Sabaz, Daher, Gordon, & Strettles, 2014; Spreij et al., 2014).

1.4. Le handicap « invisible »

Les LCA sont considérées comme des causes majeures de décès et de handicap (Fakhry, Trask, Waller, Watts, & IRTC Neurotrauma Task Force, 2004) et les TC en particulier constituent la première cause de handicap dans le monde (Maas et al., 2017; Quaglio et al., 2017).

En France, « constitue un handicap [...] toute limitation d'activité ou restriction de participation à la vie en société subie dans son environnement par une personne en raison d'une altération substantielle, durable ou définitive d'une ou plusieurs fonctions physiques, sensorielles, mentales, cognitives ou psychiques, d'un polyhandicap ou d'un trouble de santé invalidant » (Article L114 du Code l'action sociale et des familles modifié par la loi n°2005-102 du 11 février 2005). Cette définition légale se réfère à la modélisation de la Classification Internationale du Fonctionnement, du handicap et de la santé (CIF ; Organisation Mondiale de la Santé, 2001) (Barrès, 2010), notamment en prenant en compte le rôle de l'environnement et en adoptant une conception situationnelle du handicap (« être en situation de handicap du fait de certains troubles et en lien avec un contexte social »), s'éloignant des conceptions essentialiste (« être handicapé ») et qualificative (« avoir un handicap ») (Dussart, 2012). La CIF propose en effet un modèle multidimensionnel du handicap et du fonctionnement, reposant sur une interaction dynamique entre plusieurs composantes (voir **Figure III**).

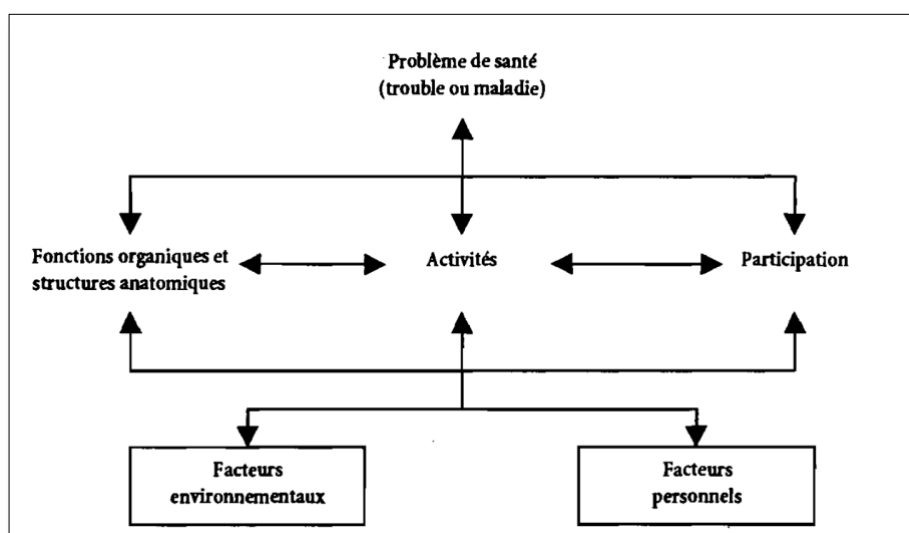


Figure III. Interaction dynamique entre les composantes de la Classification

Internationale du Fonctionnement, du Handicap et de la Santé

(d'après l'Organisation Mondiale de la Santé, 2001).

En prenant en compte la multi-dimensionnalité du handicap, certains changements suite à une LCA, tels que les séquelles cognitives, comportementales et thymiques, ne sont pas immédiatement perceptibles par la société ; on parle alors de handicap « invisible » (Irwin & Fortune, 2014; Jones, Jetten, Haslam, & Williams, 2012; Rutland-Brown, Langlois, Thomas, & Xi, 2006). Du fait de son « invisibilité », les conséquences de ce handicap sur la qualité de vie et sur la réinsertion socio-professionnelle des personnes victimes d'une LCA peuvent être sous-estimées, surtout lorsqu'elles minimisent ou ne divulguent pas leur état de santé (Jones et al., 2012), volontairement ou du fait de l'anosognosie (Long, Rager, & Adams, 2014) ou du déni (Kortte, Wegener, & Chwalisz, 2003). Cela conduit par ailleurs à des difficultés d'accès aux services compétents d'accompagnement vers la réinsertion, notamment lorsque la réinsertion est en outre freinée par une atteinte des compétences sociales (Mahar & Fraser, 2011).

Selon l'épidémiologie des LCA, une partie de la population concernée est dans la tranche d'âge correspondant aux études supérieures (Venville et al., 2016). Leur handicap « invisible » compromet la poursuite de leurs études (Hux et al., 2010; Willmott, Ponsford, Downing, & Carty, 2014) et la probabilité de les réussir se voit réduite (Schutz, Rivers, McNamara, Schutz, & Lobato, 2010). Une trajectoire scolaire perturbée aurait une incidence sur leur emploi, leur projet professionnel et leur situation financière (Mealings, Douglas, & Olver, 2012).

Mais la jeune population n'est pas la seule concernée par la formation professionnelle. En effet, lorsqu'une LCA survient chez des personnes professionnellement actives, les troubles associés à cette LCA peuvent conduire à un besoin de se réorienter afin d'adapter leur travail ou de se former complètement à une autre profession dont l'exercice serait moins impacté par ces troubles (Bade, 2010; Bardenhagen et al., 1999; Grauwmeijer, Heijenbrok-Kal, Haitsma, & Ribbers, 2012; Holzberg, 2001).

Du fait de sa complexité et de sa minimisation, le handicap « invisible » peut constituer un frein, notamment, en matière de réinsertion sociale (Martelli, Zasler, & Tiernan, 2012).

2. La prise en charge et le suivi des personnes cérébrolésées

2.1. Parcours sanitaire et médico-social

L'accompagnement des personnes victimes d'une LCA est particulièrement complexe et s'adapte à leur situation, à la fois sur le plan personnel, familial, relationnel et sociétal. Du fait de sa complexité, il s'appuie sur un parcours de prise en charge et de suivi pluridisciplinaire, mêlant à la fois les milieux sanitaires, médico-sociaux et sociaux.

Lors de la survenue d'un événement neurologique, il est primordial de maintenir les fonctions vitales et de prévenir des lésions secondaires (Pradat-Diehl, 2010). A cet effet, les services et structures à disposition des patients sont le Service d'Aide Médicale Urgente (SAMU), les Structures Mobiles d'Urgences et de Réanimation (SMUR), les services d'Urgences et de

Réanimation en lien avec des services médicaux et chirurgicaux spécialisés. A la sortie de Réanimation, le patient est orienté vers des services d'accueil à savoir des Services de Rééducation Post-Réanimation (SRPR) s'il nécessite une surveillance et des soins médicaux continus ou dans des Unités d'Eveil si son état est stable (Circulaire N°DHOS/SDO/01/DGS/SD5D/DGAS/PHAN/3B/2004/280 du 18 juin 2004). Des hospitalisations et/ou consultations de suivi peuvent ensuite être mises en place dans des services de Médecine Physique et de Réadaptation (MPR), comme par exemple dans les services de Soins de Suite et de Réadaptation (SSR), lesquels ont « pour objet de prévenir ou de réduire les conséquences fonctionnelles, physiques, cognitives, psychologiques ou sociales des déficiences et des limitations de capacité des patients et de promouvoir leur réadaptation et leur réinsertion » (Article R. 6123-118 du Code de la santé publique). Ces services sont en lien ou accueillent des Unités de soins dédiées aux personnes en état végétatif chronique ou en état pauci-relationnel (Circulaire DHOS/02/DGS/SD5D/ DGAS n° 2002-288 du 3 mai 2002).

Pour réintégrer son milieu de vie dans des conditions adaptées, un réseau médico-social de réinsertion spécifique à la cérébrolésion peut s'appuyer sur des offres de consultations de suivi, sur des équipes mobiles d'orientation et d'insertion ou sur un accompagnement associatif (Pradat-Diehl, 2010). La loi n° 2005-102 du 1 février 2005 a créé les Maisons Départementales des Personnes Handicapées (MDPH), qui sont devenues l'interlocuteur principal des structures médico-sociales. En effet, elles décident, par le biais de leur Commission des droits et de l'autonomie des personnes handicapées (CDAPH), des droits de la personne handicapée, tels que la reconnaissance du handicap (Reconnaissance de la Qualité de Travailleur Handicapé, cartes d'invalidité ou de priorité), de la délivrance de la Prestation de Compensation du handicap ou de diverses allocations. Elles sont également décisionnaires en matière d'orientation scolaire ou professionnelle vers des offres de formation ou des services sociaux

et médico-sociaux de réinsertion, tels que les Unités d'Evaluation, de Réentrainement, et d'Orientation Socioprofessionnelle (UEROS ; voir 2.2).

Selon la gravité des séquelles suite à une LCA, l'intégration du milieu de vie peut se faire en hébergement institutionnel. Dans le cas de grande dépendance, les Foyers d'Accueil Médicalisés (FAM) et les Maisons d'Accueil Spécialisées (MAS) proposent des hébergements permanents pour les personnes ayant besoin d'aide pour les actes de la vie quotidienne ou d'un suivi médical régulier (Articles R. 314-140 à R. 314-146, R. 344-1 et R 344.2 du Code de l'action sociale et des familles). Pour les cas moins graves (autrement dit, plus autonomes), le retour à domicile, des hébergements temporaires ou des accueils de jour sont possibles, toujours en lien avec des services d'accompagnement, tels que les réseaux de santé, les Groupes d'Entraide Mutuelle (GEM ; articles L. 114-1-1 et L. 114-3 du Code de l'action sociale et des familles), les Services d'Aide à Domicile (SAD ; articles L. 311-4, L. 311-5, L. 311-5-1, L. 312-1 II ; L. 313-1-2 et L313-1-3 ; L. 313-11-1 du Code de l'action sociale et des familles), les Services d'Accompagnement à la Vie Sociale (SAVS ; articles D. 312-162 à D. 312-165 du Code de l'action sociale et des familles), les Services de Soins Infirmiers A Domicile (SSIAD ; article D. 312-1 du Code de l'action sociale et des familles) ou les Services d'Accompagnement Médico-Social pour Adultes Handicapés (SAMSAH ; articles D. 312-155-9 à D. 312-155-12 du Code de l'action sociale et des familles).

Toujours selon la gravité des séquelles suite à une LCA, l'insertion professionnelle des personnes en situation de handicap peut se faire en milieu ordinaire ou en milieu protégé (Loi n° 2005-102 du 11 février 2005). Le milieu ordinaire comprend les entreprises classiques et les entreprises adaptées, telles que les Centres de distribution de travail à domicile (CDTD ; articles L. 5213-13 à L. 5213-19-1 du Code du travail ; article L. 243-6 du Code de l'action sociale et des familles) adaptés aux personnes en incapacité de se déplacer. Le milieu protégé comprend

des établissements médico-sociaux, tels que les Etablissements et Services d'Aide par le Travail (ESAT ; articles L. 243-4 à L. 243-7, L. 311-4, L. 344-1-1, L. 344-2 à L. 344-7, L. 313-23-1 à L. 313-23-3, R. 344-6 à R. 344-15, R. 314-128 à R. 314-129, D. 313-18 du Code de l'action sociale et des familles) dont les conditions de travail sont adaptées aux personnes porteuses d'un lourd handicap.

Bien que les trajectoires d'accompagnement soient diverses et fonction de chaque cas, elles tendent toutes à faire évoluer les personnes victimes de LCA du milieu hospitalier vers leur milieu de vie, en passant par des structures de réinsertion sociale et professionnelle, lorsqu'elles le nécessitent (voir **Figure IV**).

Le rapport Piveteau intitulé « Zéro sans solution » (Piveteau, 2014), commandé par le Gouvernement, a conduit l'Agence Régionale de Santé à mettre en place le dispositif « une Réponse Accompagnée Pour Tous » (RAPT) sur l'ensemble du territoire, octroyant le droit de demander l'élaboration d'un plan d'accompagnement global et individualisé, tel qu'introduit dans la loi de modernisation de notre système de santé (Loi n° 2016-41 du 26 janvier 2016). Dans la région des Hauts-de-France, plusieurs départements ont adopté ce dispositif, comme le Pas-de-Calais et l'Aisne depuis 2016, ou le Nord, l'Oise et la Somme depuis 2017, selon la fiche action RAPT de l'ARS Hauts-de-France dans le cadre des Contrats Pluriannuels d'Objectifs et de Moyens des Etablissements et Services Médico-Sociaux de 2018. Sa généralisation est intervenue au 1^{er} janvier 2018.

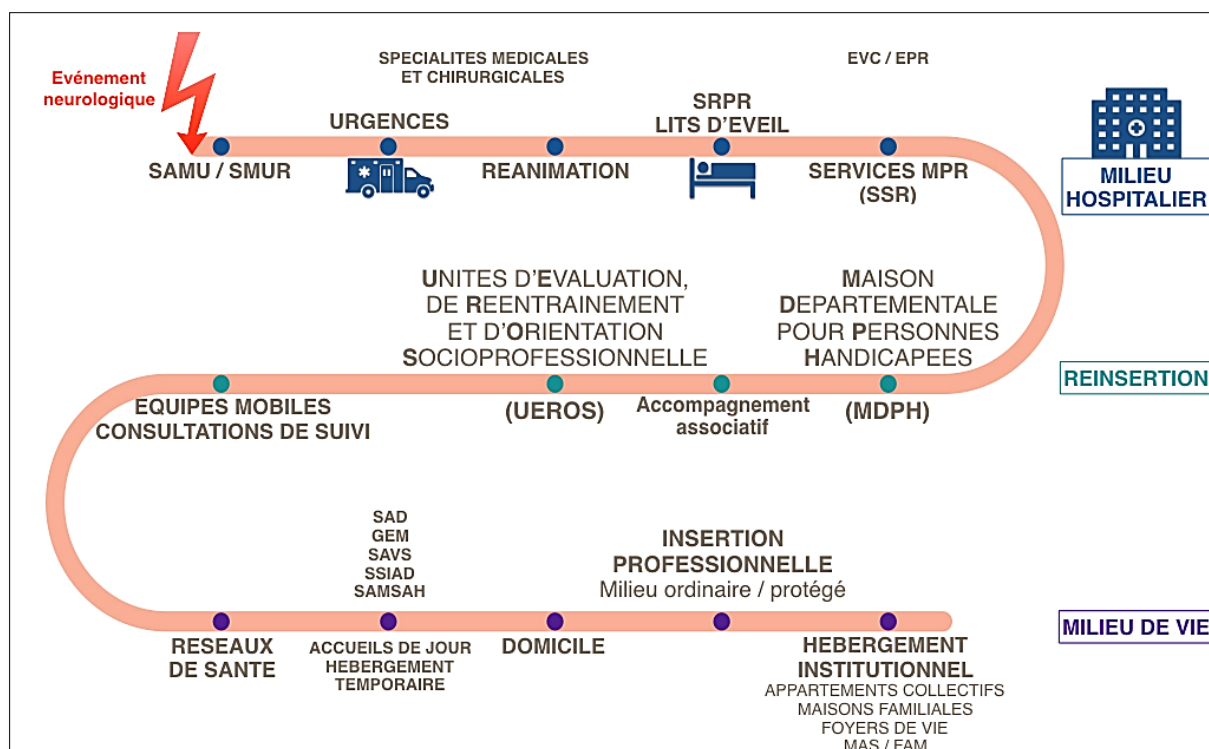


Figure IV. Evolution et structures de prise en charge et d'accompagnement potentielles des personnes victimes d'une lésion cérébrale acquise (d'après Pradat-Diehl, 2010).

EVC / EPR : Unités de soins, dédiées aux personnes en état végétatif chronique ou en état pauci-relationnel ; **FAM** : Foyer d'Accueil Médicalisé ; **GEM** : Groupe d'Entraide Mutuelle ; **MAS** : Maison d'Accueil Spécialisé ; **SAD** : Service d'Aide à Domicile ; **SAMSAH** : Service d'Accompagnement Médico-Social pour Adultes Handicapés ; **SAMU** : Service d'Aide Médicale Urgente ; **SAVS** : Service d'Accompagnement à la Vie Sociale ; **SMUR** : Structures Mobiles d'Urgences et de Réanimation ; **SRPR** : Service de Rééducation Post-Réanimation ; **SSIAD** : Service de Soins Infirmiers A Domicile ; **SSR** : Soins de Suite et de Réadaptation.

2.2. La réhabilitation professionnelle en Unités d'Evaluation, de Réentraînement et d'Orientation Sociale et professionnelle pour personnes cérébrolésées

Pour répondre au besoin des personnes victimes d'une LCA d'être orientées en matière d'insertion socio-professionnelle, les UEROS ont été créées à titre expérimental (Circulaire dite « Bauduret », DAS/DE/DSS n° 96-428 du 4 juillet 1996) puis ont été incluses dans la liste des établissements et services sociaux et médico-sociaux (Article L. 312-1(11°) du Code de l'action sociale et des familles). Dans les années 1990-2000, les UEROS étaient souvent rattachées aux SSR ou aux services de Pré-Orientation des Centres de Rééducation Professionnelle, en fonction de leur implantation régionale, créant des disparités de fonctionnement des UEROS selon les régions.

Elles ont acquis un fonctionnement pérenne, leur organisation et leur fonctionnement étant réglementés par le Décret n° 2009-299 du 17 mars 2009 ; ces unités « accueillent et accompagnent les personnes [...] dont le handicap, lié en tout ou partie à des troubles cognitifs ou des troubles du comportement et de la relation affective, résulte d'un traumatisme crânien ou de toute autre lésion cérébrale acquise. Ces unités contribuent à garantir la continuité de l'accompagnement de ces personnes en assurant les passages, au besoin itératifs, entre le secteur sanitaire, notamment en soins de suite et réadaptation, le secteur médico-social et social, le secteur éducatif et le secteur du travail » (Article D. 312-161-2 du Code de l'action sociale et des familles). Leur mission est « d'accueillir, d'informer ou de conseiller » les personnes victimes d'une LCA quant à leur projet professionnel post-lésion (Article D. 312-161-3 du Code de l'action sociale et des familles).

La Fédération des associations, groupements et établissements pour la réadaptation des personnes en situation de handicap (FAGERH) recense à ce jour 34 UEROS sur l'ensemble du territoire français.

Conformément au Décret n°2009-299, dans un premier temps, les UEROS proposent des entretiens de préadmission afin de déterminer si l'utilisateur peut bénéficier d'un programme de réentraînement. De plus, les UEROS peuvent accueillir les personnes victimes d'une LCA seulement si elles bénéficient d'une RQTH et d'une décision d'orientation UEROS, droits soumis à la décision de la CDAPH (Article R. 241-24 du Code de l'action sociale et des familles) au sein de la MDPH.

En intégrant une UEROS, les usagers sont rémunérés en tant que stagiaires de la formation professionnelle et l'accompagnement par cette structure « ne peut excéder une durée cumulée de six mois par période de trois ans » (Article D. 312-161-3 du Code de l'action sociale et des familles). Cette durée comprend alors (1) une évaluation exhaustive des potentialités et des difficultés de l'utilisateur, effectuée par l'équipe pluridisciplinaire de l'UEROS, à la fois sur le plan médical (évaluation MPR), cognitif (bilan neuropsychologique), comportemental (évaluation psychologique, évaluation de l'autonomie par une ergothérapeute et/ou un éducateur spécialisé), social (diagnostic social), relationnel et affectif (évaluation psychologique) ; (2) un programme de réentraînement visant à améliorer l'autonomie de l'utilisateur, à la fois sur le plan social et des activités de la vie quotidienne, avec la possibilité de mises en situation sur le terrain ; (3) la construction, avec l'utilisateur et son environnement familial / social, d'un projet d'insertion sociale et professionnelle, sur la base de l'évaluation et du programme de réentraînement (Cogné, Wiart, Simion, Dehail, & Mazaux, 2017).

A la fin du stage en UEROS, un suivi du projet d'insertion peut être assuré pendant deux ans par le chargé de mission socio-professionnelle (Article D. 312-161-3 du Code de l'action

sociale et des familles). Ce suivi permet notamment de connaître l'issue d'une formation entamée à la suite du stage en UEROS ou de continuer l'accompagnement si des difficultés d'intégration en milieu professionnel persistent.

3. Problématique

Les personnes atteintes d'une LCA présentent des séquelles cognitives et comportementales, couramment désignées par l'expression handicap « invisible », lesquelles ont un impact sur leur intégration ou réintégration en milieu socio-professionnel. En France, les UEROS accueillent ces personnes afin de les aider dans l'élaboration de leur projet professionnel, en fonction de leurs propres capacités, lesquelles sont évaluées de manière pluridisciplinaire et dans le cadre de mises en situation. Les difficultés que ces personnes rencontrent en milieu professionnel peuvent les conduire à opter pour une réorientation. Cette réorientation se concrétise, notamment, par l'intermédiaire d'une formation qualifiante, laquelle requiert l'efficacité d'un certain nombre de processus cognitifs et comportementaux. La question de la formation se pose notamment compte tenu de l'âge des personnes atteintes d'une LCA, qui sont relativement jeunes. Toutefois, à notre connaissance, l'impact du handicap « invisible » sur l'issue d'une formation qualifiante suite à une LCA n'a jamais été étudié. De plus, dans le cadre de la « réponse accompagnée pour tous », pouvoir conseiller de la manière la plus individualisée possible les personnes souffrant d'une LCA sur leur retour en formation est primordial.

Dans ce contexte, l'objectif de cette recherche était d'identifier des profils cognitivo-comportementaux compatibles ou incompatibles avec un retour en formation au stade séquellaire après une LCA. In fine, cela permettrait d'améliorer les conseils prodigués à cette population clinique en matière d'orientation professionnelle, et de prévenir les ruptures de parcours pouvant être dues à des échecs lors de la reprise d'une formation (Piveteau, 2014).

4. Axes et méthodes de recherche

Dans un premier temps, nous avons cherché à identifier les facteurs cognitivo-comportementaux impliqués dans la réinsertion professionnelle chez des personnes victimes d'une LCA. En menant une revue systématique de la littérature, nous avons cherché à déterminer quelles performances cognitives et comportementales permettaient de prédire l'issue professionnelle dans les phases post-aigües d'un TC, donc à un stade séquellaire, à savoir au moins 12 mois après le TC (Sacco et al., 2016). Les résultats de cette revue de littérature nous ont conduits à une réflexion sur la méthodologie à adopter pour prédire l'issue du retour en formation de personnes victimes d'une LCA (**Partie II**).

Dans un deuxième temps, il nous est apparu nécessaire d'adapter nos outils pour évaluer plus finement les troubles cognitifs et comportementaux des personnes victimes d'une LCA, avant de tester leur pouvoir prédictif. De ce fait, nous avons adapté un outil d'évaluation des processus de consolidation en mémoire verbale et évalué son intérêt chez les personnes souffrant de TC sévère. Nous avons également évalué l'intérêt d'une échelle de fatigue chez les personnes victimes d'une LCA (**Partie III**).

Dans un troisième temps, nous avons étudié le lien entre les performances cognitives et comportementales évaluées à l'entrée en UEROS et la réussite / l'échec d'une formation qualifiante après une LCA. Pour ce faire, nous avons adopté une méthodologie rétrospective et une méthodologie prospective, et avons utilisé une méthode d'analyse des données particulièrement innovante : l'apprentissage automatique (*Machine learning*) (**Partie IV**).

Enfin, l'ensemble des résultats a été discuté au regard de modèles décrits dans la littérature et des perspectives de recherche ont été élaborées (**Partie V**).

PARTIE II :

COGNITION, COMPORTEMENT ET REINSERTION

PROFESSIONNELLE DES PERSONNES CEREBRO-LESEES

Soixante-quinze pour cent des personnes victimes d'une LCA seraient en âge de travailler (Foy, 2014). Pourtant, ces personnes rencontrent des difficultés pour retrouver un emploi (Donker-Cools, Daams, Wind, & Frings-Dresen, 2016; Ketchum et al., 2012; Matérne, Lundqvist, & Strandberg, 2017; Radford et al., 2013; Trygged, Ahacic, & Kåreholt, 2011). En effet, la proportion des personnes employées après une LCA est très variable selon les études, allant de 11 à 85% dans le cas de lésions dues à un AVC (Trygged et al., 2011) et allant de 11 à 82 % dans le cas de lésions dues à une LCA d'origine traumatique (Radford et al., 2013). De plus, une revue systématique de la littérature a montré que, parmi les individus ayant eu un emploi avant leur LCA, seuls 40% avaient retrouvé un emploi dans un délai de deux ans après leur LCA (Frank & Thurgood, 2006).

Ces difficultés sont dues au handicap conséquent à une LCA, qu'il soit physique et/ou « invisible ». En effet, les difficultés cognitives, émotionnelles et comportementales que rencontrent les personnes victimes d'une LCA et qui sont objectivées par les évaluations neuropsychologiques, sont un frein pour retrouver une situation professionnelle stable (Brasure et al., 2013; Donker-Cools et al., 2016; Foy, 2014; Hooson, Coetzer, Stew, & Moore, 2013). Or, retrouver un emploi est une perspective essentielle pour tout individu (Matérne et al., 2017; Murphy et al., 2006).

Dans cette **Partie II**, nous avons cherché à identifier les facteurs cognitivo-comportementaux impliqués dans la réinsertion professionnelle chez des personnes victimes d'une LCA, en se focalisant sur l'étiologie avec la plus grande incidence (TC) et qui toucherait des personnes en âge de travailler. Pour ce faire, nous avons mené une revue systématique de la littérature incluant des personnes atteintes d'un TC en phase post-aigüe, à savoir au moins 12 mois après le TC (Sacco et al., 2016). Les résultats de cette revue de littérature nous ont conduit à nous interroger sur la méthodologie à adopter pour prédire l'issue du retour en formation de personnes victimes d'une LCA.

**1. Article 1 : Impact du fonctionnement cognitif et comportemental sur
l'issue professionnelle après un traumatisme crânien : revue systématique
de la littérature**

Manoli, R., Delecroix, H., Daveluy, W., & Moroni, C. (submitted). Impact of cognitive and behavioral functioning on vocational outcome following traumatic brain injury: A systematic review.

Title: Impact of cognitive and behavioral functioning on vocational outcome following traumatic brain injury: A systematic review

Running head: Cognition, behavior & vocational outcome in TBI

Article category: Review

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Title: Impact of cognitive and behavioral functioning on vocational outcome following traumatic brain injury: A systematic review

ABSTRACT

Purpose: Patients suffering from traumatic brain injury often present injury-related cognitive and behavioral sequelae hindering a successful professional outcome, even many years after injury. The aim of this study was to investigate cognitive and behavioral factors predicting vocational outcome in the post-acute stages of traumatic brain injury (at least one year after injury).

Methods: A systematic review of empirical research about vocational outcome of patients with traumatic brain injury was conducted. Studies published in PubMed and PsycINFO from January 1998 to May 2019 were screened. Only studies using the same injury severity criteria (the Glasgow Coma Scale score and/or the duration of post-traumatic amnesia) were selected.

Results: We found that (1) self-reported symptoms, (2) Functional Independence Measure and Mayo-Portland Adaptability Inventory Scores, (3) alcohol abuse and mood disorders, and (4) Differentiated Outcome Scale Cognitive Scores in patients with traumatic brain injury were highly predictive of the vocational outcome.

Conclusion: This systematic review emphasized the link between cognitive and behavioral functioning and vocational rehabilitation in patients with traumatic brain injury. However, scientific literature lacks cognitive and behavioral models predicting vocational outcome of these patients, including academic or vocational training. Such models would allow clinicians to improve vocational guidance of these patients.

Key words: *Brain Injuries, Traumatic; Cognition; Neuropsychology; Rehabilitation, Vocational; Return to Work; Systematic Review.*

Implications for rehabilitation

- Subjective estimation of traumatic brain injury-related sequelae is associated with vocational outcome
- Cognitive and behavioral assessment is highly important even many years after traumatic brain injury, especially in a social and professional rehabilitation context
- Cognitive and behavioral models are needed to predict vocational outcome and improve vocational guidance.

INTRODUCTION

Traumatic brain injury (TBI) is the main cause of residual disability in young adults [1]. Disability and Health as the “result of a complex relationship between an individual’s health condition and personal factors, and of the external factors that represent the circumstances in which the individual lives” [2]. Disability has a major impact on return to work (RTW), especially in patients with TBI-related cognitive and/or behavioral sequelae [3]. Cognitive sequelae after TBI interfere with patients’ quality of life [4]. Identifying cognitive and behavioral abilities strongly related with vocational outcome might allow professionals to adapt the vocational rehabilitation of these patients, in order to improve their autonomy.

Cognitive and behavioral sequelae following TBI

In at least 50% of patients with a severe TBI, sequelae affect physical, cognitive, affective or/and behavioral spheres [5]. Cognitive and behavioral impairments widely determine the long-term outcome of patients with TBI [6]. Memory impairment [7-8], especially episodic memory, is one of the most frequent cognitive sequelae following TBI. It may include difficulty in working memory [6,9] and in learning new information (anterograde memory impairment) [10]. Impairments of attentional abilities are also very common [7], and may be due to a

slowdown in information processing and cognitive fatigability [6,9-10]. In patients with moderate to severe TBI, the fact that memory and attention deficits are the most frequent deficits is presumed to be due to the irregular bony contours of the skull in the frontal and temporal regions make these cerebral areas more vulnerable [11-12].

From a behavioral perspective, irritability [7,10], impulsiveness [13], disinhibition [10,14] and loss of initiative [10] are the most commonly reported disorders following TBI. Furthermore, patients with TBI are often not fully aware of their own deficits [15-16]. Sleeping disorders associated with depression, anxiety and/or pain [17] occur in 30 to 70% of patients, even in patients with a mild TBI.

Vocational outcome and RTW

Patients with moderate or severe TBI might experience changes in their socio-professional activities [18]. Furthermore, alteration of social behavior could be associated with a decreasing probability of being re-employed after TBI [19].

RTW after TBI can be modulated according to pre-injury social and demographical (i.e. age, education, type of occupation) and post-injury factors (i.e. functional status, presence of comorbidities, delay from injury) [20-21]. Post-injury factors might also include patients' life plan and the kind of professional activity they desire, which could be incompatible with their TBI related disability. Post-injury neuropsychological and cognitive functioning have also been related to vocational outcome in patients with TBI [3]. These relationships have been widely investigated in the literature. However, there is a lack of consensus about post-traumatic characteristics predicting the RTW [22].

How to evaluate the link between post-injury sequelae and professional outcome?

A persistent cognitive impairment many years after a brain injury would be associated with poor long-term professional performance [23]. On the contrary, successfully reemployed patients with TBI appeared to have better scores on cognitive and behavioral functioning than unemployed patients [24]. Several qualitative studies [24, 25] support the necessity of a comprehensive neuropsychological assessment as part of post-injury professional evaluation. Indeed, performance during cognitive tests is directly linked to working world requirements: for instance, attention and memory are greatly involved in most jobs [26]. Neuropsychological assessment could be highly predictive of RTW [9,23,27-30]. From a psychological and behavioral standpoint, emotional and behavioral disorders appear to be key factors to predict an effective professional reintegration and employment stability [25,31].

Current literature evokes links between cognitive/behavioral factors and professional outcome in patients with TBI. However, some of these patients experience serious vocational rehabilitation difficulties even in the post-acute stages, even years after their injury. A cognitive profile could be considered as stable at least 12 months after injury [32]. Hence, which post-injury factors, assessed at least 12 months after injury, would give a significant preview of long-term professional integration? Identifying factors predicting professional / vocational outcome would lead to a refinement of cognitive and behavioral assessment of patients with TBI. For this, we conducted a systematic review of empirical research on vocational outcome in patients with TBI.

METHODS

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement guidelines [24,25] were followed whilst conducting this systematic review.

Protocol and Registration

The protocol for this review was not previously registered.

Eligibility criteria

All studies assessing cognitive, behavioral functioning and vocational outcome of patients with TBI were eligible. Inclusion criteria were: (i) publication date between 1998 and 2018, (ii) written in English or French, (iii) published in a peer-reviewed journal and (iv) conducted in adult population. Studies excluded from this review were: (i) proceedings, (ii) reviews and theoretical papers, (iii) qualitative and case studies, (iv) studies including participants with acquired brain injury without etiological distinction, (v) studies including patients with TBI occurred during childhood, military active duty or sport activity, possibly leading to greater sequelae [33-35].

Information sources and search

A database search was performed in PsycINFO and PubMed. We last run database search on June 10th, 2019.

(“traumatic brain injury” AND “return to work”)

OR (“traumatic brain injury” AND “vocational outcome”)

OR (“traumatic brain injury” AND “vocational training”)

OR (“traumatic brain injury” AND “job training”)

These terms were searched along with the following restriction operators: species – humans; ages > 18 years old; source – peer-reviewed journals; publication dates – 1998/01/01-2019/05/31; languages – English, French.

Study selection

First of all, duplicates papers were removed. Then, papers were screened according to title and abstract. After this screening, a full-text articles assessment of eligibility was conducted (*see Fig.1*). More precisely, we selected studies using the same TBI severity criteria according to the Glasgow Coma Scale (GCS) score cut-off [36] and/or according to the duration of post-traumatic amnesia (PTA) [37]. Thus, a mild TBI was considered if the GCS score was between 13 and 15 and/or the PTA duration was inferior to 24 hours; a moderate TBI if the GCS score was between 9 and 12 and/or the PTA duration between 1 and 7 days; and a severe TBI if the GCS score was between 3 and 8 and/or the PTA duration superior to 7 days. On the contrary, articles were excluded if these severity criteria were not met. Other criteria of exclusion were the lack of a behavioral or cognitive functioning assessment and/or the lack of the vocational outcome and/or a delay of the cognitive or functional assessment inferior to 12 months from the TBI.

Data collection

Data extraction was conducted independently and, for each study, we extracted the following information: (i) name of authors and year of the publication, (ii) size of the sample, (iii) age of participants, (iv) delay between time of injury and behavioral/neuropsychological assessment, (v) tested behavioral/neuropsychological abilities, (vi) vocational outcome, (vii) delay between time of injury and vocational outcome assessment, (viii) predictors of vocational outcome, and (ix) statistics.

RESULTS

Fifteen studies were selected for this systematic review (see **Fig.1**).

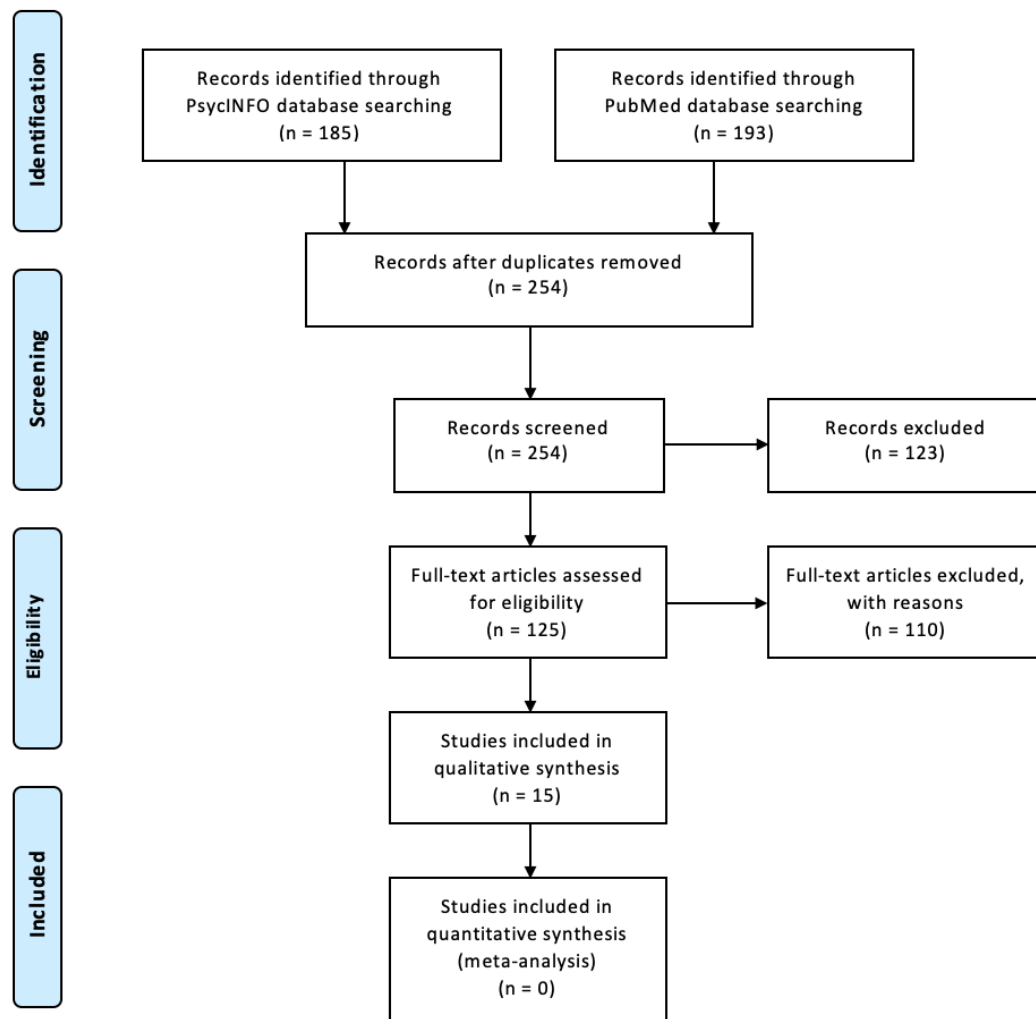


Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram of scientific papers selection.

Screening: Papers were screened on the basis of their title and abstract; we excluded proceedings, review and theoretical papers, qualitative and case studies, studies including participants with acquired brain injury without etiological distinction, studies including patients with a TBI occurred during childhood, military active duty or during sports. Eligibility: Articles were excluded after full-text assessment if severity criteria were not met, if neuropsychological functioning and/or vocational outcome was not evaluated and if patients were assessed during the first year after injury.

We identified six studies conducted in patients with all TBI severities combined (**Table 1**). Three studies showed a link between vocational outcome and mental health conditions. Indeed, alcohol abuse associated or not to another dependence and mood disorders appeared to be good predictors of a poor vocational outcome at one-year-follow-up [40]. From one to three post-injury years, self-reported cognitive and behavioral difficulties as well as self-reported anxiety and depression scores accurately differentiated patients who remained employed to those who did not [41]. Five years after injury, employment status was related to the Hospital Anxiety and Depression score [42]. Another factor related to vocational outcome and found in four studies was cognitive abilities. Indeed, two years after TBI, the scores on “Cognitive Impairment” and “Metacognition” items from the Neurobehavioral Rating Scale – Revised [43,44] could differentiate between employed and not employed patients [42]. Also at 2 years post-injury, RTW evaluated with a 5-point rating scale was predicted by cognitive and motor scores of the Functional Independence Measure [45,46]. According to Franulic et al. [42], the Neurobehavioral Rating Scale – Revised total score, and the scores on the “cognitive impairment” and “metacognition” factors from the Neurobehavioral Rating Scale – Revised were related to employment.

In addition to mental health and cognitive factors, communication skills and functional outcome were also found to be related to vocational outcome. At least 2 years after injury, the total score of the “La Trobe Communication Questionnaire” [47] was also found to be related to employment status, i.e. patients in the employed group and their relatives reported less frequent difficulties than those in the unemployed group [48]. After a mean delay of 10 years (follow-up between 6 and 15 years), RTW categorized as full, part-time or not productive, was predicted by scores to the Mayo-Portland Adaptability Inventory – 4th version [49], with lower scores predicting better outcome [50].

Table 1. Selected studies (N=6) in participants with mild, moderate and severe traumatic brain injury, without injury severity distinction.

Reference	Sample size	Age (years) Mean (SD)	Post-injury assessment delay after TBI mean(SD)	Independent variables	Vocational outcome	Vocational outcome assessment delay	Predictors of RTW	Statistics
[40]	158	> 18	1 year	Alcohol abuse and/or dependence Mood disorders SFE	RTW (Yes/No)	1 year	Age GCS SFE Alcohol abuse/dependence Mood disorders	Whole model: log likelihood, $\chi^2_6=19.2$, $p=.004$ Wald $\chi^2_1=4.9$, $p=.03$ Wald $\chi^2_1=4.9$, $p=.03$
[41]	236	34.2(13.65) 18-77	1 year	Structured Outcome Questionnaire	Remain employed for all 3 years (Yes/No)	1-3 years	Level of mobility Independence in driving <u>Self-reported cognitive difficulties</u> Memory Planning Speed of thinking <u>Self-reported behavioral difficulties</u> Lack of initiative Self-centeredness Inappropriate behavior Self-reported anxiety Self-reported depression	$\chi^2_{1,231}=44.5$, $p<0.001$ $\chi^2_{1,202}=13.48$, $p<0.001$ $\chi^2_{1,234}=8.59$, $p=0.003$ $\chi^2_{1,234}=13.49$, $p<0.001$ $\chi^2_{1,233}=7.11$, $p=0.01$ $\chi^2_{1,233}=7.65$, $p=0.01$ $\chi^2_{1,233}=7.63$, $p=0.01$ $\chi^2_{1,232}=5.59$, $p=0.02$ $\chi^2_{1,232}=8.35$, $p=0.004$ $\chi^2_{1,231}=4.11$, $p=0.04$
[42]	38 32	EMP 37.3 UNEMP 40.9	2 years	HADS NRS-R	EMP vs UNEMP	2 years	HADS Anxiety score HADS Depression score NSR-R total NSR-R Factor I Cognitive impairment NSR-R Factor II Emotional control NSR-R Factor III Metacognition NSR-R Factor IV Negative affectivity	EMP vs UNEMP <i>ns</i> EMP vs UNEMP <i>ns</i> EMP vs UNEMP <i>ns</i> EMP < UNEMP $p<0.05$ EMP vs UNEMP <i>ns</i> EMP < UNEMP $p<0.05$ EMP vs UNEMP <i>ns</i>

EMP: patients who returned to and maintained employment; **GCS:** Glasgow Coma Scale; **HADS:** Hospital Anxiety and Depression Scale; **NRS-R:** Neurobehavioral Rating Scale – Revised; **SFE:** Social Functioning Examination; **TBI:** traumatic brain injury; **RTW:** return to work; **UNEMP:** patients who did not return to and maintain employment.

Table 1. Continues

Reference	Sample size	Age (years) Mean (SD)	Post-injury assessment delay after TBI mean(SD)	Independent variables	Vocational outcome	Vocational outcome assessment delay	Predictors of RTW	Statistics
[42]	40 32	EMP 40.5 UNEMP 43.4	5 years	HADS NRS-R	EMP vs UNEMP	5 years	HADS Anxiety score HADS Depression score NSR-R total NSR-R Factor I Cognitive impairment NSR-R Factor II Emotional control NSR-R Factor III Metacognition NSR-R Factor IV Negative affectivity	EMP vs UNEMP <i>ns</i> EMP < UNEMP $p \leq 0.05$ EMP < UNEMP $p \leq 0.05$ EMP < UNEMP $p < 0.05$ EMP < UNEMP $p < 0.05$ EMP < UNEMP $p < 0.05$ EMP vs UNEMP <i>ns</i>
	40 18	EMP 36.3 UNEMP 39.3	10 years			10 years	HADS Anxiety score HADS Depression score NSR-R total NSR-R Factor I Cognitive impairment NSR-R Factor II Emotional control NSR-R Factor III Metacognition NSR-R Factor IV Negative affectivity	EMP < UNEMP $p \leq 0.05$ EMP vs UNEMP <i>ns</i> EMP < UNEMP $p \leq 0.05$ EMP < UNEMP $p < 0.05$ EMP vs UNEMP <i>ns</i> EMP < UNEMP $p < 0.05$ EMP vs UNEMP <i>ns</i>
[46]	79	39(16)	24.5(2.6) months	FIM	RTW scale	2 years	FIM cognitive FIM motor	$\beta = 2.695$; correctly classified 63%; significance of predictor 0.0001 $\beta = 3.435$; correctly classified 63%; significance of predictor 0.0003
[48]	46	EMP 36.74 (7.63) UNEMP 40.00 (13.99)	≥ 2 years	LCQ	EMP vs UNEMP	≥ 2 years	LCQ total score	EMP vs UNEMP $t = 1.74$; $p = 0.045$, one-tailed test; $d = 0.52$
[50]	74	43(13) Range 19-64	10 years (6 to 15)	MPAI-4	Fully, partly, not productive	10 years (6 to 15)	Lower scores on MPAI-4 predicted better outcome	OR=1.25, CI (1.07,1.46), $p < .01$

EMP: patients who returned to and maintained employment; **FIM:** Functional Independence Measure; **HADS:** Hospital Anxiety and Depression Scale; **LCQ:** La Trobe Communication Questionnaire; **MPAI-4:** Mayo-Portland Adaptability Inventory, 4th version; **NRS-R:** Neurobehavioral Rating Scale – Revised; **ns:** not significant; **RTW:** return to work; **TBI:** traumatic brain injury; **UNEMP:** patients who did not return to and maintain employment.

In patients with **mild TBI** (*Table 2*), the RTW was associated with two factors: (i) the presence of a chronic post-concussion syndrome encompassing TBI-related symptoms (as headaches, sleep disturbance) lasting at least one year post-TBI [38] and (ii) the number of affective and cognitive self-reported symptoms during a temporal window from 12 to 36 months after the injury [39]. The affective self-reported symptoms were changes in personality, restlessness, nervousness, irritability and feelings of frustration or impatience. The cognitive self-reported symptoms were a slowdown of their reaction times, mental fatigue, memory problems or forgetfulness, poor concentration and trouble thinking.

In patients with **moderate-to-severe TBI** (GCS 3-12 and/or PTA duration ≥ 24 hours; *Table 3*), the personal estimation in percentage of the extent of their recovery (the pre-injury level corresponding to 100%) and the psychosocial functioning score on the Sickness Impact Profile [51] were related to RTW at a follow-up between 2 and 5 years after injury [52]. Between 2 and years post-injury, subjective behavior, anger and affect were also related to complete vs incomplete RTW [53].

Table 2. Selected studies (N=2) in participants with mild traumatic brain injury (GCS score 13-15 and/or PTA duration <24 hours).

Reference	Sample size	Age (years) Mean (SD)	Post-injury assessment delay after TBI mean(SD)	Independent variables	Vocational outcome	Vocational outcome assessment delay	Predictors of RTW	Statistics
[38]	42	34.4 (15.5) Range 18-64	15 months	PCL	RTW	15 months	Presence (+) / absence (-) of chronic PCS	PCS+ vs PCS- $p<0.001$
[39]	85	Range 15-65	12 to 36 months	MTBI Follow-up Questionnaire, developed after the RHFUQ	RTW (Yes/No)	12 to 36 months	Total number of symptoms reported <u>Affective symptoms</u> Changes in personality Restlessness Nervousness – anxiety/stress Emotional – sensitivity Irritability – easily angered Feelings of depression or tearfulness Feelings of frustration or impatience <u>Cognitive symptoms</u> Slow reactions Mental fatigue Memory problems, forgetfulness Poor concentration Trouble thinking	$b=-0.17, s=0.04, p<0.001, exp(B)=0.84$ <u>RTW vs no RTW</u> $\chi^2 = 6.85, p<0.01$ $\chi^2 = 7.16, p<0.01$ $\chi^2 = 7.31, p<0.01$ $\chi^2 = 12.29, p<0.001$ $\chi^2 = 14.27, p<0.001$ $\chi^2 = 2.99, NS$ $\chi^2 = 18.98, p<0.001$ $\chi^2 = 5.75, p<0.05$ $\chi^2 = 15.33, p<0.001$ $\chi^2 = 10.05, p<0.01$ $\chi^2 = 14.27, p<0.001$ $\chi^2 = 12.24, p<0.001$

GCS: Glasgow Coma Scale; **MTBI:** mild traumatic brain injury; **PCL:** Problem Checklist (New York Head Injury Family Interview); **PCS:** Post-Concussion Syndrome; **PTA:** post-traumatic amnesia; **RHFUQ:** Rivermead Head Injury Follow-up Questionnaire; **RTW:** Return to Work; **TBI:** traumatic brain injury.

Table 3. Selected studies (N=2) in participants with moderate to severe traumatic brain injury (GCS score 3-12 and/or PTA duration ≥ 24 hours).

Reference	Sample size	Age (years) Mean (SD)	Post-injury assessment delay after TBI mean(SD)	Independent variables	Vocational outcome	Vocational outcome assessment delay	Predictors of RTW	Statistics
[52]	51	32.2(12.0) Range 15-59	40.6(12) months 25-66 months	Executive Route-Finding Task GOS-E DOS PoR SIP	RTW Former work resumed vs not resumed	2-5 years	PoR SIP	In patients <u>with</u> focal frontal pathology on neuroimaging in the first 6 months post-injury PoR, RTW: $r_s=-0.31$, <i>ns</i> SIP, RTW: $r_s=0.53$, $p<0.05$
								In patients <u>without</u> focal frontal pathology on neuroimaging in the first 6 months post-injury PoR, RTW: $r_s=-0.83$, $p<0.01$ SIP, RTW: $r_s=0.74$, $p<0.01$
[53]	186	14-81	2-16 years	Questions about changes in behavior and affect DOS	RTW complete vs uncomplete	2-16 years	Subjective behavior Subjective anger Subjective affect	$r_s=0.34$, $p<0.01$ $r_s=0.24$, $p<0.01$ $r_s=0.41$, $p<0.01$

DOS: Differential Outcome Scale; **GCS:** Glasgow Coma Scale; **GOS-E:** Glasgow Outcome Scale – Extended; **ns:** not significant; **PoR:** subjective percentage of recovery; **PTA:** post-traumatic amnesia; **RTW:** return to work; **SIP:** Sickness Impact Profile; **TBI:** traumatic brain injury.

In patients with **severe TBI** (*Table 4*), two studies highlighted that functional outcome was a good predictor of vocational outcome. According to Benedictus, Spikman, & van der Naalt [54], RTW was predicted by the Differentiated Outcome Scale [55] assessed one year after TBI. The Differentiated Outcome Scale allows outcome evaluation in social, behavioral, cognitive and physical domains with a five-point scale, from persistent vegetative state (1) to complete recovery (5). Here precisely, the RTW was predicted by scores on the cognitive subscale. At the same delay after injury, Jourdan et al. [56] found that scores on the Glasgow Outcome Scale – Extended [57] differentiated patients who returned to work and those who did not. Assessment at one year post-TBI of both Glasgow Outcome Scale – Extended and the total score on the Dysexecutive Questionnaire completed by a close relative allowed authors to distinguish between employed and unemployed patients at a four-year follow-up [58].

After a mean delay of 18 months (17.8 ± 5.7), personality changes, PTA duration [37] and physical role functioning domain scores on the Medical Outcomes Study 36-item Short-Form Health Survey [59] predicted RTW [60]. Another factor related to vocational outcome in patients with severe TBI was executive dysfunction. At a mean delay of 4 years after injury (*range 40-60 months*), total score to the Dysexecutive Questionnaire [61] completed by the patients correlated with elementary and extended activities of daily living (Barthel Index) [62] and differentiated between patients who returned to work to those who did not [63].

Table 4. Selected studies (N=5) in participants with severe traumatic brain injury (GCS score 3-8 and/or PTA duration > 7 days).

Reference	Sample size	Age (years) Mean (SD)	Post-injury assessment delay after TBI mean(SD)	Independent variables	Vocational outcome	Vocational outcome assessment delay	Predictors of RTW	Statistics
[54]	156	32.8(16.2)	12 months	GOS-E DOS	RTW (Yes/No)	12 months	DOS – Physical DOS – Cognitive DOS – Behavioral	OR=1.172; CI, 0.52-2.66; <i>p</i> =0.705 OR=8.440; CI, 3.17-22.46; <i>p</i>=0.000 OR=1.423; CI, 0.59-3.45; <i>p</i> =0.435
[56]	134	> 18	Med 14.3 months	DEX-R GOS-E	RTW (Yes/No)	1 year	DEX-R GOS-E	<i>p</i> =0.3 <i>p</i>=0.0001
[58]	133	34 (10.8)*	1 year	GOS-E DEX-R	RTW (Yes/No)	4 years	GOS-E DEX-R	OR=-1.7; 95%CI[2.1;-1.3]; <i>p</i>>0.001 OR=9.3; 95%CI[3.5;15.1]; <i>p</i>=0.01
[60]	43	≥ 18 years	17.8(5.7) months	PTA General medical condition SF-36 SCID-I HADS	RTW (Yes/No)	18 months	HADS Depressive disorder Personality changes Anxiety disorder Alcohol/drug dependence PTA SF-36 Physical SF-36 Physical Role SF-36 Bodily Pain	<i>p</i> =0.87 OR=1.30; 95%CI, 0.3-3.6; <i>p</i> =0.96 OR=17.60; 95%CI, 3.6-87.1; <i>p</i>=0.0001 OR=2.61; 95%CI, 0.6-11.7; <i>p</i> =0.21 OR=0.50; 95%CI, 0.1-2.8; <i>p</i> =0.43 OR=6; 95%CI, 1.50-24.0; <i>p</i>=0.01 OR=2.2; 95%CI, 0.5-9.4; <i>p</i> =0.29 OR=4.75; 95%CI, 1.2-18.4; <i>p</i>=0.02 OR=2.2; 95%CI, 0.5-9.4; <i>p</i> =0.29
[63]	147	32.5(14.2)	50.9(6.4) months 40-67 months	GOS-E NRS-R HADS DEX	ADL (Barthel Index)	4 years	Mean DEX score	DEX, Elementary ADL <i>r</i> _s = -0.23, <i>p</i>=0.013
					RTW (Yes/No)			DEX, Extended ADL <i>r</i> _s = -0.49, <i>p</i><0.0001 RTW > no RTW, <i>p</i><0.02

ADL: activities of daily living; **DEX-R:** Dysexecutive Questionnaire completed by a close relative; **DOS:** Differentiated Outcome Scale; **GCS:** Glasgow Coma Scale; **GOS-E:** Glasgow Outcome Scale – Extended; **HADS:** Hospital Anxiety and Depression Scale; **Med:** median; **NRS-R:** Neurobehavioral Rating Scale – Revised; **PTA:** post-traumatic amnesia; **RTW:** return to work; **SCID-I:** Structured Clinical Interview for DSM-IV Axis I Disorders; **SF-36:** Medical Outcomes Study 36-item Short-Form Health Survey.

* At the four-year assessment.

DISCUSSION

This review highlighted specific factors related to and predicting vocational outcome, according to the injury severity, at post-acute stages of TBI, when patients' cognitive and behavioral functioning is considered stable [32]. We selected 15 studies including a neuropsychological / behavioral assessment of patients with TBI which was administered at least 12 months post-injury. From these studies, several factors have been identified as being related to vocational outcome after TBI and these factors included cognitive as well as emotional functioning. The strongest predictor of vocational outcome found in this systematic review was the Mayo-Portland Adaptability Inventory (4th version) scores assessed after a mean delay of 10 years after TBI; these scores were indeed associated with small confidence intervals, indicating a high precision of the odds ratios [64]. In patients with mild and moderate-to-severe TBI, several self-reported symptoms were found to be associated with RTW. In patients with severe TBI, RTW appeared to be predicted by functional outcome measures as well as executive functioning.

These results highlight the impact of cognitive and behavioral factors on vocational outcome in patients with TBI. However, most of the variables found to be related to vocational outcome were self-reported measures. There were very few studies that directly measure the cognitive and emotional functioning after a minimal delay of 12 months from injury and relying on self-reported measures could bias research studies since it was found that self-awareness and depression could have an impact on self-reported measures [65] and that self-reported post-concussion symptoms could increase when patients with TBI have fewer family resources and are young [66].

Database search using the terms “traumatic brain injury” AND “vocational training” AND “traumatic brain injury” AND “job training” identified only 9 studies [67-75]. These studies were not included in our final sample because of the missing injury severity scores and the lack of exploration of the link between post-injury factors and professional training. Thus, it appears

that the impact of cognitive and behavioral sequelae on vocational or academic training has apparently never been studied; yet, this issue is of major importance. Indeed, in 2013 in the United States, 1,080.7 per 100,000 population among individuals between 15 and 24 years old suffered from a TBI [76], and these individuals would want or need to resume vocational training or academic education [77].

Nevertheless, some limitations to this systematic review could be considered. Our selection of studies was limited to the most used injury severity criteria, i.e. the GCS and duration of PTA scores. Yet, different measures defining injury severity had been identified in a meta-analysis: PTA, disability rating scale, GCS, duration of inpatient hospital stay, orientation, abbreviated injury scale, Injury Severity Score (ISS), revised trauma score, and the trauma score-ISS [78]. When comparing different injury severity measures, ISS has been identified as the best measure to predict RTW in patients with TBI [79], however it is rarely used in scientific papers (59 studies found through database search of “injury severity score (ISS)” in PsycINFO on September 17th 2018, including studies published between January 1998 and August 2018 vs 115 studies using the duration of PTA (search of “amnesia (PTA)”) and 293 using the GCS score (search of “Glasgow coma scale (GCS)”). Finally, even if injury related measures are often a good indicator of vocational outcome, these measures are often missing from patients’ medical files examined in retrospective studies, even more when their professional integration takes several years after injury. Another limitation is the heterogeneity of selected studies. Indeed, different cognitive and behavioral variables were investigated, at different delays after injury, and their impact on vocational outcome was also assessed at different follow-ups. Even vocational outcome variable was operationalized in various ways across studies, one using a 5-point RTW rating scale, others using variables dichotomized in different ways, as employed vs unemployed, return to previous work (yes vs no), complete vs incomplete employment, or employment maintained during a precise period (yes vs no). Therefore, comparisons between

studies were not relevant. The type of professional career or intensity of job/vocation was not tested as a factor in these studies. This would likely drive what variables would be most important, as higher level positions may rely more on cognitive functioning whereas outcomes in lower level positions may be predicted by other variables. Most of the selected studies had assessed all the variables with the same delay after injury. Thus, relationships between independent variables and professional outcome might be bi-directional. Indeed, we could suppose that having difficulties in returning to work could influence patients' mood or behavior [80], which could influence cognitive functioning [81]. Yet, the effect of professional integration on cognitive and behavioral functioning has not been investigated in these studies. Notwithstanding these limitations, our results are consistent with the assumption that cognitive factors are highly predictive of vocational outcome in patients with TBI [81]. This should be investigated with objective measures, as scores from neuropsychological batteries, which implicate a specialized evaluation of cognitive functions, identifying the nature of the cognitive deficit. Shedding light on specific impairment is necessary when patients must develop a conceivable plan of professional rehabilitation. It also allows clinicians to propose adequate compensatory strategies.

CONCLUSION

This systematic review highlighted the interest in using an integrative approach for the assessment of patients with TBI during their vocational rehabilitation, including an integrative evaluation based on cognitive, psychological, behavioral and functional assessment.

It also underlined a gap in literature regarding the return to an academic or vocational training of patients with TBI, whereas they are often young and some of them might be in a training course at the time of the brain injury.

Future studies should focus on cognitive/behavioral factors and their predictive power of vocational outcome within specific rehabilitation units, so clinicians could rely on specific factors to improve vocational guidance of patients with TBI. A clear distinction should be made, in terms of vocational outcome, between RTW, vocational / academic training, and return to school, as these different occupations may require different cognitive / behavioral profiles.

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2. Comment prédire le retour en formation des personnes avec lésion cérébrale acquise ?

2.1. *Evaluation neuropsychologique et comportementale*

Notre revue systématique de la littérature (**Article 1**) a mis en évidence plusieurs facteurs en lien avec la reprise d'une activité professionnelle de personnes atteintes d'un TC, incluant à la fois la présence de troubles liés à l'usage de l'alcool et de l'humeur, le nombre de symptômes auto-rapportés, une hétéro-évaluation de la récupération post-lésionnelle (*Differentiated Outcome Scale*), et une auto-évaluation de l'adaptabilité (*Mayo-Portland Adaptability Inventory*) et du fonctionnement (*Functional Independence Measure*). Toutefois, dans cette revue, seules 14 études ont été recensées incluant des personnes à distance de leur TC, à savoir avec au moins 12 mois d'intervalle depuis l'accident. Dans la mesure où les déficits cognitifs et comportementaux (Bales, Wagner, Kline, & Dixon, 2009; Klein, Houx, & Jolles, 1996; Velikonja, Warriner, & Brum, 2010) ainsi que les difficultés d'insertion professionnelle (Fleming, Tooth, Hassell, & Chan, 1999; Hillier, Sharpe, & Metzger, 1997; Olver, Ponsford, & Curran, 1996; Schalén, Nordström, & Nordström, 1994) persistent au-delà de la période aiguë, il était primordial d'étudier l'impact de ces déficits sur l'insertion professionnelle à distance de la LCA.

Afin de couvrir l'ensemble des déficits qui pourraient empêcher une insertion professionnelle réussie, le profil cognitif et comportemental des personnes victimes d'une LCA doit être analysé de manière exhaustive. De ce fait, cette analyse doit couvrir différentes fonctions cognitives, comme la cognition sociale (Cattran, Oddy, Ramos, Goodson, & Wood, 2018; Ubukata et al., 2014), les capacités visuo-instrumentales (Vries et al., 2018), les fonctions mnésiques (Lindeløv, Overgaard, & Overgaard, 2017; Whyte, Skidmore, Aizenstein, Ricker, & Butters, 2011), exécutives (Coetzer, Stein, & Toit, 2001; Owen, Freyenhagen, Martin, &

David, 2017) et attentionnelles (Markovic et al., 2018), ainsi que la fatigabilité (Jonasson, Levin, Renfors, Strandberg, & Johansson, 2018; Mollayeva et al., 2014), et les changements comportementaux (Jonker, Weeda, Rauwerda, & Scherder, 2019), identifiés dans la littérature comme étant des domaines particulièrement sensibles aux LCA.

En étudiant le lien entre une évaluation exhaustive des fonctions cognitives et comportementales des personnes victimes d'une LCA et leur issue professionnelle post-LCA, nous pourrions identifier les facteurs cognitifs et comportementaux les plus pertinents pour prédire l'issue professionnelle, et plus particulièrement l'issue d'une reprise de formation, laquelle n'est pas encore ou est très peu étudiée dans la littérature.

2.2. Nouvelle méthode d'analyse des données : l'apprentissage automatique

L'évaluation exhaustive des fonctions cognitives et comportementales suppose le recueil d'un grand nombre de données (*big data*), sachant que plusieurs tests sont requis pour les différentes fonctions (par exemple, la mémoire) et les différents sous-domaines d'une fonction (par exemple, la mémoire de travail, la mémoire épisodique, etc.), et que la passation de chaque test implique le recueil de plusieurs mesures (par exemple, temps de réalisation, scores totaux, indices, etc.). Pour analyser les liens prédictifs entre ces données et les données binaires concernant l'issue de la formation (réussite / échec) après une LCA, une méthode particulièrement innovante en neuropsychologie apparaît adéquate : l'apprentissage automatique (*machine learning*). Il s'agit d'une sous-discipline de l'intelligence artificielle consacrée à l'analyse de grands ensembles complexes de données (Mitchell, 1997) dont l'objectif principal est de faire des prédictions (Schütze et al., 2018).

L'apprentissage automatique peut être de deux types, à savoir non-supervisé ou supervisé (Zhao & Liu, 2007). L'apprentissage non-supervisé (*unsupervised learning*) extrait des inférences à partir de données constituées de variables indépendantes, sans définir des variables dépendantes. Dans ce cas, la technique la plus utilisée est le « regroupement » (*clustering*), utilisée pour l'analyse exploratoire des données afin d'identifier des patterns au sein des données (MathWorks®, 2016). L'apprentissage supervisé (*supervised learning*) permet, grâce à des méthodes computationnelles, d'extraire l'information contenue dans un grand volume de données de manière automatique et donc d'« apprendre » (*learn*) à partir d'un échantillon d'apprentissage dont la variable dépendante est connue. Cet apprentissage aboutit à l'élaboration de modèles permettant de prédire la variable dépendante dans un nouvel échantillon de données (Balcázar, Bonchi, Gionis, & Sebag, 2010; MathWorks®, 2016; Mitchell, 1997). Le choix des algorithmes d'apprentissage supervisé dépend du type de données à prédire : des algorithmes de classification sont utilisés dans le cas de variables discrètes et des algorithmes de régression sont utilisés dans le cas de variables continues (MathWorks®, 2016) (voir **Figure V**).

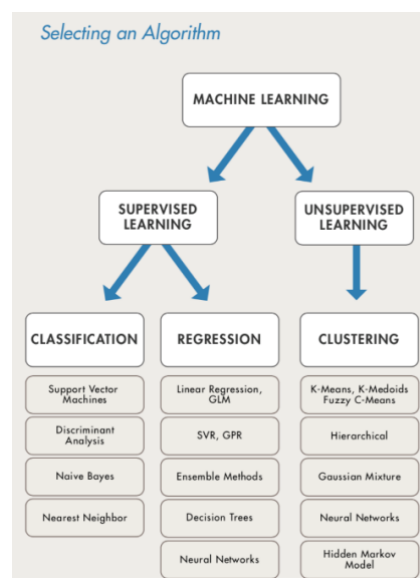


Figure V. Sélection des algorithmes d'apprentissage automatique

(d'après MathWorks®, 2016).

L'apprentissage automatique supervisé permettrait ainsi d'identifier des liens prédictifs entre les données cognitives et comportementales et les données binaires concernant l'issue de la formation (réussite / échec) après une LCA.

3. Discussion

Dans cette **Partie II**, nous avons identifié, au sein de la littérature scientifique actuelle, les facteurs cognitifs et comportementaux évalués à distance d'une LCA et qui sont liés à l'issue professionnelle de personnes victimes d'une LCA.

La revue systématique de la littérature nous a permis de souligner le manque d'études investiguant d'autres types d'issues professionnelles, comme l'issue d'une formation professionnelle qualifiante entamée à la suite d'une LCA, et l'impact que les déficits post-LCA auraient sur ces issues. Une évaluation exhaustive des fonctions cognitives et comportementales, adaptée aux personnes souffrant d'une LCA, nous a semblé pertinente. Cette évaluation implique une analyse de données de grande dimension, particulièrement innovante en neuropsychologie, et qui permet d'identifier des modèles prédictifs : l'apprentissage automatique (*machine learning*). L'utilisation de cette technique apparaît, pour le moment, limitée à la détection et au diagnostic de pathologies (Bakator & Radosav, 2018; Sajda, 2006) et son utilisation en neuropsychologie est relativement restreinte aux maladies neurodégénératives, comme la Maladie d'Alzheimer (Battista, Salvatore, & Castiglioni, 2017; Grassi et al., 2019).

Il s'agira, dans la Partie III, d'identifier le type d'adaptation et d'outils que l'évaluation exhaustive des fonctions cognitives et comportementales requiert, avant d'étudier l'impact de ces fonctions sur l'issue en formation de personnes victimes d'une LCA (**Partie IV**).

PARTIE III :

ADAPATATION DES OUTILS POUR UNE EVALUATION

PLUS FINE DES TROUBLES COGNITIFS ET

COMPORTEMENTAUX DES PERSONNES

CEREBROLESEES

Dans les **Parties I et II**, nous avons vu que les personnes souffrant d'une LCA présentent des troubles affectant à la fois les sphères cognitive, physique et comportementale. Au niveau cognitif, quelle que soit leur étiologie, les LCA sont souvent à l'origine de déficits mnésiques (**Partie I ; Partie II, Article 1**) et de plaintes de la part des patients concernant leur niveau de fatigue, les deux étant en lien avec le retour à l'emploi (**Partie II, Article 1**).

Dans la littérature scientifique, les plaintes mnésiques des patients souffrant d'une LCA ne sont pas toujours objectivées par des mesures neuropsychologiques (Aben et al., 2011; Byrne, Coetzer, & Addy, 2017). Concernant l'évaluation de la fatigue, de nombreux outils existent, mais très peu sont validés en Français (Debouverie, Pittion-Vouyovitch, Louis, & Guillemin, 2007; Gentile, Delarozière, Favre, Sambuc, & San Marco, 2003) et/ou testés chez les personnes souffrant d'une LCA (Malley, 2017).

Dans cette **Partie III**, nous avons cherché à identifier les outils permettant d'évaluer l'ensemble des processus déficitaires de la mémoire verbale et le niveau de fatigue liés à la survenue d'une LCA. Pour ce faire, nous avons, d'une part, adapté un test neuropsychologique évaluant la mémoire épisodique verbale et testé son utilité chez les patients souffrant d'un TC sévère, et d'autre part, testé la sensibilité d'une échelle de fatigue dans une population souffrant d'une LCA.

1. Evaluation des processus de consolidation en mémoire verbale

1.1. Article 2 : Evaluation de la consolidation en mémoire verbale étendue à une semaine



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Extension to One Week of Verbal Memory Consolidation Assessment

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Objective: Although impairments of long-term recall affect everyday life, they may be missed by standard delayed recall tests, which typically assess the ability to retain new information within a few minutes, without encompassing the consolidation process. We adapted a verbal memory test to evaluate long-term memory consolidation in healthy volunteers. **Method:** A sample of 238 participants ($M = 42.23$ years old, $SD = 16.45$) was administered an adapted version of the French RL/RI-16 (Van der Linden & the members of GREMEM, 2004), the One-Week Free and Cued Selective Reminding Test—word version, in which special feature relies on a 30-min and a 1-week-delayed recall after encoding. We proposed normative data on 4 indicators, depending on participants' own performance during the test, to measure their encoding, storage and consolidation abilities, with a method using an ascendant step-by-step linear regression model and a percentile procedure. **Results:** Results showed a better performance in women than in men for encoding and cueing scores ($p < .01$ and $p < .05$, respectively). We also highlighted an increase of the forgetting score according to the recall delay after encoding (30 min vs. 7 days; $Z = 12.49$, $p < .001$), the forgetting percentage 7 days after encoding being largely influenced by participants' age and gender ($F[2, 236] = 248.1$, $p < .001$; adjusted $R^2 = 67\%$). **Conclusions:** This study emphasized the role of demographic factors on long-term memory consolidation. The demographically adjusted normative data we provide for the One-Week Free and Cued Selective Reminding Test—word version make it a sensitive tool for long-term memory consolidation assessment in clinical and forensic practice.

General Scientific Summary

Our study highlighted the interest in evaluating memory performance with greater delay after encoding than it is usually assessed. The normative data provided for our adapted verbal memory test will allow refined memory evaluation in patients with memory impairment. It is crucial to detect such deficit to adapt patients' professional rehabilitation.

Keywords: normative data, verbal memory, long-term consolidation, Free and Cued Selective Reminding Test

Supplemental materials: <http://dx.doi.org/10.1037/neu0000403.supp>

New memories are gradually transformed from an initially labile state (in which they are vulnerable to disruption) to a more per-

manent state (in which they are resistant to disruption); this is known as the consolidation process (McGaugh, 2000; Sara & Hars, 2006).

Mounting evidence implicates sleep in the consolidation of various kinds of memories (Axmacher, Draguhn, Elger, & Fell, 2009; Axmacher, Haupt, Fernandez, Elger, & Fell, 2008; Gais & Born, 2004; Stickgold & Walker, 2005), and this memory consolidation sleep-mediation would depend on initial learning and encoding processes (Himmer, Müller, Gais, & Schönauer, 2017). The hippocampal-neocortical interactions underlying memory consolidation appear to be mediated by slow-wave sleep (Paller, 2010). Sleep also has a vital role in decreasing the negative effect of interference on memory recall (Ellenbogen, Hulbert, Jiang, & Stickgold, 2009), thus preserving consolidation process from interfering stimuli.

A large body of literature based on animal and human data highlights the crucial role of the time interval on the consolidation

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process (Hupbach, Gomez, Hardt, & Nadel, 2007; McGaugh, 2000). However, the time interval that sustains complete consolidation has not yet been clarified; thus, consolidation might encompass a period ranging from weeks to years (Moscovitch & Nadel, 1998; Squire & Alvarez, 1995). More recently, Barry, Coogan, and Commins (2016) investigated the consolidation process from a neurobiological perspective and found that spatial memory consolidation would take at least 2 weeks. This question of time interval is a key point in neuropsychological assessment of long-term memory (LTM) in patients.

Several cases of patients with relatively normal acquisition and initial retention of new memories but abnormally fast forgetting of these memories over several days or weeks have been reported (Ahern et al., 1994; Cassel, Morris, Koutroumanidis, & Kopelman, 2016; De Renzi & Lucchelli, 1993; Evans, Elliott, Reynders, & Isaac, 2014; Kapur et al., 1996, 1997; Lucchelli & Spinnler, 1998; O'Connor, Sieggreen, Ahern, Schomer, & Mesulam, 1997; Wilkinson et al., 2012). This pattern of forgetting appears to represent a memory consolidation disorder instead of an encoding deficit (Hoefijzers, Dewar, Della Sala, Zeman, & Butler, 2013). Indeed, learning and delayed recall at 30 min have been reported as preserved in patients with temporal lobe epilepsy or transient epileptic amnesia, whereas an accelerated long-term forgetting has been highlighted with a delayed recall at 24 hours (Jansari, Davis, McGibbon, Firminger, & Kapur, 2010; Lah, Mohamed, Thayer, Miller, & Diamond, 2014; Mulhert, Milton, Butler, Kapur, & Zeman, 2010; Ricci, Mohamed, Savage, Boserio, & Miller, 2015), 6 weeks (Kapur et al., 1997; Manes, Graham, Zeman, de Lujan Calcagno, & Hodges, 2005; Tramoni et al., 2011) or 8 weeks (Blake, Wroe, Breen, & McCarthy, 2000). However, in these studies, patients' performance was compared with small groups of normal controls (i.e., from four to 16 participants; Blake, Wroe, Breen, & McCarthy, 2000; Kapur et al., 1997; Mayes et al., 2003).

Long-term consolidation cannot always be assessed because entire neuropsychological assessment is often limited in time. It is one of the reasons most studies led in amnesic patients used memory tests that typically assess the ability to retain new information over a period of about 30 min (e.g., Wechsler Memory Scale; Wechsler, 1997, 2009), whereas tests with a retention period of 1 or more days are rare (e.g., Jones-Gotman et al., 1997, 24 hours). For instance, French neuropsychologists generally assess verbal episodic memory with a free and cued selective reminding procedure: the RL/RI-16 test (for details, see Van der Linden & the members of GREMEM, 2004). This procedure relies on a semantic encoding and cueing underlying a deep processing, leading to better long-term memory performance in comparison with shallow processing (Craik & Lockhart, 1972). Hence, this could ensure that performance to the test is not related to an eventual complexity of test material. However, delayed recalls are assessed 20 min after encoding, and this delay does not appear to provide crucial information on LTM consolidation because it has been demonstrated in studies among patients with brain damage. Thus, neuropsychological assessment of LTM needs an adaptation of standard memory tests using appropriate delays to better understand and give an objective basis of patients' complaint in a professional rehabilitation process.

Another problem of memory assessment is that the raw scores correspond to the number of word recalled or recognized and do not consider participants' own performance throughout the test.

Thus, long-term memory forgetting rates may appear to be more sensitive to identify subtle memory problems (Butler & Zeman, 2008). To obtain sensitive memory indicators, each memory score should be related to participants' own performance throughout the test and to their own demographic data.

This study had two main purposes: (a) to adapt an existing verbal memory assessment tool leading to a refined measure of LTM performance encompassing consolidation process and (b) to obtain demographically adjusted normative data for future studies in brain-damaged patients.

For these purposes, 238 neurologically healthy volunteers were administered an adapted version of the French RL/RI-16 (Van der Linden & the members of GREMEM, 2004), the One-Week Free and Cued Selective Reminding Test—word version (1W-FCSRT-word). Two modifications have been considered: the delayed recall of 20 min has been replaced by a 30-min-delay, which is commonly used in neuropsychological memory assessment in clinical practice (e.g., Rey's Auditory Verbal Learning test, Rey, 1964; Wechsler Memory Scale, Wechsler, 1997, 2009) and a delayed recall of 7 days after encoding has been added to capture the LTM consolidation processes. A forgetting score was calculated for these two delays after encoding. We assumed that memory performance would decline, depending on the retrieval delay after encoding. More precisely, we expected an increase of the percentage of words forgotten 7 days after encoding in comparison with the one at 30 min. It is crucial to evaluate this difference in forgetting in healthy participants to have a baseline in detecting eventual consolidation impairment in patients with brain damage.

Method

Participants

Two hundred thirty-eight participants (124 women and 114 men) ranging in age from 18 to 81 years old ($M = 42.23$, $SD = 16.45$) were recruited in the Lille area (France) through a local campaign. All participants were native French speakers and their demographic and sociocultural characteristics are representative of French population. It has been ensured that participants' number of years of education correspond to the age composition of the French population as it is described by the French National Institute of Economic and Statistical Information (INSEE, 2016). All participants older than 50 years included in this study had a normal general intellectual efficiency and were self-reliant. The distribution of participants by age group, gender, and years of education is indicated in Table 1.

Our campaign specified that only volunteers who did not match the exclusion criteria could apply for the research study. Before starting the procedure, exclusion criteria had been screened with a questionnaire. The exclusion criteria were as follows: history of neurological disease, psychiatric illness, or head injury or stroke. None received any financial compensation for their participation. According to the Helsinki Declaration (World Medical Association, 2013), participants gave full informed consent.

Procedure

The 1W-FCSRT—word version, a modified version of the French RL/RI-16 items (Van der Linden & the members of GREMEM,

Table 1
Distribution of Participants According to Age Group, Gender and Education Level and Raw Data for 1W-FCSRT-Word Memory Scores

Demographic data				Raw data					
Age group	Gender	Education level		Learn (%)	Cued (%)	FR30 (/16)	FR30-forget (%)	FR7d (/16)	FR7d-forget (%)
1	18–29 years	F = 22	1 n = 11	62.53 (21.43)	94.68 (7.33)	14.82 (.98)	8.07 (12.68)	10.27 (3.50)	–25.64 (24.50)
			2 n = 11	66.28 (18.32)	88.89 (12.25)	14.27 (1.56)	1.24 (7.80)	11.27 (2.61)	–19.55 (19.83)
		M = 39	1 n = 27	41.63 (31.85)	88.86 (12.28)	13.78 (1.34)	10.69 (18.62)	9.15 (2.44)	–26.75 (20.22)
			2 n = 12	57.49 (26.96)	83.85 (15.58)	13.33 (1.78)	–.31 (16.94)	8.50 (2.47)	–36.54 (20.08)
2	30–49 years	F = 50	1 n = 33	55.97 (26.58)	91.70 (9.59)	13.24 (1.98)	.46 (11.75)	10.61 (3.11)	–18.90 (25.15)
			2 n = 17	58.96 (26.53)	89.12 (14.60)	14.18 (2.13)	6.14 (14.16)	10.65 (3.12)	–20.79 (21.07)
		M = 59	1 n = 36	38.83 (27.29)	85.28 (13.47)	12.28 (1.81)	4.24 (16.57)	7.64 (2.42)	–35.59 (19.11)
			2 n = 23	52.83 (32.38)	86.95 (14.20)	13.83 (1.99)	6.68 (12.55)	9.87 (3.86)	–26.11 (25.85)
3	50–64 years	F = 29	1 n = 20	63.25 (18.56)	91.23 (9.53)	12.60 (2.26)	–4.16 (18.31)	7.25 (2.10)	–45.41 (14.34)
			2 n = 9	42.61 (25.37)	90.82 (9.32)	11.89 (2.52)	–1.62 (15.97)	8.56 (4.56)	–29.68 (37.16)
		M = 11	1 n = 7	61.76 (20.92)	93.38 (7.83)	12.43 (1.62)	.08 (15.26)	6.00 (3.27)	–49.03 (36.12)
			2 n = 4	42.68 (18.45)	88.11 (8.93)	12.25 (2.36)	5.86 (11.29)	6.75 (1.26)	–41.46 (7.89)
4	65–81 years	F = 23	1 n = 19	46.31 (33.54)	89.44 (11.85)	12.21 (2.07)	–4.35 (12.42)	6.63 (3.76)	–49.01 (27.31)
			2 n = 4	57.29 (8.59)	92.56 (10.89)	12.00 (4.24)	–11.68 (29.49)	4.25 (2.06)	–68.13 (16.37)
		M = 5	1 n = 3	41.67 (31.46)	94.86 (.68)	10.33 (2.08)	–4.25 (24.93)	2.67 (1.15)	–76.28 (6.43)
			2 n = 2	53.57 (5.05)	100.00 (.00)	12.50 (.71)	–3.85 (5.44)	5.50 (4.95)	–57.69 (38.07)

Note. M = male; F = female; education level 1, ≤12; level 2, >12 years. Raw data are presented as *mean (SD)*.

2004) replacing the delayed recall at 20 min by one at 30 min and the addition of a 7-day-delayed recall, was administered to our healthy volunteers. This assessment was divided between two sessions.

In the first session, 16 words were presented to the participants, four at a time on four successive cards. After a semantic cue was given to the participants (e.g., *fruit*), they were asked to name and point out the target word. When all four words of one card were accurately identified, the words were hidden and an immediate cued recall of these words was administered, allowing an encoding control. This identification procedure followed by a cued recall was carried out for all four cards (16 words). Then, three successive recall trials were performed. Within a trial, participants were invited to recall as many words as they remember (free recalls; FR1, FR2, FR3) and then a semantic cue was provided for the missing items (cued recalls; CR1, CR2, CR3), and a feedback was given if participants failed to recall the target word given the cue. Total recall scores corresponded to the sum of free and cued recall (e.g., TR1 = FR1 + CR1). Each recall trial was preceded by a distracting task (counting backward from the indicated number during 20 seconds) so participants would not use their phonological loop to retain the word list (Baddeley, 2006). Then followed a recognition phase; a list of 48 words (16 target words and 32 distractors) was orally presented to our participants and they were asked to identify the words they remember having learned. A delayed free (FR30) and a cued recall (CR30) were administered after a 30-min delay, instead of a 20-min delay as in the RL/RI-16 test (Van der Linden & the members of GREMEM, 2004).

In the second session carried out 7 days later, participants performed only a free recall (FR7d) and a cued recall (CR7d) (see Figure 1 for the 1W-FCSRT-word administration procedure). Participants were not aware that words learned in Session 1 would be recalled in Session 2. The two sessions were carried out in the same place, on the same day of the week, and at the same hour of the day to ensure consistency in the spatiotemporal context of the assessment.

Scoring

The four distinct memory indicators analyzed in this study were computed as follows:

1. A learning score (Learn), corresponding to the percentage of words encoded relatively to the first free recall, was calculated as follows: $Learn = \frac{FR_3 - FR_1}{16 - FR_1} \times 100$.
2. A cueing score (Cued), corresponding to the effect of cued recall on learning, was calculated as follows: $Cued = (\Sigma TR_{1+2+3} - \Sigma FR_{1+2+3}) / (48 - \Sigma FR_{1+2+3}) \times 100$.

We explored forgetting as the inability to retrieve information at a precise moment whereas it could have been retrieved previously (Tulving, 1974). Indeed, we calculated forgetting percentages using a formula that included the learning phase last free recall.

3. A short-term consolidation score (FR30-Forget), corresponding to the forgetting percentage for the FR30 after encoding was calculated as follows: $FR30 - Forget = \frac{FR_{30} - FR_3}{FR_3} \times 100$.
4. A long-term consolidation score (FR7d-Forget), corresponding to the forgetting percentage for the Free Recall 7 days after encoding was calculated as follows: $FR7d - Forget = \frac{FR_{7d} - FR_3}{FR_3} \times 100$.

For both consolidation scores, a negative value reflected better performance in the third trial of the initial learning phase than in delayed recall and vice versa for a positive value.

According to Squire (1986) and Sutherland et al. (2001), forgetting and consolidation processes are linked. Consolidation process could not be measured without taking into account the initial learning. For example, a delayed recall of three words does not have the same meaning when the participant initially learned 16 words or three words among the 16 presented in the procedure.

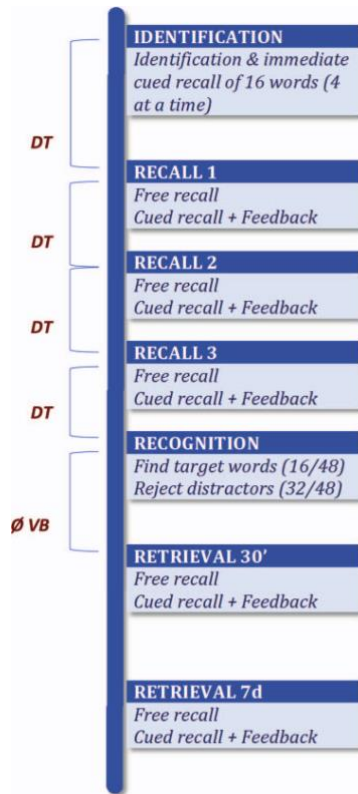


Figure 1. 1W-FCSRT-word administration procedure. DT: distracting task (counting backwards from the indicated number during 20 sec); VB: no verbal task was administered during this time interval. See the online article for the color version of this figure.

Thus, we analyzed consolidation performance in terms of forgetting scores. It allowed us to identify whether there was a difference between the 30-min-delayed free recall and participants' initial learning, hence refining our memory scores interpretation in generally used memory tests. Furthermore, in analyzing the performance difference between the 7-day-delayed free recall and participants' initial learning, it would emphasize the value of a long-term delayed memory evaluation.

All indicators from the 1W-FCSRT-word for which we provide normative data are presented in supplementary material.

Data Analysis

Raw data for 1W-FCSRT-word memory scores are presented in Table 1.

To analyze the link between memory scores 30 min after the learning phase and memory scores after a 1-week delay, we carried out Spearman correlational analyses.

Norms for 1W-FCSRT-word memory performance indicators were established with different methods. First, we used the method of Barona, Reynolds, and Chastain (1984) by means of an ascendant step-by-step linear regression model including three predictive factors: age group (Group 1: 18–29 years; Group 2: 30–49 years; Group 3: 50–64 years; and Group 4: 65–81 years), education level (1: ≤ 12 years; 2: > 12 years of formal education), and gender (0, *female*; 1, *male*). For all models with statistically significant regression coefficients, we tested the normality of residuals distribution. Linear regression assumptions were satisfied only for the model predicting FR7d-Forget.

Therefore, norms for Learn, Cued, and FR30-Forget were obtained using a classical percentile procedure (Dancey & Reidy, 2007). Nonparametric tests were conducted to evaluate the effect of age group, gender, or years of education on memory performance.

In supplementary material, norms for raw scores for which linear regression assumptions were not satisfied (FR2, FR3, and FR30) were assessed using the method developed by Crawford, Garthwaite, and Slick (2009) to determine percentiles associated with a confidence interval.

All analyses were performed using R software (version 3.3.2). The significance level was set at $p < .05$.

Results

Memory Score Characteristics

Learn and Cued scores. No performance difference was found in Learn score according to age group ($\chi^2[3, 238] = 1.12, p = .77$) or years of education ($W = 5693.5, p = .16, r[95\% \text{ confidence interval (CI)}] = 0.09 [-0.04, 0.22]$), but performance was greater in women ($M = 56.64, SD = 25.53$) than in men ($M = 46.16, SD = 29.17$) ($W = 8526, p < .01, r[95\% \text{ CI}] = 0.18 [0.05, 0.3]$). No performance difference was found in Cued according to age group ($\chi^2[3, N = 238] = 1.78, p = .62$) or years of education ($W = 6734.5, p = .49, r[95\% \text{ CI}] = 0.04 [-0.08, 0.17]$), but performance was greater in women ($M = 90.90, SD = 10.68$) than in men ($M = 87.42, SD = 13.0$) ($W = 8148.5, p = .03, r[95\% \text{ CI}] = 0.14 [0.01, 0.26]$).

FR30-Forget. An effect of age group was found on performance for this score ($\chi^2[3, 238] = 14.22, p < .01$).

FR30-Forget and FR7d-Forget scores. In general, forgetting percentage appeared to increase with temporal delay after encoding ($Z = 12.49, p < .001$), and this applied to all age groups (Group 1: $Z = 6.64, p < .001$; Group 2: $Z = 8.08, p < .001$; Group 3: $Z = 5.13, p < .001$; Group 4: $Z = 4.58, p < .001$) (see Figure 2).

Spearman correlational analyses emphasized a low positive correlation between FR30 and FR7d ($r_s = .44, p < .001$) and negligible correlations between CR30 and CR7d ($r_s = .22, p < .001$), between TR30 and TR7d ($r_s = .27, p < .001$), and between FR30-Forget and FR7d-Forget ($r_s = .27, p < .001$) (Hinkle, Wiersma, & Jurs, 2003).

Normative Data

Percentiles for Learn and Cued scores were calculated according to gender (see Table 2). Percentiles for FR30-Forget score were calculated according to age group (see Table 3).

Participants' age group and gender both predicted in a statistically significant manner FR7d-Forget ($F[2, 236] = 248.1, p < .001$; $\hat{y} = -12.46$ age group $- 11.21$ gender; residual standard error = 23.58; adjusted $R^2 = 67\%$). The regression equation allows calculation of FR7d-Forget Z-scores for clinical use.

Discussion

This study had a dual purpose. First, we aimed to adapt an existing verbal memory assessment tool that could give a memory performance score encompassing consolidation process. Second, we meant to obtain demographically adjusted normative data on specific indicators, depending on participants' own performance throughout the entire test, underlying their encoding, storage and consolidation abilities.

For these purposes, we administered to our participants an adapted version of the French RL/RI-16 (Van der Linden & the members of GREMEM, 2004), the 1W-FCSRT-word, which relies on two substantial modifications: insertion of delayed recall tasks 30 min (instead of 20 min) and 7 days after encoding. We evaluated their memory performance with composite scores that take into account participants' own performance throughout the entire test. Indeed, we investigated LTM performance with forgetting scores.

Our main results showed that LTM performance was modulated by demographic variables, especially age group and gender. Forgetting percentage for the 30-min-delayed free recall (FR30-Forget score) was modulated by age group factor, whereas forgetting percentage for the 7-day-delayed free recall (FR7d-Forget score) was modulated by both age group and gender. Indeed, 30 min after the learning phase, forgetting increased along with participants' age, and 7 days after encoding, it was more stressed out in men than in women.

Table 2

Percentiles Calculated With a Classical Method (Dancey & Reidy, 2007) for Learn and Cued Scores

Percentiles	Women		Men	
	Learn	Cued	Learn	Cued
0	-50.00	42.86	-33.33	38.89
5	20.00	73.16	.00	65.83
10	26.07	76.61	.00	72.11
15	33.33	80.00	12.50	75.95
20	37.50	82.35	20.00	77.44
25	40.00	83.99	25.89	78.93
50	57.14	93.10	50.00	90.00
75	75.69	100.00	66.67	100.00
100	100.00	100.00	100.00	100.00

A gender effect was found on encoding/storage memory performance. Indeed, for the encoding score corresponding to the percentage of word encoded during learning relatively to the first free recall and for the storage score corresponding to the cueing effect during learning, women generally performed better than men. This result is often seen in episodic memory studies (see Herlitz, Nilsson, & Backman, 1997, for a review; Peterson, 2011; Pillemer, Wink, DiDonato, & Sanborn, 2003). One possible explanation of this gender effect is that our adapted memory test is verbal. Indeed, the superiority of women's performance in episodic memory tasks has been underlined for recall or recognition tasks using verbal items such as words, stories, names, or concrete pictures (Lewin, Wolgers, & Herlitz, 2001) but also for encoding tasks (Grysmen, 2017). Furthermore, Herlitz, Airaksinen, and Nordstrom (1999) reported that the gender difference in episodic memory tasks is around one quarter of a standard deviation and is higher in free recall than in recognition tasks. According to Lewin et al. (2001), the superiority of women could be explained by their better performance on tasks involving verbal production rather than by better overall memory abilities. As far as recall tasks are concerned, women present higher scores because they seem to use a

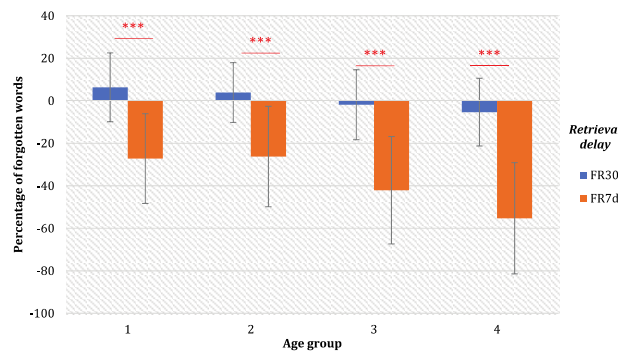


Figure 2. Percentage of forgotten words, according to the retrieval delay after encoding and age group. FR30 and FR7d, 30-minute-delayed and the 7-day-delayed free recalls. *** $p < .001$. See the online article for the color version of this figure.

Table 3
Percentiles Calculated With a Classical Method (Dancey & Reidy, 2007) for FR30-Forget Score

Percentile	Age groups			
	18–29 years	30–49 years	50–64 years	65–81 years
0	–28.57	–25.00	–46.15	–53.85
5	–15.38	–18.18	–26.87	–28.12
10	–13.33	–13.33	–21.59	–26.85
15	–8.33	–8.33	–16.89	–20.00
20	–7.14	–6.67	–13.52	–19.27
25	–7.14	.00	–12.50	–10.31
50	7.69	.00	–3.13	.00
75	15.38	10.00	9.09	.00
100	66.67	50.00	30.00	22.22

semantic strategy to encode information (Berenbaum, Baxter, Seidenberg, & Hermann, 1997). Using the California Verbal Learning Test and matching women and men according to their abilities to analyze semantic chunks, Berenbaum et al. (1997) observed a reduction in women's superiority in a word recall task. Otero Dadin, Rodríguez Salgado, and Andrade Fernandez (2009) have also suggested that the use of a semantic strategy to encode words plays a role in this regard. Similarly, the FCSRT is based on a reinforcement of a semantic strategy to encode words, so it is not surprising to observe superior performance in women.

Comparisons between memory scores according to the delay after encoding showed a statistical significant effect of the delay on forgetting percentage (30 min vs. 7 days). Indeed, performance significantly decreased from 30-min-delayed recall to 7-day-delayed recall.

According to Brown and Lewandowsky (2010), forgetting does not necessarily mean memory decay or consolidation failure. It also can be defined as an inability to recall something at a particular moment but that could be retrieved later (Habib & Nyberg, 2008; Sadeh, Ozubko, Winocur, & Moscovitch, 2014). However, following the definition of Tulving (1974), initial learning could be modified, and retained information, even when repeated, can be forgotten at a particular moment, recollection being particularly sensitive to decay (Viskontas, Carr, Engel, & Knowlton, 2009). As in the 1W-FCSRT-word procedure, participants' learning was facilitated through repeated recall trials during the learning phase, and a pathological forgetting percentage may highlight a consolidation impairment in patients with memory complaints in comparison with our healthy volunteers.

Our study nevertheless has some limitations. First, very few older participants were administered the memory test, possibly weakening normative data for those between 65 and 81 years old. However, it is important to mention that this type of procedure appears to be difficult for older people, so it may not be the first choice to assess memory performance. Second, provided normative data do not concern the existing parallel version of the test. This parallel version is used for memory evaluation retest to avoid a bias because of the material.

Our adaptation of the RL/RI 16 test with demographically adjusted normative data for composite scores is a useful task to highlight potential long-term amnesia (LTA), in particular among patients with traumatic brain injury. Demonstrating the presence of

LTA in these patients could support their memory complaints and thereby allow a more precise professional guidance. This first study conducted in healthy young participants confirms the importance of demographic factors in patients' memory performance and especially after a delay of 7 days.

Our study could also clarify the neural basis of memory consolidation. The medial temporal structures are often affected in LTA patients. It is well known that the time course of memory consolidation is orchestrated by hippocampal-neocortical connections, whose role is strongly debated in models of consolidation. According to the standard model (Squire & Alvarez, 1995), the role of the hippocampus in retrieval is time limited and the content of memories remains unchanged throughout the consolidation process. Similarly, the Multiple Trace Model posits that the establishment of long-term memories involves lengthy hippocampo-neocortical connections (Moscovitch & Nadel, 1998; Nadel, Campbell, & Ryan, 2007; Nadel & Moscovitch, 1997, 2001; Noulhiane et al., 2007). However, this model suggests that the hippocampus remains an integral part of the memory trace and is thus always involved in the retrieval of long-term episodic memories, regardless of the age of the memory. The consolidation and stabilization processes occurring after new encoding are not yet well established in human memory, although several authors have investigated this issue. For instance, studies have explored memory consolidation and its relationship with sleep after 6 months (Rauchs et al., 2008). One study addressed the question of the neural correlates of trace stabilization by comparing brain activity related to the retrieval of newly learned memory traces trained in a massed scheme (labile condition) with a spaced learning scheme (stabilized condition) across a period of 8 days (Takashima et al., 2007). Administration of standardized functional neuroimaging protocol will allow us to specify the involvement of the hippocampal-neocortical interaction during the first week following encoding and better understand the impairment observed in LTA patients.

Our data highlighted the relevance of assessing LTM consolidation using a delayed recall task extended over several days and pointed to the influence of demographic factors. By assessing many participants distributed in groups related to age and gender, our findings constitute baseline performance, which will help in assessing memory performance of brain-damaged patients in neuropsychological and forensic practice as well as clarifying the neural basis of LTM consolidation.

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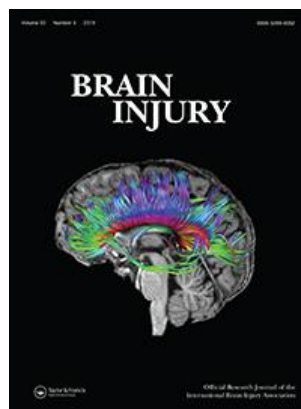
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1.2. Article 3 : Pourquoi évaluer le rappel verbal à une semaine chez les patients souffrant d'un traumatisme crânien grave ?



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Why evaluate one-week-delayed verbal recall in patients with severe traumatic brain injury?

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ABSTRACT

Primary objective: The aim of this study was to propose new measures to evaluate memory processes in patients with severe traumatic brain injury (TBI). In this purpose, we analyzed learning and consolidation processes depending on own patient's performance during a memory test.

Methods: One-week Free and Cued Selective Reminding Test – word version (1W-FCSRT-word), which special feature relies on a 30-min and a 1-week-delayed recall after encoding, was administered to a group of 43 patients with severe TBI (age range from 20 to 54 years) and a group of neurologically healthy volunteers matched for age and gender.

Results: Patients performed worse than healthy volunteers for the learning score. Their forgetting percentage was above healthy volunteers' performance and difference between the two groups increased with the delay from the learning phase.

Conclusion: In patients with severe TBI, our results underlined an altered learning and an impairment of long-term consolidation. It is crucial to detect these deficits in the aim to highlight, with a better accuracy, these patients' memory complaints and to propose a better professional rehabilitation.

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Introduction

Verbal memory impairment has been described in patients with traumatic brain injury (TBI) (1–3) up to 1 year (4–8) and even 5 years after injury (9). However, the specific altered memory process, between learning, consolidation and/or retrieval, is still discussed (10).

Verbal retrieval process, defined as the ability to search a specific verbal information previously learned (11), appears to be impaired in patients with TBI (12), especially in the case of temporal lobe lesions (13). Memory acquisition or encoding process can be defined as the ability to learn and recall information through a set of immediate trials (14). It was found that patients with moderate-to-severe TBI needed more learning trials to reach the required acquisition criterion (15) due to difficulties to organize new information within the encoding process (16). However, in a group of patients, this difficulty seemed to normalize itself between 6 months to 1 year after brain injury (14).

Consolidation process has been described as the long-term storage of encoded information (17) and appeared to be impaired in patients with TBI (1). Wright et al. (18) proposed two indexes to evaluate encoding and consolidation impairment: an encoding deficit index and an acquisition adjusted consolidation deficit index. Using these indexes, patients with TBI appeared to present both encoding and consolidation deficits within 7 months after injury and even at 1 year after injury (19).

Although few studies used long-term consolidation paradigm, most of them support the consolidation process impairment

hypothesis to explain memory deficit in patients with TBI (14,19). Memory tests included in usual neuropsychological assessments explore memory processes within a short delay such as 30 min (e.g. RAVLT (20); Wechsler memory scale (21,22);) whereas consolidation process might cover a period of time ranging from weeks to years (23,24). Memory tests using greater recall delays should be integrated in a neuropsychological assessment to investigate consolidation impairment in patients with TBI. Moreover, memory complaints as well as memory impairment in patients with TBI persist long time after injury. Yet, after a long period from the injury, only a global memory assessment has been carried out to detect an eventual memory deficit (25–27). However, this global assessment is not sufficient to identify the cognitive origin of the memory deficit. Memory deficit impede professional and/or social life reintegration of these patients. Investigating specific altered memory processes in patients with TBI is crucial to plan a revalidation program and to guide their professional rehabilitation (28,29).

This study focused on new measures to detect verbal memory impairment in patients with TBI. For this purpose, we analyzed learning and consolidation processes depending on each patient's performance during the learning phase of the test. Indeed, we assumed that learning process would be underlined by the percentage of words encoded during the learning phase. We also supposed that consolidation process would be emphasized by the percentage of words forgotten between learning phase and retrieval, forgetting being the result of consolidation impairment (30). We hypothesized that learning process would

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be weakened in patients with severe TBI, in comparison with healthy volunteers. Forgetting would rather increase in these patients, and even more with a longer delay between learning phase and retrieval: forgetting percentage would be larger after 7 days than 30 min.

Methods

Participants

Forty-three participants with a severe TBI were included in this study from 2003 to 2016. Brain injury severity was estimated according to the criteria established by Teasdale and Jennett (31) (Glasgow Coma Scale score: 3–8). All participants had undergone a neuropsychological assessment in a Health and Social Structure (UROS – evaluation, rehabilitation and socio-professional orientation structure) in Lille (France). All participants were adults (age range at the time of assessment from 20 to 54 years; $M = 31.23$, $SD = 8.24$) and stable from a sensorimotor, cognitive and behavioral perspective, after a mean delay of 5.01 years post-TBI (range from 1 to 16 years). Moreover, the delay from the brain injury was between 4 and 9 years for 58.14% of the patients, between 1 and 3 years for 34.88% and between 14 and 16 years for 6.98%. Exclusion criteria were: (1) psychiatric or neurological history previous to their actual injury, (2) pregnancy, (3) juveniles, and (4) limited French proficiency. Patients' performance was compared to performance of 168 neurologically healthy volunteers matched for age and gender, recruited in the Lille area (France) through a local campaign. According to the Helsinki Declaration (World Medical Association, 2013), participants gave a full informed consent.

Demographic data of our samples are presented in Table 1.

Material

All participants were administered the 1-Week Free and Cued Selective Reminding Test – word version (1W-FCSRT-word (32)). This test is a modified version of the French RL/RI-16 items test (33). The major modification consisted in replacing the 20-min-delayed recall with a 30-min-delayed recall and adding a 7-days-delayed recall. Words were visually presented with a semantic cue orally and simultaneously given by the neuropsychologist. The learning phase corresponded to three immediate and successive recall trials, participants being invited to recall as many words as

they remember (free recalls: FR1, FR2, FR3). Delayed free recall was administered 30 min and 7 days after the learning phase. Participants were not aware of these two delayed recall phases.

Scoring

Three memory indicators (32) were analyzed: (1) a learning score (*Learn*), corresponding to the percentage of words encoded at the end of the learning phase relatively to the first free recall (FR1); (2) a rapid consolidation score (*FR30-Forget*), underlined by the forgetting percentage for the Free Recall 30 min after encoding; and (3) a slow consolidation score (*FR7d-Forget*), highlighted by the forgetting percentage for the Free Recall 7 days after the learning phase. For both consolidation scores, a negative value reflected better performance in the end of the initial learning phase than in delayed recall, and vice versa for a positive value.

Data analysis

We adopted two different methods to analyze collected data.

First, we investigated differences in terms of memory performance between patients and healthy controls, considering patients' performance as altered as soon as they performed statistically significantly worse than the healthy volunteers. For this purpose, non-parametric tests were conducted for all three memory scores (*Learn*, *FR30-Forget*, and *FR7d-Forget*). As in the validation article of 1W-FCSRT (32) authors have found a gender effect on *Learn* score, an age group effect on *FR30-Forget* and an effect of both factors (age group and gender) on *FR7d-Forget*, we investigated the impact of these factors on differences of performance between patients and healthy volunteers. In order to evaluate the pertinence of calculating a long-term forgetting score (*FR7d-Forget*) in patients with severe TBI, we conducted, within each sample (patients and healthy controls), non-parametric tests to compare *FR30-Forget* and *FR7d-Forget* performance. Through a backward stepwise regression analysis, we investigated the effect of demographical factors (age group, gender and education level) and the recall delay (30 min vs 7 days) on the forgetting score according to the group (patients vs. healthy controls). We also compared the difference in performance between patients and healthy controls, according to the recall delay (30 min vs 7 days). And we analyzed if there

Table 1. Demographic data of participants.

			Participants with sTBI (N = 43)	Healthy volunteers (N = 168)	MWW
AGE GROUP	20–29 yo	n	23	45	$p = 0.45$
		Gender	20M/3F	32M/13F	
		Years of education	15.48(1.73)	15.13(2.19)	
	30–49 yo	n	18	109	$p < 0.001$
		Gender	14M/4 F	59M/50F	
		Years of education	16.50(2.79)	13.94(3.57)	
50–54 yo		n	2	14	$p = 0.69$
		Gender	2M/0 F	4M/10F	
		Years of education	13.50(3.54)	12.64(3.20)	

Years of education are presented in terms of mean(SD). F: female; M: male; MWW: Mann-Whitney-Wilcoxon test; sTBI: severe traumatic brain injury; yo: years old. *P*-values in bold are of statistical significance.

was an interaction effect of both recall delay and group on the forgetting score.

Second, we adopted a clinical approach to determine the percentage of patients with TBI who obtained an impaired performance. So, patients' performance was analyzed according to the demographically adjusted normative data (according to age group and/or gender) of 1W-FCSRT-word (32), and we considered a performance as impaired when standardized scores were inferior or equal either to -1.65 z-score or to the fifth percentile.

All analyses were performed using R software (<https://www.r-project.org/>). The significance level was set at $p < 0.05$.

Results

A statistically significant difference was found between patients and healthy volunteers for the *Learn* score (Mann-Whitney Test, Z -adjusted = 2.66, $p < 0.01$). Indeed, patients ($M = 34.23$, $SD = 36.25$) performed worse than healthy volunteers ($M = 50.63$, $SD = 28.68$). However, this difference appeared to be accurate only in men (Z -adjusted = 2.09, $p < 0.05$).

A statistically significant difference was found between patients and healthy volunteers for the *FR30-Forget* score (Z -adjusted = 2.67, $p < 0.01$). Patients ($M = -2.55$, $SD = 27.00$) performed worse than healthy volunteers ($M = 4.36$, $SD = 14.90$). However, this difference appeared to be significant only in patients between 20 and 29 years old (Z -adjusted = 2.87, $p < 0.01$).

A statistically significant difference was found between patients and healthy volunteers for the *FR7d-Forget* score (Z -adjusted = 5.12, $p < 0.001$). Patients ($M = -49.77$, $SD = 23.39$) performed worse than healthy volunteers ($M = -27.92$, $SD = 23.39$). However, this difference appeared to be significant

both in men and women between 20 and 29 years old (Kruskal-Wallis test, respectively, $H(1,52) = 17.70$, $p < 0.001$; $H(1,16) = 6.91$, $p < 0.01$) and also in women between 30 and 49 years old ($H(1,54) = 3.87$, $p < 0.05$).

Forgetting percentage was higher after a delay of 7 days than after a delay of 30 min in both groups: healthy controls (Wilcoxon signed-rank test; $W = 24914$, $p < 0.001$) and patients ($W = 1718$, $p < 0.001$) (see Figure 1).

A statistically significant difference in terms of age (Wilcoxon signed-rank test; $W = 4816.5$, $p < 0.001$), gender ($W = 2630.5$, $p < 0.01$) and education level ($W = 1481.5$, $p < 0.001$) was found between the patients and the control group. Therefore, age, gender and education level were introduced in regression analysis. Using a backward stepwise regression, only group (controls vs severe TBI) and delay (30 min vs 7 days) were found to be predictive of the forgetting score ($F(2,419) = 164.33$, $p < 0.001$, adjusted $R^2 = 0.44$). A statistically significant interaction effect of these factors was found on forgetting score, difference between patients and healthy controls being greater 7 days after learning phase than after a delay of 30 min ($t(1,419) = -7.26$, $p < 0.001$; see Figure 1).

According to normative data, an impaired performance was found in 16% (7/43) of patients for the *Learn* score, 28% (12/43) for the *FR30-Forget* score and 35% (15/43) for the *FR7d-Forget* score. From the seven patients with an impaired *Learn* score, only one patient had impaired both *FR30-Forget* and *FR7d-Forget* scores. From the subgroup of 12 patients with an impaired *FR30-Forget* score, 7 patients also had an impaired *FR7d-Forget* score. Finally, from the subgroup of 15 patients with an impaired *FR7d-Forget* score, 6 patients had *Learn* and *FR30-Forget* scores in the normal range.

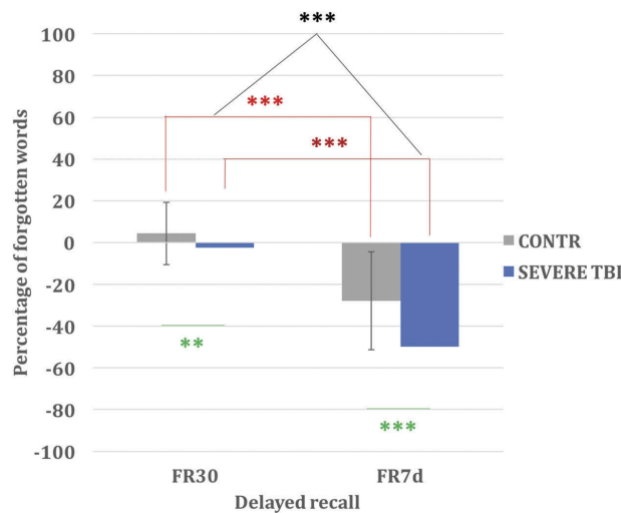


Figure 1. Percentage of forgotten words as a function of delayed recall.

Percentage of forgotten words was calculated comparing the delayed recall with the third free recall of the learning phase. ** $p < 0.01$, *** $p < 0.001$; CONTR: healthy controls; FR30: 30-min-delayed free recall; FR7d: 7-days-delayed free recall; TBI: traumatic brain injury.

Discussion

The aim of this study was to identify new measures that would allow clinicians to focus on the specific mnemonic altered process in patients with severe TBI. For this purpose, we analyzed learning and consolidation processes as a function of each patient's performance during a memory test; learning was operationalized as the percentage of words encoded during the learning phase and consolidation as the percentage of forgotten words. We analyzed rapid and slow consolidation, according to the recall delay after the learning phase (30 min vs. 7 days). Impairment in these processes was interpreted according to the demographically adjusted norms of 1W-FCSRT-word (32).

Memory performance in patients with severe TBI was less effective in comparison with healthy volunteers, concluding to less effective learning and consolidation processes. Memory impairment as calculated according to demographically adjusted normative data (32) affected few patients in their learning process, meaning that patients with severe TBI would still have abilities to learn new verbal information. However, learning abilities did not seem to normalize, as it had been found in the literature (14). In these patients, we found a greater impairment of consolidation processes, a higher percentage of patients having slow consolidation impairment more than rapid consolidation impairment. Difference in terms of forgetting score between patients and healthy controls was found to be greater 7 days after the learning phase than after a delay of 30 min. Consolidation deficit in these patients appeared to grow over larger delays than the usual assessment time. Hence, patients with severe TBI presented a slow verbal memory consolidation deficit and assessment of this deficit needs to be adapted to this finding. Indeed, using the *FR7d-Forget* score allowed us to identify slow verbal memory consolidation deficit in six patients who did not appear to have any memory impairment within the 30-min delay. With usual scoring and memory evaluation within 30-min delay, we might have missed memory impairment in these patients.

Therefore, the slow consolidation score seems to be a more sensitive measure of consolidation process in patients with severe TBI than the rapid consolidation score. The lack of information about the brain lesions location of all patients included in this study could not allow us to explore the cerebral causes of this consolidation impairment. Another comment to this study could be the different time span for the two groups, since patients were evaluated between 2003 and 2016, whereas data collection in healthy volunteers covered a shorter period.

Our results underlining a reduction of learning abilities in patients with severe TBI in comparison with healthy volunteers is consistent with the literature (15,34). Thus, a diminished verbal learning should be considered in neuropsychological assessment and, as it can be impacted by executive and attentional dysfunction, it should be interpreted in combination with attention and executive functions performances (34,35).

The performance pattern found in our set of patients is consistent with studies supporting an impairment of the

consolidation process in patients with severe TBI (14,19) and this even several years after brain injury. However, this impairment did not appear to be obvious within a 30-min-delayed recall as it was already noticed in literature. This may be due to our composite scoring, based on participants' own performance during encoding phase. However, this scoring methodology is necessary for a more sensitive evaluation of memory processes and could highlight difficulties underlined in memory complaints of patients with brain injury. A forgetting score after a delay of 7 days from encoding may also encompass the consolidation process (23,24) which might not be completed over 30 min.

Memory impairment appeared to be the most frequent cognitive sequelae after a TBI (36). As memory is greatly involved in most jobs (29), it is highly associated with professional rehabilitation of these patients (28). Hence, the major interest of this study lies in using a long-term forgetting score to detect consolidation impairment in patients with severe TBI, and adapt their vocational rehabilitation in line with this impairment. Indeed, detecting impairments that would hinder a successful vocational rehabilitation might improve vocational guidance of these patients and maybe prevent them from failure in resuming work or vocational training. This particular memory assessment also appears to be valuable for a forensic expertise, that contributes to the recognition of patients' deficits. Contrary to the usual memory tests that assess only the ability to retain new information within 30 min and may underestimate the cognitive consequences of brain injury, the 1W-FCSRT-word appeared to be a sensitive tool of memory impairment in patients with TBI.

Conclusions

Even several years post-injury, patients with a severe TBI seem to conserve an alteration of the encoding process and a long-term consolidation impairment. From clinical and forensic perspective, it is crucial to detect this deficit and to adapt the professional rehabilitation of patients with severe TBI.

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Disclosure Statement

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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Conflicts of interest

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2. Evaluation du niveau de fatigue spécifique aux LCA (Article 4)

Article 4 : L’inventaire multidimensionnel de fatigue (MFI-20) est-il adéquat pour mesurer le niveau de fatigue chez les personnes souffrant d’une lésion cérébrale acquise ?

Title: Is Multidimensional Fatigue Inventory (MFI-20) adequate to measure brain injury related fatigue?

Running head: BRAIN INJURY RELATED FATIGUE

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Conflict of interest

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Abstract

Background. Fatigue is a common symptom in patients with acquired brain injury (ABI) related disability while its multidimensionality has never been investigated, and specifically its relationship with patients' cognitive functioning.

Objective. This study aimed to evaluate the validity of the Multidimensional Fatigue Inventory (MFI-20) in patients suffering from ABI-related disability.

Methods. Four hundred twenty-six participants divided in three different groups (ABI-related disability, physical-related disability without an ABI, and healthy volunteers with no disability) were administered the French version of the Multidimensional Fatigue Inventory. We investigated the link between these fatigue measures and neuropsychological assessment in patients with ABI. Performance on this tool was compared according to the group and we calculated normative data for the Multidimensional Fatigue Inventory based on healthy volunteers' performance.

Results. In patients with ABI, fatigue measures significantly correlated with neuropsychological measures of attention, memory and executive functions. We found higher scores on Mental Fatigue and Reduced Activities dimensions in patients with ABI in comparison with the patients with physical disability ($p<0.05$) and healthy controls ($p<0.01$).

Conclusions. The Multidimensional Fatigue Inventory appeared to be a sensitive tool to detect ABI-related fatigue, fatigue levels being higher than in patients with physical disability and in healthy volunteers. As fatigue appeared to be related to memory, executive and attentional functioning of patients with ABI-related disability who often face unemployment, its impact on vocational outcome following ABI should be further investigated.

Keywords: *acquired brain injury, disability, multidimensional fatigue inventory, normative data, validity.*

Introduction

Fatigue is a common symptom in patients with acquired brain injury (ABI) (Malley, 2017), affecting between 21 and 70% of patients suffering from a traumatic brain injury (TBI) (Cantor et al., 2008, 2014), between 20 and 92% of patients with stroke (Duncan, Wu, & Mead, 2012; Nadarajah & Goh, 2015) and over 80% of patients with brain tumor (Asher, Fu, Bailey, & Hughes, 2016; Lovely, Miaskowski, & Dodd, 1999).

Fatigue has been widely defined in the literature. A complete and precise definition was provided by Aaronson et al., fatigue corresponding to “the awareness of a decreased capacity for physical and/or mental activity due to an imbalance in the availability, utilization, and/or restoration of resources needed to perform activity.” (Aaronson et al., 1999, p.46). A consensus was reached on its multidimensionality (Malley, 2017), fatigue including physical and psychological, motivational and situational, and activity-related dimensions (Cantor et al., 2014; Malley, 2017). A gender difference in fatigue was commonly found in the literature: in the general population, the number of fatigue complaints appeared to be higher in women than in men (Bensing, Hulsman, & Schreurs, 1999; Fuhrer & Wessely, 1995; Peretti-Watel et al., 2009). Different models to explain ABI-related fatigue were proposed. According to the coping hypothesis, fatigue would be the result of compensating processes for ABI-related cognitive impairment (van Zomeren & van den Burg, 1985) since several studies highlighted that neuropsychological performance was linked to the fatigue level of patients with TBI (Azouvi et al., 2004; Belmont, Agar, Hugeron, Gallais, & Azouvi, 2006; Belmont, Agar, & Azouvi, 2009; van Zomeren & van den Burg, 1985; Ziino & Ponsford, 2006a, 2006b). In patients with TBI, it was found that attentional performance (especially vigilance) predicted fatigue and fatigue increased depression and anxiety symptoms (Ponsford, Schönberger, & Rajaratnam, 2015), related to the return to work (Xiong, Martin, Sravanapudi, Colantonio, & Mollayeva,

2016). More generally, slower return to work was found to be predicted by self-reported fatigue (Jonasson, Levin, Renfors, Strandberg, & Johansson, 2018; Wäljas et al., 2014).

Assessment of fatigue following ABI in its multidimensionality is a challenging question, since the existing fatigue scales do not address both ABI context and multidimensionality. For example, the Fatigue Severity Scale (Krupp, LaRocca, Muir-Nash, & Steinberg, 1989) and the Barrow Neurological Institute Fatigue Scale (Borgaro, Gierok, Caples, & Kwasnica, 2004) evaluate one general fatigue dimension, and the Mental Fatigue Scale (Johansson, Starmark, Berglund, Rödhölm, & Rönnbäck, 2010) evaluate a particular fatigue dimension. However, to our knowledge, existing multidimensional scales had never been validated in patients with ABI, including both traumatic and non-traumatic (such as patients with a cerebral stroke or a cerebral tumor) etiologies. For example, the Modified Fatigue Impact Scale (Fisk et al., 1994) was validated only in patients with mild to moderate TBI (Schiehser et al., 2015), the Neurological Fatigue Index (Mills, Young, Pallant, & Tennant, 2010) and Fatigue Impact Scale (Debouverie, Pittion-Vouyovitch, Louis, & Guillemin, 2007) were developed only in patients with multiple sclerosis and the Neurological Fatigue Index was validated only in patients with stroke (Mills et al., 2012). The Multidimensional Fatigue Inventory (MFI-20) (Smets, Garssen, Bonke, & De Haes, 1995) and the Fatigue Impact Scale (Debouverie et al., 2007) both are psychometric tools evaluating multidimensional fatigue and validated in French. Since the MFI-20 is shorter (20 items) than the Fatigue Impact Scale (40 items), it appeared to be more adapted to patients with ABI who experience simultaneously a wide range of cognitive, psychological and behavior injury-related sequelae (Beni et al., 2017; Simblett, Ring, & Bateman, 2017; Spitz, Alway, Gould, & Ponsford, 2017). A validation of the MFI-20 in patients with ABI-related disability would lead to a more accurate assessment of fatigue and of its effects on cognitive functions. The aims of this study were therefore to evaluate the validity of the MFI-20 in patients suffering

from ABI-related disability and to provide demographically adjusted normative data for this tool in order to determine cut-off scores.

Method

Participants

Based on a volunteer participation, we included 426 participants divided in three different groups: 109 patients with disability due to an ABI (disability-ABI group), 79 patients with disability due to a physical cause in absence of an ABI (disability-noABI group), and 238 healthy volunteers with no disability (no-disability group). All participants were French fluent speakers. In the disability-ABI group, participants were 44.98 ($SD=15.80$) years old, the majority were men (70%) and they were included in this study at a mean delay of 4.28 years ($SD=5.33$) after their ABI. In the disability-noABI group, participants were 42.39 ($SD=8.34$) years old and the majority were men (62%). In the no-disability group, participants were 33.05 ($SD=11.85$) years old and the majority were women (64%).

The research was completed in accordance with the Helsinki Declaration (World Medical Association, 2013). Ethical approval for this study was obtained (2017-5-S55).

Procedure

Based on a volunteer participation, patients in the disability-ABI group were administered a fatigue evaluation during their neuropsychological assessment. We followed the same procedure for fatigue assessment in the three groups. Indeed, all participants were asked to complete the MFI-20 questionnaire. A single-item visual analogue scale (VAS) was administered to test the construct validity of the MFI-20. Both tools investigated their fatigue level during the previous week.

The VAS corresponded to a 10 cm long vertical bar. It was anchored by ‘total absence of fatigue’ (in French, “absence totale de fatigue”) at the bottom of the scale and by ‘complete exhaustion’ (in French, “épuisement complet”) at the top. Participants were asked to place a mark on the bar that described how tired they felt during the previous week. Fatigue intensity was scored by measuring in centimeters from the bottom of the scale to participants’ mark. As for the MFI-20, a higher score on the VAS indicated a higher level of fatigue. As some of our participants had an ABI inducing visuo-spatial deficit, such as spatial neglect, we decided to use a vertical VAS so neglect patients would not experience overwhelming difficulties in performing the task (Scott & Huskisson, 1979).

In the disability-ABI group, neuropsychological assessment was available in 43 patients. It included 172 variables corresponding to scores on different neuropsychological tests (see **Table 1**). According to patients’ limitations and/or their ABI-related complaints, the 172 variables were not necessarily available for all patients. In the no-disability group, 106 participants completed a paper version and 132 participants completed an online version of the MFI-20 on LimeSurvey. Among those who completed a paper version, 45 participants completed the VAS.

Data analysis

In the disability-ABI group, convergent validity was evaluated through Pearson or Kendall’s Tau correlation tests between VAS and MFI-20 scores. We ran regression analyses to investigate the influence of age, gender, education and etiology on the following fatigue measures: VAS score, MFI-20 total score, and on the four dimensions of the MFI-20, as to say General Fatigue, Mental Fatigue, Reduced Activities and Motivation (Gentile, Delarozière, Favre, Sambuc, & San Marco, 2003). Within this subgroup, we analyzed the link between the fatigue measures and neuropsychological performance through Pearson or Kendall’s Tau correlation test.

Table 1. List of neuropsychological tests administered to patients with ABI.

Test / Battery	Assessed cognitive function
One-Week Free and Cued Selective Reminding Test (Manoli et al., 2018)	Episodic verbal memory
Rey-Osterrieth Complex Figure (Meyers & Meyers, 1995)	Episodic visual memory Visual-constructive abilities
Doors Test (Baddeley, Emslie, & Nimmo-Smith, 1994)	Episodic visual memory
Dual task (Baddeley, Della Sala, Papagno, & Spinnler, 1997)	Working memory
Brown-Peterson Test (Geurten, Vincent, Van der Linden, Coyette, & Meulemans, 2016)	
D2 cancellation test (Brickenkamp & Zillmer, 1998)	Attention
Test Battery of Attentional Performance (TAP version 2.3.1; French adaptation by Michel Leclercq) (Zimmermann & Fimm, 2002)	
Trail Making Test (Roussel & Godefroy, 2008; Tombaugh, 2004)	Reactive mental flexibility
Stroop Test (Roussel & Godefroy, 2008)	Inhibition
The Multiple Errand Test (Martin, 1972)	Planning
Tower of London (Coyette & Van der Linden, 1993; Rainville et al., 2002)	
Wisconsin Card Sorting Test (Heaton, 1993)	Flexibility Planning
Block Design test from the Wechsler Adult Intelligence Scale – Fourth Edition (WAIS-IV) (Wechsler, 2008)	Visual-constructive abilities
Verbal fluency test (Cardebat, Doyon, Puel, Goulet, & Joannette, 1990)	Spontaneous mental flexibility
« Reading the mind in the eyes » Test – revised version (Baron-Cohen, Wheelwright, Hill, Raste, & Plumb, 2001)	Social cognition
Empathy Quotient (Baron-Cohen & Wheelwright, 2004)	

In the no-disability group, we evaluated the impact of socio-demographical characteristics on the fatigue measures using the method of Barona, Reynolds, and Chastain (1984) by means of an ascendant step-by-step linear regression model including three predictive factors: age, number of years of formal education, and gender. We then analyzed the MFI-20 scores according to the version administered and the subgroups combining the statistically significant predictors.

We compared performance of the three groups (disability-ABI, disability-noABI and no-disability) on the fatigue measures using Kruskal-Wallis multiple comparison tests and reported

the results among multiple pairwise comparisons using Dunn's test (Dunn, 1964), adjusting p-values with the Benjamini-Hochberg method (Benjamini & Hochberg, 1995).

We investigated the effect of the group on the fatigue measures according to gender through moderation analyses. We applied Hayes's Model 1 (Bolin, 2014; Hayes, 2013) with gender as the moderator. We examined the interaction between gender and the group (firstly, disability vs no-disability, secondly, disability-ABI vs no-disability). Then, using a pick-a-point approach, i.e. a simple-slopes analysis, we estimated the conditional effect of each group on fatigue measures for the two values of the gender moderator (Bolin, 2014; Cohen, Cohen, West, & Aiken, 2014; Hayes, 2013). The pick-a-point approach is a method of probing an interaction on a specific value of the moderator (Montoya, 2019). The significance of the indirect effect was tested using bias-corrected bootstrap (5000 times resampling) 95% confidence intervals and only standardized coefficients were reported (Bolin, 2014; Hayes, 2013).

In order to establish norms for the MFI-20 scores, we relied on the performance of the no-disability group and to the linear regression models testing the impact of socio-demographical characteristics on fatigue measures. For all models with statistically significant regression coefficients, we tested the normality of residuals distribution. As the assumption of normality of residuals distribution was not confirmed, norms were obtained using a classical percentile procedure (Dancey & Reidy, 2007).

Statistical analyses were performed using R version 3.5.3 (<https://www.r-project.org/>), only moderation analysis required using the PROCESS macro (Bolin, 2014; Hayes, 2013) on IBM SPSS Statistics 20.0 (<https://www-01.ibm.com/support/docview.wss?uid=swg21509012>).

Results

Disability-ABI group

Convergent validity of the MFI-20 was good; the correlations between all the MFI-20 scores and the VAS were statistically significant, even if low for MFI-20 total score ($\tau=0.43$, $p<0.001$), General Fatigue ($\tau=0.48$, $p<0.001$) and Mental Fatigue dimension ($\tau=0.33$, $p<0.001$), and negligible for Reduced Activities ($\tau=0.15$, $p=0.03$) and Motivation dimension ($\tau=0.17$, $p=0.02$) (Hinkle, Wiersma, & Jurs, 2003).

Age, gender and education did not significantly predict the VAS score (respectively, $p=0.99$, $p=0.16$, $p=0.44$), the MFI-20 total score (respectively, $p=0.47$, $p=0.33$, $p=0.63$), General Fatigue (respectively, $p=0.74$, $p=0.07$, $p=0.67$), Mental Fatigue (respectively, $p=0.32$, $p=0.61$, $p=0.73$), Reduced Activities (respectively, $p=0.84$, $p=0.10$, $p=0.19$) and Motivation dimension scores (respectively, $p=0.26$, $p=0.26$, $p=0.45$). Etiology significantly predicted the MFI-20 total score ($p=0.02$), the General Fatigue dimension score ($p=0.04$) and the Reduced Activities dimension score ($p<0.01$), patients with TBI and stroke having higher scores than those with brain tumor. It did not significantly predict the VAS score ($p=0.87$), the Mental Fatigue dimension score ($p=0.20$) and the Motivation dimension score ($p=0.07$).

Correlation analyses underlined that Motivation dimension of the MFI-20 significantly correlated with the delay from injury ($\tau=0.28$, $p=0.02$). Neuropsychological performance significantly correlated with the VAS and MFI-20 (see **Table 2**).

Table 2. Statistically significant correlations between neuropsychological scores and fatigue measures in patients with ABI.

	VAS	MFI-20 total score	General Fatigue	Mental Fatigue	Reduced Activities	Motivation
1W-FCSRT	CR2: <i>tau</i> =0.35, <i>p</i> =0.02	<i>ns</i>	TR2: <i>tau</i> =0.33, <i>p</i> =0.02; TR30: <i>tau</i> =0.33, <i>p</i> =0.03	PC TR7d: <i>tau</i> =-0.33, <i>p</i> =0.03	<i>ns</i>	<i>ns</i>
ROCF test	<i>ns</i>	<i>ns</i>	<i>ns</i>	<i>ns</i>	<i>ns</i>	IR time: <i>tau</i> =0.30, <i>p</i> =0.04
TAP	Alertness index: <i>tau</i> =0.36, <i>p</i> =0.01	Vigilance2: <i>tau</i> =0.35, <i>p</i> =0.04; Vigilance2 omiss: <i>r</i> =0.64, <i>p</i> <0.01; Vigilance tot omiss: <i>r</i> =0.62, <i>p</i> <0.01; PC Vigilance tot omiss: <i>tau</i> =-0.36, <i>p</i> <0.05	<i>ns</i>	PC omiss AudST Divided Attention: <i>tau</i> =-0.35, <i>p</i> <0.05; Vigilance2: <i>tau</i> =0.35, <i>p</i> <0.05; Vigilance2 omiss: <i>r</i> =0.61, <i>p</i> <0.01; Vigilance tot omiss: <i>r</i> =0.56, <i>p</i> =0.01; PC Vigilance tot omiss: <i>tau</i> =-0.40, <i>p</i> =0.03	Vigilance1: <i>r</i> =0.35, <i>p</i> <0.05; Vigilance2: <i>tau</i> =0.35, <i>p</i> <0.05; Vigilance2 omiss: <i>r</i> =0.49, <i>p</i> =0.03; Vigilance tot omiss: <i>r</i> =0.47, <i>p</i> =0.04; PC Vigilance tot omiss: <i>tau</i> =-0.38, <i>p</i> =0.04	WM err: <i>tau</i> =-0.43, <i>p</i> =0.01; PC WM err: <i>tau</i> =0.43, <i>p</i> =0.01; PC GoNoGo err: <i>tau</i> =0.49, <i>p</i> =0.03; PC Incompatibility err: <i>tau</i> =0.43, <i>p</i> =0.01

CR2: second cued recall; **IR time:** total duration of the immediate recall; **ns:** non-significant; **PC GoNoGo err:** percentile of the number of errors on the Go/NoGo subtest; **PC Incompatibility err:** percentile of the total number of errors on the Incompatibility subtest; **PC omiss AudST Divided Attention:** percentile of the total number of omissions during the auditory simple task of the Divided Attention subtest; **PC TR7d:** percentile of seven-days-delayed total recall; **PC Vigilance tot omiss:** percentile of vigilance total number of omissions; **PC WM err:** percentile of the number of errors on the Working Memory subtest; **TR2:** second total recall; **TR30:** 30-minutes-delayed total recall; **Vigilance tot omiss:** Vigilance total number of omissions; **Vigilance1:** raw score during the 1st part of the Vigilance subtest; **Vigilance2 omiss:** number of omissions during the 2nd part of the Vigilance subtest; **Vigilance2:** raw score during the 2nd part of the Vigilance subtest; **WM err:** number of errors on the Working Memory subtest.

Table 2. (Continues)

	VAS	MFI-20 total score	General Fatigue	Mental Fatigue	Reduced Activities	Motivation
ToL test	<i>ns</i>	mov 6N: $\tau=-0.43, p=0.04$; Z-score mov 6N: $\tau=-0.42, p<0.01$; Z-score time 3N: $\tau=0.36, p=0.01$; time 5N: $\tau=0.30, p=0.03$	mov 6N: $\tau=-0.45, p<0.01$; Z-score time 3N: $\tau=0.34, p=0.02$; time 5N: $\tau=0.30, p=0.03$	<i>ns</i>	time 3N: $\tau=-0.29, p<0.05$	time 3N: $\tau=0.30, p=0.03$
Verbal fluency	<i>ns</i>	Z-score on “animal” fluency: $r=0.43, p=0.04$; raw score on “P”-letter fluency: $r=0.36, p=0.02$; Z-score on “P”-letter fluency: $r=0.47, p=0.02$	Z-score on “animal” fluency: $r=0.58, p<0.01$; raw score on “P”-letter fluency: $r=0.38, p=0.02$; Z-score on “P”-letter fluency: $r=0.46, p=0.03$	<i>ns</i>	<i>ns</i>	<i>ns</i>
Block Design subtest (WAIS-IV)	<i>ns</i>	<i>ns</i>	<i>ns</i>	$r=-0.44, p=0.03$	<i>ns</i>	<i>ns</i>

mov 6N: number of movements performed by the patients when solving problems requiring at least six movements while the first evident movement is neutral; **ns:** non-significant; **time 3N:** total time needed by the patients to solve problems requiring at least three movements while the first evident movement is neutral; **time 5N:** total time needed by the patients to solve problems requiring at least five movements while the first evident movement is neutral; **WAIS-IV:** Wechsler Adult Intelligence Scale – Fourth Edition.

No-disability group

In the no-disability group, participants completed either a paper ($N_{paper}=106$) or an online version of the MFI-20 ($N_{online}=132$). Those who completed the online version had a greater female/male ratio (*Pearson's Chi-squared test with Yates' continuity correction*, $X^2=9.2417$, $p<0.01$) and a higher level of formal education (*Exact Wilcoxon rank sum test*, $W=7115.5$, $p<0.001$) than those who completed the paper version. When comparing the scores of those who completed the paper version with those who completed the online version, significant statistical differences were found for MFI-20 total score (*Asymptotic Wilcoxon rank sum test*, $W=8988$, $p<0.001$), General Fatigue ($W=9062.5$, $p<0.001$), Reduced Activities ($W=8759.5$, $p<0.001$) and Motivation ($W=8324.5$, $p=0.01$) dimensions. Yet, this difference might not be due to the version administrated, since age and gender were both significant predictors of the MFI-20 total score ($F=10.0$, $p<0.001$, *adjusted* $R^2=0.11$), General Fatigue ($F=9.63$, $p<0.001$, *adjusted* $R^2=0.10$), Mental Fatigue ($F=9.25$, $p<0.001$, *adjusted* $R^2=0.09$), and Reduced Activities ($F=8.74$, $p<0.001$, *adjusted* $R^2=0.09$) dimensions, and since age was a statistically significant predictor of the Motivation dimension ($F=4.77$, $p=0.03$, *adjusted* $R^2=0.02$). Thus, we categorized participants' age in three age groups: group 1 corresponding to those between 18 and 29 years old, group 2 to those between 30 and 44 years old and group 3 to those between 45 and 71 years old. These age groups were combined with the gender variable (Male/Female) and we analyzed the MFI-20 scores according to these combinations age group x gender (Male*Group1, Male*Group2, Male*Group3, Female*Group1, Female*Group2, Female*Group3; see **Table 3**) or according to age group alone. Based on the results presented in **Table 3** and given the fact that women were overrepresented in the online version, we decided to pool together the data of all participants with no disability, regardless of the version of the MFI-20 administered.

Table 3. MFI-20 scores in the no-disability group, according to the version administered and the subgroups combining age group and gender.

Scores Subgroups	Paper vs Online version				
	MFI-20 total score	General Fatigue	Mental Fatigue	Reduced Activities	Motivation
Male*Group1	W=247.5, <i>p</i> =0.72	W=265.5, <i>p</i> =0.43	W=176, <i>p</i> =0.19	W=220, <i>p</i> =0.78	W=2695, <i>p</i> = 0.05
Female*Group1	<i>t</i>=2.77, <i>p</i><0.01	<i>t</i>=2.75, <i>p</i><0.01	W=1099.5, <i>p</i> =0.18	W = 1340.5, <i>p</i><0.001	
Male*Group2	<i>t</i> =1.32, <i>p</i> =0.21	<i>t</i> =1.39, <i>p</i> =0.18	<i>t</i> =1.34, <i>p</i> =0.19	W=73.5, <i>p</i> =0.95	W=447.5, <i>p</i> =0.67
Female*Group2	<i>t</i> =-0.41676, <i>p</i> =0.68	<i>t</i> =-0.49461, <i>p</i> =0.63	<i>t</i> =-0.06, <i>p</i> =0.95	<i>t</i> =0.09, <i>p</i> =0.93	
Male*Group3	<i>t</i> =0.44, <i>p</i> =0.67	<i>t</i> =0.22, <i>p</i> =0.83	W=38.5, <i>p</i> =0.38	<i>t</i> =-0.49, <i>p</i> =0.63	W=311, <i>p</i> =0.06
Female*Group3	<i>t</i>=2.46, <i>p</i>= 0.03	<i>t</i>=2.41, <i>p</i>=0.03	W=135, <i>p</i> =0.07	W=167, <i>p</i><0.001	

t: Welch Two Sample *t*-test; *W*: Exact Wilcoxon rank sum test

Statistical significant relationships are in bold (confidence interval = 5 %).

Disability-ABI vs disability-noABI vs no-disability

In the disability-ABI group, age, gender and education did not significantly predict the VAS (age: *p*=0.99, gender: *p*=0.16, education: *p*=0.44), the MFI-20 total score (age: *p*=0.47, gender: *p*= 0.33, education: *p*=0.63), General Fatigue (age: *p*=0.74, gender: *p*=0.07, education: *p*=0.67), Mental fatigue (age: *p*=0.32, gender: *p*=0.61, education: *p*=0.73), Reduced Activities (age: *p*=0.84, gender: *p*=0.10, education: *p*=0.19), an Motivation dimension (age: *p*=0.26, gender: *p*=0.26, education: *p*=0.45).

Therefore, comparisons between the three groups (disability-ABI, disability-noABI, and no-disability) were conducted regardless of the socio-demographic characteristics on the fatigue scores. A statistical significant difference was found on the VAS according to the group (Kruskal-Wallis *chi-squared*=26.66, *p*<0.001), scores being higher in the disability-noABI group in comparison with the disability-ABI group (Dunn's Test, *Z*=-4.64, *p*<0.001) and with

the no-disability group (*Dunn's Test*, $Z=4.11$, $p<0.001$), but no statistical significant difference was found between the disability-ABI group and the no-disability group (*Dunn's Test*, $Z=0.34$, $p=0.73$). A statistical significant difference was found on the MFI-20 total score according to the group (*Kruskal-Wallis chi-squared*=27.91, $p<0.001$), scores being higher in the disability-ABI (*Dunn's Test*, $Z=4.26$, $p<0.001$) and the disability-noABI (*Dunn's Test*, $Z=4.19$, $p<0.001$) groups in comparison with the no-disability group, but no statistical significant difference was found between the disability-ABI group and the disability-noABI group (*Dunn's Test*, $Z=-0.34$, $p=0.73$). A statistical significant difference was found on the General Fatigue dimension according to the group (*Kruskal-Wallis chi-squared*=42.49, $p<0.001$), scores being higher in the disability-ABI (*Dunn's Test*, $Z=3.38$, $p=0.001$) and the disability-noABI (*Dunn's Test*, $Z=6.30$, $p<0.001$) groups in comparison with the no-disability group, and scores being higher in the disability-noABI group in comparison with the disability-ABI group (*Dunn's Test*, $Z=-2.88$, $p=0.004$). A statistical significant difference was found on the Mental Fatigue dimension according to the group (*Kruskal-Wallis chi-squared*=10.93, $p=0.004$), scores being higher in the disability-ABI group in comparison with the disability-noABI group (*Dunn's Test*, $Z=2.32$, $p=0.03$) and with the no-disability group (*Dunn's Test*, $Z=3.23$, $p=0.004$), but no statistical significant difference was found between the disability-noABI group and the no-disability group (*Dunn's Test*, $Z=0.24$, $p=0.81$). A statistical significant difference was found on the Reduced Activities dimension according to the group (*Kruskal-Wallis chi-squared*=32.38, $p<0.001$), scores being higher in the disability-ABI group in comparison with the disability-noABI group (*Dunn's Test*, $Z=3.96$, $p<0.001$) and with the no-disability group (*Dunn's Test*, $Z=5.57$, $p<0.001$), but no statistical significant difference was found between the disability-noABI group and the no-disability group (*Dunn's Test*, $Z=0.46$, $p=0.65$). No statistically significant difference was found on the Motivation dimension according to the group (*Kruskal-Wallis chi-squared*=5.49, $p=0.06$).

A moderator effect of gender?

We tested a moderation model with group as the independent variable, fatigue measures as the outcome variable, and gender as a moderator. In the first analysis, the two modalities of the group were disability (including the groups disability-ABI and disability-noABI) and no-disability. In the second analysis, the two modalities of the group were disability-ABI and no-disability. In both analyses, the fatigue measures were VAS, MFI-20 total score, General Fatigue, Mental Fatigue, Reduced Activities, and Motivation. Only statistically significant moderator effects were reported hereafter.

In the first analysis, using group (disability vs no-disability) as the independent variable, Reduced Activities as the outcome variable, and gender as a moderator, we found a significant interaction between group and gender (see **Figure 1a**), $t(418)=2.89$; $p<0.01$ ($B=2.45$, $SE=0.85$, 95% CI 0.78 to 4.12): group predicted Reduced Activities for men, $t(418)=-4.78$; $p<0.001$ ($B=-2.75$, $SE=0.58$, 95% CI -3.89 to -1.61), but not for women, $t(418)=-0.48$; $p=0.63$ ($B=-0.30$, $SE=0.62$, 95% CI -1.52 to 0.93).

In the second analysis, using group (disability-ABI vs no-disability) as the independent variable, Reduced Activities as the outcome variable, and gender as a moderator, we found a significant interaction between group and gender (see **Figure 1b**), $t(339)=2.54$; $p=0.01$ ($B=2.66$, $SE=1.05$, 95% CI 0.60 to 4.72): group predicted Reduced Activities for men, $t(339)=-5.98$; $p<0.001$ ($B=-3.93$, $SE=0.66$, 95% CI -5.22 to -2.64), but not for women, $t(339)=-1.56$; $p=0.12$ ($B=-1.27$, $SE=0.81$, 95% CI -2.87 to 0.33).

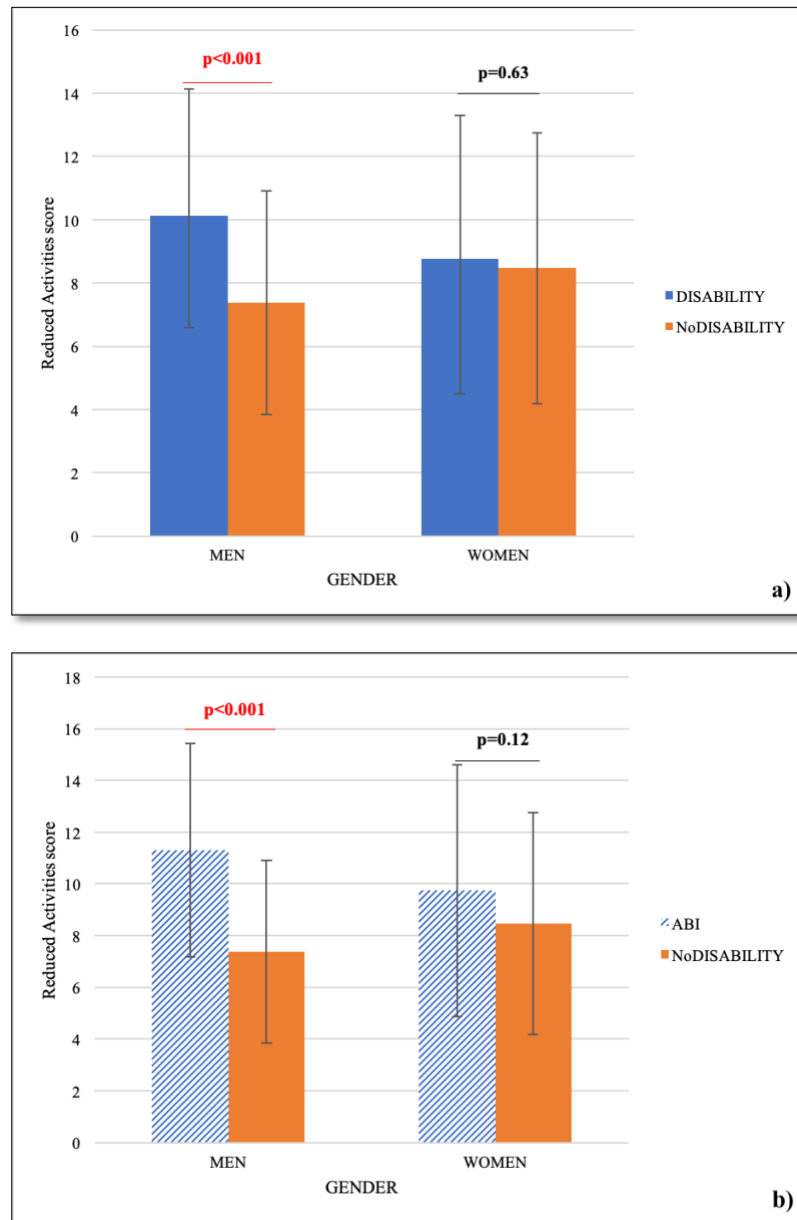


Figure 1. Scores on the Reduced Activities dimension of the Multidimensional Fatigue Scale, according to gender and group: a) disability vs no-disability, b) acquired brain injury vs no-disability.

ABI: acquired brain injury.

MFI-20 Normative data

Percentiles were calculated according to age and gender (see *Table 4*).

Table 4. Percentiles Calculated With a Classical Method (Dancey & Reidy, 2007) for MFI-20 measures.

MFI-20 TOTAL SCORE							
	Age group	G1		G2		G3	
	Gender	Male	Female	Male	Female	Male	Female
Percentiles	0	89.00	120.00	89.00	103.00	89.00	91.00
	5	80.00	102.00	80.00	89.20	80.75	84.60
	10	75.00	96.10	78.00	81.80	74.50	80.80
	15	72.80	89.95	73.80	77.00	70.75	75.40
	20	63.80	86.00	71.40	75.20	70.00	71.20
	25	59.00	83.75	67.00	69.00	65.50	70.00
	50	45.00	64.00	53.00	61.00	54.00	47.00
	75	39.00	50.25	41.00	47.00	38.75	39.00
	100	25.00	27.00	34.00	30.00	20.00	20.00

GENERAL FATIGUE							
	Age group	G1		G2		G3	
	Gender	Male	Female	Male	Female	Male	Female
Percentiles	0	46.00	60.00	47.00	63.00	50.00	41.00
	5	42.00	50.10	42.00	44.60	47.00	41.00
	10	41.20	48.00	37.60	40.80	44.00	41.00
	15	36.60	46.00	36.40	40.00	39.25	38.80
	20	30.20	45.00	35.20	38.20	31.00	38.00
	25	28.00	43.75	31.00	36.00	31.00	35.00
	50	21.00	33.00	23.00	29.00	27.00	26.00
	75	17.00	23.25	18.00	23.00	19.50	20.00
	100	9.00	10.00	13.00	10.00	9.00	9.00

MENTAL FATIGUE							
	Age group	G1		G2		G3	
	Gender	Male	Female	Male	Female	Male	Female
Percentiles	0	33.00	40.00	26.00	34.00	33.00	27.00
	5	26.80	33.10	25.60	28.40	31.50	25.20
	10	22.20	29.10	24.00	26.00	27.00	24.00
	15	19.00	28.30	23.40	25.20	22.50	20.40
	20	18.20	27.00	22.20	23.80	21.00	17.40
	25	18.00	25.00	22.00	22.00	19.50	17.00
	50	15.00	19.50	17.00	18.00	12.50	13.00
	75	13.00	13.00	14.00	15.00	8.00	10.00
	100	6.00	6.00	7.00	9.00	6.00	6.00

REDUCED ACTIVITIES							
	Age group	G1		G2		G3	
	Gender	Male	Female	Male	Female	Male	Female
Percentiles	0	19.00	20.00	14.00	16.00	11.00	17.00
	5	14.60	17.00	13.60	11.40	11.00	13.20
	10	12.00	16.00	12.00	11.00	10.50	12.00
	15	11.00	15.00	12.00	10.20	10.00	11.80
	20	11.00	14.00	12.00	9.00	10.00	9.80
	25	10.00	13.00	11.00	9.00	9.25	8.00
	50	6.00	9.00	8.00	7.00	7.00	6.00
	75	5.00	6.00	4.00	5.00	4.75	4.00
	100	3.00	3.00	3.00	3.00	3.00	3.00

MOTIVATION							
	Age group	G1		G2		G3	
	Gender	Male	Female	Male	Female	Male	Female
Percentiles	0	13.00		14.00		13.00	
	5	8.00		9.00		11.40	
	10	7.00		8.00		8.00	
	15	6.90		7.45		7.00	
	20	5.20		7.00		7.00	
	25	5.00		6.00		7.00	
	50	4.00		5.00		5.00	
	75	2.50		3.00		3.00	
	100	2.00		2.00		2.00	

G1: 18-29 years; G2: 30-44 years; G3: 45-71 years old.

Discussion

The aim of this study was to evaluate the validity of the MFI-20 in patients suffering from ABI-related disability. For this purpose, 426 participants divided in three different groups (disability due to an ABI, disability due to a physical cause in absence of an ABI, and healthy volunteers with no disability) were administered the MFI-20 and a single-item VAS. We investigated the link between these fatigue measures and neuropsychological assessment in the disability-ABI group. Performance on these tools was compared according to the group and we calculated normative data for the MFI-20 based on healthy volunteers' performance.

In patients with ABI, MFI-20 measures and VAS correlated with memory and attention performance. MFI-20 measures additionally correlated with planning, spontaneous mental flexibility and visuo-constructive performance. A higher level of fatigue was found in patients with disability due to an ABI in comparison with patients with physical disability and healthy volunteers on Mental Fatigue and Reduced Activities dimensions of the MFI-20. Thus, these two dimensions of the MFI-20 appeared to highlight ABI-related fatigue. Higher levels of fatigue were found in patients with disability, either due to an ABI or not, in comparison with healthy volunteers on MFI-20 total score and General Fatigue. Thus, these three measures appeared to highlight disability-related fatigue.

Fatigue either due to a physical disability or an ABI could not be underlined only with the VAS score. However, giving that VAS correlated with MFI-20 scores and neuropsychological measures of memory and attention, this tool could be useful in patients with severe sequelae who would not be able to respond to a full 20-items-questionnaire, as it was already used in patients with severe TBI (Belmont et al., 2009).

We found a moderating effect of gender on the relation between group (patients with disability vs healthy controls, and patients with ABI vs healthy controls) and Reduced Activities dimension measuring the ability to physically do (or not) something (Gentile et al., 2003). The

score on the Reduced Activities dimension was higher in patients with physical and ABI-related disability in comparison with healthy controls, but only in men. Thus, in these two groups, men would be more impacted than women on their ability to physically do something. Even if healthy women would experience a higher level of fatigue in comparison to men on this specific point, this level would not be impacted by the presence of a disability. This could have been influenced by the fact that the male/female ratio was greater in patients with disability (73/31 for patients with ABI; 49/30 for patients with physical disability) than in the group of healthy volunteers (86/152). Indeed, in medical and social structures for patients with disability, the male/female ratio is representative of the physical and ABI disability incidence (Vagnerova, Koerner, & Hurn, 2008), whereas in general population it was found that women were more likely to participate to surveys than men (Curtin, Presser, & Singer, 2000; Moore & Tarnai, 2002; Singer, van Hoewyk, & Maher, 2000). Another possible explanation of this moderating effect would be the fact that fatigue in women's life was found to be associated with environmental demands on their lives, as self-esteem, menstrual cycle phases or number of children (Lee, Lentz, Taylor, Mitchell, & Woods, 1994).

Conclusions

The Multidimensional Fatigue Inventory appeared to be a sensitive tool to detect ABI-related fatigue, fatigue levels being higher than in patients with physical disability and in healthy volunteers. We provided normative data for this tool based on healthy volunteers' performance, according to gender and age group. As fatigue appeared to be related to neuropsychological functioning of patients with ABI-related disability who often face unemployment, its impact on vocational outcome following ABI should be further investigated.

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3. Discussion

L'objectif de cette **Partie III** était d'identifier les outils permettant d'évaluer l'ensemble des processus déficitaires de la mémoire épisodique verbale et la fatigue générale, qui sont souvent retrouvés chez les personnes victimes d'une LCA.

D'une part, nous avons, dans l'**Article 2** (Manoli et al., 2018), proposé l'adaptation d'une épreuve existante, le test du Rappel libre/Rappel indicé à 16 items (RL/RI-16 ; Van der Linden & the members of GREMEM, 2004). Cette adaptation, le *One-Week Free and Cued Selective Reminding Test-word version* (1W-FCSRT-word), comportait, comme dans le test du RL/RI-16, une phase d'apprentissage en trois essais, cependant le délai du rappel différé a été modifié à 30 minutes (par rapport au délai initial de 20 minutes) et un rappel différé supplémentaire à sept jours après le dernier rappel de la phase d'apprentissage a été rajouté. Cette adaptation a également souligné l'importance de calculer les performances mnésiques en fonction des performances pendant la phase d'apprentissage. Ainsi, nous avons fourni des données normatives pour quatre mesures sous-tendant des processus mnésiques différents : un score d'apprentissage sous-tendant le processus d'encodage, un score d'indilage sous-tendant le processus de stockage, et deux scores d'oubli pour les rappels différés (30 minutes et sept jours), sous-tendant ainsi deux processus de consolidation en mémoire verbale, l'un rapide (30 minutes) et l'autre lent (sept jours). Dans l'**Article 3** (Manoli, Chartaux-Danjou, Delecroix, Daveluy, & Moroni, 2018), nous avons évalué les processus mnésiques de patients souffrant de TC sévère et de participants contrôles neurologiquement sains au moyen de l'épreuve 1W-FCSRT. Les patients avaient des performances mnésiques inférieures aux participants contrôles, pour le score d'apprentissage ainsi que pour les deux scores d'oubli. En s'appuyant sur les données normatives fournies dans l'**Article 2** (Manoli et al., 2018), des scores mnésiques déficitaires ont été mis évidence chez 16% des patients pour le score d'apprentissage, chez 28% pour le score d'oubli à 30 minutes et 35% pour le scores d'oubli à sept jours. En utilisant cette

épreuve adaptée, nous avons retrouvé un déficit de la consolidation lente chez six patients qui ne présentaient aucun déficit mnésique, ni en phase d'apprentissage, ni après un délai de 30 minutes. Avec des épreuves classiques utilisant une évaluation de la mémoire dans un délai de 30 minutes, on aurait pu conclure à tort à une préservation des capacités mnésiques, alors que celles-ci sont hautement liées à la réintégration professionnelle des personnes cérébrolésées (Boake et al., 2001; Green et al., 2008).

D'autre part, nous avons, dans l'**Article 4**, testé l'utilité d'un questionnaire de fatigue, le *Multidimensional Fatigue Inventory* (Gentile et al., 2003; Smets et al., 1995), pour mesurer le niveau de fatigue spécifique d'une LCA. Pour ce faire, nous avons administré cet outil à trois groupes de participants : un groupe de patients porteurs d'un handicap dû à une LCA, un groupe de patients porteurs d'un handicap physique non causé par une LCA, et un groupe de participants contrôles neurologiquement sains. Chez les patients souffrant d'une LCA, les scores de fatigue corrélaient significativement avec les mesures neuropsychologiques d'attention, mémoire et fonctions exécutives, et étaient significativement plus élevés par rapport aux patients porteurs d'un handicap physique non causé par une LCA et par rapport aux participants contrôles. De ce fait, le *Multidimensional Fatigue Inventory* est apparu comme un outil suffisamment sensible pour détecter le niveau de fatigue spécifique d'une LCA. Cet outil était par ailleurs corrélé aux mesures de mémoire épisodique verbale de l'épreuve adaptée proposée dans l'**Article 2**, et notamment avec le rappel à sept jours, chez des personnes souffrant d'une LCA.

L'ensemble de ces résultats nous ont permis de justifier l'utilisation de ces deux outils afin d'investiguer le lien entre performances cognitives, comportement et probabilité de réussir / échouer en intégrant une formation après une LCA. Ils ont été inclus dans la méthodologie des études présentées dans la **Partie IV** ayant pour objet cette investigation.

PARTIE IV :

PERFORMANCES COGNITIVES ET PROBABILITE

DE REUSSIR / ECHOUER EN INTEGRANT UNE

FORMATION APRES UNE LESION CEREBRALE

ACQUISE

Dans la **Partie II**, la revue systématique de la littérature (**Article 1**) nous a permis de mettre en évidence le manque d'études explorant d'autres types d'issues professionnelles, comme l'issue d'une formation entamée à la suite d'une LCA, et l'impact que les déficits post-LCA peuvent avoir sur ces issues.

Dans cette **Partie IV**, nous avons étudié le lien entre les performances cognitives et comportementales évaluées à l'entrée en Unités d'Évaluation, de Réentraînement et d'Orientation Sociale et/ou professionnelle pour personnes cérébro-lésées (UEROS) et la réussite / l'échec d'une formation qualifiante entreprise après une LCA. Pour ce faire, une évaluation exhaustive des fonctions cognitives et comportementales, adaptée aux personnes souffrant d'une LCA, nous a semblé primordiale. Dans cette évaluation, nous avons pris en compte de nouvelles mesures et de nouveaux outils proposés dans la **Partie III**, à savoir les mesures de l'épreuve *One-Week Free and Cued Selective Reminding Test* (1W-FCSRT) présentée dans les **Articles 2 et 3** et le questionnaire *Multidimensional Fatigue Inventory* (MFI-20) qui a fait l'objet de l'**Article 4**. L'étude du lien entre performances cognitives et comportementales et l'issue d'une formation professionnelle impliquait une analyse de données de grande dimension, particulièrement innovante en neuropsychologie, et qui permet d'identifier des modèles prédictifs : l'apprentissage automatique ou *machine learning*.

1. Volet rétrospectif

1.1. Article 5 – *Etude préliminaire : Comment évaluer l'impact des séquelles cognitives sur le retour en formation des patients souffrant de lésion cérébrale acquise ?*

Manoli, R., Duwooz, A., Chartaux-Danjou, L., Delecroix, H., Daveluy, W., Torre, F., & Moroni, C. (unsubmitted). How to evaluate the impact of cognitive sequelae on vocational outcome in patients with acquired brain injury? A retrospective study.

Running head: Vocational outcome and brain injury

Title: How to evaluate the impact of cognitive sequelae on vocational outcome in patients with acquired brain injury? A retrospective study

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Title: How to evaluate the impact of cognitive sequelae on vocational outcome in patients with acquired brain injury? A retrospective study

ABSTRACT

Objective: To highlight cognitive abilities hindering the return to vocational training after an acquired brain injury.

Design: A retrospective study.

Setting: Data were collected in two Health and Social units for individuals with brain injury (in French: *UEROS, Unités d'Evaluation, de Réentraînement et d'Orientation Sociale et/ou professionnelle*) in Berck-sur-Mer and Lille, France.

Participants: Thirty-five individuals suffering from acquired brain injury were included in this study. All participants had completed a vocational rehabilitation program, between 2003 and 2014, and resumed a vocational training afterwards.

Interventions: Not applicable.

Main Outcome Measures: Vocational outcome defined as success or failure in resuming an accredited vocational training.

Results: Neuropsychological data collected from participants' assessment during the rehabilitation program, after a mean delay of six years post-injury, were processed through machine learning algorithms with supervised learning classification methods. Neuropsychological scores underlying attention performance and executive functioning were the most related to vocational outcome.

Conclusion(s): Our results emphasized neuropsychological factors that would explain the success or failure in resuming vocational training. Increasing the number of participants could allow us to identify neuropsychological scores predicting vocational training outcome.

Key words: vocational training, cognition, brain injury, machine learning.

Abbreviations:

ABI	Acquired brain injury
BORB	Birmingham Object Recognition Battery
TAP	Test battery of Attentional Performance
TBI	Traumatic brain injury
TMT	Trail Making Test
WAIS	Wechsler Adult Intelligence Scale
WCST	Wisconsin Card Sorting Test
WMS	Wechsler Memory Scale

Acquired brain injury (ABI), either with a traumatic or non-traumatic etiology,¹ is a major cause of death or disability.² In France for example, 704 per 100 000 adults presented traumatic brain injury related disabilities.³ Brain injury sequelae can affect many areas, including cognition and behavior.⁴ Cognitive disabilities appeared to be correlated to functional outcome in patients with brain injury,⁵ especially with a traumatic etiology.⁶ Functional outcome seemed to have an impact on patients' quality of life.²

Different cognitive sequelae affecting memory, attention and executive functioning were identified in patients with ABI,⁷ including patients with tumor.⁸⁻⁹ Executive impairment was found in patients with ABI,¹⁰⁻¹¹ whether suffering from traumatic brain injury (TBI),¹²⁻¹³ stroke¹⁴⁻¹⁵ or brain tumor.¹⁶ For example, weaker spontaneous and reactive mental flexibility as well as weaker automatic response inhibition performance was found in patients with TBI in comparison with neurologically healthy individuals.¹⁷ This pattern was also observed with a non-verbal material in patients with stroke.¹⁸

Regarding attentional processes, patients with TBI present difficulties in sustained,¹⁹⁻²⁰ focused and divided attention.²¹ Attention deficits,²² including information processing speed,¹⁸ were also underlined in patients with stroke or in patients with a brain tumor for visual material.²³

Impairments in verbal short-term memory, visuospatial and verbal working memory were found in patients with TBI.²⁴ Memory impairments also appeared to affect episodic and autobiographical memory in mild TBI,²⁵ verbal encoding in patients with left-hemisphere stroke²⁶ and spatial memory in patients with ischemic stroke.²⁷

All these deficits have an impact on patients' autonomy and productivity.²⁸ Patients with brain tumor, for example, experience particular difficulties in work assignments, as remembering important dates or appointments, or also shifting between professional tasks.²⁹

Forty percent of individuals return to work one or two years after an ABI.³⁰ However, patients and employers reported sensory overload and fatigue as work barriers.¹ Indeed, cognitive fatigue is often reported to hinder activities of daily living of patients with brain injury.³¹ Cognitive impairments were identified as negative predictors of return to work after stroke.³² Memory, attentional, problem solving or planning deficits appeared to affect work performance of patients with traumatic brain injury.³³ Regarding executive functioning, patients with ABI performing on average or higher were more independent in employment than patients with low executive performance.³⁴ To our knowledge, the impact of cognitive sequelae on return to vocational training has not yet been investigated. Since identifying such cognitive factors would require an exhaustive neuropsychological assessment, this investigation would need a specific data analysis. Indeed, as neuropsychological assessment usually contains many measures and vary in terms of tests administered inducing missing data from one patient to another, the most adequate data analysis appears to be machine learning,³⁵ which works with large data and even with missing data as it occurs in retrospective studies.³⁶

The aim of this study was to highlight cognitive profiles that would hinder a return to vocational training after an ABI. In this purpose and through machine learning algorithms, we sought to evaluate the impact of cognitive deficits following a brain injury on return to vocational training and to determine whether success or failure in resuming a vocational training would be predicted by patients' cognitive abilities. More specifically, we presumed that memory, attention and executive functions impairment would have a negative impact on learning processes during a vocational training and hence this impairment would be directly linked to vocational outcome of individuals suffering from brain injury. Thus, we hypothesized the existence of cognitive profiles predicting success or failure in vocational training of these individuals.

METHOD

Participants

This retrospective study included 35 patients with ABI who resumed a vocational training after a social-professional rehabilitation program, from 2003 to 2014, in two Health and Social Structures (28 participants in the UEROS Lille and seven in the UEROS Berck-sur-Mer, France). All participants were adults, French native speakers and, according to their physiatrist, stable from a sensorimotor, cognitive and behavioral perspective.

Since functional outcome does not seem to be correlated to etiology of ABI,² we included patients regardless of the etiology (80% TBI, 14% stroke and 6% brain tumor). The participants' average age at the time of the injury was 25.71 ($\pm$ 9.27) and 31.29 ($\pm$ 9.12) when they had integrated the rehabilitation program. The average delay between the time of the injury and the rehabilitation program was 5.57 years ($\pm$ 5.33). Twenty-five participants (71%) from our sample succeeded in their vocational training.

Procedure

During the rehabilitation program, participants were administered a neuropsychological assessment, consisting in exploring five cognitive domains: memory, attention, executive functions, visual instrumental abilities and social cognition (see **Table 1**).

Table 1. Neuropsychological assessment.

Evaluated cognitive functions		Test and batteries	Procedure
MEMORY	Short term memory	Digit span (WAIS-III; Wechsler, 2000)	Forward and backward verbal recall of sequences of digits presented orally
		Spatial span (WMS-III; Wechsler, 2001)	Forward and backward visuo-spatial recall of sequences of digits presented visuo-spatially
	Working memory	Brown-Peterson Test (Geurten et al., 2016)	Verbal recall of visually presented trigrams after a delay of 0, 5, 10, and 20 seconds; the delay comprised or not an interference task (backward recall of pairs of numbers visually presented)
		Dual task (Baddeley et al., 1997)	A tracking task concomitantly performed with a verbal recall of sequences at participants' own span, during 2 minutes
	Episodic verbal long-term memory	RL/RI-16 items (Van der Linden et al., 2004)	Learning and recall of 16 words during 3 trials
		1W-FCSRT (Manoli et al., 2018)	Delayed recall of 16 words, 30 min and 7 days after encoding

1W-FCSRT: One Week – Free and Cued Selective Reminding Test; **RL/RI**: “*rappel libre / rappel indicé*”, corresponding to a free and cued selective reminding test of verbal material; **WAIS**: Wechsler Adult Intelligence Scale; **WMS**: Wechsler Memory Scale.

Table 1. (Continues)

MEMORY	Episodic visual long-term memory	Rey-Osterrieth Complex Figure (Meyers & Meyers, 1995)	Incidental immediate (3 min after encoding) and delayed (30 min after encoding) grapho-motor recall of a complex figure
		Doors Test (Baddeley et al., 1994)	Recognition of visually presented doors
ATTENTION		Test Battery of Attentional Performance (version 2.3.1; French adaptation by Michel Leclercq; Zimmermann, & Fimm, 2002)	Computerized battery including 13 subtests: Alertness: reaction time measures, with or without a preceding cue Working Memory: when a sequence of numbers is visually presented, press the key when the number shown is the same as the n-back number, n deferring from a condition to another Eye-Movement: reaction time measures Crossmodal Integration: reaction time measures for the combination of two specified stimuli Sustained Attention: reaction time measures whenever two successive stimuli have the same color and/or shape and/or size and/or filling Flexibility: reaction time in switching between two stimuli Visual Field / Neglect: <i>a peripheral flicker stimulus appears on an otherwise empty background / the screen is filled with a mask of numbers in order to provoke extinction</i>

Table 1. (Continues)

ATTENTION	Test Battery of Attentional Performance (version 2.3.1; French adaptation by Michel Leclercq; Zimmermann, & Fimm, 2002)	Divided Attention: two parallel visual/auditory reaction time tasks Go/NoGo: press the key for target stimuli (1 of 2 or 2 amongst 5) Incompatibility: <i>depending on the direction of the stimulus, respond with the right or left hand irrespective of the side on which the stimulus is presented</i> Covert Shift of Attention: reaction time measures, with a correct/incorrect preceding cue Vigilance: detect a specified auditory or visual pattern Visual Scanning: detect a stimulus in exploring a matrix
	D2 cancellation test (Brickenkamp, 1998)	Cross out only specified items as many as possible within the time limit
EXECUTIVE FUNCTIONS	Trail Making Test (Roussel & Godefroy, 2008; Tombaugh, 2004)	A) Connect a sequence of consecutive numbers; B) Connect a sequence of consecutive numbers and letters, alternating between numbers and letters
	Stroop Test (Roussel & Godefroy, 2008)	1) read color names; 2) <i>name different color patches</i> ; 3) <i>name the color of the ink instead of reading the word, color-words being printed in an inconsistent color ink</i>
	The Multiple Errands Test (Martin, 1972)	Perform multiple everyday tasks in a real-world environment, according to different conditions
	Trail Making Test (Roussel & Godefroy, 2008; Tombaugh, 2004)	A) Connect a sequence of consecutive numbers; B) Connect a sequence of consecutive numbers and letters, alternating between numbers and letters

Table 1. (Continues)

EXECUTIVE FUNCTIONS	Stroop Test (Roussel & Godefroy, 2008)	1) read color names; 2) <i>name different color patches</i> ; 3) <i>name the color of the ink instead of reading the word, color-words being printed in an inconsistent color ink</i>
	The Multiple Errands Test (Martin, 1972)	Perform multiple everyday tasks in a real-world environment, according to different conditions
EXECUTIVE FUNCTIONS	Tower of London (Coyette & Van der Linden, 1993)	Problem solving in reproducing the presented model, with different levels of difficulty, according to the number of movements (3, 4, 5, 6) required to solve the problems and/or according to the type of first required movement (neutral, positive, negative)
	Wisconsin Card Sorting Test (Heaton et al., 1993)	Match stimuli according to inferred rules
	Verbal Fluency Test (Cardebat et al., 1990)	Produce as many words as possible from a category within the time limit
VISUAL INSTRUMENTAL ABILITIES	Block design (WAIS-III; Wechsler, 2000)	Rearrange blocks to match presented models
	Birmingham Object Recognition Battery (Riddoch & Humphreys, 1993)	Matching (orientation, size, length, position of objects), figure-ground distinction in overlapping figures, recognition, object decision, functional and associative matching, picture naming

Table 1. (Continues)

SOCIAL COGNITION	« Reading the mind in the eyes » Test – revised version (Baron-Cohen et al., 2001)	<i>Describing the emotional/mental state of a person based on only an image of their eyes, in a fixed-choice paradigm</i>
	Empathy Quotient (Baron-Cohen & Wheelwright, 2004)	Degree of agreement with a list of statements (on a 4-point scale, from strongly agree to strongly disagree)

Data analysis

Raw scores and standardized scores (percentiles and/or Z-scores) to the neuropsychological tests corresponded to our independent variables (i.e. 189 variables). The dependent variable was the vocational training outcome, with two modalities: success and failure. We sought to identify which scores would explain or predict the success or failure in resuming a vocational training after a brain injury.

For this purpose, data were analyzed through machine learning algorithms with supervised learning classification methods. First, we performed a decision tree learning, generally used for inductive inference,⁵⁵ using the C4.5 algorithm.⁵⁶⁻⁵⁷ Then, we performed a rule-based machine learning method called association rule learning with Globo,⁵⁸ one of the main learners of Volata, a machine learning system implemented in Java.⁵⁹ Finally, we used a boosting method on the decision tree (random decision forests) and association rule learnings respectively with the C5.0 algorithm⁵⁷ and GloBoost in Volata.⁵⁹⁻⁶⁰

RESULTS

The C4.5 algorithm generated a concise decision tree with four attributes (**Fig. 1**). The first attribute corresponded to the GZ-F index, an error-corrected quantitative performance on the D2 cancellation test,⁴⁴ calculated by subtracting the total number of errors to the total number of items processed. The second attribute corresponded to a performance score to the Tower of London test, namely the Z-score of the number of movements realized in the problems requiring at least five movements and containing a “positive trigger” (the first movement facilitates the resolution of the problem).^{49,61} The third attribute of the decision tree corresponded to the Z-score of the number of common words starting with the letter “p” generated during the Verbal Fluency Test.⁵⁰ The fourth attribute corresponded to the percentage of correct answers for the 20-second-distracting-task conditions of the Brown-Peterson Test.³⁹

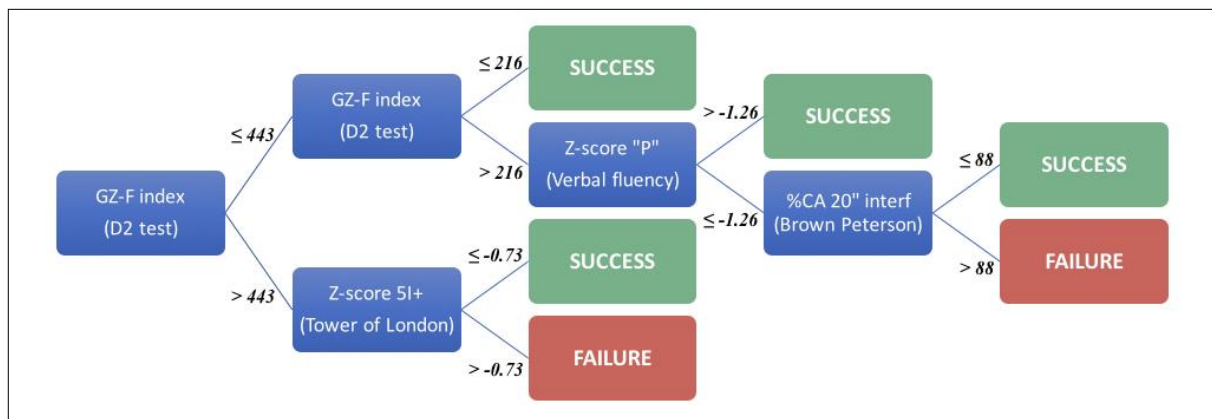


Figure 1. Neuropsychological measures associated with success or failure in resuming vocational training after brain injury: a decision tree generated with the C4.5 algorithm

%CA 20" interf: percentage of correct answers (raw score) for the 20-second-distracting-task conditions of the Brown-Peterson Test; 5I+: number of movements realized in the problems requiring at least five movements and containing a "positive trigger" during the Tower of London test; GZ-F: an error-corrected quantitative performance on the D2 test, calculated by subtracting the total number of errors to the total number of items processed; "P": number of common words starting with the letter "p" generated during the Verbal Fluency Test.

Association rule learning identified five models implicating 17 attributes. According to each model, a specific neuropsychological performance was linked either to success or failure in resuming vocational training (**Table 2**). The C5.0 algorithm generated a forest of 10 decision trees implicating 16 attributes. The most implicated attribute in these forest of decision trees was the percentile of the number of errors on the flexibility subtest (press the right or left button according to the right or left location of the target on the screen) of the TAP⁴⁵ (**Table 3**).

Table 2. Attributes implicated in the five models identified with an association rule learning.

NEUROPSYCHOLOGICAL TEST/BATTERY	ATTRIBUTES	SCORE	COGNITIVE FUNCTION	MODEL	PREDICTED OUTCOME
Doors Test	Part A+B	Raw score	Episodic visual memory	1	SUCCESS
D2 test	GZ score = quantitative performance index	Raw score	Visual selective attention	1	SUCCESS
D2 test	GZ-F score = global performance index	Raw score	Visual selective attention	1 2	SUCCESS SUCCESS
D2 test	GZ score = quantitative performance index	Percentile	Visual selective attention	2	SUCCESS
Wechsler adult intelligence scale – Third version	Digit span forwards	Raw score	Short-term verbal memory	2	SUCCESS
Divided attention (Test Battery of Attentional Performance)	Number of omissions – auditory simple task	Raw score	Divided attention	2	SUCCESS
Divided attention (Test Battery of Attentional Performance)	Number of omissions – visual simple task	Raw score	Divided attention	2	SUCCESS
Flexibility (Test Battery of Attentional Performance)	Flexibility – Time	Percentile	Cognitive flexibility	3	SUCCESS
Flexibility (Test Battery of Attentional Performance)	Flexibility – Number of errors	Percentile	Cognitive flexibility	3	SUCCESS
Wechsler adult intelligence scale – Third version	Block design	Raw score	Visuo-construction	3 4	SUCCESS FAILURE
Wechsler Memory Scale – Third version	Spatial span – total score	Raw score	Short-term visual memory	4	FAILURE
Dual Task	Efficiency (%)	Raw score	Central executive, working memory	4	FAILURE
D2 test	SB score = variation interval	Raw score	Constancy in performance	4	FAILURE
Tower of London	Number of movements realized in the neutral problems requiring at least five movements	Z-score	Planning	4	FAILURE
Tower of London	Number of movements realized in the problems requiring at least five movements containing a “negative trigger”	Z-score	Planning	4	FAILURE
Wisconsin Card Sorting Test	Number of correct answers	Raw score	Rules deduction and elaboration	4	FAILURE
Alertness (Test Battery of Attentional Performance)	Alertness without warning tone (time)	Percentile	Alertness	5	FAILURE

Table 3. Attributes implicated in the forest of decision trees generated with C5.0 algorithm.

NEUROPSYCHOLOGICAL TEST/BATTERY	MEASURE	SCORE	COGNITIVE FUNCTION	PERCENTAGE OF IMPLICATION
Flexibility (Test Battery of Attentional Performance)	Number of errors	Percentile	Cognitive flexibility	94%
Trail Making Test	Part B-A – Time (Tombaugh, 2004)	Percentile difference	Reactive mental flexibility	80%
Alertness (Test Battery of Attentional Performance)	Alertness index	Percentile	Alertness	74%
Stroop	Interference-denomination – Time	Raw score	Automatic response inhibition	74%
Tower of London	Number of movements realized in the problems requiring at least five movements containing a “positive trigger”	Z-score	Planning	74%
Alertness (Test Battery of Attentional Performance)	Alertness without warning tone – Time	Percentile	Alertness	71%
Flexibility (Test Battery of Attentional Performance)	Flexibility – Time	Raw score	Cognitive flexibility	71%
Wechsler Memory Scale – Third Version	Spatial span – Total score	Raw score	Short-term visual memory	69%
Verbal fluency test	Number of generated words – Letter P	Z-score	Spontaneous mental flexibility	60%
Rey figure	Copy task	Percentile	Visuo-construction	51%
Stroop	Interference-denomination – Time	Percentile	Automatic response inhibition	51%
Vigilance (Test Battery of Attentional Performance)	Vigilance – Median time	Percentile	Vigilance	43%
Multiple Errands Test	Total score	Raw score	Ecological executive functions	40%
Doors Test	Part A	Percentile	Episodic visual memory	31%
Wisconsin Card Sorting Test	Total number of perseverative responses	Percentile	Rules deduction and elaboration	29%
Wisconsin Card Sorting Test	Total number of non-perseverative errors	Percentile	Rules deduction and elaboration	23%

Boosting of association rule learning generated 605 different rules using 128 attributes. Among these attributes, only six were shared with the forest of decision trees: (1) percentile of the number of errors and (2) median execution time on the flexibility subtest, and (3) percentile of simple reaction time measure on the alertness subtest of the TAP⁴⁵; (4) raw and (5) standardized (percentiles) time score in the color-word interference condition of the Stroop Test⁴⁶; and (6) percentile of the Doors Test part A.⁴³

DISCUSSION

The aim of this study was to identify cognitive abilities hindering the vocational training outcome in patients with ABI. We found concise explanatory machine learning theories including neuropsychological attributes. The attributes identified as linked to vocational training outcome in every supervised learning classification method were the GZ-F index on the D2 cancellation test⁴⁴ and the percentile of the number of errors on the flexibility subtest of the TAP.⁴⁵ The GZ-F index is an error-corrected quantitative performance, calculated by subtracting the total number of errors to the total number of items processed. This attribute underlies visual selective attention abilities,⁶² as scanning accuracy and speed.⁶³ This error-corrected measure is crucial since patients with TBI have a high error percentage on the D2 test.⁶⁴ The flexibility subtest of the TAP corresponds to an attentional set shifting task assessing cognitive flexibility.⁶⁵ The TAP was found to be a sensitive tool to assess executive and attentional impairment in adults with closed head injury⁶⁶ and in children with mild TBI.⁶⁷ Thus, our results underlined that performance on these two neuropsychological measures would explain the success or failure in resuming a vocational training after an ABI. This suggests that these particular cognitive abilities (visual attention/speed and cognitive flexibility) would be implicated in vocational outcome even before considering the return to employment.

At a lesser extent, other neuropsychological factors were also found to be implicated in explaining vocational training outcome. Cognitive measures underlying executive functioning, attentional and memory abilities were involved in different models found through machine learning algorithms and representing success or failure in resuming a vocational training.

According to literature, memory, attentional and executive performance also appeared to affect work performance of patients with traumatic brain injury.³³ However, besides cognitive factors, psychological and behavioral factors were also found to be related to the return to work in patients with ABI, as anxiety and depression,⁶⁸⁻⁶⁹ fatigue,⁷⁰⁻⁷¹ personality changes^{68,72} or alcohol dependence/abuse.⁷³ These psychological and behavioral factors should also be investigated in the context of return to vocational training.

Study limitations

The fact that the identified factors were only explanatory of vocational training outcome may be due to the sample size. Thus, increasing the number of participants could permit to highlight predictive relationships between cognitive performance and vocational outcome.

Another limitation was the number of missing data which could have also weakened the relationships between our variables. Yet, missing data are common in retrospective studies.³⁶ Conducting prospective studies, with a same neuropsychological protocol for each participant, would overcome this limitation.

CONCLUSIONS

Cognitive sequelae after ABI highlighted with a neuropsychological assessment would not all have the same impact on the vocational outcome. We identified cognitive factors that would explain the success or failure in resuming vocational training. Further studies should confirm these findings. Predictive power of psychological and behavioral factors should also be

investigated. Increasing the sample size could allow us to highlight predictive relationships between cognitive/behavioral factors and vocational outcome.

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***1.2. Article 6 : Identifier l'issue du retour en formation à partir de
l'évaluation neuropsychologique des patients avec lésion cérébrale :
Apports de l'apprentissage automatique***

Manoli, R., Chartaux-Danjou, L., Delecroix, H., Daveluy, W., Torre, F., & Moroni, C. (under review). The relationship between cognition and vocational training in persons with acquired brain injury: Contribution of Machine Learning.

Title: The relationship between cognition and vocational training in persons with acquired brain injury: Contribution of Machine Learning

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ABSTRACT

Objective: Patients suffering from brain injury often experience unemployment or difficulties to reintegrate a social and professional environment, especially due to their brain injury related cognitive sequelae. The aim of our study was to identify specific cognitive patterns related to long-term vocational training outcome in these patients.

Method: Twenty-eight records of patients who entered a professional rehabilitation program, were retrospectively processed in order to extract neuropsychological scores. Relationships between these scores and patients' vocational training outcome after a rehabilitation program were analyzed through machine learning algorithms.

Results: Data analysis identified cognitive patterns related to both vocational training outcomes: succeeded or failed, each pattern including performance intervals on three neuropsychological measures. The cognitive pattern related to a successful vocational outcome included performance intervals on measures underlying verbal memory consolidation, visual memory incidental recall, problem solving and planning. The cognitive pattern explaining failure included performance intervals on measures underlying planning and solving of difficult problems.

Conclusions: From a comprehensive neuropsychological battery, memory and executive measures appeared to be the best attributes related to vocational training outcome in patients with brain injury. However, our study suggests that even with cognitive functioning above the pathological threshold, patients with brain injury could fail in their vocational training. Thus, the most related to vocational outcome attributes would be more a specific cognitive level of functioning rather than an interpretation of neuropsychological scores only based on a normal vs pathological distinction. Hence, clinicians may identify cognitive profiles related to a successful vocational outcome.

Key-words: *brain injury; machine learning; neuropsychological performance; vocational outcome.*

Introduction

Acquired brain injury (ABI) is an injury to the brain which generally occurs after birth and has either a traumatic, or a non-traumatic cause as stroke or tumors (Brain Injury Association of America; Wilson et al., 2018). With a 12% prevalence of Traumatic Brain Injury (TBI) in the world (Frost, Farrer, Primosch, & Hedges, 2013), and a prevalence of stroke ranging from 1.5% to 3% in Europe and in the USA (Zhang, Chapman, Plested, Jackson, & Purroy, 2012), ABI represents a common cause of death and disability (Fryer, Thomas & Barnes, 2017).

Cognitive complaints and/or impaired performance in neuropsychological tests have been underlined in patients with ABI (Joode et al., 2012), due to a traumatic (Ngwenya et al., 2018; Trahan, Ross, & Trahan, 2001) or a non-traumatic cause (Passier et al., 2010; van Rijsbergen, Mark, de Kort, & Sitskoorn, 2014). According to Ngwenya et al. (2018), 60% of patients with mild TBI reported cognitive complaints associated with memory and executive impairments. Patients with moderate-to-severe TBI reported memory dysfunction complaints, associated to actual memory and learning neuropsychological impairment (Jamora, Young, & Ruff, 2012). In patients with stroke, subjective cognitive complaints also appeared to be associated with objective impairment on neuropsychological tests (van Rijsbergen, Mark, Kop, de Kort, & Sitskoorn, 2017). However, the association between complaints and neuropsychological performance is not always observed (Stulemeijer, Vos, Bleijenberg, & van der Werf, 2007). Five years after a TBI, neuropsychological evaluation of these patients identified that sustained attention, planning abilities and anterograde episodic memory deficits were the most common cognitive deficits (Caron et al., 2018). In patients suffering from ischemic stroke, poor memory

performance and a reduced visuospatial and executive functioning were also underlined (Mellon et al., 2015).

These injury-related cognitive sequelae were found to be related to delayed professional reintegration (Kahan et al., 2018; Libeson, Downing, Ross, & Ponsford, 2018), since these deficits are frequent and this even eight (Ruet, Bayen, Jourdan, Pradat Diehl, & Azouvi, 2018) or ten years after a TBI (Draper & Ponsford, 2008). According to a qualitative study, patients with TBI reported injury-related cognitive and mood problems as the most common factors hindering the return to work (Libeson et al., 2018; Scaratti et al., 2017). The predictive power of neuropsychological factors on patients' return-to-work was widely investigated. Therefore, different factors were underlined to hinder a successful return to work, such as the persistence of attention and memory difficulties from 3 to 4 weeks after a mild TBI (Wäljas et al., 2014), processing speed performance difficulty one year after a severe TBI (Sigurdardottir et al., 2018), or social cognition and executive functions deficits six years after an ABI (Yeates et al., 2016).

Given the heterogeneity of findings reported in the literature, especially due to studies focusing only on specific cognitive functions, one solution would be to explore comprehensive neuropsychological assessments of patients with ABI, including evaluation of a high number of cognitive processes. With a flexible neuropsychological battery approach (i.e., using different tests according to patients' complaints), data might contain missing values (Casaletto & Heaton, 2017). When it comes to analysis of a dataset containing many variables with missing values, machine learning would be one of the suitable techniques (Altman & Bland, 2007; Battista, Salvatore, & Castiglioni, 2017). In fact, machine learning algorithms extract automatically information contained in a dataset and generalize it in data models, highlighting predictive relationships between variables (Mitchell, 1997). With a supervised machine

learning, new data increase accuracy of predictive models (Lopes, Machado, Rabêlo, Fernandes, & Lima, 2016). Indeed, a supervised learning analyses available data inferring a rule which links different variables, and this rule is tested and updated in new data (Russell & Norvig, 2009). Furthermore, unlike regression analyses relying on a knowledge-based model, machine learning would seek a predictive model from available data (Goulon, Duprat, & Dreyfus, 2006). Therefore, machine learning exploration of neuropsychological assessment in patients with ABI would identify vocational outcome predictors.

Under the French law (Decree N° 2009-299 of March 17th 2009), patients with ABI-related cognitive and behavioral sequelae who face many difficulties to (re)integrate a working environment could be referred to special vocational rehabilitation units. These units ensure the transitions between healthcare, medico-social, education and labor sectors. Their missions are to inform and guide patients with ABI towards a vocational project taking into consideration patients' cognitive, behavioral and/or physical limitations. But this guidance is often based on professionals' own expertise and not on an objective or theoretical model, and in absence of such a model, professionals may avoid advising patients to undertake training for fear that they will not succeed. This additional failure might contribute to turning in on oneself and to a social withdrawal. Several studies highlighted the interest of neuropsychological assessment for patients seeking to resume work (Mani, Cater, & Hudlikar, 2017; Sigurdardottir et al., 2018). However, to our knowledge, the impact of cognitive performance on vocational training after ABI has never been investigated. This issue is of major importance. Indeed, TBI appeared to occur in 1,080.7 per 100,000 population among individuals between 15 and 24 years old (Taylor, Bell, Breiding, & Xu, 2017) who would want or need to resume vocational training or academic education (MacLennan & MacLennan, 2008).

Therefore, the aim of our study was to identify specific cognitive patterns related to long-term vocational training outcome in patients with ABI, so neuropsychologists could rely on patients' objective cognitive performance to guide them towards an appropriate vocational training. For this purpose, we sought to explore neuropsychological assessments of patients with ABI through machine learning. We hypothesized that, among all neuropsychological objective measures, executive functions (Alvarez & Emory, 2006) as well as learning and memory retrieval performances would be the best attributes to explain their return to vocational training after ABI, as these factors are often implicated in abilities acquisition and in the return to work.

Method

Participants

We included patients with ABI who were facing difficulties to return to an active life, even many years later after injury. We retrospectively processed all the records of patients who joined a specific professional rehabilitation program, from 2002 to 2017. The objective of this program was to support and guide the development of their professional project according to their abilities and limitations. This program included multidisciplinary assessments of their injury-related sequelae, evaluations of their difficulties in daily life and in real-life professional situations. After the rehabilitation program, the rehabilitation team stated about a vocational guidance for each patient, according to his strengths and limitations: either an ordinary working environment, or a sheltered employment, or a vocational training in order to learn a new trade, more adequate to his sequelae. A regular annual follow-up concerning the professional reintegration was proposed to all patients.

We screened 343 records of patients and, at the time of data collection, 28 patients had completed a Vocational Training after the rehabilitation program ($N_{VT}=28$). The training was considered as successful when patients obtained a specific qualification for the training. Failure

included either training abandon or failed examination. Most patients had a TBI, only 24% had a non-traumatic ABI. Their average age at the time of the neuropsychological assessment during the rehabilitation program was 31.29 years old ($SD=9.18$; *range 19-56*), 57% of patients were male and their number of years of formal education was on average 11.46 years ($SD=2.60$; *range 6-17*). They had been referred to the rehabilitation program as part of a professional reorientation process after a mean delay of 6.14 years ($SD=5.74$; *range 1.37-23.00*) from their injury. This variation of the delay from injury was due to the professional instability variation between patients. Indeed, some patients had been referred to the rehabilitation program soon after their injury, and some others experienced a relatively long recovery and professional instability before they took or a social care professional took for them the decision to follow a professional rehabilitation program.

All participants were French fluent speakers and their brain injury related sequelae were stable, according to the physiatrist of the rehabilitation unit. All of them had diffuse cognitive difficulties and not only a focal neuropsychological syndrome based on the hemispheric specialization (such as aphasia or neglect syndrome).

Data collection was conducted according to a reference methodology (MR-003), not requiring participants' express or written consent, according to French Law (decision n° 2016-263 of French data protection commission, on July 21st, 2016). The research was completed in accordance with the Helsinki Declaration (World Medical Association, 2013). Ethical approval for this study was obtained (REF 2017-1-S52).

Procedure

During the rehabilitation program, all participants were administered a neuropsychological assessment, consisting in exploring five cognitive domains.

1. **Memory abilities** were explored as follows:

- Short term memory: **Digit span** (Wechsler Adult Intelligence Scale-Third Edition, WAIS-III; Wechsler, 2000), **Spatial span** (Wechsler Memory Scale-Third Edition, WMS-III; Wechsler, 2001);
 - Working memory: **Brown-Peterson Test** (Geurten et al., 2016), **Dual task** (Baddeley, Della Sala, Papagno, & Spinnler, 1997);
 - Episodic long-term memory: **Free and Cued Selective Reminding Test** (in French, *Rappel Libre / Rappel Indiqué à 16 items*; Van der Linden et al., 2004) and **One Week Free and Cued Selective Reminding Test** (1W-FCSRT; Manoli et al., 2018) for verbal memory; **Rey-Osterrieth Complex Figure** (Meyers & Meyers, 1995), **Doors Test** (Baddeley, Emslie, & Nimmo-Smith, 1994) for visual memory.
2. **Attentional abilities** were explored with: **D2 cancellation test** (Brickenkamp, 1988), **Test Battery of Attentional Performance** (TAP; version 2.3.1; French adaptation by Michel Leclercq; Zimmermann & Fimm, 2002).
 3. **Executive functions** were explored with: **Trail Making Test** (TMT; Roussel & Godefroy, 2008; Tombaugh, 2004), **Stroop Test** (Roussel & Godefroy, 2008), **Wisconsin Card Sorting Test** (WCST; Heaton et al., 1993), **Tower of London** (Coyette & Van der Linden, 1993), **Verbal Fluency Test** (Cardebat, Doyon, Puel, Goulet, & Joannette, 1990), **Multiple Errands Test** (Martin, 1972).
 4. **Visual instrumental abilities** were explored with: **Block design** subtest (WAIS-III; Wechsler, 2000), **Birmingham Object Recognition Battery** (BORB; Riddoch & Humphreys, 1993).
 5. **Social cognition** was assessed with: « **Reading the mind in the eyes** » **Test – revised version** (Baron-Cohen, Wheelwright, Hill, Raste, & Plumb, 2001), **Empathy Quotient** (Baron-Cohen & Wheelwright, 2004).

According to patients' records, the neuropsychological assessment was administered during several sessions of one or two hours, averaging a total of eight hours. According to patients' limitations, they could not all receive the entire battery of tests, resulting in missing values in neuropsychological data.

Machine Learning

Performance during neuropsychological assessment (raw and standardized scores) corresponded to 315 attributes, containing many missing values (37.68%). The vocational training outcome corresponded to the dependent variable, divided in two classes: success and failure. Given the number of attributes, their relationships with the dependent variable were analyzed through machine learning algorithms. We adopted a Knowledge Discovery and Data Mining (KDD) approach, which relies on meaningful extractions of information from data, so the procedures were not fully automated and allowed human intelligence intervention (Diday, 2017; Singh & Dubey, 2018). The main aims of this analysis were: (1) to obtain rules, as to say concurrences of attributes (scores from neuropsychological assessment), explaining the two classes, and (2) to obtain one rule per class concurring as few attributes as possible. Indeed, each rule had to be complete, namely it had to cover all the observations of a class; e.g. a rule explaining success had to apply to all the participants who had actually succeeded. And each rule had to be correct, namely it should not cover observations of the other class; e.g. a rule explaining success should not apply to participants who had actually failed their vocational training.

We generalized the continuous attributes in creating performance intervals per attribute per outcome (success or failure). Then, performance was normalized according to performance of all the patients who entered the program even if they did not complete a vocational training (i.e. $N=343$). This normalization consisted in considering the minimal and maximal values in the

performance of all the patients from the rehabilitation program ($N=343$) and in replacing each value “ v ” of an attribute by $(v-min)/max-min$). Attribute-value theories were learned with GloBoost (Torre, 2005) in Volata, a machine learning system instantiated with least general generalization operators (Torre, 2013). Rules including n attributes identified with these algorithms could be represented in the Euclidean plane as hyperrectangles or n -dimensional rectangles. The Euclidian plane being a geometrical representation of an observation according to its different characteristics, we could represent our patients on this plan according to their performance on the neuropsychological attributes. We used the Euclidean distance, as to say the straight-line distance between two observations in the Euclidean plane, in order to determine the distance between individuals’ localization in the plane according to their performance and the pattern of performance predicting vocational training outcome (Hastie, Tibshirani, & Friedman, 2009). Then, following the principle of Occam’s razor, which gives higher probabilities to sampler rules (Alpaydin, 2004; Gamberger & Lavrač, 1997), we identified the rules using the fewest attributes to explain patients’ vocational training outcome. These rules were further tested on the patients from the rehabilitation program who did not start a vocational training but to whom it was recommended ($N=13$ patients from the 343 records).

Results

The first machine learning identified one rule predicting vocational training failure and two rules predicting success of patients with ABI, but one of these two rules predicting success was only applicable in one patient (*ind35* who succeeded in his vocational training). This patient had a neuropsychological assessment in another structure one year before entering the rehabilitation program, so actually only additional tests were administered instead of a comprehensive assessment, which would explain the large percentage of missing values (75%) for this patient. Even if machine learning analysis was chosen precisely because our data set

contained missing values, a percentage of 75% of missing values for a particular patient was exceptional. Assuming that this data set was atypical, we excluded this patient's data from further analysis. The second machine learning identified a rule including two patients with different vocational training outcomes (*ind6* had succeeded, *ind4* had failed). One of these patients had several neuropsychological assessments before joining the rehabilitation program, so during the program he did not benefit from a comprehensive assessment. Furthermore, after the rehabilitation program he started a vocational training, but he abandoned it for unknown reasons. The other patient reported a high level of fatigue during the neuropsychological assessment and this could have influenced his performance. In order to avoid the implication of two different classes in a rule explaining one class, these two patients were also excluded from further analysis.

We ran the learning algorithms with the 25 remaining observations (16 patients had succeeded; 9 patients had failed; see **Table 1**).

We identified 4014 distinct rules (using different combinations of attributes), 93 related to success and 3921 related to failure in resuming a vocational training after ABI. Following the principle of Occam's razor, we found only one rule including three attributes among rules explaining failure. Similarly, among rules predicting success, we found nine rules with four attributes (see **Figure 1**).

Table 1. Final sample characteristics.

<i>Gender</i>	<i>Age</i>	<i>Years of formal education</i>	<i>Etiology</i>	<i>Delay from injury</i>	<i>Severity evaluation</i>	<i>Severity interpretation</i>	<i>Vocational training outcome</i>
F	21	11	TBI	1.37	-	-	Success
M	26	11	TBI	2.67	-	-	Success
M	19	8	TBI	1.55	-	Severe*	Success
M	35	10	TBI	17.63	Coma 3w	Severe	Failure
M	30	10	TBI	2.82	Coma	Severe*	Success
F	26	12	TBI	11.38	Coma	-	Success
F	40	14	TBI	7.65	Coma 4w	Severe	Success
M	23	10	TBI	2.27	Coma 2w	Severe	Success
F	20	10	TBI	11.37	GCS=3	Severe	Success
M	27	17	TBI	4.56	Coma 6w	Severe	Success
M	33	12	Brain Tumor	4.67	Grade III astrocytoma	-	Success
F	30	14	Stroke	1.92	Rankin 2	Slight disability	Success
M	31	11	Stroke	4.13	Rankin 3	Moderate	Failure
F	25	17	Stroke	2.18	Extubation at day 7	-	Success
M	36	8	TBI	3.57	GCS 3	Severe	Failure
F	43	6	Stroke	8.00	-	-	Success
M	29	14	TBI	4.04	GCS 8	Severe	Failure
M	27	12	TBI	2.72	GCS 5	Severe	Failure
M	25	8	TBI	4.56	GCS 5	Severe	Failure
M	37	9	Brain Tumor	5.09	WHO grade I ganglioglioma	-	Success
M	27	12	TBI	3.15	GCS 7	Severe	Success
F	56	10	TBI	14.23	-	-	Success
M	37	12	TBI	17.59	-	-	Success
F	24	13	Stroke	1.73	NIHSS 4	Minor	Failure
F	53	14	TBI	1.74	GCS 10	Moderate	Failure
M=15 F=10	Mean 31.20 ±9.36	Mean 11.40 ±2.6	TBI=72% Stroke =20% Tumor =8%	Mean 5.70 ±4.93		Severe=48% No info=36%	Success =68% Failure =32%

**Severity interpretation only stated in patient's medical record in absence of severity evaluation criteria.*

GCS=Glasgow Coma Scale score; d=days; F=female; M(gender)=male; MAX=maximum value; MIN=minimum value; NIHSS=National Institutes of Health Stroke Scale score; PTA=post-traumatic amnesia; TBI=traumatic brain injury; w=weeks; WHO=World Health Organization.

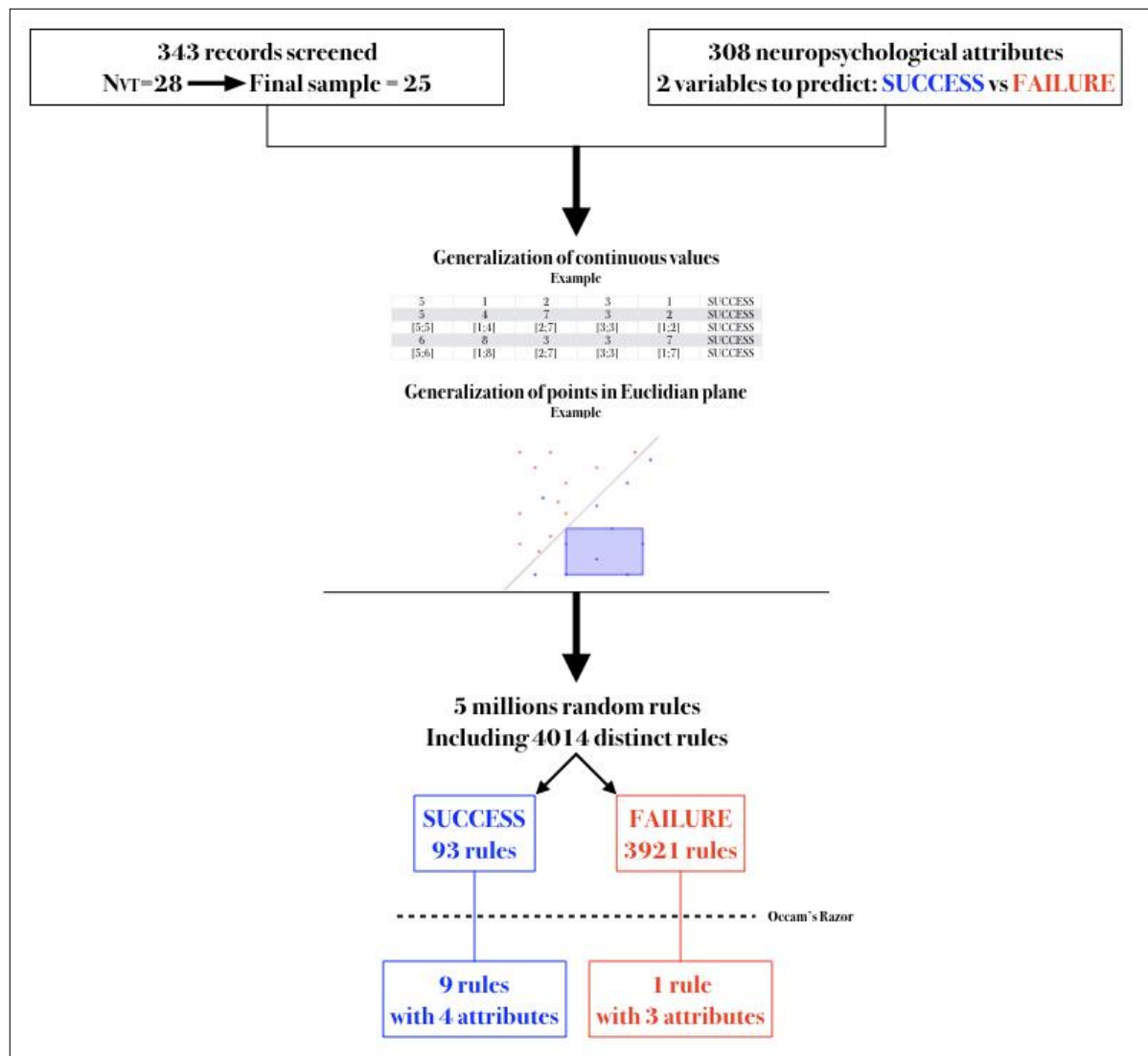


Figure 1. Data analysis and rules obtained through machine learning.

N_{VT}: number of participants who completed a vocational training.

The nine rules explaining success used simultaneously three attributes corresponding to three measures from three different neuropsychological tests: (1) a 30-min delayed recall forgetting score from the One Week Free and Cued Selective Reminding Test (FR30-Forget 1W-FCSRT; Manoli et al., 2018); (2) an Immediate Recall Incidental Element Accuracy score from the Rey-Osterrieth Complex Figure (Imm Recall ROCF; Meyers & Meyers, 1995); (3) a Z-score from the Tower of London Test (Z-score time 5i- ToL; Coyette & Van der Linden, 1993), corresponding to the Z-score of total time needed by the patients to solve the problems requiring at least five movements while the first evident movement would block the solving. In the Euclidean plane, this rule corresponded to a 3-dimensional rectangle (see **Figure 2a**).

The rule related to failure used simultaneously other three attributes, corresponding to three different scores from the ToL (Coyette & Van der Linden, 1993): (1) the Z-score of the number of movements performed by the patients when solving problems requiring at least five movements while the first evident movement would help the solving (Z-score mov 5i+ ToL); (2) the Z-score of total time needed by the patients to solve problems requiring at least five movements while the first evident movement is neutral (Z-score time 5n ToL); and (3) the Z-score of total time needed by the patients to solve problems requiring at least six movements while the first evident movement is neutral (Z-score time 6n ToL). The rule related to failure also corresponded to a 3-dimensional rectangle in the Euclidean plane (see **Figure 2b**).

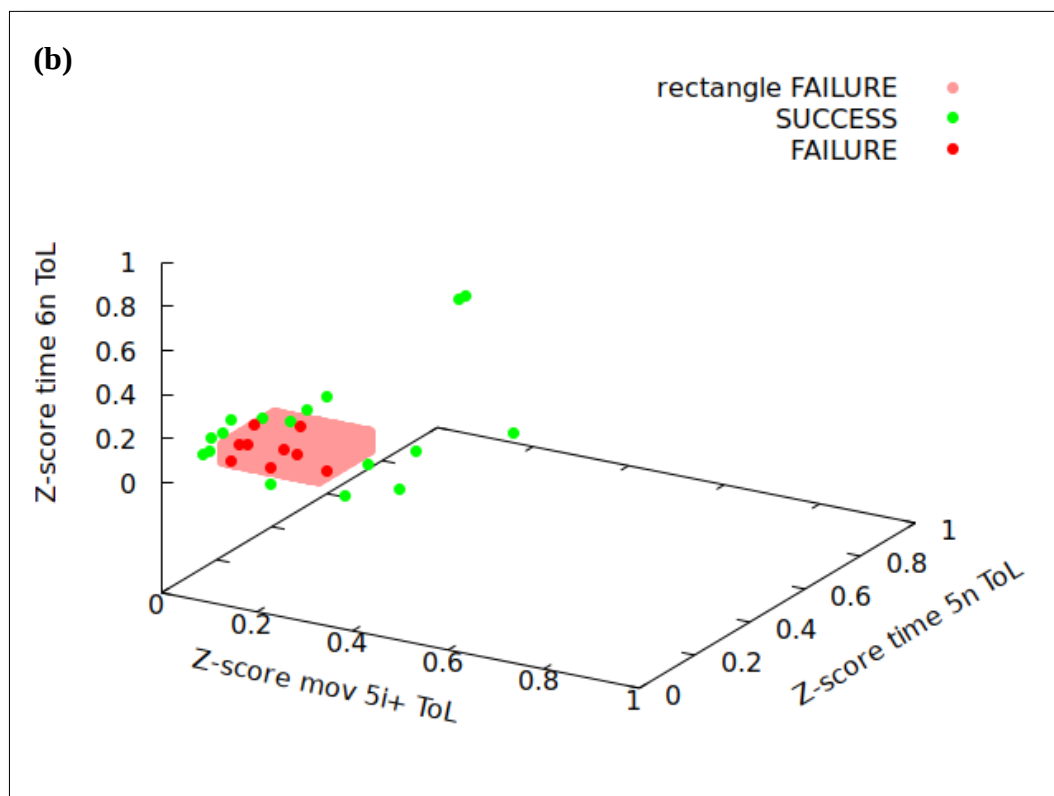
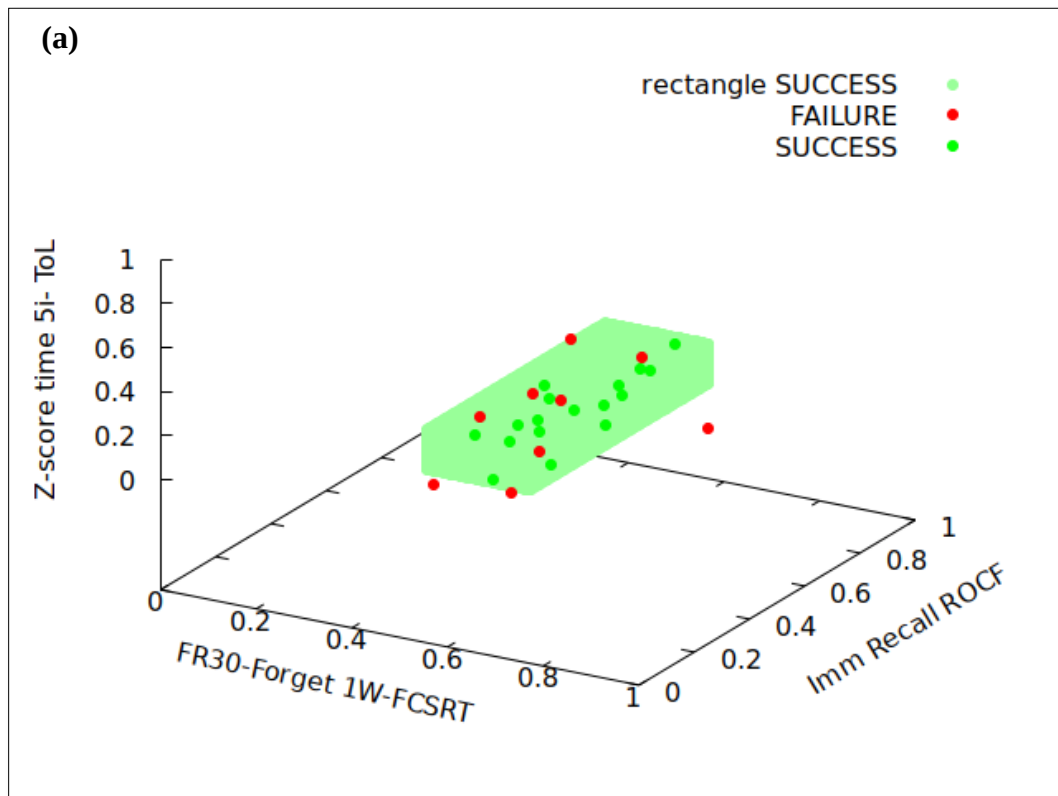


Figure 2. Neuropsychological performance explaining vocational training success (a) and failure (b) in patients with acquired brain injury.

More precisely, machine learning algorithms identified specific patterns of performance for these attributes, identifying whether a patient is more likely to succeed or to fail when resuming a vocational training. Hence, a patient is more likely to have a successful vocational outcome if his performance is simultaneously within the following intervals: a 1W-FCSRT FR30-Forget raw score (%) $\in [-18.18; 25.00]$; a ROCF Imm Recall raw score ≥ 13.00 ; and a ToL Z-score time 5i- ≤ 5.36 . Similarly, a patient is more likely to experience failure in resuming vocational training, if his performance is simultaneously within the following intervals: a ToL Z-score mov 5i+ $\in [-0.74; -0.27]$; a ToL Z-score time 5n $\in [-1.26; 0.94]$; and a ToL Z-score time 6n $\in [-0.68; -0.02]$.

These two patterns of cognitive rules were challenged with the patients' data to whom a vocational training was recommended at the end of the rehabilitation program, i.e. 13 participants from the 343 screened in the rehabilitation program. Using the Euclidean distance, we identified that among these 13 patients, their cognitive performance matched with the 3-dimensional rectangle explaining success in 11 patients (85%). For the two participants left, one was near the rectangle and the other was near to the 3-dimensional rectangle explaining failure in resuming a vocational training.

Discussion

The aim of our study was to identify specific cognitive patterns related to long-term vocational training outcome in patients with brain injury. Using machine learning procedure, we identified two specific patterns of cognitive performance, each pattern including performance intervals on three neuropsychological measures. The cognitive pattern explaining a successful vocational outcome included performance intervals on a verbal memory measure from the 1W-FCSRT, a visual memory measure from the ROCF and a problem-solving measure from the ToL. The

cognitive pattern explaining failure included performance intervals on three other problem-solving measures from the ToL.

Even data analysis with machine learning is not theory-driven, our findings are consistent with the literature, providing us with an additional argument against any random selection of the best attributes. First, verbal memory appeared to be related to the professional outcome.

This has been highlighted in the literature; patients suffering from TBI with higher scores on Verbal Memory Index from the Wechsler Memory Scale – Revised version (WMS-R; Wechsler, 1987) were found to be more likely to return to work (O'Connell, 2000). Nevertheless, the Verbal Memory Index is a global measure of verbal memory and performance on this index could be affected by a specific verbal memory difficulty regarding learning or retrieval or other memory processes. In our study, we identified a specific verbal memory process functioning related to vocational training outcome, as to say a rapid long-term consolidation process (Manoli et al., 2018). Visual memory impairment in patients with TBI has been already described in literature (Winardi et al., 2014) but it appeared to be related to the return to work only in one study including veterans from Vietnam War 15 years after penetrating head-injuries (Schwab, Grafman, Salazar, & Kraft, 1993). In our study, we underlined the implication of verbal incidental memory specific performance in a successful vocational training. This could be due to a usual requirement, in a vocational training, of an incidental learning and retrieval, information being continuously processed and used to perform different tasks (Ericsson, 2008). Problem-solving and planning, also found in literature under the term of prospection, again appeared to be related to employment abilities in only one study underlining predictive relationships between ToL performance of patients with mild TBI and their instrumental activities of daily living, including employment (Zakzanis, Grimes, Uzzaman, & Schmuckler, 2016). Even if the ToL version used in this study is not strictly the

same of our version, both tasks evaluate prospection abilities and this cognitive process appears to be related to employment and to vocational training.

Strengths and limitations

To our knowledge, it is the first study focusing on the relationship between cognitive factors and the return to vocational training in patients with ABI. We also adopted a relatively new approach when it comes to explore cognitive performance from a comprehensive neuropsychological assessment. Indeed, machine learning techniques have come into use recently, especially in research studies in patients with Alzheimer's Disease (Battista, Salvatore, & Castiglioni, 2017), mild cognitive impairment or dementia (Weakley, Williams, Schmitter-Edgecombe, & Cook, 2015). The strength of this approach is to analyze all at once the cognitive measures extracted from a neuropsychological assessment, even with missing data (Altman & Bland, 2007). Given that our data contained many missing values, with usual regression-based analyses we would have had to use different strategies to impute the missing data, otherwise we could not have run these analyses. Given our large data, with usual regression-based analyses we would have had to impose penalty to the logistic model. The risk with this type of analysis would be to minimize the relationships between neuropsychological factors and training outcome.

With the GloBoost procedure, we found 4014 different rules. Following the principle of Occam's razor, we decided to focus only on rules with fewest attributes. If we included other rules with more attributes, these rules would necessarily explain fewer cases of the learning set. Instead, the selected rules explained vocational outcome with an accuracy of 80.8%. And, when we tested the two patterns of cognitive performance in patients who did not start a vocational training but to whom it was recommended, we highlighted that, according to the rules we

identified, 85% of patients with a vocational training recommendation would have succeeded if they would had entered a training.

Our results constitute another scientific proof that a neuropsychological assessment can inform and improve professional guidance of patients with ABI. But this does not mean that a neuropsychological assessment of patients with ABI should be limited only to the six factors from three neuropsychological tests highlighted in this study. On the one hand, at this stage, we cannot say whether only these six scores allow us to decide on the ability of patients with ABI to return to training or whether it can be predicted by particular performance involving cognitive processes that would be found with other scores measuring these same cognitive functions. Hence, neuropsychological assessment must be exhaustive in order to refine prediction models. On the other hand, our results are only applicable for a specific objective which is to predict the return to training. In France, patients with ABI could benefit from a neuropsychological assessment in different types of medico-social facilities. At the national level, there is a divergence in the use of neuropsychological tests when the purpose of the assessment is the same, especially in the case of vocational rehabilitation. So, our results could also provide evidence of the need to standardize an assessment procedure to better respond to patients' needs in terms of vocational rehabilitation.

Additionally, our study suggests a new approach to assess cognitive abilities even if patients' performance was within a normal range. Indeed, machine learning identified specific levels of performance associated with vocational outcome. Furthermore, machine learning rule predicting failure identified cognitive performance intervals within normal range. The normal/pathological distinction seems no longer relevant, since, in our sample, patients with neuropsychological performance in the normal range on the predictive factors failed a vocational training.

However, some limits could be mentioned. Our participants constituted a small sample. Indeed, to collect data for this kind of study could take many years: patients have to perform a complete cognitive assessment supported by a complete assessment of the activities of daily living, to find a vocational training (they want to follow), the training would last one or two years, and only afterwards we would know these patients' vocational training outcome. So further studies should be conducted in samples including a larger number of patients who had retrieved a vocational training, in order to validate and refine the vocational outcome-related cognitive patterns found in this study. Moreover, retrospectively, we only had access to the neuropsychological assessment scores. Yet, the impact of behavioral factors and/or fatigue should also be evaluated, since they were found to be related to professional outcome following brain injury (Colantonio et al., 2016; Stéfan, Mathé, & SOFMER group, 2016).

Conclusion

From a comprehensive neuropsychological battery, particular visual and verbal memory performance as well as problem solving and planning abilities appeared to be the best attributes related to vocational training outcome in patients with brain injury. Furthermore, since these patterns of cognitive performance were not impaired and relied on several levels of functioning, our study suggests that normal vs pathological categorization would not be relevant when deciding of patients' ability to retrieve a vocational training. Hence, according to patients' performance on neuropsychological tests, clinicians may identify cognitive profiles that are most likely to succeed or fail in resuming a vocational training after a brain injury. These cognitive patterns should be refined in further studies, notably in investigating the possibility to predict vocational training from neuropsychological assessment.

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1.3.Article 7 : Etude de cas

Manoli, R., Chartaux-Danjou, L., Delecroix, H., Daveluy, W., Torre, F., & Moroni, C. (submitted). Machine Learning modelling of neuropsychological performance could determine vocational training outcome following a brain injury: A case study.

Title: Machine Learning modelling of neuropsychological performance could determine vocational training outcome following a brain injury: A case study

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ABSTRACT

Objective: Using two different Machine Learning approaches, cognitive patterns related to vocational training outcome following a brain injury were found. The aim of our case study was to test these patterns in a patient suffering from an acquired brain injury (ABI).

Method: NB, a 38-year-old female, suffering from a left-temporal brain injury, had integrated a vocational rehabilitation program, during which she benefited from a neuropsychological assessment. After this program, she successfully completed a vocational training. Her neuropsychological performance was screened according to the cognitive patterns previously found as related to vocational training outcome.

Results: All the previously found cognitive patterns related to success or failure in vocational training predicted NB's success. These cognitive patterns included memory and executive functioning.

Conclusions: NB's vocational outcome could have been predicted before entering the training by relying on her memory and executive functioning. Her neuropsychological assessment showed very few cognitive deficits and her vocational training success might seem obvious. However, relying on such cognitive patterns before entering a vocational training would help clinicians to guide vocational rehabilitation of patients with brain injury. These cognitive patterns should be further tested in large groups of patients in order to calculate an accuracy index and/or refine these patterns.

Key-words: *Brain Injuries; Epilepsy; Cognition; Neuropsychology; Rehabilitation; Vocational Education.*

Introduction

Acquired brain injury (ABI) is a non-congenital and non-degenerative injury to the brain occurring after birth (Byrne, Coetzer, & Addy, 2017; King & Dean, 2009). ABI involves neurological (Godbolt et al., 2015; Ventura, Balcer, & Galetta, 2014), cognitive (Simblett, Ring, & Bateman, 2017; Watter, Copley, & Finch, 2017), emotional (Byrne et al., 2017; Spitz, Alway, Gould, & Ponsford, 2017) and behavioral changes (Beni et al., 2017; Martínez-Pernía et al., 2016). Neurological changes may include a post-traumatic epilepsy (Plumley, Kotloski, & Hermann, 2017), seizures being a common complication of traumatic brain injury (TBI) and other types of ABI (Duarte & Fishman, 2007). ABI-related cognitive impairment may be complicated by the epilepsy and impact patients' quality of life and vocational-social rehabilitation (Donker-Cools, Daams, Wind, & Frings-Dresen, 2016; Lin, Mula, & Hermann, 2012; Plumley et al., 2017).

Return to employment following ABI vary between studies, with a 11 to 85% rate in case of stroke (Trygged, Ahacic, & Kåreholt, 2011) and from 11 to 82% rate in case of TBI (Radford et al., 2013). However, within a delay of two years after ABI, only 40% of individuals would retrieve the employment they had before ABI (Frank & Thurgood, 2006). Finding an employment after ABI might also imply a change of profession (Chang et al., 2016; Klonoff & Lage, 1995), to move towards a profession more adequate to ABI-related sequelae. This move could need a vocational training. However, few studies investigated this particular aspect which is the return to vocational training and/or its outcome in patients with ABI (Inge, Strobel, Wehman, Todd, & Targett, 2000; Johnstone, Mount, et al., 2003; Johnstone, Price, et al., 2003; Johnstone, Vessell, Bounds, Hoskins, & Sherman, 2003; Man, Poon, & Lam, 2013; Parente & Stapleton, 1999; Rumrill et al., 2016; Wesolowski, Zencius, & Rodriguez, 1999). And none of them investigated the link between cognitive-behavioral changes and vocational training outcome.

Recently, using two different machine learning methods, we explored this link in two samples of patients suffering from ABI. These machine learning methods identified two models of cognitive patterns related to vocational training outcome following a brain injury. The first model corresponded to a decision tree including scores underlying the efficiency of working memory, attention and executive functions, related to success or failure of vocational training. The second model included two rules, one explaining success and the other explaining failure. The rule explaining success used simultaneously three intervals of verbal memory, visual memory and executive functions measures. The rule explaining failure used simultaneously three intervals of executive functions measures.

The aim of this case study was to test these models in a patient suffering from ABI who underwent a vocational training. More precisely, it would allow us to determine if this patient's vocational training outcome could have been predicted based on his cognitive skills.

Case presentation

“NB”, a 38-year-old right-handed woman with 11 years of formal education, was referred to a vocational rehabilitation unit following the diagnosis of a left temporal posterior lesion in the Heschl's area causing a partial intractable epilepsy. The lesion was non-progressive, but its nature was unknown. Seizure frequency was between 10 and 15 per month, without generalization, but NB had to suspend any activity during the seizures in which NB experienced a feeling of emptiness, hearing problems and epigastric pain. NB was under medical treatment (topiramate 150 mg/day and lamotrigine 150 mg 2/day) and refused to consider a surgical treatment.

Regarding the employment status, NB was a stay-at-home mother before her first seizure. When she wanted to retrieve an employment, she entered a professional upgrading program, which

she had to abandon for medical reasons. After the vocational rehabilitation program, she successfully completed a vocational training.

Procedure

During the vocational rehabilitation program, and prior to her successful vocational training, NB benefited from an exhaustive neuropsychological assessment, evaluating her memory, visuoconstructive abilities, executive functioning, attention and social cognition (see **Table 1**). We screened her neuropsychological performance according to the cognitive patterns previously found as related to vocational training outcome. Indeed, we focused on her performance on neuropsychological measures found to be implicated in successful or failed vocational training. As we knew that her vocational training was successful, this allowed us to verify the accuracy of the neuropsychological models found to predict vocational training outcome. This verification was made by comparing NB's scores and the score intervals of neuropsychological measures related to training success and failure.

Table 1. NB's neuropsychological assessment.

COGNITIVE FUNCTION	TEST	MEASURE/SUBTEST	RAW SCORE	STANDARD SCORE	INTERPRETATION
SHORT TERM MEMORY	WAIS-III	Digit Span	10.0	6.00	NORMAL
	WMS-III	Spatial Span	17.0	10.00	NORMAL
EPISODIC VERBAL MEMORY	1W-FCSRT	FR1	9.0	Z=-0.51	NORMAL
		TR1	14.0	PC=19	NORMAL
		FR2	15.0	PC=95	NORMAL
		TR2	16.0	PC≥61	NORMAL
		FR3	15.0	PC=78	NORMAL
		TR3	16.0	PC≥58	NORMAL
		Learn	0.9	PC=75	NORMAL
		Cued	0.8	PC=10	NORMAL
		FR30	16.0	PC≥89	NORMAL
		TR30	16.0	PC≥57	NORMAL
		FR30-Forget	6.7	PC=50	NORMAL
		FR7d	12.0	Z=0.7	NORMAL
		TR7d	15.0	PC=47	NORMAL
		FR7d-Forget	-20.0	Z=0.21	NORMAL
EPISODIC VISUAL MEMORY	Doors Test	A	10.0	PC=10	NORMAL
		B	6.0	PC=10	NORMAL
		A+B	16.0	PC=10	NORMAL
	ROCF	Immediate Recall	20.5	PC=34	NORMAL
		Immediate Recall-time (sec)	297.0	Z=0.49	NORMAL
VISUOCONSTRUCTION	ROCF	Delayed Recall	18.0	PC=16	NORMAL
		Copy	34.0	PC>16	NORMAL
	WAIS-III	Copy-time (sec)	265.0	Z=0.42	NORMAL
		Block Design	21.0	4.00	NORMAL
WORKING MEMORY	Brown-Peterson Task	5s	94.0	Z=-0.70	NORMAL
		10s	100.0	Z=0.60	NORMAL
		20s	83.0	Z=-0.58	NORMAL
	Dual-task	"Mu" index	68.1	Z=-2.33	PATHOLOGICAL
EXECUTIVE FUNCTIONS	Errands Test	Test Score	42.0	-	NORMAL
	TMT	TMT-A	39.0	Z=1.04	NORMAL
		TMT-B	59.0	Z=0.03	NORMAL
	Stroop	Reading duration	39.0	Z=-0.19	NORMAL
		Reading errors	0.0	Z=-0.52	NORMAL
		Denomination duration	46.0	Z=-0.91	NORMAL
		Denomination errors	0.0	Z=-0.52	NORMAL
		Interference duration	72.0	Z=-1.27	NORMAL
		Interference errors	0.0	Z=-0.78	NORMAL

1W-FCSRT: One-Week Free and Cued Selective Reminding Test—word version; **Cued:** cueing score, corresponding to the effect of cued recall on learning; **FR1:** 1st free recall; **FR2:** 2nd free recall; **FR3:** 3rd three recall; **FR30:** 30-minute-delayed free recall; **FR30-Forget:** short-term consolidation score, corresponding to the forgetting percentage for the 30-minute-delayed recall; **FR7d:** seven-day-delayed free recall; **FR7d-Forget:** long-term consolidation score, corresponding to the forgetting percentage for the seven-day-delayed free recall; **Learn:** learning score, corresponding to the percentage of words encoded on the 3rd first recall relatively to the first free recall; **ROCF:** Rey-Osterrieth Complex Figure test; **TR1:** 1st total recall; **TR2:** 2nd total recall; **TR3:** 3rd total recall; **TR30:** 30-minute-delayed total recall; **TR7d:** seven-day-delayed total recall; **WAIS:** Wechsler Adult Intelligence Scale; **WMS:** Wechsler Memory Scale.

Table 1. (continues)

COGNITIVE FUNCTION	TEST	MEASURE/SUBTEST	RAW SCORE	STANDARD SCORE	INTERPRETATION
EXECUTIVE FUNCTIONS	ToL	Mov3N	3.0	Z=-0.35	NORMAL
		Mov4N	5.0	Z=-0.37	NORMAL
		Mov5N	13.6	Z=1.56	NORMAL
		Mov5I+	5.0	Z=-0.92	NORMAL
		Mov5I-	11.6	Z=1.03	NORMAL
		Mov6N	8.0	Z=-1.78	NORMAL
		Time3N	8.0	Z=-0.45	NORMAL
		Time4N	12.6	Z=-0.40	NORMAL
		Time5N	75.6	Z=5.06	PATHOLOGICAL
		Time5I+	11.3	Z=-1.06	NORMAL
		Time5I-	34.0	Z=1.52	NORMAL
		Time6N	27.0	Z=-0.31	NORMAL
	WCST	Correct answers	65.0	PC=84	NORMAL
		Errors	12.0	PC=16	NORMAL
		Total perseverative answers	8.0	PC=10	NORMAL
		Perseverative errors	7.0	PC=9	NORMAL
		Nonperseverative errors	5.0	PC=6	NORMAL
		Conceptual answers	62.0	PC=81	NORMAL

Mov 3N: number of movements performed by the patients when solving problems requiring at least three movements while the first evident movement is neutral; **Mov 4N:** number of movements performed by the patients when solving problems requiring at least four movements while the first evident movement is neutral; **Mov 5N:** number of movements performed by the patients when solving problems requiring at least five movements while the first evident movement is neutral; **Mov 5I+:** number of movements performed by the patients when solving problems requiring at least five movements while the first evident movement would help the solving; **Mov 5I-:** number of movements performed by the patients when solving problems requiring at least five movements while the first evident movement would block the solving; **Mov 6N:** number of movements performed by the patients when solving problems requiring at least six movements while the first evident movement is neutral; **PC:** percentile; **Time 3N:** total time needed by the patients to solve problems requiring at least three movements while the first evident movement is neutral; **Time 4N:** total time needed by the patients to solve problems requiring at least four movements while the first evident movement is neutral; **Time 5N:** total time needed by the patients to solve problems requiring at least five movements while the first evident movement is neutral; **Time 5I+:** total time needed by the patients when solving problems requiring at least five movements while the first evident movement would help the solving; **Time 5I-:** total time needed by the patients to solve the problems requiring at least five movements while the first evident movement would block the solving; **Time 6N:** total time needed by the patients to solve problems requiring at least six movements while the first evident movement is neutral; **ToL:** Tower of London; **WCST:** Wisconsin Card Sorting Test; **Z:** Z-score.

Table 1. (continues)

COGNITIVE FUNCTION	TEST	MEASURE / SUBTEST	RAW SCORE	STANDARD SCORE	INTERPRETATION
ATTENTION	D2	GZ	473.0	PC=54	NORMAL
		GZ-F	415.0	PC=38.2	NORMAL
		SB	18.0	PC>10	NORMAL
	TAP-Alertness	No warning	215.0	PC=62	NORMAL
		Warning	221.0	PC=38	NORMAL
		Index	0.0	PC=50	NORMAL
	TAP-Working Memory	Duration	984.0	PC=8	NORMAL
		Errors	2.0	PC=50	NORMAL
		Omissions	5.0	PC=8	NORMAL
	TAP-Flexibility	Duration (median)	707.0	PC=54	NORMAL
		Errors	1.0	PC=79	NORMAL
	TAP-Divided Attention	Auditive dual task	616.0	PC=46	NORMAL
		Auditive dual task omissions	1.0	PC=31	NORMAL
		Visual dual task	796.0	PC=50	NORMAL
		Visual dual task omissions	0.0	PC=82	NORMAL
		Auditive simple task	521.0	PC=34	NORMAL
		Auditive simple task omissions	1.0	PC=14	NORMAL
		Visual simple task	821.0	PC=54	NORMAL
		Visual simple task omissions	0.0	PC>66	NORMAL
	TAP-Incompatibility	Duration (median)	120.0	PC=54	NORMAL
		Errors	3.0	PC=54	NORMAL
	TAP-Vigilance	Total score	1017.0	PC=12	NORMAL
		Errors	3.0	PC=42	NORMAL
		Omissions	4.0	PC=50	NORMAL
	TAP-Visual Scanning	Missing target duration	5470.0	PC=42	NORMAL
		Present target omissions	5.0	PC=46	NORMAL
SOCIAL COGNITION	RMET	Total score	36.0	Z=-0.33	NORMAL
	CBS	Total score	47.0	Z=0.81	NORMAL

CBS: Cambridge Behaviour Scale; **GZ:** number of items processed; **GZ-F:** calculated by subtracting the total number of errors to the total number of items processed; **PC:** percentile; **RMET:** “Reading the mind in the eyes” test; **SB:** performance variation interval; **TAP:** Test of Attentional Performance; **Z:** Z-score.

Results

In one study, a concise decision tree was generated through the C4.5 algorithm, a learning algorithm used for inductive inference (Quinlan, 1993, 2018; Mitchell, 1997). It included four attributes: the GZ-F index from the D2 cancellation test (Brickenkamp & Zillmer, 1998), a performance score to the Tower of London test (Coyette & Van der Linden, 1993; Rainville, 2002), the Z-score of the letter “p” generation from the Verbal Fluency Test (Cardebat, Doyon, Puel, Goulet, & Joannette, 1990), and the percentage of correct answers for the 20-second-distracting-task conditions of the Brown-Peterson Test (Geurten, Vincent, Van der Linden, Coyette, & Meulemans, 2016).

According to the decision tree, the first step corresponded to the GZ-F index (D2 cancellation test), calculated by subtracting the total number of errors to the total number of items processed. NB obtained 415, which lead us to provide NB's Z-score of the number of common words starting with the letter "p" generated (Verbal Fluency Test). However, NB was not administered this test. Thus, according to the score she would have had, the decision tree would either have answered "Success" or it would have requested the score for the following attribute, i.e. the percentage of correct answers for the 20-second-distracting-task conditions (Brown-Peterson Test), which was 83. Giving this score, the decision tree answered "Success". This meant that, regardless of the NB's Z-score of the letter "p" generation, the decision tree would have predicted a successful vocational training for NB (see **Figure 1**).

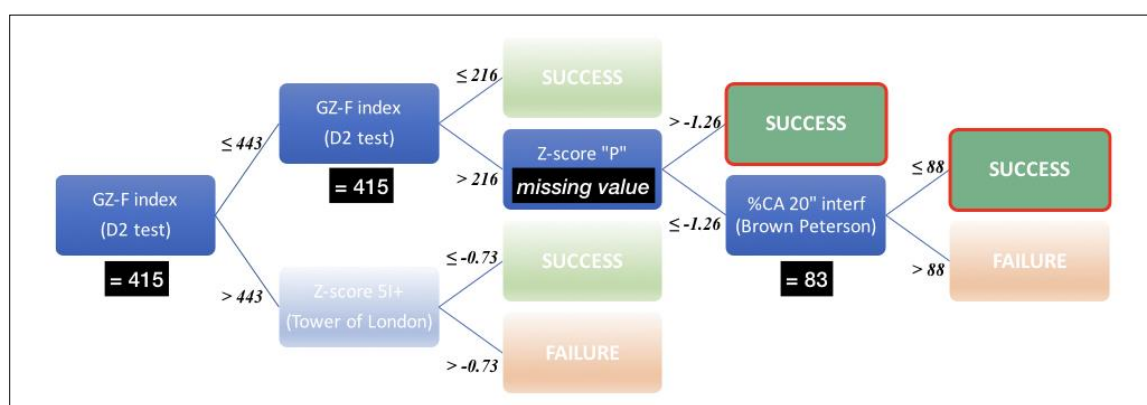


Figure 1. Neuropsychological scores of NB according to the decision tree generated with C4.5 algorithm allowing to predict success or failure in resuming vocational training after brain injury.

Boxes filled with color gradient were irrelevant according to NB's scores.

%CA 20" interf: percentage of correct answers (raw score) for the 20-second-distracting-task conditions of the Brown-Peterson Test; 5I+: number of movements realized in the problems requiring at least five movements and containing a "positive trigger" during the Tower of London test; GZ-F: an error-corrected quantitative performance on the D2 test, calculated by subtracting the total number of errors to the total number of items processed; "P": number of common words starting with the letter "p" generated during the Verbal Fluency Test.

In another study, following a least general generalization approach (Torre, 2005), a cognitive pattern was identified, including a rule explaining success and another rule explaining failure of vocational training.

The rule explaining success used simultaneously three attributes: (1) a 30-min delayed recall forgetting score from the One Week Free and Cued Selective Reminding Test (FR30-Forget 1W-FCSRT) (Manoli et al., 2018); (2) an Immediate Recall Incidental Element Accuracy score from the Rey-Osterrieth Complex Figure (Imm Recall ROCF) (Meyers & Meyers, 1995); (3) a Z-score from the Tower of London Test (Z-score time 5i- ToL) (Coyette & Van der Linden, 1993) corresponding to the Z-score of total time needed by the patients to solve the problems requiring at least five movements while the first evident movement would block the solving. Specific intervals on these measures were associated with a successful vocational training:

- FR30-Forget 1W-FCSRT $\in [-18.18; 25.00]$; NB's score was 6.67
- Imm Recall ROCF ≥ 13.00 ; NB's score was 20.50
- Z-score time 5i- ToL ≤ 5.36 ; NB's score was 1.52.

NB's performance was simultaneously within the intervals of the "Success" rule, concluding to a successful vocational training. If we represent on a graph her performance simultaneously on the three attributes, it would be comprised in the "Success" 3-dimensional rectangle representing the three intervals of possible performance associated with success (see **Figure 2a**).

The rule explaining failure used simultaneously other three attributes, corresponding to three different scores from the ToL (Coyette & Van der Linden, 1993): (1) the Z-score of the number of movements performed by the patients when solving problems requiring at least five movements while the first evident movement would help the solving (Z-score mov 5i+ ToL); (2) the Z-score of total time needed by the patients to solve problems requiring at least five movements while the first evident movement is neutral (Z-score time 5n ToL); and (3) the Z-

score of total time needed by the patients to solve problems requiring at least six movements while the first evident movement is neutral (Z-score time 6n ToL). Specific intervals on these measures were associated with a failed vocational training:

- Z-score mov 5i+ $\in [-0.74; -0.27]$; NB's score was -0.92
- Z-score time 5n ToL $\in [-1.26; 0.94]$; NB's score was 5.06
- Z-score time 6n ToL $\in [-0.68; -0.02]$; NB's score was -0.31 .

Since NB's performance was not simultaneously within the three intervals of the "Failure" rule, we could not conclude to a failed vocational training. If we represent on a graph her performance simultaneously on the three attributes, it would be distant from the "Failure" 3-dimensional rectangle representing the three intervals of possible performance associated with failure (see **Figure 2b**).

Discussion

The aim of our case study was to test in a single case two different models found to explain the link between cognitive functioning and vocational training outcome following ABI. The patient in this study successfully completed a vocational training, and both models predicted success based on patients' neuropsychological evaluation.

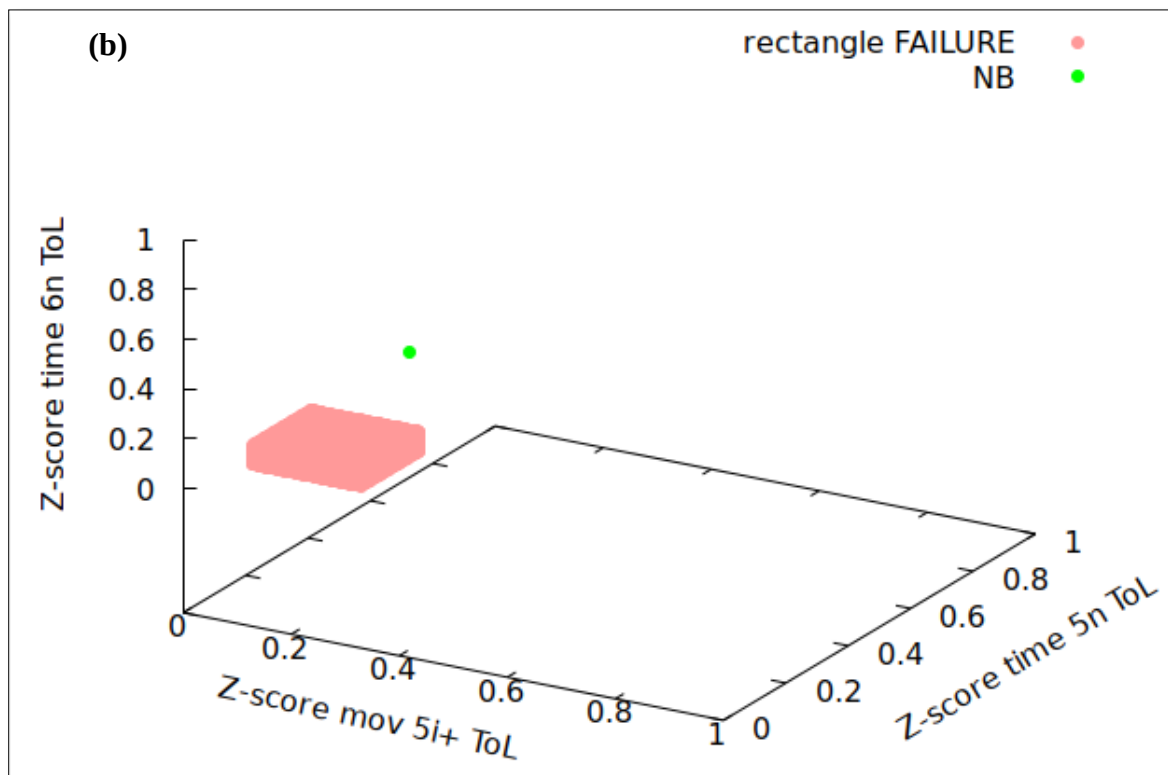
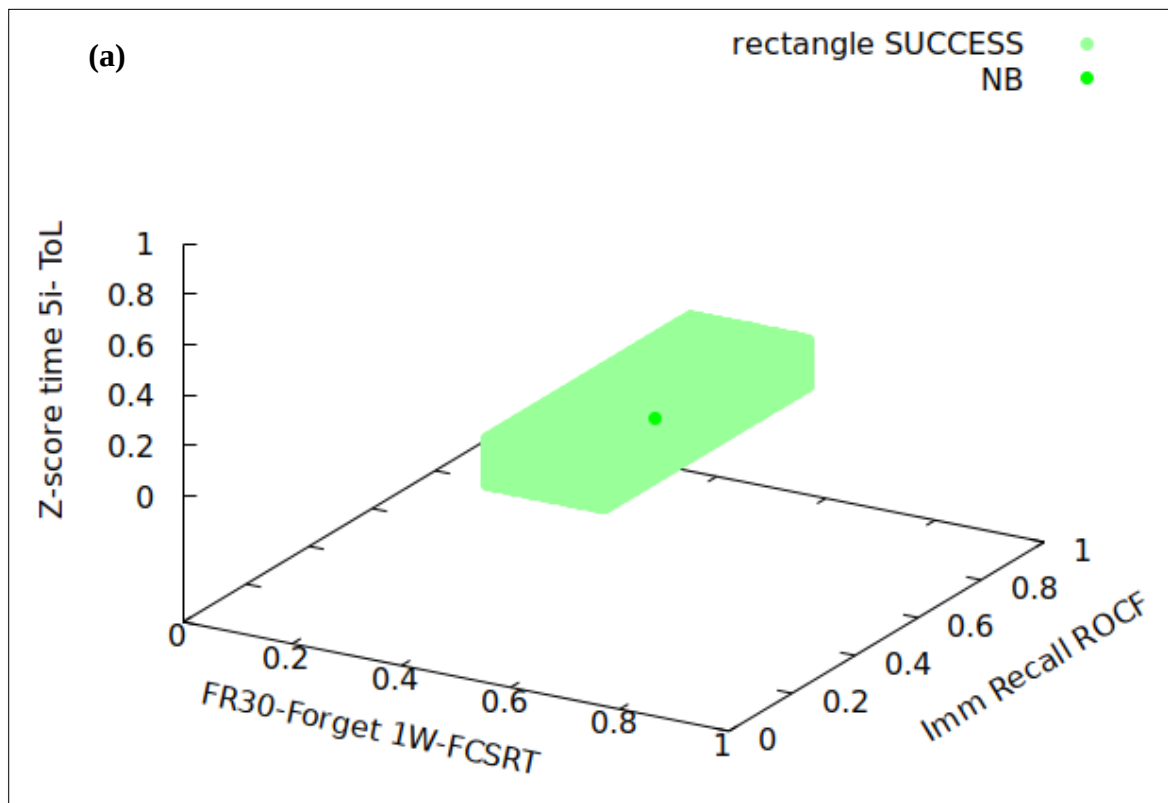


Figure 2. Neuropsychological performance of NB according to cognitive pattern explaining vocational training success (a) and failure (b) in patients with ABI.

In this case both models were accurate, meaning that attention measures with the D2 test of attention, executive functions measures with the ToL test and memory measured with 1W-FCSRT and ROCF were highly related to vocational training outcome following ABI. In the literature, the ToL (Shallice, 1982) was also found to be associated to the instrumental activities of daily living, including employment (Zakzanis, Grimes, Uzzaman, & Schmuckler, 2016) and ROCF scores were related to the return to work (Watt & Penn, 2000). Return to work following ABI was more generally predicted by the cognitive functions highlighted in these models, as attention (Watt & Penn, 2000), verbal (Drake, Gray, Yoder, Pramuka, & Llewellyn, 2000; O'Connell, 2000; Sigurdardottir et al., 2018) and visual memory (Sigurdardottir et al., 2018; Watt & Penn, 2000) and executive functions (Azouvi et al., 2015; Drake et al., 2000; Sigurdardottir et al., 2018). As attention and memory are involved in most jobs (Green et al., 2008), these cognitive functions seemed to be logically implicated in vocational training as well.

These models should be further investigated in larger groups, in order to determine their accuracy and/or refine them. Indeed, such models would allow clinicians to use objective factors to guide patients with ABI towards socio-professional reintegration, and would avoid to start a training that will fail.

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1.4. Le profil neuropsychologique peut-il permettre de prédire la réussite ou l'échec en formation des personnes cérébrolésées ? Etude multicentrique

Introduction

Les personnes souffrant d'une LCA et présentant des difficultés pour réintégrer le milieu socio-professionnel peuvent être prises en charge dans les Unités d'Évaluation, de Réentraînement et d'Orientation Socio-professionnelle (UEROS) sur orientation des Maisons Départementales des Personnes Handicapées (MDPH). Ces personnes sont relativement jeunes et souhaitent souvent reprendre une formation.

Dans l'**Article 6**, nous avons mis en évidence un modèle permettant d'associer performances cognitives et réussite ou échec en formation professionnelle chez des personnes souffrant d'une LCA. Ce modèle comprenait une règle « réussite » et une règle « échec ». La règle « réussite » correspondait à une association d'intervalles de performance pour trois scores évaluant la consolidation rapide en mémoire épisodique verbale (score FR30-Forget, de l'épreuve *One-Week Free and Cued Selective Reminding Test*, 1W-FCSRT ; Manoli et al., 2018), la mémoire visuelle incidente (score de rappel immédiat, de l'épreuve *Rey-Osterrieth Complex Figure* ; Meyers & Meyers, 1995), et les capacités de planification (score de l'épreuve *Tower of London* ; Coyette & Van der Linden, 1993; Rainville, 2002). La règle « échec » correspondait à une association d'intervalles de performance pour trois scores évaluant les capacités de planification (scores de l'épreuve *Tower of London*).

Dans la continuité des travaux exposés précédemment dans cette **Partie IV**, nous avons voulu tester ce modèle dans un nouvel échantillon de patients souffrant d'une LCA. Pour ce faire et afin d'obtenir un échantillon conséquent, nous avons mené une étude multicentrique.

Méthode

Participants

En collaboration avec plusieurs UEROS en France (Mulhouse, Berck-sur-Mer, Saint-André-de-l'Eure, Mondeville, Lyon et Fontenailles), nous avons inclus de manière rétrospective 67 patients souffrant d'une LCA qui avaient des difficultés à réintégrer le milieu socioprofessionnel. Pour pallier ces difficultés, ces patients avaient effectué un stage en UEROS, et ont entrepris une formation professionnelle à la suite de leur stage. L'issue de cette formation (réussite / échec) était connue pour l'ensemble des participants.

Lors de leur entrée en UEROS, ces patients avaient en moyenne 33,38 ans ($\pm 8,85$) et comptaient 64% d'hommes. Parmi eux, 53% avaient eu un TC, 34% un AVC et 12% présentaient une autre étiologie. Ils étaient à un délai moyen de 5,35 ans de leur événement neurologique. Concernant la formation professionnelle post-UEROS, 46 avaient réussi et 21 avaient échoué (respectivement 69% vs 31%).

Procédure

Pour l'ensemble des participants, nous avons recueilli les scores de l'évaluation neuropsychologique, effectuée au début de chaque stage en UEROS. Les scores recueillis (237 variables indépendantes) correspondaient aux épreuves suivantes :

- *Wechsler Adult Intelligence Scale* – 3^e édition (WAIS-III ; Wechsler, 2008),
- *Matrices Progressives Standard* (Raven, Raven, & Court, 2000),
- *Test de raisonnement concret et abstrait* (TRCG et TRAG) (Goguelin, 1953),

- Batterie d'efficience mnésique BEM-144 (Signoret, 1991),
- Figure de Rey ou *Rey–Osterrieth Complex Figure* (Meyers & Meyers, 1995),
- Test des portes ou *Doors Test* (Baddeley, Emslie, & Nimmo-Smith, 1994),
- *California Verbal Learning Test* (CVLT ; Hahn-Barma & Adam, 2008),
- *One-Week Free and Cued Selective Reminding Test* (1W-FCSRT; Manoli et al., 2018),
- Echelle clinique de mémoire de Wechsler – 3^e édition (MEM-III ; Wechsler, 2008),
- Double tâche (Baddeley, Della Sala, Papagno, & Spinnler, 1997; GREFEX, 2001),
- D2 (Brickenkamp & Zillmer, 1998),
- Brown-Peterson (Geurten et al., 2016),
- Test d'Evaluation de l'Attention (TAP, version 2.3.1 ; adaptation française de Michel Leclercq ; Zimmermann & Fimm, 2002),
- *Trail Making Test* (GREFEX, 2001; Roussel & Godefroy, 2008; Tombaugh, 2004),
- Stroop (Bohnen, Jolles, & Twijnstra, 1992; Roussel & Godefroy, 2008),
- Test des commissions (Martin, 1972),
- Test des 6 éléments (Garnier et al., 1998 ; GREFEX, 2001),
- Tour de Londres (Coyette & Van der Linden, 1993),
- Test de complèment de phrases de Hayling (Burgess & Shallice, 1997),
- Paced Auditory Serial Addition Test (Reuter, Baumstarck-Barrau, Loundou, Pelletier, & Auquier, 2010),
- Wisconsin Card Sorting Test (Heaton, 1993),
- Modified Card Sorting Test (GREFEX, 2001; Nelson, 1976),
- Test de Brixton (Burgess & Shallice, 1996; GREFEX, 2001),
- Fluences verbales (Cardebat et al., 1990),
- “*Reading the Mind in the Eyes*” Test (Baron-Cohen, Wheelwright, Hill, Raste, & Plumb, 2001).

Les participants n'ont pas tous eu les mêmes épreuves et/ou la totalité des épreuves ci-dessus.

Analyse des données

Etant donné les disparités entre UEROS concernant la durée de l'évaluation neuropsychologique et le type d'épreuves administrées, l'échantillon d'étude comportait 85,77% de valeurs manquantes.

Avant toute analyse des données, nous avons écarté les variables dont le taux de valeurs manquantes était supérieur à 60%, ramenant le nombre de variables indépendantes à 21, avec un taux total de valeurs manquantes de 40,63%.

Dans un premier temps, parmi les 21 variables indépendantes, nous nous sommes intéressés aux six variables composant le modèle retrouvé dans l'**Article 6**, permettant d'expliquer l'issue de la formation professionnelle après une LCA. En analysant les performances des participants par rapport aux intervalles du modèle relatifs à la réussite et à l'échec, nous avons déterminé le taux de participants pour lesquels le modèle est correct.

Dans un second temps, nous avons comparé les performances sur les 21 variables indépendantes selon l'issue de la formation des participants (réussite / échec), en utilisant le test t de Welch pour échantillons indépendants lorsque la distribution des variables indépendantes suivait une loi normale, et le test de Wilcoxon-Mann-Whitney dans le cas contraire.

Résultats

Dans un premier temps, afin de tester le modèle à six facteurs, nous avons analysé les performances des participants au regard des intervalles de la règle « réussite » et de la règle « échec » (voir **Tableau 1**). Aucun des participants n'avait l'ensemble des 6 mesures impliquées

dans le modèle, ce qui aurait permis de valider une des règles, d'en réfuter l'autre ou de réfuter les deux. De ce fait, le pourcentage d'exactitude du modèle n'a pu être calculé.

Parmi les participants ayant réussi leur formation ($N=46$), 58,70% avaient au moins un score appartenant à un intervalle de la règle « réussite » (en vert dans le **Tableau 1**) tout en n'ayant aucun score en dehors (en bleu dans le **Tableau 1**) des intervalles de la règle « réussite » et aucun score appartenant aux trois intervalles de la règle « échec » (en rouge dans le **Tableau 1**). Dans le même groupe, 13,04% avaient deux scores appartenant à un intervalle de la règle « réussite » (en vert dans le **Tableau 1**) tout en n'ayant aucun score en dehors (en bleu dans le **Tableau 1**) des intervalles de la règle « réussite » et aucun score appartenant aux trois intervalles de la règle « échec » (en rouge dans le **Tableau 1**). Pour 10,87% des participants ayant réussi leur formation, le nombre de valeurs manquantes ne nous a pas permis de statuer sur l'issue prédite par le modèle car ces participants avaient des scores dans un ou deux intervalles de la règle « réussite » et dans un ou deux intervalles de la règle « échec ». Un seul participant sur les 46 avait l'ensemble des trois mesures de la règle « réussite », cependant un des scores était en dehors de l'intervalle associé à la règle « réussite ». De ce fait, la règle « réussite » n'était pas correcte chez 2,17% de notre sous-échantillon de participants ayant réussi leur formation après une LCA.

Chez les participants ayant échoué leur formation ($N=21$), aucun n'avait l'ensemble des trois mesures de la règle « échec », un seul (4,76%) avait au moins un score appartenant à un intervalle de la règle « échec » (en rouge dans le **Tableau 1**) tout en n'ayant aucun score en dehors (en bleu dans le **Tableau 1**) des intervalles de la règle « échec » et aucun score appartenant aux trois intervalles de la règle « réussite » (en vert dans le **Tableau 1**).

Tableau 1. Test des règles « réussite » et « échec » dans l'échantillon multicentrique.

Numéro d'inclusion	Issue de la formation	REGLE "REUSSITE"			REGLE "ECHEC"		
		FR30-Forget	ROCF IR	Z time 5I-	Z mov 5I+	Z time 5N	Z time 6N
7KD	REUSSITE	12.5	?	1.42	-0.26	2.14	4.39
53ADSM	REUSSITE	8.333	12	-0.46	-0.28	0.24	?
59B	REUSSITE	44.444	20.5	?	-0.61	?	?
8CF	REUSSITE	-12.5	?	?	0.97	?	?
61L	REUSSITE	16.667	?	?	-0.13	?	?
47VO	REUSSITE	40	21	?	?	?	?
37SB	REUSSITE	-7.692	?	?	-0.02	?	?
UB19	REUSSITE	-30	?	?	?	?	?
57L	REUSSITE	0	17	?	-0.27	?	?
9DG	REUSSITE	-8.333	30	?	?	?	?
64AKR	REUSSITE	-7.143	23	?	?	?	?
56B	REUSSITE	8.333	?	?	-0.65	?	?
50TC	REUSSITE	11.111	23	?	?	?	?
45SG	REUSSITE	7.692	14	?	?	?	?
36PL	REUSSITE	0	?	?	-0.65	?	?
25OR	REUSSITE	0	26	?	?	?	?
UB7	REUSSITE	-15.385	?	?	?	?	?
UB6	REUSSITE	25	?	?	?	?	?
6FD	REUSSITE	-16.667	?	?	?	?	?
65ROC	REUSSITE	0	?	?	?	?	?
63PLU	REUSSITE	?	25	?	?	?	?
62D	REUSSITE	0	?	?	?	?	?
49NR	REUSSITE	?	23	?	?	?	?
46NG	REUSSITE	?	15	?	?	?	?
44NC	REUSSITE	?	16.5	?	?	?	?
42EB	REUSSITE	?	14	?	?	?	?
35JM	REUSSITE	?	27	?	?	?	?
34MV	REUSSITE	?	16	?	?	?	?
33AB	REUSSITE	?	27	?	?	?	?
29TVB	REUSSITE	?	28.5	?	?	?	?
28NO	REUSSITE	?	27	?	?	?	?
21BF	REUSSITE	0	?	?	?	?	?
11PP	REUSSITE	12.5	?	?	?	?	?
10MAH	REUSSITE	7.692	?	?	?	?	?
UB9	REUSSITE	?	?	?	?	?	?
UB8	REUSSITE	?	?	?	?	?	?
UB17	REUSSITE	?	?	?	?	?	?
UB16	REUSSITE	?	?	?	?	?	?
67GIR	REUSSITE	?	?	?	?	?	?
66DEB	REUSSITE	?	?	?	?	?	?
5RC	REUSSITE	?	?	?	?	?	?
52SZ	REUSSITE	?	?	?	?	?	?
4VD	REUSSITE	?	?	?	?	?	?
40BM	REUSSITE	?	?	?	?	?	?
2ML	REUSSITE	?	?	?	?	?	?
12JHR	REUSSITE	?	?	?	?	?	?

En **vert** : valeurs comprises dans les intervalles de performance de la règle « réussite » ; en **rouge** : valeurs comprises dans les intervalles de la règle « échec » ; en **bleu** : valeurs n'appartenant à aucun de ces intervalles.
 ? : valeurs manquantes ; **FR30-Forget** : pourcentage d'oubli lors du rappel libre différé à 30 minutes par rapport au 3^e rappel libre de l'épreuve 1W-FCSRT ; **ROCF-IR** : rappel incident à 3 minutes de la figure complexe de Rey ; **Z mov 5I+** : score Z du nombre de mouvements réalisés pour les items nécessitant au moins 5 mouvements avec incitateur positif à l'épreuve de la Tour de Londres ; **Z time 5I-** : score Z de la durée de réalisation pour les items nécessitant au moins 5 mouvements avec un incitateur négatif ; **Z time 5N** : score Z de la durée de réalisation pour les items nécessitant au moins 5 mouvements ; **Z time 6N** : score Z de la durée de réalisation pour les items nécessitant au moins 6 mouvements.

Tableau 1. (suite)

Numéro d'inclusion	Issue de la formation	REGLE "REUSSITE"			REGLE "ECHEC"		
		FR30-Forget	ROCF IR	Z time 5I-	Z mov 5I+	Z time 5N	Z time 6N
68CHA	ECHEC	33.333	11	?	?	?	?
60H	ECHEC	-33.333	24	?	?	?	?
39ER	ECHEC	-23.077	35	?	?	?	?
13SB	ECHEC	-33.333	13	?	?	?	?
58C	ECHEC	?	?	?	0.07	?	?
55L	ECHEC	?	?	?	1.24	?	?
38AA	ECHEC	-27.273	?	?	?	?	?
54M	ECHEC	18.182	?	?	-0.65	?	?
27CE	ECHEC	0	34	?	?	?	?
20DF	ECHEC	22.222	17.5	?	?	?	?
48CG	ECHEC	?	26.5	?	?	?	?
43JL	ECHEC	?	16.5	?	?	?	?
1CFN	ECHEC	?	22	?	?	?	?
16LF	ECHEC	0	?	?	?	?	?
14VT	ECHEC	-6.25	?	?	?	?	?
51JR	ECHEC	?	?	?	?	?	?
41MT	ECHEC	?	?	?	?	?	?
3BD	ECHEC	?	?	?	?	?	?
31GS	ECHEC	?	?	?	?	?	?
26NK	ECHEC	?	?	?	?	?	?
15MC	ECHEC	?	?	?	?	?	?

En **vert** : valeurs comprises dans les intervalles de performance de la règle « réussite » ; en **rouge** : valeurs comprises dans les intervalles de la règle « échec » ; en **bleu** : valeurs n'appartenant à aucun de ces intervalles.

? : valeurs manquantes ; **FR30-Forget** : pourcentage d'oubli lors du rappel libre différé à 30 minutes par rapport au 3^e rappel libre de l'épreuve 1W-FCSRT ; **ROCF-IR** : rappel incident à 3 minutes de la figure complexe de Rey ; **Z mov 5I+** : score Z du nombre de mouvements réalisés pour les items nécessitant au moins 5 mouvements avec incitateur positif à l'épreuve de la Tour de Londres ; **Z time 5I-** : score Z de la durée de réalisation pour les items nécessitant au moins 5 mouvements avec un incitateur négatif ; **Z time 5N** : score Z de la durée de réalisation pour les items nécessitant au moins 5 mouvements ; **Z time 6N** : score Z de la durée de réalisation pour les items nécessitant au moins 6 mouvements.

Dans un second temps, aucune différence statistiquement significative n'a été retrouvée en termes de performances cognitives pour les 21 variables indépendantes testées entre les participants qui avaient réussi et ceux qui avaient échoué leur formation professionnelle à la suite d'une LCA (voir **Tableau 2**). Cependant, les scores au TMT mettent en évidence un temps moyen plus long pour réaliser la tâche ainsi que des écart-types plus larges chez les personnes qui ont échoué leur formation, par rapport à celles qui ont réussi (voir **Tableau 2**).

Tableau 2. Performances cognitives de l'échantillon en fonction de la réussite ou l'échec de la formation professionnelle.

Fonction cognitive	Epreuve	Score	M (DS) Groupe "Réussite"	M (DS) Groupe "Echec"	Comparaison statistique
Mémoire épisodique visuelle	Figure de Rey (ROCF)	RI = Rappel incident à 3min	21,34 (5,64)	22,17 (8,58)	Test de Welch pour échantillons indépendants $t = 0,26, p = 0,78$
Mémoire épisodique verbale	One-Week Free and Cued Selective Reminding Test (1W-FCSRT)	FR1 = 1 ^{er} Rappel libre	8,24 (2,33)	7,80 (1,93)	Test de Welch pour échantillons indépendants $t = -0,57, p = 0,57$
		CR1 = 1 ^{er} Rappel indicé	5,52 (2,00)	5,70 (1,83)	Test de Welch pour échantillons indépendants $t = 0,26, p = 0,80$
		TR1 1 ^{er} Rappel total	13,76 (2,49)	13,70 (2,31)	Test de la somme des rangs de Wilcoxon $W = 118,5, p = 0,82$
		FR2 = 2 ^e Rappel libre	10,16 (2,48)	9,10 (2,85)	Test de Welch pour échantillons indépendants $t = -1,03, p = 0,32$
		CR2 = 2 ^e Rappel indicé	4,68 (1,95)	5,50 (2,51)	Test de Welch pour échantillons indépendants $t = 0,93, p = 0,37$
		TR2 = 2 ^e Rappel total	15,24 (2,89)	14,60 (1,07)	Test de la somme des rangs de Wilcoxon $W = 91, p = 0,20$
		FR3 = 3 ^e Rappel libre	10,6 (2,80)	10,5 (2,68)	Test de Welch pour échantillons indépendants $t = -0,10, p = 0,92$
		CR3 = 3 ^e Rappel indicé	4,68 (2,54)	4,10 (2,69)	Test de Welch pour échantillons indépendants $t = -0,59, p = 0,57$
		TR3 = 3 ^e Rappel total	15,36 (1,19)	14,60 (1,90)	Test de la somme des rangs de Wilcoxon $W = 90, p = 0,16$

DS : déviation standard ; **M** : moyenne.

Tableau 2. (suite)

Fonction cognitive	Epreuve	Score	Groupe "Réussite" Moyenne (écart-type)	Groupe "Echec" Moyenne (écart-type)	Comparaison statistique
Mémoire épisodique verbale	One-Week Free and Cued Selective Reminding Test (1W-FCSRT)	FR30 = Rappel libre à 30min	11,29 (2,71)	9,80 (2,90)	Test de la somme des rangs de Wilcoxon $W = 85, p = 0,19$
		FR30-Forget = % oublié à 30min	4,02 (16,85)	-4,95 (24,10)	Test de Welch pour échantillons indépendants $t = -1,07, p = 0,30$
		TR30 = Rappel total à 30min	9,04 (6,17)	9,40 (6,24)	Test de la somme des rangs de Wilcoxon $W = 124,5, p = 0,88$
	Wechsler Memory Scale (MEM-III)	HIST-I = « Mémoire Logique » rappel immédiat	20,82 (13,00)	20,73 (10,92)	Test de la somme des rangs de Wilcoxon $W = 96, p = 0,92$
		HIST-II = « Mémoire Logique » rappel différé	14,67 (7,41)	14,40 (3,53)	Test de la somme des rangs de Wilcoxon $W = 98, p = 0,53$
Attention	D2	GZ	362,61 (96,61)	361,20 (76,53)	Test de Welch pour échantillons indépendants $t = -0,05, p = 0,96$
		GZ-F	339,56 (90,30)	335,13 (75,97)	Test de Welch pour échantillons indépendants $t = -0,14, p = 0,89$
		SB	13,63 (6,06)	10,50 (3,59)	Test de la somme des rangs de Wilcoxon $W = 68, p = 0,12$
Flexibilité mentale réactive	TMT	A	37,04 (15,13)	62,80 (93,41)	Test de la somme des rangs de Wilcoxon $W = 100, p = 0,12$
		B	83,92 (35,92)	125,80 (112,03)	Test de la somme des rangs de Wilcoxon $W = 137, p = 0,67$
		B-A	46,83 (29,97)	66,78 (73,47)	Test de la somme des rangs de Wilcoxon $W = 112, p = 0,74$

DS : déviation standard ; **M** : moyenne.

Discussion

L'objectif de cette étude était de tester le modèle cognitif en lien avec l'issue d'une formation professionnelle à la suite d'une LCA mis en évidence dans l'**Article 6**. Ce modèle était composé de deux règles, l'une sous-tendant la réussite et l'autre l'échec de la formation. Chacune des règles comportait simultanément trois intervalles de performances correspondant à trois mesures neuropsychologiques. La règle « réussite » comportait des intervalles de performances correspondant à des mesures de consolidation en mémoire épisodique verbale, de mémoire épisodique visuelle et de planification. La règle « échec » comportait des intervalles de performances correspondant à trois mesures de planification. Afin de tester ce modèle, nous avons recueilli de manière rétrospective les données de personnes souffrant d'une LCA ayant intégré une formation professionnelle à la suite de leur stage en UEROS.

Dans notre échantillon d'étude, les six variables impliquées dans le modèle à tester comportaient un nombre très élevé de valeurs manquantes, ne nous permettant pas de calculer le pourcentage d'exactitude du modèle dans cette nouvelle population. Parmi les participants ayant réussi leur formation, près de 60% avaient au moins un des trois scores permettant de prédire la réussite, en l'absence de scores réfutant cette règle. Parmi ces 60%, aucun des participants n'avait l'ensemble des trois scores permettant de vérifier la règle. Chez les participants ayant échoué leur formation, aucun n'avait l'ensemble des trois mesures de la règle « échec » et un seul (4,76%) avait au moins un des trois scores permettant de prédire l'échec, en l'absence de scores réfutant cette règle.

Par ailleurs, en comparant les participants ayant réussi et ceux ayant échoué sur les variables indépendantes, aucune différence statistiquement significative n'a été relevée. Cela voudrait dire qu'une seule variable ne peut déterminer la réussite ou l'échec à la suite d'une LCA. Ces résultats plaident en faveur d'un modèle plus complexe, comme celui mis en évidence à l'**Article 6**, dont nous n'avons pu évaluer l'exactitude dans cette étude. Ainsi, ce modèle devrait

être testé sur un autre échantillon comprenant les données pour les six variables qui rentrent en jeu dans le modèle. De manière prospective, nous pourrions administrer un bilan neuropsychologique complet et identique pour tous les participants, incluant ces six variables, mais aussi en rajoutant des variables comportementales, comme la fatigue (**Partie III, Article 4**), pour arriver à un modèle cognitivo-comportemental le plus exact possible.

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2. Volet prospectif – Etude multicentrique

Dans le volet rétrospectif présenté précédemment, nous avons mis en évidence des modèles cognitifs en lien avec la réussite ou l'échec en formation professionnelle des personnes souffrant d'une LCA. En effet, ces modèles nous permettaient d'*expliquer* la réussite ou l'échec à l'aide d'un certain nombre de mesures neuropsychologiques. Cependant, ils ne nous renseignaient pas sur le pouvoir *prédictif* de ces mesures quant à la réussite ou l'échec.

L'objectif de cette nouvelle étude était d'évaluer ce pouvoir prédictif et l'implication d'autres facteurs cognitivo-comportementaux dans l'issue professionnelle, nous avons mis en place une méthodologie prospective multicentrique avec plusieurs UEROS en France. L'aspect prospectif nous permettait de contrôler le taux de valeurs manquantes et l'aspect multicentrique nous permettait d'avoir un échantillon suffisamment grand pour satisfaire les prérequis des analyses de données.

Tous les usagers entrant en stage dans les UEROS collaborant à ce projet étaient invités à participer à l'étude. Les participants ont été inclus entre septembre 2017 et avril 2019.

Par ailleurs, l'intégration d'une formation, si tel est le projet de l'utilisateur, se fait plusieurs mois voire plusieurs années après le stage en UEROS. De ce fait, l'issue de la formation professionnelle pour les participants qui ont intégré une formation parmi l'ensemble des participants inclus dans l'étude ne sera connue que dans plusieurs mois ou années.

2.1. Variables d'intérêt de l'évaluation neuropsychologique

Concernant l'aspect cognitif, les variables d'intérêt étaient les six mesures correspondant au modèle cognitif retrouvé dans l'**Article 6** ainsi que les autres mesures habituellement recueillies lors de l'évaluation neuropsychologique en début de stage UEROS. Parmi ces variables, il y

avait notamment les mesures de l'épreuve *One-Week Free and Cued Selective Reminding Test* (1W-FCSRT) qui a fait l'objet des **Articles 2 et 3**.

2.2. Variables d'intérêt de l'évaluation comportementale

Dans les études rétrospectives présentées précédemment, seul l'aspect cognitif avait été investigué, les évaluations comportementales en UEROS manquant d'outils quantitatifs. Avec une approche prospective, nous avons voulu inclure l'aspect comportemental dans la construction de modèles prédictifs de l'issue professionnelle après une LCA.

Dans les **Parties I et II** de ce travail de thèse, le niveau de fatigue et les changements comportementaux après une LCA semblaient primordiaux pour la réintégration du milieu socio-professionnel. De ce fait, nous avons voulu inclure dans le volet prospectif une évaluation du niveau de fatigue en proposant la passation du *Multidimensional Fatigue Inventory* (MFI-20) (Gentile, Delarozière, Favre, Sambuc, & San Marco, 2003; Smets, Garssen, Bonke, & De Haes, 1995), qui a fait l'objet de l'**Article 4**. Nous avons également proposé une évaluation des changements comportementaux à l'aide de l'Echelle des Changements de Comportement Socio-Émotionnel de Genève (ECCSEG), validée auprès d'une population souffrant d'un TC (Beni et al., 2017).

2.3. Retombées scientifiques

Cette nouvelle méthode d'étude nous permettra de tester les modèles cognitifs retrouvés précédemment et/ou d'identifier d'autres modèles cognitifs, comportementaux ou cognitivo-comportementaux permettant de prédire un retour efficace en formation professionnelle à la suite d'une LCA. Les retombées cliniques permettront aux professionnels de s'appuyer sur des critères objectifs pour guider les usagers vers une formation professionnelle.

3. Discussion

Dans cette **Partie IV**, nous avons identifié plusieurs modèles cognitifs permettant de faire le lien avec l'issue professionnelle de personnes victimes d'une LCA, en adoptant une méthode d'analyse des données particulièrement innovante, l'apprentissage automatique ou *machine learning*.

Dans l'**Article 5**, nous avons mis en évidence que les processus cognitifs les plus impliqués dans l'issue d'une formation professionnelle étaient les processus attentionnels, suivis des fonctions exécutives et des processus mnésiques. Ces processus ont permis de créer un modèle cognitif reposant sur un arbre de décision permettant d'expliquer la réussite ou l'échec de la formation. Dans l'**Article 6**, nous avons présenté un modèle cognitif reposant sur deux règles, l'une prédisant la réussite et l'autre prédisant l'échec en formation. Les deux règles reposaient chacune sur une combinaison de trois intervalles pour trois mesures neuropsychologiques différentes. La règle « réussite » reposait sur des mesures de mémoire épisodique verbale, mémoire épisodique visuelle et planification (fonction exécutive). La règle « échec » reposait sur des mesures de planification (fonction exécutive). Ce modèle a été validé dans le cadre d'une étude de cas (**Article 7**), mais son pourcentage d'exactitude n'a pu être calculé dans le cadre de l'étude rétrospective multicentrique, l'échantillon présentant un très grand nombre de valeurs manquantes pour nos variables d'intérêt. Il sera à nouveau testé dans le cadre d'une étude prospective multicentrique lorsque les informations quant à l'issue de la formation professionnelle des participants seront renseignées. Cette étude prospective multicentrique permettra également d'ajuster le modèle, notamment selon l'aspect comportemental.

Cette **Partie IV** nous a permis de démontrer l'utilité d'un bilan neuropsychologique complet et exhaustif dans le cadre d'un stage en UEROS. En effet, grâce aux modèles cognitifs proposés, le bilan neuropsychologique permet d'apporter des informations-clés quant à la probabilité de

réussir ou échouer une formation professionnelle et d'améliorer les conseils d'orientation professionnelle pour les patients souffrant d'une LCA. Ces modèles cognitifs ont également souligné l'importance de prendre en compte une combinaison de processus cognitifs lorsque l'on s'interroge sur les capacités d'une personne souffrant d'une LCA à réintégrer le milieu socio-professionnel, et ne pas se focaliser sur un seul processus, comme par exemple la mémoire, ou dichotomiser les performances en termes de normal et pathologique.

PARTIE V :

DISCUSSION GENERALE ET PERSPECTIVES

1. Discussion générale

1.1. Principaux résultats

L'objectif général de cette thèse était d'identifier des profils cognitivo-comportementaux compatibles ou incompatibles avec un retour en formation au stade séquellaire après une LCA. Ainsi, l'intérêt était porté sur les aspects fonctionnels en lien avec une LCA qui permettraient ou non le retour en formation, et non à l'impact de lésions cérébrales spécifiques sur le retour en formation de personnes victimes d'une LCA.

Dans un premier temps, nous avons voulu identifier, dans les phases post-aigües d'une LCA, les facteurs cognitivo-comportementaux impliqués dans la réinsertion professionnelle des personnes souffrant d'une LCA d'origine traumatique, dans la mesure où cette étiologie a l'incidence la plus élevée et affecte surtout les personnes en âge de travailler (**Partie II**). En menant une revue systématique de la littérature (**Article 1**), nous avons mis en évidence que le nombre de symptômes auto-rapportés, les habiletés fonctionnelles et cognitives, les troubles thymiques et les troubles liés à l'usage de l'alcool étaient hautement prédictifs de l'issue professionnelle des personnes souffrant d'une LCA d'origine traumatique. Ces résultats mettent en lumière l'intérêt d'adopter une approche intégrative dans l'évaluation des personnes souffrant d'une LCA dans un contexte de réintégration socio-professionnelle, à la fois sur les aspects cognitif, psychologique, comportemental et fonctionnel. Cette revue a cependant permis de souligner le manque d'études investiguant d'autres types d'issues professionnelles, comme l'issue d'une formation entamée à la suite d'une LCA, et l'impact que les déficits post-LCA auraient sur ces issues.

Dans un deuxième temps, il nous est apparu nécessaire d'adapter nos outils pour évaluer plus finement les troubles cognitifs et comportementaux des personnes victimes d'une LCA, avant

de tester leur pouvoir prédictif (**Partie III**). De ce fait, nous avons, d'une part, adapté un outil d'évaluation des processus de consolidation en mémoire épisodique verbale (**Article 2**) et évalué son intérêt chez les personnes souffrant de TC sévère (**Article 3**). D'autre part, nous avons évalué l'intérêt d'une échelle de fatigue chez les personnes victimes d'une LCA (**Article 4**).

Dans l'**Article 2**, nous avons adapté l'épreuve du RL/RI-16 items (Van der Linden & the members of GREMEM, 2004) en remplaçant le rappel différé à 20 minutes après la phase d'apprentissage par un délai de 30 minutes et en rajoutant un rappel différé supplémentaire à sept jours. Cette adaptation, appelée *One-Week Free and Cued Selective Reminding Test* (1W-FCSRT), reposait également sur de nouvelles mesures d'apprentissage, stockage et consolidation en mémoire verbale qui prennent en compte les propres performances du participant au cours du test. Ainsi, chez des participants neurologiquement sains, nous avons pu distinguer des processus de consolidation distincts, l'un rapide correspondant au score d'oubli lors du délai de 30 minutes après la phase d'apprentissage et l'autre lent correspondant au score d'oubli lors du délai de sept jours. Ces processus ont été évalués chez des personnes souffrant d'un TC sévère (**Article 3**). Les patients avaient des scores d'oubli plus élevés que les participants neurologiquement sains, et ce d'autant plus que le délai du rappel différé était grand. En se basant sur des normes établies sur une population neurologiquement saine (**Article 2**), nous avons pu mettre en évidence que les patients avec TC sévère présentaient des déficits de consolidation en mémoire épisodique verbale, surtout dans sa composante lente. Détecter ce type de déficit permettrait, d'une part, d'objectiver les plaintes des patients et, d'autre part, d'adapter leur réintégration socio-professionnelle en fonction de la sévérité de leurs troubles mnésiques.

Dans l'**Article 4**, nous avons évalué l'utilité du *Multidimensional Fatigue Inventory* ou MFI-20 (Gentile, Delarozière, Favre, Sambuc, & San Marco, 2003; Smets, Garssen, Bonke, & De

Haes, 1995) chez des patients souffrant d'une LCA. Chez ces patients, les mesures du MFI-20 étaient liées à des mesures neuropsychologiques d'attention, de mémoire et de fonctions exécutives. Cet outil nous a permis d'évaluer la fatigue liée au handicap dû à une LCA, et la distinguer de celle liée à un handicap physique sans atteinte cérébrale focale et celle survenant chez des personnes en bonne santé générale (sans handicap).

Dans un troisième temps, nous avons étudié le lien entre les performances cognitives et comportementales évaluées à l'entrée en UEROS et la probabilité de réussir/échouer en intégrant une formation après une LCA. Pour ce faire, nous avons adopté une méthodologie rétrospective et une méthodologie prospective, et avons utilisé une méthode d'analyse des données particulièrement innovante : l'apprentissage automatique (*Machine learning*) (**Partie IV**). Dans une étude préliminaire (**Article 5**), nous avons inclus de manière rétrospective des personnes souffrant d'une LCA ayant effectué un stage à l'UEROS de Lille (UGECAM Hauts-de-France) ou à l'UEROS de Berck-sur-Mer (Fondation Hopale) et qui avaient complété une formation professionnelle qualifiante à la suite de ce stage. À l'aide d'algorithmes d'apprentissage automatique supervisé par arbre de décision, nous avons étudié le lien entre les scores obtenus par les participants à l'évaluation neuropsychologique effectuée en début de stage UEROS et le résultat de l'issue de leur formation professionnelle post-UEROS (réussite vs échec). Nous avons mis en évidence un modèle cognitif permettant d'expliquer la réussite et l'échec en formation professionnelle après une LCA ; ce modèle comprenait des mesures d'attention, de mémoire de travail, de planification, et de flexibilité mentale spontanée. De la même manière, dans l'**Article 6**, nous avons inclus de manière rétrospective des personnes souffrant d'une LCA ayant effectué un stage à l'UEROS de Lille (UGECAM Hauts-de-France) et qui avaient complété une formation professionnelle qualifiante à la suite de ce stage. À l'aide d'algorithmes d'apprentissage automatique supervisé par rectangles aléatoires, nous avons

étudié le lien entre les scores obtenus par les participants à l'évaluation neuropsychologique effectuée en début de stage UEROS et le résultat de l'issue de leur formation professionnelle post-UEROS, afin d'identifier des patterns de performance expliquant la réussite et d'autres expliquant l'échec. Nous avons mis en évidence que chacune des issues en formation professionnelle à la suite d'une LCA (réussite/échec) reposait sur une combinaison de trois intervalles pour trois mesures neuropsychologiques différentes, la réussite reposant sur des mesures de mémoire épisodique verbale, mémoire épisodique visuelle et planification, l'échec reposant sur trois mesures de planification. Les modèles obtenus dans les **Articles 5 et 6** ont été testés dans la cadre d'une étude de cas, chez une patiente souffrant d'une LCA temporelle postérieure non évolutive dans la région de Heschl, à l'origine d'une épilepsie pharmaco-résistante. Cette patiente avait réussi sa formation professionnelle qualifiante débutée à la suite de son stage à l'UEROS de Lille (UGECAM Hauts-de-France). Selon les modèles des **Articles 5 et 6**, ses performances cognitives telles qu'évaluées en début de stage UEROS auraient prédit la réussite d'une formation professionnelle. Afin de confirmer ces résultats et de tester la validité du modèle de l'**Article 6** sur un nouvel échantillon, nous avons mené une étude multicentrique, incluant des patients souffrant d'une LCA ayant effectué un stage dans une autre UEROS française ayant souhaité collaborer à cette étude (Mulhouse, Berck-sur-Mer, Saint-André-de-l'Eure, Mondeville, Lyon et Fontenailles) et ayant intégré une formation professionnelle à la suite de ce stage. Dans ce nouvel échantillon d'étude, les six variables impliquées dans le modèle à tester (trois pour la réussite, trois pour l'échec) comportaient un nombre très élevé de valeurs manquantes, ne nous permettant pas de calculer le pourcentage d'exactitude du modèle.

Afin de pallier les limites rencontrées en adoptant une démarche rétrospective, nous avons débuté une étude prospective multicentrique. Lorsque les informations quant à l'issue de la formation professionnelle des participants seront renseignées, les modèles mis en évidence dans

les **Articles 5 et 6** seront testés à nouveau et affinés, en fonction notamment d'autres facteurs, comme la fatigue et les changements comportementaux.

1.2. Interprétation des résultats

Les résultats de notre revue systématique de la littérature (**Partie II, Article 1**) ont montré qu'une évaluation exhaustive des habiletés fonctionnelles et cognitives était nécessaire, même dans les phases post-aigües du TC, pour pouvoir prédire l'issue professionnelle des personnes souffrant d'une LCA d'origine traumatique. Nous nous sommes ainsi focalisés, dans la **Partie IV**, sur l'évaluation neuropsychologique des personnes souffrant d'une LCA, telle que menée dans les UEROS, conformément aux dispositions du Décret n° 2009-299 du 17 mars 2009 relatif aux conditions d'organisation et de fonctionnement des UEROS, afin de prédire l'issue d'une formation professionnelle intégrée à la suite du stage UEROS. Parmi les différentes mesures de l'évaluation neuropsychologique, des scores à des épreuves spécifiques se sont érigés en facteurs explicatifs :

- (1) Indice GZ-F au test du D2 (Brickenkamp & Zillmer, 1998), calculé par une soustraction du nombre total d'erreurs au nombre total d'items traités, et évaluant les processus attentionnels ;
- (2) Pourcentage de réponses correctes au test de Brown-Peterson (Geurten, Vincent, Van der Linden, Coyette, & Meulemans, 2016) lorsque les tâches distractrices durent 20 secondes, et évaluant les processus de mémoire de travail auditivo-verbale ;
- (3) Score d'oubli à 30 minutes de délai après la phase d'apprentissage de l'épreuve 1W-FCSRT, adaptée de l'épreuve RL/RI-16 items (Van der Linden & the members of GREMEM, 2004) dans l'**Article 2 (Partie III)**, et évaluant les processus de consolidation rapide en mémoire épisodique verbale ;

- (4) Score de rappel immédiat au test de la Figure de Rey (Meyers & Meyers, 1995), et évaluant les processus de récupération en mémoire épisodique visuelle ;
- (5) Score au test de fluences verbales phonémiques pour la lettre « P » (Cardebat, Doyon, Puel, Goulet, & Joannette, 1990), et évaluant la flexibilité mentale spontanée ;
- (6) Quatre scores différents au test de la Tour de Londres (Coyette & Van der Linden, 1993; Rainville, 2002), à savoir le score Z du nombre de mouvements réalisés par les patients pour résoudre les problèmes nécessitant au moins cinq mouvements tandis que le premier mouvement évident favoriserait la résolution, le score Z du temps total mis par les patients pour résoudre les problèmes nécessitant au moins cinq mouvements tandis que le premier mouvement évident bloquerait la résolution, le score Z du temps total mis par les patients pour résoudre les problèmes nécessitant au moins cinq mouvements tandis que le premier mouvement évident est neutre, et le score Z du temps total mis par les patients pour résoudre les problèmes nécessitant au moins six mouvements tandis que le premier mouvement évident est neutre.

Les performances au test du D2 n'ont, à notre connaissance, jamais été étudiées en lien avec la réhabilitation socio-professionnelle des personnes souffrant d'une LCA. Cependant, Kay et Silver (1988) ont souligné que les déficits d'attention et de concentration seraient des obstacles à une réhabilitation réussie, les personnes ayant des déficits attentionnels nécessitant une minimisation des distracteurs dans l'environnement de travail ou la focalisation sur une seule tâche à la fois. Un protocole pour une étude randomisée et contrôlée a été proposé pour tester l'effet d'un entraînement attentionnel au cours de la première année post-LCA sur le retour à l'emploi de personnes souffrant d'une LCA (Bartfai, Markovic, Landahl, & Schult, 2014).

Les performances au test de Brown-Peterson n'ont, à notre connaissance, jamais été étudiées en lien avec la réhabilitation socio-professionnelle des personnes souffrant d'une LCA.

Cependant, des auteurs ont montré qu'une rééducation des processus de mémoire de travail chez des personnes souffrant d'une LCA avait un effet bénéfique sur le perçu subjectif de leur fonctionnement en vie quotidienne (Björkdahl, Akerlund, Svensson, & Esbjörnsson, 2013; Lundqvist, Grundström, Samuelsson, & Rönnberg, 2010). Une étude qualitative a souligné le lien entre mémoire de travail verbale et la reprise d'un travail à la suite d'un TC (Meulenbroek, Bowers, & Turkstra, 2016).

Les performances à l'épreuve 1W-FCSRT ont été évaluées en lien avec l'issue d'une formation professionnelle à la suite d'une LCA pour la première fois dans le cadre de ces travaux de thèse, cet outil ayant été proposé dans la **Partie III (Article 1)**. De ce fait, l'impact des processus de consolidation rapide et lente en mémoire épisodique verbale, mis en évidence dans l'**Article 1**, sur la réhabilitation socio-professionnelle n'a jamais été testé dans la littérature. Cependant, une étude qualitative a mis en évidence que la mémoire épisodique verbale, et plus précisément l'apprentissage, était liée au retour à un emploi de niveau intermédiaire (*mid-level job*) après un TC (Meulenbroek et al., 2016). La mémoire verbale, telle qu'évaluée par l'index de mémoire verbale de l'Echelle de Mémoire de Wechsler – Révisée (Wechsler, 1987), serait liée au retour à l'emploi après un TC (O'Connell, 2000). Les processus d'apprentissage et de rappel indicé, tels qu'évalués par le *California Verbal Learning Test* (Delis, Kramer, Kaplan, & Ober, 1983), permettraient de différencier les militaires ayant retrouvé un service complet de ceux ayant un service militaire limité après un TC léger (Drake, Gray, Yoder, Pramuka, & Llewellyn, 2000). Les performances au test de la Figure de Rey n'ont, à notre connaissance, jamais été étudiées en lien avec la réhabilitation socio-professionnelle des personnes souffrant d'une LCA. De manière générale, l'impact de la mémoire visuelle sur la réhabilitation de ces personnes est très peu étudié ou alors cet impact apparaît statistiquement non significatif (Rusbridge, Walmsley, Griffiths, Wilford, & Rees, 2013).

Les performances au test des fluences verbales dans sa forme couramment utilisée en France (Cardebat et al., 1990) n'ont, à notre connaissance, jamais été étudiées en lien avec la réhabilitation socio-professionnelle des personnes souffrant d'une LCA. Une étude quantitative sur un petit échantillon a mis en évidence que, les processus de flexibilité mentale spontanée, tels qu'évalués par le subtest Fluence Verbale de la batterie *Delis–Kaplan Executive Function System* (Delis, Kaplan, & Kramer, 2001), permettaient de différencier les patients souffrant d'un TC modéré à sévère et les participants contrôles neurologiquement sains, et corrélaient significativement avec des mesures évaluant la capacité des patients à faire les courses, une activité de vie quotidienne (Cralidis & Salley, 2017). Les processus de flexibilité mentale spontanée, tels qu'évalués par le *Controlled Oral Fluency Test* (Benton & Hamsher, 1983), permettaient de différencier les militaires ayant retrouvé un service complet de ceux ayant un service militaire limité après un TC léger (Drake et al., 2000).

Les performances au test de la Tour de Londres n'ont, à notre connaissance, jamais été étudiées en lien avec la réhabilitation socio-professionnelle des personnes souffrant d'une LCA. Cependant, des auteurs ont montré que les processus de planification, tels qu'évalués par le test du Zoo de la batterie *Behavioral Assessment of Dysexecutive Syndrome* (Wilson, Evans, Emslie, Alderman, & Burgess, 1998), prédisaient le score à un questionnaire (*Role Resumption List for Return To Work* ; Spikman, Boelen, Lamberts, Brouwer, & Fasotti, 2010; Zomerén & Burg, 1985) évaluant le retour à l'emploi de personnes souffrant d'un TC modéré à sévère (Westerhof- Evers, Fasotti, van der Naalt, & Spikman, 2019). Or, dans le cadre de ces travaux de thèse, un des scores de la Tour de Londres était présent dans les deux modèles retrouvés dans la **Partie IV (Articles 5 et 6)** ; il s'agissait en effet du score Z du nombre de mouvements réalisés par les patients pour résoudre les problèmes nécessitant au moins cinq mouvements tandis que le premier mouvement évident favoriserait la résolution. Cela montre que les

processus de planification évalués au moyen de la Tour de Londres permettraient d'anticiper la réussite ou l'échec en formation professionnelle de personnes souffrant d'une LCA.

Des auteurs ont montré, à l'aide de plusieurs études de cas, que des stratégies de réhabilitation cognitive axées sur l'attention, la mémoire et les fonctions exécutives pourraient améliorer la capacité des patients souffrant d'un TC à gérer les tâches et les exigences du milieu de travail (Mateer & Sira, 2006). De ce fait, l'ensemble des mesures cognitives ayant un impact sur le retour en formation à la suite d'une LCA, que nous avons mis en évidence dans ces travaux de thèse, devraient faire l'objet d'études ultérieures, sur d'autres échantillons de patients souffrant d'une LCA. Par ailleurs, comme nous l'avons souligné dans l'**Article 1 (Partie II)**, les habiletés fonctionnelles et cognitives ne seraient pas les seuls prédicteurs de l'issue professionnelle à la suite d'une LCA, et l'impact des troubles comportementaux, tels que l'usage de l'alcool, sur le retour en formation devrait également être évalué. C'est pourquoi nous avons intégré la passation de l'Echelle des Changements de Comportements Socio-Emotionnels de Genève (Beni et al., 2017) dans notre étude prospective multicentrique. Des auteurs ont proposé un modèle illustrant les facteurs « en faveur » et ceux qui entravent la réhabilitation socio-professionnelle (voir **Figure VI**), selon le vécu des patients (Glintborg, Thomsen, & Hansen, 2018). La fatigue y est représentée comme un facteur négatif récurrent.

Ce modèle additionné aux résultats retrouvés dans l'**Article 4 (Partie III)**, selon lesquels les performances à l'échelle de fatigue MFI-20 permettraient de mettre en évidence la fatigue liée au handicap dû à une LCA et seraient corrélées aux performances cognitives d'attention, de mémoire et de fonctions exécutives, a justifié la passation du MFI-20 (Gentile et al., 2003; Smets et al., 1995) dans notre étude prospective multicentrique.

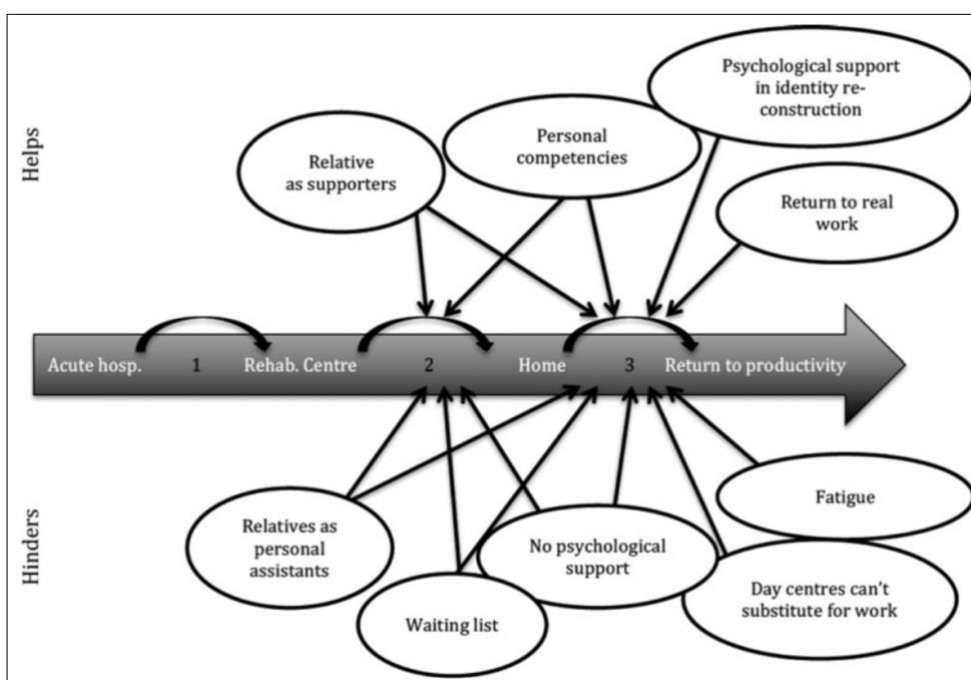


Figure VI. Les facteurs qui aident / entravent la réhabilitation socio-professionnelle des personnes souffrant d'une LCA, selon leur propre expérience

(d'après Glinborg et al., 2018).

1.3.Limites globales

Les résultats des études constituant ce travail de thèse se sont heurtés à plusieurs limites scientifiques et institutionnelles.

1.3.1. Limites scientifiques

Concernant la revue de littérature (**Article 1, Partie II**), les critères d'inclusion et d'exclusion des études pourraient sembler stricts, notamment en ce qui concerne le critère de sévérité des LCA, limité aux intervalles du score à l'échelle de Glasgow (Teasdale & Jennett, 1974) et/ou à ceux de la durée de l'amnésie post-traumatique (Stein, 1996). Toutefois, il s'agit des critères les plus utilisés dans la littérature (**Article 1, Partie II**). De plus, l'identification des facteurs

en lien avec la réhabilitation professionnelle selon la sévérité de la LCA nous a semblé primordial, étant donné que la plupart des usagers effectuant un stage en UEROS souffriraient d'une LCA modérée à sévère (Cogné, Wiart, Simion, Dehail, & Mazaux, 2017; Le Gall et al., 2007).

Les études de la **Partie IV** se sont heurtées à deux grandes limites, à savoir un nombre trop restreint d'observations et un nombre trop élevé de données neuropsychologiques manquantes. Le nombre réduit d'observations était dû au fait que, seuls certains usagers ayant bénéficié d'un stage en UEROS souhaitaient une (ré)orientation professionnelle et ont donc suivi une formation qualifiante. En effet, selon les études, 9 à 10% des usagers auraient suivi une formation après leur stage en UEROS (Cogné et al., 2017; Le Gall et al., 2007). De plus, le nombre de places est différent d'une UEROS à une autre ; il y a, par exemple, 15 places à l'UEROS de Lille (Rapport d'activité 2017 de l'UGECAM Nord-Pas-de-Calais-Picardie) alors qu'il n'y en a que 6 à l'UEROS de Saint-André-de-l'Eure (Rapport d'activité 2017 de LADAPT). Par ailleurs, le temps de travail des équipes pluridisciplinaires est réparti différemment d'une UEROS à une autre, peu d'UEROS bénéficiant d'un équivalent temps plein pour les neuropsychologues.

Le nombre de données manquantes a peut-être été à l'origine d'une sous-pondération de certaines variables indépendantes sous-représentées mais qui pourraient avoir un lien étroit avec notre variable dépendante. Ces données manquantes étaient dues notamment à une hétérogénéité des évaluations neuropsychologiques entre les UEROS, l'évaluation neuropsychologique à l'UEROS de Lille ayant été réalisée sur huit heures en moyenne réparties sur plusieurs semaines, alors que dans certaines autres UEROS l'évaluation était réalisée sur une durée d'une à deux heures. Pour pallier cette limite, des analyses davantage qualitatives auraient pu être menées, en définissant les variables indépendantes par les fonctions cognitives évaluées et non pas par un score à une épreuve neuropsychologique. Cependant les résultats

auraient été imprécis ; nous n'aurions eu aucune indication sur les épreuves les plus sensibles au contexte de formation professionnelle à la suite d'une LCA.

Une autre limite dans les études de la **Partie IV** résidait dans l'utilisation de deux algorithmes différents (arbres de décision, rectangles aléatoires) ayant conduit à deux modèles. Utiliser le même algorithme sur deux échantillons aurait pu nous conduire à un modèle plus robuste. Toutefois, l'utilisation d'un second algorithme (rectangles aléatoires) était justifiée par l'investigation des facteurs en lien avec la réussite et des facteurs en lien avec l'échec en formation professionnelle, et non plus une intrication de facteurs conduisant à la réussite ou l'échec (arbre de décision). Enfin, nous n'avons pas étudié l'impact des aspects psychologiques des participants souffrant d'une LCA sur leur retour en formation professionnelle, alors que les troubles thymiques influenceraient grandement le retour à l'emploi (**Article 1, Partie II**).

1.3.2. Limites d'ordre institutionnel

La limite d'ordre scientifique évoquée ci-dessus concernant le faible nombre d'observations était en réalité la conséquence d'une limite d'ordre institutionnel dans la mise en place de notre collaboration avec les UEROS. En effet, nous avons proposé une collaboration à plusieurs UEROS adhérant à la Fédération des Associations, Groupements et Etablissements pour la Réadaptation des personnes en situation de Handicap (FAGERH). Parmi les sept UEROS qui se sont portées volontaires pour collaborer à ce projet, seules deux collaborations ont abouti, notamment à cause de dysfonctionnements institutionnels et/ou d'absence de réponse au moment du lancement du projet. Nous avons, dans ce contexte, contacté les UEROS entretenant des liens professionnels avec l'UEROS de Lille et avons pu obtenir une collaboration avec six autres UEROS. Par ailleurs, dans certaines UEROS, le nombre des usagers qui ont suivi une formation après leur stage était très bas, notamment à cause de la politique de ces structures, qui était de ne pas orienter les usagers vers une formation qualifiante pour leur éviter un énième

échec. L'identification, dans le cadre de ces travaux de thèse, des facteurs expliquant la réussite et des facteurs expliquant l'échec en formation professionnelle conduirait peut-être ces structures à abandonner ce genre de politique et à orienter le plus objectivement possible les personnes souffrant d'une LCA.

La limite d'ordre scientifique évoquée ci-dessus concernant le nombre élevé de données neuropsychologiques manquantes était en réalité la conséquence d'une limite tenant à la pratique neuropsychologique dans les UEROS, caractérisée par une hétérogénéité des durées d'évaluation, lesquelles influencent le nombre et le type d'épreuves administrées. L'uniformisation des pratiques neuropsychologiques en France dans les UEROS pourrait être une solution permettant de pallier cette limite. A cet égard, des lignes directrices pourraient être proposées, comme c'est déjà le cas s'agissant des patients atteints d'épilepsie pharmaco-résistante en contexte péri-chirurgical en Europe (Vogt et al., 2017) et en France (*soumission en cours*).

1.4. Modèle hypothétique des relations entre les facteurs cognitivo-comportementaux et l'issue d'une formation professionnelle à la suite d'une LCA

En nous appuyant sur les résultats de ces travaux de thèse, sur le modèle de fatigue survenant à la suite d'un TC modéré à sévère (voir **Figure VII**) proposé par Ponsford, Schönberger et Rajaratnam (2015), ainsi que sur l'étude de Holmqvist, Lindstedt et Möller (2018), nous avons proposé un modèle hypothétique illustrant les relations entre les facteurs cognitifs et comportementaux et l'issue professionnelle après une LCA (voir **Figure VIII**).

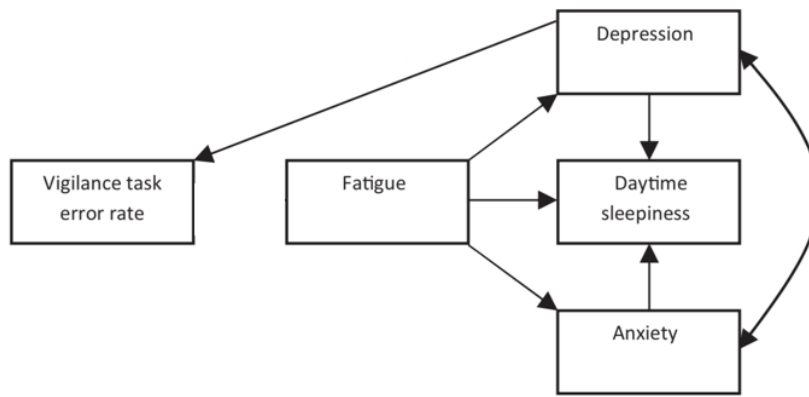


Figure VII. Modèle de fatigue à la suite d'un TC

(d'après Ponsford, Schönberger, & Rajaratnam, 2015).

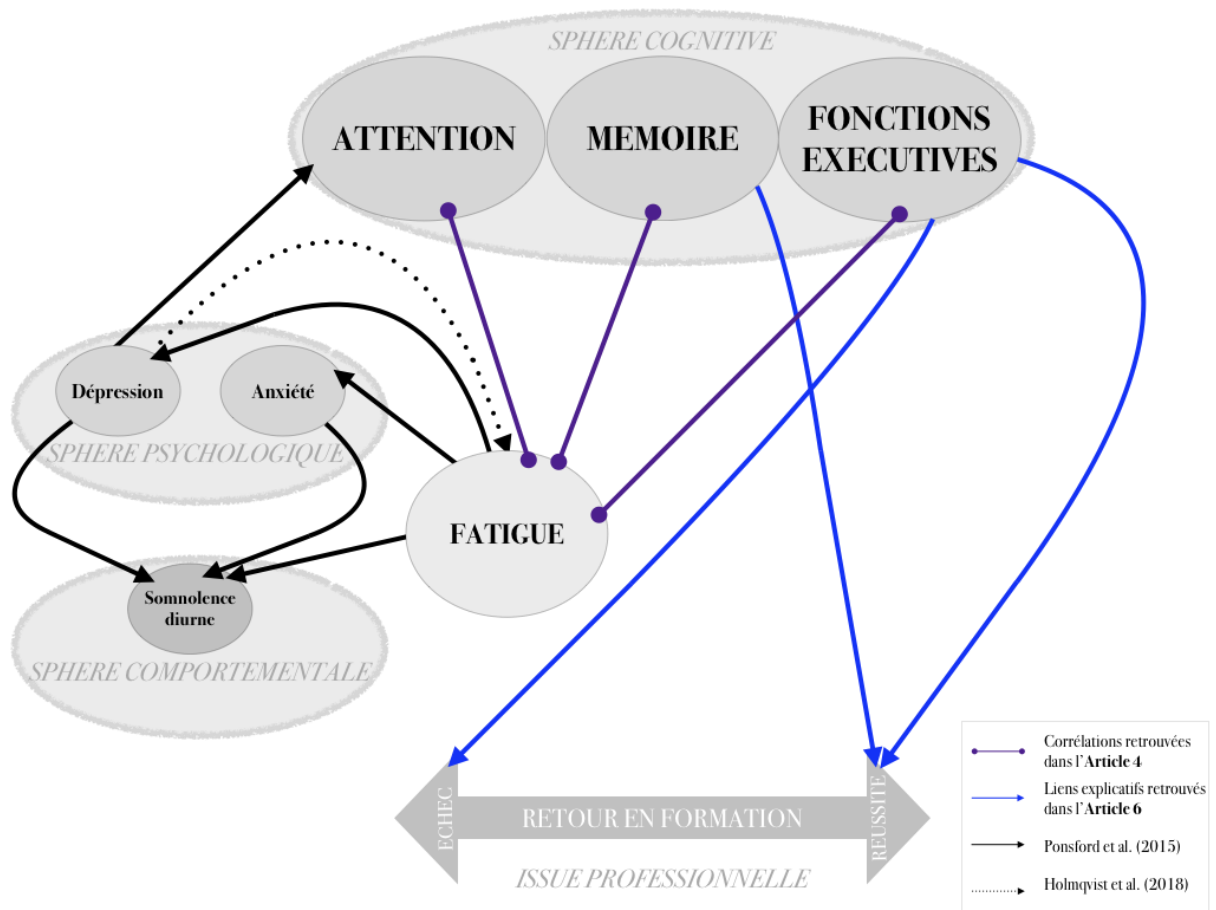


Figure VIII. Modèle hypothétique illustrant les relations entre les facteurs cognitifs et comportementaux et l'issue professionnelle après une lésion cérébrale acquise.

Dans ce modèle hypothétique, nous avons illustré les liens entre la fatigue et les sphères psychologique, comportementale et cognitive, tels que proposés dans la littérature (Holmqvist et al., 2018; Ponsford et al., 2015) : la fatigue aurait une influence sur la dépression, l'anxiété et la somnolence diurne, cette dernière étant influencée par la dépression et l'anxiété qui sont étroitement liées, et la dépression influencerait à son tour le niveau de fatigue et les performances attentionnelles.

Nous avons également illustré les relations entre la fatigue et la sphère cognitive en s'appuyant sur les résultats obtenus dans l'**Article 4 (Partie III)**. En effet, les corrélations retrouvées entre les mesures du MFI-20 et les performances aux épreuves neuropsychologiques indiqueraient un lien entre fatigue et fonctionnement attentionnel, mnésique et exécutif chez des personnes souffrant d'une LCA.

A son tour, la sphère cognitive aurait un impact sur l'issue professionnelle. En effet, en s'appuyant sur les résultats obtenus dans l'**Article 6 (Partie IV)**, les performances mnésiques et exécutives expliqueraient un retour en formation réussi, et les performances exécutives seules suffiraient à expliquer l'échec d'un retour en formation à la suite d'une LCA.

2. Perspectives de recherche

Avant même d'évoquer la question des perspectives de recherche, il convient de rappeler qu'à l'horizon 2021 nous disposerons des résultats de l'étude prospective multicentrique débutée au cours de ces travaux de thèse, lesquels permettront de valider les modèles cognitifs retrouvés précédemment et/ou d'identifier d'autres modèles cognitifs, comportementaux ou cognitivo-comportementaux permettant de prédire un retour efficace en formation professionnelle à la suite d'une LCA.

Quant aux perspectives de recherche, il s'agira de tester dans des études ultérieures le modèle hypothétique présenté précédemment, afin de confirmer les liens entre les différentes sphères et l'issue d'une formation professionnelle après une LCA. Nous pourrions également investiguer l'impact du niveau de fatigue sur la relation entre les fonctions cognitives et l'issue de la formation, ainsi que l'implication des sphères psychologiques et comportementales sur l'issue d'une formation entreprise à la suite d'une LCA.

Les études portant sur les modèles cognitivo-comportementaux prédisant la réussite ou l'échec en formation pourraient être le point de départ pour l'uniformisation des pratiques neuropsychologiques en UEROS. En effet, l'identification des mesures neuropsychologiques les plus pertinentes dans ce contexte permettrait de construire une batterie de base à destination des neuropsychologues en UEROS. Cette batterie répondrait à une question spécifique, portant sur les répercussions fonctionnelles d'une LCA sur la réinsertion socio-professionnelle. En cela elle se distinguerait des évaluations neuropsychologiques à visée diagnostique. Une telle uniformisation des pratiques en UEROS ne se cantonnerait pas spécifiquement à la pratique neuropsychologique ; en effet, des évaluations uniformisées, dans ce même contexte de retour en formation, pourraient être proposées dans d'autres disciplines impliquées dans les programmes de réhabilitation en UEROS, comme par exemple en psychologie clinique ou ergothérapie. Cette uniformisation favoriserait les collaborations scientifiques entre les UEROS et pourrait aboutir à un protocole de réhabilitation. L'utilité de ce protocole de réhabilitation pourrait être estimée en mettant en place une évaluation supplémentaire, en fin de stage en UEROS, afin d'identifier les éventuels effets par rapport à l'évaluation de début de stage. Enfin, l'orientation socio-professionnelle et plus particulièrement le retour en formation professionnelle seraient argumentés par les résultats de l'évaluation finale et les éventuels effets du protocole de réhabilitation.

3. Conclusion générale

Dans le cadre de ces travaux de thèse, en utilisant une approche relativement innovante en neuropsychologie, celle des algorithmes d'apprentissage automatique (*machine learning*), nous avons identifié, sur le plan théorique, des modèles cognitifs explicatifs de la réussite et de l'échec en formation professionnelle de personnes souffrant d'une lésion cérébrale acquise. Sur le plan clinique, ils permettront aux professionnels des Unités d'Évaluation, de Réentraînement et d'Orientation Sociale et/ou professionnelle pour personnes cérébrolésées de guider ces personnes vers la réinsertion socio-professionnelle en s'appuyant sur des indices objectifs.

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ANNEXES

A. Manuel d'utilisation de l'épreuve 1W-FCSRT

ONE-WEEK FREE AND CUED SELECTIVE REMINDING TEST – WORD VERSION (1W-FCSRT)

TEST DU RAPPEL LIBRE / RAPPEL INDICE A SEPT JOURS – VERSION MOTS

Matériel, consignes et données normatives

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PRESENTATION DES AUTEURS

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AVANT-PROPOS

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ADMISTRATION ET CONSIGNES

1. Présentation de l'épreuve : matériel et procédure

Le test proposé ici, appelé *One-Week Free and Cued Selective Reminding Test – word version* (1W-FCSRT ; en français, Test du Rappel Libre / Rappel Indiqué à Sept Jours – version mots), est une adaptation de l'épreuve RL/RI 16 items, élaborée par Van Der Linden et al (2004). Il utilise le même matériel soit « une liste de 16 mots appartenant à 16 catégories sémantiques différentes. Ces items ont été sélectionnés à partir des listes de production d'exemplaires de **Dubois (1982)** ainsi que de données que nous avons spécifiquement recueillies pour des catégories non reprises dans **Dubois (1982)**, de sorte qu'ils ne constituent pas les exemplaires les plus prototypiques de leur catégorie : les items qui occupent les deux premières positions dans les listes de production d'exemplaires ont ainsi été exclus. Ces items ont un rang de typicalité qui se situe entre 3 et 22 (moyenne : 11,9 et écart-type : 6,4). Parallèlement, 16 autres mots appartenant aux mêmes catégories sémantiques ont été sélectionnés selon les mêmes critères de typicalité (rang de typicalité entre 4 et 22 ; moyenne : 10,4 et écart-type : 4,7). Enfin, 16 mots non reliés sémantiquement aux items cibles ont été choisis. Ces 32 mots serviront d'items distracteurs (sémantiques ou neutres) lors de la phase de reconnaissance. [...] »

Les 16 mots à mémoriser sont présentés sur des fiches par groupes de quatre dans le même ordre pour tous les participants (voir ci-dessous, schéma 1, pour la présentation de chaque fiche [...] avec la disposition spatiale des items [...]). Chaque fiche correspond à une feuille format A4 standard disposée en mode paysage. La feuille est alors séparée en quatre parties égales. Les items sont disposés au centre de chaque partie. La police de caractère est le « Times », taille 80, format italique et non-gras. Attention, il est important de respecter ces paramètres ainsi que la disposition spatiale des items dans la mesure où l'étalonnage a été réalisé strictement sur ce matériel. »

1	gilet jonquille domino hareng	2	dentiste groseille harpe cuivre
3	mésange céleri judo tilleul	4	tabouret valse géographie rougeole

Schéma 1 : Matériel commun entre le RL/RI 16 items et le 1W-FCSRT.

2 - Procédure et consignes

La procédure que nous utilisons est la même que lors de la RL-RI 16 items, elle se différencie par l'ajout d'une phase de rappel libre et de rappel indicé à 7 jours. La procédure débute par :

Phase d'encodage (d'après [Van der Linden et al., 2004](#))

« L'examineur présente au participant, une fiche à la fois. Pour chaque fiche de 4 items, l'examineur demande à la personne de chercher et de lire à voix haute l'item (par exemple, *jonquille*) correspondant à l'indice catégoriel fourni (par exemple, *fleur*). L'examineur fournit des consignes suivantes :

« Je vais vous présenter des fiches ; sur chaque fiche, sont inscrits quatre mots ; je vous demande de mémoriser tous les mots inscrits sur les fiches. Voici la première fiche : parmi ces quatre mots, dites-moi quel est le poisson ? (réponse). Quel le vêtement ? (réponse), etc. ».

L'ordre des catégories sémantiques proposées par l'examineur est fixé et suit l'ordre noté sur le modèle de protocole (voir Feuille de réponse). Il n'y a pas de limite de temps pour obtenir une réponse durant cette phase d'encodage. Si la personne est en difficulté à cette étape, par exemple suite à des troubles sémantiques importants, l'épreuve est interrompue. Il est essentiel de noter qu'il s'agit d'une phase d'encodage intentionnel. »

Rappel indicé immédiat (IMR) (d'après [Van der Linden et al., 2004](#))

« Quand les quatre items d'une fiche ont été correctement identifiés, l'examineur retire la fiche et administre un test de rappel indicé immédiat (IMR) des quatre mots : il fournit l'indice catégoriel à voix haute et la personne doit rappeler l'item appartenant à cette catégorie. L'examineur fournit des consignes suivantes :

« Maintenant, je reprends la fiche et vous allez me dire quel était le poisson qui était inscrit sur cette fiche ? (réponse). Quel était le vêtement ? (réponse), etc. ».

Il n'y a pas de limite de temps pour cette phase de rappel indicé immédiat. L'examineur fournit un feed-back immédiat (correct - pas correct) sur la qualité de la réponse. Si certains mots ne sont pas récupérés (réponses fausses ou absence de réponse) lors de ce rappel indicé immédiat, l'examineur représente la fiche correspondante, propose le nom de la catégorie du (ou des) item(s) non rappelés (et uniquement de ceux-là), et la personne doit à nouveau identifier et lire le (ou les) item(s) en réponse à sa (leur) catégorie. Ensuite, l'examineur retire la fiche et propose à nouveau un test de rappel indicé immédiat, uniquement pour le (ou les) item(s) non évoqué(s) précédemment. Si le participant commet encore une erreur ou ne peut répondre, l'examineur lui proposera un troisième et dernier encodage sélectif avec rappel indicé immédiat.

On procède de la même manière pour les 3 autres fiches de 4 items. »

Tâche distractive (d'après [Van der Linden et al., 2004](#))

« Après la présentation et le rappel indicé immédiat réussi de la quatrième fiche, le participant est soumis à une tâche distractive de 20 secondes (comptage à rebours par 1, à partir de 374). »

Rappel libre (FR) et indicé (CR) des 16 items (d'après [Van der Linden et al., 2004](#))

« Après la phase de rappel indicé immédiat et le délai de 20 secondes (rempli par la tâche de comptage à rebours), on procède à la phase de rappel libre : on demande au participant de rappeler l'ensemble des mots qui lui ont été présentés sur les fiches, dans n'importe quel ordre. L'examineur propose des consignes suivantes :

« Je vous demande de rappeler le plus grand nombre de mots qui vous ont été présentés précédemment sur les fiches. Vous disposez de deux minutes ».

La phase de rappel libre dure 2 minutes. L'examineur note, sur les feuilles de données brutes, les mots émis par le participant (qu'ils soient corrects ou non) ainsi que le décours temporel (marquer un trait toutes les 15 secondes dans la liste des réponses du patient). Durant le rappel, il transcrit les réponses correctes par exemple en notant un signe « + » à côté de l'item correspondant sur la feuille de réponses. L'examineur ne signale pas, durant le rappel libre, les mots faux et les mots doubles (mais il les note).

La phase de rappel libre est suivie d'une étape de rappel indicé et ce, uniquement pour les items non évoqués par le participant en rappel libre ou pour les items pour lesquels la personne a produit une erreur. L'examineur fournit oralement la catégorie sémantique correspondant aux items non récupérés ou incorrects et le participant doit rappeler l'item correspondant. L'examineur fournit des consignes suivantes :

« Vous n'avez pas pu rappeler certains mots (et/ou certains n'étaient pas corrects), je vous propose d'essayer de les retrouver. Sur les fiches que je vous ai présentées précédemment, quel(le) était le (la) ... (nom de la catégorie) ? ».

Le participant dispose de 10 secondes par item pour le rappel indicé. Si, durant la phase de rappel indicé, l'item n'est toujours pas rappelé ou si la personne propose une réponse incorrecte, l'examineur fournit oralement la réponse correcte au participant au terme de la période de 10 secondes, du moins pour les rappels indicés 1 et 2 : lors du troisième rappel indicé, l'examineur ne fournit plus aucune réponse et feed-back au participant.

La procédure de rappel libre puis de rappel indicé est répétée 3 fois. Les trois essais sont séparés par une tâche distractive de comptage à rebours d'une durée de 20 secondes (comme par exemple, à partir de respectivement 329, 267, et 188). Il importe de fournir systématiquement au participant des consignes de récupération explicites, lui indiquant clairement que les items qu'il doit rappeler lui ont été présentés auparavant sur des fiches. En l'absence de telles consignes, le test pourrait prendre la forme d'un test de mémoire implicite (« je fournis les premiers mots qui me viennent à l'esprit en réponse à la catégorie »).

L'examineur note le nombre d'évocations correctes pour chaque rappel libre (FR1, FR2, FR3), le nombre d'évocations correctes pour chaque rappel indicé (CR1, CR2, CR3), et le nombre total d'évocations correctes ($TR1 = FR1 + CR1$; $TR2 = FR2 + CR2$; $TR3 = FR3 + CR3$). »

Reconnaissance (HITS, FAS, FAN) (d'après Van der Linden et al., 2004)

Immédiatement après le comptage à rebours qui suit le troisième essai de rappel indicé, un test de reconnaissance oui/non est proposé : le participant a pour tâche de reconnaître les 16 items-cibles mélangés à 16 distracteurs sémantiques et à 16 distracteurs neutres. Les 48 items sont présentés un à un sur des cartons (écriture Times, italique, taille 80), leur ordre de présentation est figé pour tous les participants (voir *Feuille de réponse*, p.17).

L'examineur fournit les consignes suivantes :

« Maintenant, je vais vous présenter une série de mots. Certains de ces mots appartiennent à la liste de mots que vous venez d'apprendre et qui étaient présentés sur des fiches, d'autres sont nouveaux. Je vous demande pour chaque mot de me dire si oui ou non vous l'avez vu précédemment. Voici le premier mot, l'avez-vous déjà vu oui ou non dans la phase précédente ? ».

La personne doit impérativement répondre par OUI ou NON. Il n'y a pas de limite de temps de réponse. L'examineur relève le nombre de reconnaissances correctes (HITS) et le nombre de fausses alarmes : acceptations d'un distracteur sémantique (FAS [...]) et acceptations d'un distracteur neutre (FAN). [...] »

Rappel libre et indicé différés

- Rappel libre à 30 minutes (FR30) et rappel indicé à 30 minutes (CR30)

Trente minutes après la phase de reconnaissance (et sans qu'une tâche de nature verbale n'ait été présentée durant ce délai), se déroule une phase de rappel libre et de rappel indicé des 16 items. En ce qui concerne le rappel libre, l'examineur fournit des consignes suivantes :

« Tout à l'heure, je vous ai présenté une liste de mots sur 4 fiches, et je vous ai demandé de les apprendre. Pouvez-vous m'en rappeler le plus possible, dans n'importe quel ordre ? Vous disposez de deux minutes ».

Durant le rappel, les mots faux et doubles ne sont pas signalés au participant (mais ils sont relevés sur le protocole de notation). En ce qui concerne le rappel indicé, les consignes suivantes sont présentées :

« Vous n'avez pas pu rappeler certains mots (et/ou certains n'étaient pas corrects), je vous propose d'essayer de les retrouver. Sur les fiches que je vous ai présentées tout à l'heure, quel(le) était le (la) ... (nom de la catégorie) ».

L'examineur octroie 10 secondes par item pour le rappel indicé. Il importe à nouveau de fournir, de façon systématique, des consignes mettant clairement en évidence le caractère explicite de la récupération.

Pour l'épreuve du 1W-FCSRT, nous avons introduit une phase de rappel libre et de rappel indicé à 7 jours :

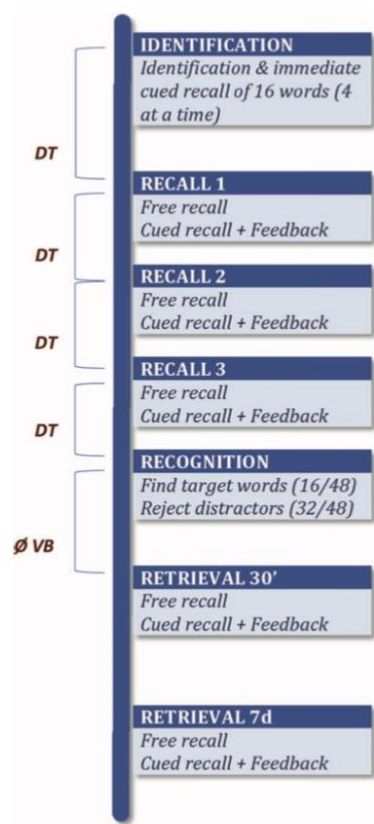
- Rappel libre à 7 jours (FR7d) et rappel indicé à 7 jours (CR7d)

Les mêmes consignes sont administrées sept jours après l'apprentissage des 16 items.

Pour ces deux phases de rappel différé, l'examineur relève le nombre d'évocations correctes en rappel libre (FR30 et FR7d), le nombre d'évocations correctes en rappel indicé (CR30 et CR7d) et le nombre total d'évocations correctes ($TR30 = FR30 + CR30$ et $TR7d = FR7d + CR7d$).

Récapitulatif de l'ensemble de la procédure

- Identification et rappel immédiat des items 4 par 4 (IMR)
- Tâche distractive (20 secondes)
- Rappel libre 1 (FR1) + Rappel indicé 1, avec feed-back (CR1) = TR1
- Tâche distractive (20 secondes)
- Rappel libre 2 (FR2) + Rappel indicé 2, avec feed-back (CR2) = TR2
- Tâche distractive (20 secondes)
- Rappel libre 3 (FR3) + Rappel indicé 3, sans feed-back (CR3) = TR3
- Tâche distractive (20 secondes)
- Reconnaissance
- Après 20 minutes : rappel libre différé (FR30) + rappel indicé différé (CR30) = TR30
- Après 7 jours : rappel libre différé (FR7d) + rappel indicé différé (CR7d) = TR7d



3 – Participants :

La normalisation de l'épreuve 1W-FCSRT a été élaborée à partir des performances de 238 participants (124 femmes et 114 hommes) âgés de 18 à 81 ans (moyenne d'âge = 42,23, écart-type = 16,45). Ces participants ont été recrutés dans la région de Lille. Tous les participants sont de langue maternelle française. Les participants ont été recrutés selon les critères d'inclusion suivant : être indemne de troubles neurologiques et/ou psychiatriques, être indemne d'accident neurologique d'étiologie vasculaire ou traumatique. Tous ont été informés des objectifs de notre étude et ont signé un formulaire de consentement. La répartition selon leurs caractéristiques sociodémographiques est présentée dans le tableau ci-dessous.

Demographic data				
	Age group	Gender	Education level	
1	18–29 years	F = 22	1	<i>n</i> = 11
			2	<i>n</i> = 11
		M = 39	1	<i>n</i> = 27
			2	<i>n</i> = 12
2	30–49 years	F = 50	1	<i>n</i> = 33
			2	<i>n</i> = 17
		M = 59	1	<i>n</i> = 36
			2	<i>n</i> = 23
3	50–64 years	F = 29	1	<i>n</i> = 20
			2	<i>n</i> = 9
		M = 11	1	<i>n</i> = 7
			2	<i>n</i> = 4
4	65–81 years	F = 23	1	<i>n</i> = 19
			2	<i>n</i> = 4
		M = 5	1	<i>n</i> = 3
			2	<i>n</i> = 2

COTATION

1. Scores recueillis (/16)

Plusieurs indicateurs sont recueillis au cours de cette épreuve :

FR1	Nombre de mots correctement rappelés librement lors du 1 ^{er} essai.
TR1	Nombre total de mots correctement rappelés lors du 1 ^{er} essai (librement + à l'aide d'indices).
FR2	Nombre de mots correctement rappelés librement lors du 2 ^e essai.
TR2	Nombre total de mots correctement rappelés lors du 2 ^e essai (librement + à l'aide d'indices).
FR3	Nombre de mots correctement rappelés librement lors du 3 ^e essai.
TR3	Nombre total de mots correctement rappelés lors du 3 ^e essai (librement + à l'aide d'indices).
FR30	Nombre de mots correctement rappelés librement 30 minutes après la phase d'encodage.
TR30	Nombre total de mots correctement rappelés 30 minutes après la phase d'encodage (librement + à l'aide d'indices)
FR7d	Nombre de mots correctement rappelés librement 7 jours après la phase d'encodage.
TR7d	Nombre total de mots correctement rappelés 7 jours après la phase d'encodage (librement + à l'aide d'indices)

A partir de ces scores bruts sont calculés des indices composites.

2. Scores composites

- Score d'apprentissage (**Learn**) : pourcentage de mots appris au bout des 3 essais par rapport à FR1 ;

- $\text{Learn} = \frac{FR_3 - FR_1}{16 - FR_1} \times 100$

- Score d'indication (**Cued**) : pourcentage de mots totaux restitués à l'aide d'indication par rapport aux rappels libres ;

- $\text{Cued} = \frac{(\sum TR_{1+2+3} - \sum FR_{1+2+3})}{(48 - \sum FR_{1+2+3})} \times 100.$

- Score de consolidation rapide (**FR30-Forget**) : pourcentage d'oubli lors du rappel libre à 30 minutes (FR30) ;

- $\text{FR30-Forget} = \frac{FR_{30} - FR_3}{FR_3} \times 100$

- Score de consolidation lente (**FR7d-Forget**) : pourcentage d'oubli lors du rappel libre à 7 jours

- $\text{FR7d-Forget} = \frac{FR_{7d} - FR_3}{FR_3} \times 100.$

ETALONNAGE

Pour établir les normes à l'épreuve 1W-FCSRT, nous avons utilisé la méthode de régressions linéaires ascendantes pas-à-pas proposée par [Barona, Reynolds et Chastain \(1984\)](#) en considérant les facteurs sociodémographiques suivants : groupe d'âge (Groupe 1 : 18-29 ans ; Groupe 2 : 30-49 ans ; Groupe 3 : 50-64 ans ; et Groupe 4 : 65-81 ans), niveau d'éducation (1, ≤ 12 ans ; 2 : > 12 ans d'éducation), et sexe (0, *femme* ; 1, *homme*). Pour tous les modèles avec des coefficients de régression statistiquement significatifs, nous avons testé la normalité de la distribution des résidus. Les conditions d'application des régressions linéaires n'étaient remplies que pour les modèles prédisant **FR1**, **FR7d** et **FR7d-Forget**.

Pour les score recueillis non prédits par des équations de régression, nous avons calculé des normes en utilisant la méthode développée par [Crawford, Garthwaite et Slick \(2009\)](#) pour déterminer les percentiles associés à des intervalles de confiance.

Les normes pour les scores composites n'étant pas prédits par des équations de régression, à savoir **Learn**, **Cued** et **FR30-Forget**, ont été obtenues en utilisant une procédure classique de calcul des percentiles ([Dancey & Reidy, 2007](#)).

UTILISATION DU FICHIER DE CALCUL AUTOMATIQUE

Etape 1 – Indiquer obligatoirement l'âge et le sexe du participant.

Age participant Normes établies sur un échantillon âgé de 18 à 81 ans
 Sexe (F/M) F = Femme ; M = Homme

Il est important de noter que les normes ont été établies pour des personnes âgées entre 18 et 81 ans.

Le niveau socio-culturel (années d'étude) n'est pas à spécifier dans le fichier de calcul automatique car cette variable démographique ne contribue pas aux résultats au test.

Dans l'exemple choisi, il s'agit d'une femme âgée de 43 ans.

Etape 2 – Indiquer les valeurs des scores recueillis

Les valeurs des scores recueillis sont à saisir dans les **cases grises** de la colonne « Scores bruts ». Les scores composites sont calculés automatiquement (cases blanches) à partir des scores recueillis.

Les **scores normés** apparaissent sous le format **score Z** ou **percentile**.

Scores EN	Scores FR	Score Brut	Score Z	Percentile
FR1	Rappel Libre 1	10	0.02	-
TR1	Rappel Total 1	12		< 5
FR2	Rappel Libre 2	9	-	6
TR2	Rappel Total 2	15		15
FR3	Rappel Libre 3	10	-	< 5
TR3	Rappel Total 3	14		< 5
Learn	Tx d'apprentissage	0.00	-	< 5
Cued	Sensibilité à l'indiciage	63.16	-	< 5
FR30	Rappel Libre 30min	10	-	6
TR30	Rappel Total 30min	14		< 5
FR30-Forget	Tx d'oubli RL 30min	0.00	-	50
FR7d	Rappel Libre 7j	11	0.38	-
TR7d	Rappel Total 7j	12		9
FR7d-Forget	Tx d'oubli RL 7j	10.00	1.48	-

Etape 3 –Interprétations des résultats.

Score Z	Interprétation clinique
$Z \leq -1.65$	Performance déficitaire
$-1.64 < Z < -1$	Limite
$-0.9 < Z < 0.9$	Moyenne
$1 < Z < 1.64$	Supérieure à la moyenne
$Z > 1.65$	Très supérieure à la moyenne

Percentile	Interprétation clinique
≤ 5	Performance déficitaire
6-8	Limite
9-24	Moyenne faible
25-74	Moyenne
75-90	Moyenne élevée
91-97	Supérieure à la moyenne
≥ 98	Très supérieure à la moyenne

Comment interpréter un taux d'oubli (lors du rappel différé à 30 minutes ou 7 jours) ?

Le taux d'oubli varie de -100% à 100%.

- Lorsqu'il est compris entre -100% et 0 (exclu), cela veut dire que le participant a rappelé moins de mots lors du rappel différé que lors du 3^e rappel libre de la phase d'apprentissage.
- Lorsqu'il est de 0%, cela veut dire que le participant a rappelé autant de mots lors du rappel différé que lors du 3^e rappel libre de la phase d'apprentissage.
- Lorsqu'il est compris entre 0% (exclu) et 100%, cela veut dire que le participant a rappelé plus de mots lors du rappel différé que lors du 3^e rappel libre de la phase d'apprentissage.

Le taux d'oubli s'interprète par rapport aux scores standardisés qui sont calculés automatiquement, comme cela a été présenté dans le tableau p.16.

Si l'on prend l'exemple présenté dans le tableau p.16, c'est-à-dire d'une femme âgée de 43 ans et qui a obtenu les scores indiqués, son taux d'oubli à 30 minutes est de 0%, correspondant au percentile 50. Nous pouvons en conclure que cette personne a des processus de consolidation rapide dans la moyenne. Son taux d'oubli à 7 jours est de 10% (ce qui veut dire qu'elle a rappelé plus de mots lors du rappel libre différé à 7 jours que lors du 3^e rappel libre de la phase d'apprentissage), correspondant au score $Z=1,48$. Nous pouvons en conclure que cette personne a des processus de consolidation lente supérieurs la moyenne.

Si l'on prend l'exemple d'un homme de 32 ans, avec un taux d'oubli à 30 min de -40% (percentile <5) et un taux d'oubli à 7 jours de -50% (score $Z=-0,59$), nous pouvons en conclure que cette personne a des processus de consolidation rapide déficitaires, mais des processus de consolidation lente dans la moyenne.

FEUILLE DE REPONSE – 1W-FCSRT-WORD VERSION

One Week Free and Cued Selective Reminding Test (1W-FCSRST) – word version

Nom : _____ Prénom : _____ Age : _____ Date : _____

Catégorie	Item	Rappel 1		Rappel 2		Rappel 3		Rappel à 30 min		Rappel à 7 jours	
		IMR	FR1	CR1	FR2	CR2	FR3	CR3	FR30	CR30	FR7d
poisson	hareng										
vêtement	gilet										
jeu	domino										
fleur	jonquille										
profession	dentiste										
fruit	groseille										
métal	cuivre										
inst. mus.	harpe										
oiseau	mésange										
arbre	tilleul										
sport	judo										
légume	céleri										
danse	valse										
maladie	rougeole										
meuble	tabouret										
science	géographie										
Rép. Correctes											
Score total (FR+CR)											
Faux											
Doubles											

PROTOCOLE DE RECONNAISSANCE

Nom : Prénom : Age : Date :

Items	Réponse	Items	Réponse
1 <u>plombier</u>		25 <u>angine</u>	
2 Gilet		26 <i>chalet</i>	
3 <u>clarinette</u>		27 tabouret	
4 <i>hélicoptère</i>		28 <i>lait</i>	
5 domino		29 <u>aluminium</u>	
6 <i>soleil</i>		30 <i>fourchette</i>	
7 Judo		31 <i>tenaille</i>	
8 <i>colonel</i>		32 jonquille	
9 <i>doigt</i>		33 rougeole	
10 <u>sardine</u>		34 <u>abricot</u>	
11 <i>train</i>		35 <i>tracteur</i>	
12 <u>divan</u>		36 <u>platane</u>	
13 <u>puzzle</u>		37 mésange	
14 groseille		38 <i>ail</i>	
15 valse		39 cuivre	
16 <i>bouteille</i>		40 <u>tango</u>	
17 <u>corbeau</u>		41 harpe	
18 hareng		42 <u>épinards</u>	
19 <i>cave</i>		43 céleri	
20 <u>mathématiques</u>		44 tilleul	
21 dentiste		45 <u>muguet</u>	
22 géographie		46 <i>mazout</i>	
23 <i>tasse</i>		47 <i>sabre</i>	
24 <u>équitation</u>		48 <u>bonnet</u>	

	Sujet	Contrôles
Reconnaissances correctes :	/ 16	
Acceptations de distracteurs sémantiques :	/ 16	
Acceptations de distracteurs neutres :	/ 16	

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B. Echelle MFI-20 et échelle visuelle analogique

MFI-20

(Gentile, Delarozière, Favre, Sambuc, & San Marco, 2003)

Consigne :

Sur une échelle en sept points, allant de « *oui, c'est vrai* » à « *non, ce n'est pas vrai* », indiquez à quel point chaque énoncé proposé s'applique à vous, au cours de cette dernière semaine.

Nom :

Prénom :

Date de naissance :

MFI-20

(Gentile, Delarozière, Favre, Sambuc, & San Marco, 2003)

1. Je me sens en forme.	Oui, C'est vrai	☐	☐	☐	☐	☐	☐	☐	Non, ce n'est pas vrai
2. Physiquement, je ne me sens pas capable de faire grand-chose.	Oui, C'est vrai	☐	☐	☐	☐	☐	☐	☐	Non, ce n'est pas vrai
3. Je me sens très actif.	Oui, C'est vrai	☐	☐	☐	☐	☐	☐	☐	Non, ce n'est pas vrai
4. J'ai envie de faire des tas de choses agréables.	Oui, C'est vrai	☐	☐	☐	☐	☐	☐	☐	Non, ce n'est pas vrai
5. Je me sens fatigué(e).	Oui, C'est vrai	☐	☐	☐	☐	☐	☐	☐	Non, ce n'est pas vrai
6. Je pense que je fais beaucoup de choses dans une journée.	Oui, C'est vrai	☐	☐	☐	☐	☐	☐	☐	Non, ce n'est pas vrai
7. Quand je fais quelque chose je peux me concentrer dessus.	Oui, C'est vrai	☐	☐	☐	☐	☐	☐	☐	Non, ce n'est pas vrai
8. Physiquement, je peux faire beaucoup.	Oui, C'est vrai	☐	☐	☐	☐	☐	☐	☐	Non, ce n'est pas vrai
9. Je redoute d'avoir des choses à faire.	Oui, C'est vrai	☐	☐	☐	☐	☐	☐	☐	Non, ce n'est pas vrai
10. Je pense que je ne fais pas grand-chose dans une journée.	Oui, C'est vrai	☐	☐	☐	☐	☐	☐	☐	Non, ce n'est pas vrai
11. J'arrive bien à me concentrer.	Oui, C'est vrai	☐	☐	☐	☐	☐	☐	☐	Non, ce n'est pas vrai
12. Je me sens reposé(e).	Oui, C'est vrai	☐	☐	☐	☐	☐	☐	☐	Non, ce n'est pas vrai
13. Me concentrer sur quelque chose me demande beaucoup d'effort.	Oui, C'est vrai	☐	☐	☐	☐	☐	☐	☐	Non, ce n'est pas vrai
14. Physiquement, je me sens en mauvais état.	Oui, C'est vrai	☐	☐	☐	☐	☐	☐	☐	Non, ce n'est pas vrai
15. J'ai un tas de projets.	Oui, C'est vrai	☐	☐	☐	☐	☐	☐	☐	Non, ce n'est pas vrai
16. Je me fatigue facilement.	Oui, C'est vrai	☐	☐	☐	☐	☐	☐	☐	Non, ce n'est pas vrai
17. Je mène peu de choses à bien.	Oui, C'est vrai	☐	☐	☐	☐	☐	☐	☐	Non, ce n'est pas vrai
18. Je n'ai rien envie de faire.	Oui, C'est vrai	☐	☐	☐	☐	☐	☐	☐	Non, ce n'est pas vrai
19. Mes pensées s'égarent facilement.	Oui, C'est vrai	☐	☐	☐	☐	☐	☐	☐	Non, ce n'est pas vrai
20. Physiquement, je me sens en parfait état.	Oui, C'est vrai	☐	☐	☐	☐	☐	☐	☐	Non, ce n'est pas vrai

Nom :

Prénom :

Date de naissance :

Echelle Visuelle Analogique (EVA)

Placez une croix, sur la ligne ci-dessous, selon votre **niveau de fatigue ressenti** au cours de cette dernière semaine, allant d'une « *absence totale de fatigue* » à un « *épuisement complet* ».

Epuisement complet



Absence totale de fatigue