



Mental Fatigue as a Consequence of Reduced
Information Processing Speed Following Mild vs.
Moderate-Severe Traumatic Brain Injury

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Abstract

Objective: To investigate the relationship between information processing speed and (mental) fatigue in patients with mild, and moderate-severe traumatic brain injury (TBI) in the chronic phase post-injury. Additionally it was examined whether anxiety, depression, and coping style were related to levels of fatigue.

Method: Patients with mild ($n = 55$), and moderate severe ($n = 25$) TBI were included, as well as a group of healthy controls (HCs; $n = 40$). Neuropsychological assessment consisted of information processing speed measures (Digit Span, Trail Making Test, Vienna Testing System) and self-report questionnaires measuring fatigue (Dutch Multifactor Fatigue Scale) anxiety and depression (Hospital Anxiety and Depression Scale), and coping style (Utrechtse Coping List).

Results: In the moderate-severe TBI group, poorer performance on a measure of basic information processing speed was related to higher levels of mental fatigue, $r = -.56, p < .001$. In the mild TBI group, no correlations were found between information processing speed measures and fatigue. However, for mild TBI, higher levels of self-reported anxiety, depression, and passive coping were related to higher levels of mental fatigue, $r = .50, p < .01$; $r = .52, p < .01$; $r = .43, p < .01$, respectively. In the moderate-severe TBI, none of these psychological factors were significantly related to mental fatigue.

Conclusions: The current study demonstrates a negative association between information processing speed and mental fatigue in the moderate-severe TBI group, and positive associations between anxiety, depression, and passive coping in the mild TBI group. This implies the need for a careful evaluation of the causes underlying reported fatigue in both patient groups when approaching them in clinical practice.

Keywords: information processing speed, fatigue, traumatic brain injury

Introduction

Traumatic brain injury (TBI) is an important public health problem worldwide, with annually millions of people sustaining a TBI, creating an increasingly high economic burden (Baldwin, Breiding & Sleet, 2016; Fu, Jing, McFaull & Cusimano, 2016; Taylor, Bell & Breiding, 2017). TBI has been defined as ‘an alteration in brain function or other evidence of brain pathology, caused by an external force’ (Menon et al., 2010). The brain injury that consequently occurs can include focal lesions as well as diffuse axonal injury (DAI). Focal lesions are coup contusions occurring at the site of impact, or contrecoup contusions in which the force of the impact causes the brain to strike the opposite side of the skull. Additionally, diffuse axonal injury can occur, in which the head makes an unrestricted movement with the brain lagging behind the movement of the skull (Silver, McAllister & Arciniegas, 2019). The severity of TBI is commonly determined using the Glasgow Coma Scale (GCS) in combination with the duration of Post Traumatic Amnesia (PTA), classifying the group of TBI patients into three subgroups: either mild, moderate, or severe (Matis & Birbilis, 2008).

In both mild TBI (mTBI) and moderate-severe TBI, fatigue is a frequently occurring and persistent complaint (Beaulieu-Bonneau & Ouellet, 2017; Johansson & Rönnbäck, 2017). Previous literature shows that many patients view fatigue as their most challenging symptom (LaChappelle & Finlayson, 1998). Fatigue following TBI often manifests as both physical and mental fatigue, and is associated with problems in social, emotional, physical, and cognitive functioning, thereby negatively affecting the patients’ quality of life (Cantor et al., 2008). Findings of the study done by Beaulieu-Bonneau & Ouellet (2017) indicate that fatigue severity generally tends to decrease over the first year following mTBI, and to remain relatively stable or increase over time after moderate-severe TBI. Independently of time, moderate-severe TBI was found to be associated with higher levels of fatigue in comparison to mTBI.

Possibly, the fatigue complaints often reported by TBI patients could be related to deficits in information processing speed. DAI generates a loss of white matter connectivity, axonal swelling and disconnection, that can lead to a slowed information processing speed (Dymowski, Owens, Ponsford & Willmott, 2015). Possibly, in order to compensate for the reduced information processing speed, the brain is required to work harder, using more mental effort to complete a task (Wilson, 2000; Ziino & Ponsford, 2006; Ziino & Ponsford, 2006). Several studies have found that during the performance of cognitive tasks, there are greater increases in blood pressure in TBI patients compared to non-injured controls (Riese, Hoedemeacker, Brouwer & Mulder, 1999; Ziino & Ponsford, 2006). Prolonged engagement in compensatory strategies requires more mental effort and could therefore result in higher levels of fatigue.

Mild TBI is the most common (80-90%) type of TBI (van der Horn et al., 2020). Most cases of mTBI do not show permanent physiological effects on standard neuroimaging techniques such as CT or MRI. Cognitive complaints commonly experienced during the early stages following mTBI include attentional problems and a reduced speed of information processing (Anderson et al., 2005; Dymowski, Owens, Ponsford & Willmott, 2015; Spikman & Van Zomeren, 2010). However, in mTBI, the majority of these deficits significantly reduce within a few months following the injury, with full recovery expected at approximately six months (Carroll et al., 2004). In general, the majority of mTBI cases have a good prognosis, and objectively measured long-lasting cognitive deficits are not common (Spencer et al., 2017). Therefore, although the fatigue experienced by mTBI patients could partly be a consequence of subtle sequelae of a reduced processing speed, it is likely that in addition, other factors play a role in the persistent complaints of fatigue in this group.

The remainder (10-20%) of TBI patients present with moderate-severe TBI. In moderate-severe TBI, structural brain damage is often present, shown on neuroimaging

techniques such as CT or MRI (Armstrong & Morrow, 2019). In contrast to the group of mTBI patients, the majority of moderate-severe TBI patients suffer from long-lasting cognitive deficits (Spikman, Timmerman, Milders, Veenstra & van der Naalt, 2012), negatively affecting the patients' quality of life. A prominent cognitive impairment in moderate-severe TBI concerns information processing speed, which is more profound than in the case of mTBI (Rakers et al., 2018; Spencer et al., 2017). This could be related to the more severe diffuse axonal injury (DAI) in moderate-severe TBI (Rabinowitz, Hart, Whyte & Kim, 2019). The cognitive impairments in moderate-severe TBI can persist for months and partly even be permanent (Armstrong & Morrow, 2019). Since information processing speed is more affected as the severity of brain injury increases (Rakers et al., 2018; Spencer, et al., 2017), it is likely that moderate-severe TBI patients need to compensate more in order to function at their premorbid level, compared to mTBI patients. Fatigue, in the moderate-severe TBI group, is more likely to be a direct consequence of the objectively measured, and more profound, impairment in information processing speed.

Experiencing a traumatic brain injury is a stressful event, which therefore is likely to be accompanied by psychological factors. Depression and anxiety are common following TBI, and persistent post-injury complaints are strongly related to these psychological factors (van der Horn, Spikman, Jacobs & van der Naalt, 2013; Osborn, Mathias, Fairweather-Schmidt & Anstey, 2017). Anxiety and depression are known to be closely related to fatigue (Lackner, Gudleski, DiMuro, Keefer & Brenner, 2013; O'Shea et al., 2016). Additionally, following a TBI, patients often present with a decreased use of active coping and an increased use of passive coping (Spitz, Schönberger & Ponsford, 2013), which has been associated with higher levels of fatigue as well (Bakker, van der Beek, Hendriksen, Bruinvels & van Poppel, 2015; Dehaghani, Kheiroddin & Esmaeilpour, 2019). Especially in mTBI, in case of persistent complaints of fatigue despite the lack of evidence of structural

brain damage (Cooksley et al., 2018, Foreman et al., 2007), psychological factors such as anxiety, depression, and coping style could possibly in part account for higher fatigue levels.

The aim of the present study primarily was to investigate the relationship between information processing speed and fatigue in patients with mTBI and patients with moderate-severe TBI. Furthermore, it was examined whether anxiety, depression and coping style were related to levels of fatigue. In addition, comparisons were made with a group of healthy controls (HCs). It was hypothesized that a greater impairment in processing speed would be related to higher levels of mental fatigue.

Method

Design and Setting

This study contains data obtained through file examination of TBI patients who have been admitted to the University Medical Centre of Groningen (UMCG), a level one trauma center. Data was acquired in compliance with the ethical regulations of the UMCG. On emergency department admission, neurological examination was performed to indicate the severity of the brain injury by determining the Glasgow Coma Scale (GSC) score and duration of posttraumatic amnesia (PTA), classifying the patients into either mild or moderate-severe TBI. The neuropsychological assessment was conducted at least six months post-injury, also considered as the chronic phase after an acquired, nonprogressive brain injury (Visser-Keizer, Hogenkamp, Westerhof-Evers, Egberink & Spikman, 2015). Neuropsychological assessment consisted of information processing speed tests and questionnaires for fatigue, coping, and mood.

Participants

The TBI patients were seen for neuropsychological assessment between January 2015 and June 2020. Mild TBI was defined by a GCS score of 13-15, PTA duration of less than 24hrs and/or a loss of consciousness of less than 30 minutes (Vos et al., 2012). Moderate-severe TBI was defined by a GCS score of less than 13, PTA duration of 24 hours or more and/or a loss of consciousness of 30 minutes or more (Lezak, Howieson, Bigler & Tranel, 2012). Patients of 16 years and older were included in the study. Participants who were suspected of showing insufficient effort, in part determined through symptom validity testing, were excluded from the study. Other general exclusion criteria were the presence of other neurological disorders and substance abuse.

Measures

Neuropsychological tests for basic information processing speed

The Digit Span Test is a part of the Wechsler Adult Intelligence Scale (WAIS) III, and is a test for working memory, attention and immediate verbal recall (Ostrosky-Solís & Lozano, 2006), which consists of three conditions. In the forward condition (Digit Span forwards) a series of digits is read out loud by the examiner, upon which these need to be repeated by the participant. The score on the Digit Span forwards condition was used as a measure on attention span. Total scores for this condition range from 0 to 16.

The Trail Making Test (TMT) is a test for attention and executive function (Mateen et al., 2018), consisting of two conditions. In Condition A, numbered circles have to be connected in ascending sequence, measuring basic mental speed (Reitan, 1958). Time on Condition A was used as a measure on attention and mental speed (TMT A).

The Vienna Testing System (VTS) is a computerized test for basic as well as complex information processing speed and attention, consisting of multiple subtests (Ong, 2015). For the current study, four subtests of the VTS were used (VTS S1, VTS S2, VTS S3, and VTS DT). In the first condition (S1), the patient has to respond to a yellow circle displayed on the computer screen by pressing a button on a panel connected to the computer as fast as possible. In the second condition (S2) the patient has to respond to a tone by pressing the button as fast as possible. The first two conditions measure basic information processing speed. In condition S1 and S2, higher time scores indicate a lower performance.

Neuropsychological tests for complex information processing speed

In the backward condition of the Digit Span Test (Digit Span backwards) of the Wechsler Adult Intelligence Scale (WAIS) III, a series of digits is read out loud by the examiner, upon which these need to be repeated backwards by the participant. The score on

the Digit Span backwards condition was used as a measure of divided attention. Total scores on this condition range from 0 to 16.

In condition B of the TMT (TMT B), numbered as well as lettered circles have to be connected in ascending sequence while alternating between the two (Reitan, 1958), measuring cognitive flexibility. Time on Condition B was used as a measure on complex information processing speed.

In the third condition of the VTS (S3) the patient has to respond to a yellow circle presented in combination with a tone by pressing the button as fast as possible, measuring inhibition. In this condition, a higher time score indicates a lower performance. In the fourth condition of the VTS (DT) the patient has to respond to different colors and different tones, by either pressing the button or pressing a pedal connected to the computer as fast as possible. This condition measures divided attention. Here, a higher score indicates a better performance.

Fatigue

The Dutch Multifactor Fatigue Scale (DMFS) is designed to measure multiple aspects of fatigue in TBI patients in the chronic phase after an acquired, nonprogressive brain injury (Visser-Keizer, Hogenkamp, Westerhof-Evers, Egberink & Spikman, 2015). The DMFS consists of 38 items total, on a 5-point Likert scale ranging from 1 (*totally disagree*) to 5 (*totally agree*). The items are divided over five subscales, each measuring an aspect of fatigue after TBI.

Impact of fatigue. This scale consists of 11 items, measuring the impact that fatigue has on the participant's daily life. Scores range from 11 to 55. Higher scores on this scale indicate a higher impact of fatigue on daily life, due to for example a high frequency of

experienced fatigue, a fatigue which is experienced as very severe, or a fatigue that the participants experiences to have no control of.

Direct consequences of fatigue. This scale consists of 9 items, measuring the direct consequences the fatigue has on the participant's daily life. Scores range from 9 to 45. Higher scores on this scale indicate that the participant is largely affected by the complaints directly linked to the fatigue. These complaints can be mental, physical, as well as emotional.

Mental fatigue. This scale consists of 7 items, measuring the relationship between mental effort and mental fatigue. Scores range from 7 to 35. Higher scores on this scale indicate a stronger relationship between mental effort and mental fatigue, which can mean that either mental effort is leading to fatigue, or that mental fatigue influences the performance of mental tasks.

Physical fatigue. This scale consists of 6 items, measuring the relationship between physical effort and physical fatigue. Scores range from 6 to 30. Higher scores on this scale indicate a stronger relationship between physical effort and physical fatigue.

Coping with the boundaries of fatigue. This scale consists of 5 items, measuring how participants cope with the boundaries that come with fatigue. Scores range from 5 to 25. Higher scores on this scale indicate a higher amount of crossing one's own boundaries of fatigue. Lower scores on this scale indicate the prevention of fatigue complaints.

Coping and Mood

The Utrecht Coping List (UCL) is a self-report questionnaire examining how participants cope with problems and stressful situations (Schreurs, Tellegen & Willige, 1984). The UCL consists of 47 items on a 4-point Likert scale ranging from 1 (*seldom or never*) to 4 (*very often*). The items are divided over seven subscales, each measuring a different aspect of coping.

The Hospital Anxiety and Depression Scale (HADS) is a questionnaire measuring psychological distress, defined in terms of depression and anxiety (Nezlek, Rusanowska, Holas & Krejtz, 2019). The scale consists of 14 items on a 4-point Likert scale, with score ranges from 0 to 28. Of the 14 items, seven measure depression (range from 0 to 14), and seven measure anxiety (range from 0 to 14). Higher scores represent a higher severity of depression and/or anxiety (Zigmond & Snaith, 1983).

Hypotheses

H1) The mild TBI group does not significantly differ from healthy controls in performance on measures of information processing speed (Digit Span forwards, Digit Span backwards, TMT A, VTS 1, VTS 2, VTS 3, and VTS DT), demonstrated by one-way AN(C)OVA.

H2) The moderate-severe TBI group performs significantly worse than the mild TBI group and healthy controls on measures of information processing speed (Digit Span forwards, Digit Span backwards, TMT A, VTS 1, VTS 2, VTS 3, and VTS DT), demonstrated by one-way AN(C)OVA.

H3) There is a significant relationship between performance on information processing speed measures (Digit Span forwards, Digit Span backwards, TMT A, VTS 1, VTS 2, VTS 3, and VTS DT), and reported fatigue (DMFS-I, DMFS-Con, DMFS-M, DMFS-Ph, and DMFS-C) in the mild TBI group and in the moderate-severe TBI group, with the strongest relationship expected in the moderate-severe TBI group, demonstrated by Pearson correlations.

H4) There is a significant relationship between reported anxiety, depression, and coping style (HADS-A, HADS-D, UCL-A, and UCL-P) and reported fatigue (DMFS-I, DMFS-Con,

DMFS-M, DMFS-Ph, and DMFS-C) in the mTBI group as well as in moderate-severe TBI group, with the strongest relationship expected in the mTBI group, demonstrated by Pearson correlations.

Statistical Analysis

For analyzing data, SPSS version 24.0 was used. Assumptions were checked. To examine differences between HCs, patients with mild and patients with moderate-severe TBI, χ^2 tests for categorical data, Kruskal-Wallis H tests for nonparametric data, and *t*-tests and one-way analysis of variance for parametric data were conducted. In case there are significant differences in demographic variables between groups, these variables will be included as covariates in subsequent analyses. In addition, post hoc analyses were computed using univariate tests under the Bonferroni correction. Associations between measures were tested with Pearson correlations. Subsequently, multiple linear regression analysis was performed. The overall alpha level was set at .05, two-sided.

Results

Participants

A total of 80 TBI patients were included, among which were 55 mild TBI and 25 moderate-severe TBI patients. In addition, 40 HCs were included. Groups were well-matched with regard to gender and hand preference. However, moderate-severe TBI patients were significantly younger than mild TBI patients and HCs. Additionally, moderate-severe TBI patients had a significantly lower level of education than mild TBI patients as well as HCs (see Table 1). Therefore, in the subsequent analyses, age and education were included as covariates.

Table 1

Participant Characteristics, M (\pm SD)

Variable	1. HC	2. Mild TBI	3. Mod-Sev TBI	Difference 1 - 2 -3	
	(n = 40)	(n = 55)	(n = 25)	F/ χ^2 /H	p
Age	50.7 (12.0)	43.5 (15.3)	34.3 (14.5)	F = 10.4	<.001
Gender, male (%)	13 (33%)	27 (49%)	15 (60%)	$\chi^2 = 5.2$.072
Education	6.0 (0.8)	5.7 (0.9)	5.0 (1.1)	H = 13.6	<.01
Hand pref., right (%)	38 (95%)	48 (87%)	19 (76%)	$\chi^2 = 5.4$.068

Note. TBI = traumatic brain injury; Mod-Sev = moderate to severe; Education = 7-point scale ranging from 1 (*primary school education only*) to 7 (*university education*); Hand pref. = Hand preference; GCS = Glasgow Coma Scale; PTA = posttraumatic amnesia.

Processing Speed Measures

Table 2 shows the differences between the group of HCs, mild and moderate-severe TBI patients on the measures of basic and complex information processing speed. Post hoc analyses revealed significant differences between the HCs compared to the mild TBI and moderate-severe TBI patients, whereas mild and moderate-severe TBI patients did not differ significantly from one another.

With regard to scores on tests for basic information processing speed, post hoc analyses revealed that mild TBI patients performed significantly worse than HCs on Digit Span forwards ($p < .05$). Both moderate-severe and mild TBI patients performed significantly worse than HCs on VTS S1 ($p < .01$ and $p < .05$, respectively). Similarly, both moderate-severe and mild TBI patients performed significantly worse than HCs on VTS S2 ($p < .000$ and $p < .05$, respectively).

With regard to scores on tests for complex information processing speed, post hoc analyses revealed that moderate-severe as well as mild TBI patients performed significantly worse than HCs on VTS S3 ($p < .01$ and $p < .05$, respectively). Additionally, moderate-severe TBI patients performed significantly worse than HCs on TMT B and VTS DT ($p < .05$ and $p < .01$, respectively).

Table 2

Comparisons of Basic and Complex Processing Speed Measures, M (\pm SD)

Variable	1. HC	2. Mild TBI	3. Mod-Sev TBI	Difference 1 - 2- 3	
	(<i>n</i> = 40)	(<i>n</i> = 55)	(<i>n</i> = 25)	F/H	<i>p</i>
Neuropsychological tests for basic information processing speed					
Digit Span forwards	10.2 (4.3)	8.7 (1.6)	8.7 (2.4)	F = 3.4	<.05
TMT A	29.5 (9.7)	29.7 (10.0)	34.4 (11.5)	F = 3.0	.053
VTS S1	264.0 (43.5)	295.7 (50.4)	326.0 (72.5)	H = 16.8	<.001
VTS S2	227.1 (45.1)	253.5 (47.8)	285.0 (71.7)	H = 16.8	<.001
Neuropsychological tests for complex information processing speed					
Digit Span backwards	8.6 (1.8)	8.3 (2.1)	7.9 (1.6)	F = .3	.746
TMT B	59.0 (17.3)	61.4 (23.0)	80.9 (40.6)	H = 6.7	.05
VTS S3	442.6 (72.3)	463.6 (84.1)	477.9 (100.0)	F = 4.7	<.05
VTS DT	235.2 (28.9)	223.6 (27.1)	206.6 (29.1)	H = 13.6	<.001

Note. HC = healthy controls; TBI = traumatic brain injury; Mod-Sev = moderate to severe; 15WT = 15 Word Test; TMT A = Trail Making Test A; TMT B = Trail Making Test B; CR = cijferreeksen; VTS = Vienna Test System.

Fatigue, Coping and Mood

Table 3 shows the differences between the mild TBI and moderate-severe TBI group on fatigue, mood and coping measures. The mild TBI group reported a significantly higher impact of fatigue compared to the moderate-severe TBI group ($p < .01$). From a clinical perspective, in the mild TBI group 72% of patients reported a ‘very high’ impact of fatigue, whereas in the moderate-severe TBI group 40% of patients did. Groups did not significantly differ on mood and coping measures.

Table 3

Comparisons of Fatigue, Anxiety, Depression, and Coping Measures, M (\pm SD)

Variable	1. Mild TBI	2. Mod-Sev TBI	Difference 1 - 2	
	($n = 55$)	($n = 25$)	t	p
Fatigue questionnaire				
DMFS-I	36.8 (11.2)	29.6 (10.8)	$t = 2.7$	$<.01$
DMFS-Con	28.6 (6.4)	28.1 (7.6)	$t = .3$.792
DMFS-M	26.5 (5.7)	24.3 (6.6)	$t = 1.6$.121
DMFS-Ph	17.8 (5.2)	16.9 (4.0)	$t = .7$.471
DMFS-C	15.1 (3.8)	15.8 (3.3)	$t = -.8$.426
Anxiety and depression questionnaire				
HADS-A	6.1 (4.0)	7.4 (4.0)	$t = -1.4$.179
HADS-D	5.6 (4.1)	6.0 (4.5)	$t = -.4$.731
Coping questionnaire				
UCL-A	2.5 (1.0)	2.2 (.8)	$t = 1.1$.293
UCL-P	2.7 (.9)	3.0 (1.0)	$t = -1.2$.217

Note. TBI = traumatic brain injury; Mod-Sev = moderate to severe; DMFS-I = subscale of the Dutch Multifactor Fatigue Scale (DMFS) measuring impact of fatigue; DMFS-Con = subscale of the DMFS measuring direct consequences of fatigue; DMFS-M = subscale of the DMFS measuring mental fatigue; DMFS-Ph = subscale of the DMFS measuring physical fatigue; DMFS-C = subscale of the DMFS measuring coping with fatigue. HADS-A = subscale of the Hospital Anxiety and Depression Scale (HADS) measuring anxiety; HADS-D = subscale of the HADS measuring depression; UCL-A = Active problem-focused coping subscale of the Utrechtse Copinglijst (UCL); UCL-P = Passive emotion-focused subscale of the UCL.

Correlations between Processing Speed and Fatigue

Table 4 presents the correlation coefficients between information processing speed measures and fatigue. Scores on basic, as well as complex information processing speed measures did not significantly correlate with reported levels of fatigue in the mild TBI group. In the moderate-severe TBI group, performance on the Digit Span forwards was highly negatively correlated with mental fatigue.

Table 4

Correlations Between Processing Speed Measures and Fatigue

Variable	1. Mild TBI <i>n</i> = 55					2. Mod-Sev TBI <i>n</i> = 25				
	DMFS-I	DMFS-Con	DMFS-M	DMFS-Ph	DMFS-C	DMFS-I	DMFS-Con	DMFS-M	DMFS-Ph	DMFS-C
Neuropsychological tests for basic information processing speed										
Digit Span forwards	-.07	-.04	-.15	.03	-.08	-.32	-.34	-.56**	-.33	-.17
TMT A	.10	.20	.14	.09	.20	.22	.30	.31	.29	.08
VTS S1	-.02	.03	.07	-.03	-.10	.01	.14	.19	.19	.17
VTS S2	.01	.09	.11	.15	-.08	.22	.36	.32	.28	.36
Neuropsychological tests for complex information processing speed										
Digit Span backwards	-.01	-.10	-.02	.03	-.07	-.21	.01	-.20	.19	-.14
TMT B	-.19	-.16	-.27	-.20	-.01	-.09	-.14	.08	.01	-.03
VTS S3	-.02	.14	.03	-.11	.03	.28	.34	.33	.19	.17
VTS DT	-.06	-.10	-.02	-.24	-.17	-.42	-.25	-.38	-.18	.10

Note. HC = healthy controls; TBI = traumatic brain injury; Mod-Sev = moderate to severe; 15WT = 15 Word Test; TMT A = Trail Making Test A; TMT B = Trail Making Test B; VTS = Vienna Test System; DMFS-I = subscale of the Dutch Multifactor Fatigue Scale (DMFS) measuring impact of fatigue; DMFS-Con = subscale of the DMFS measuring direct consequences of fatigue; DMFS-M = subscale of the DMFS measuring mental fatigue; DMFS-Ph = subscale of the DMFS measuring physical fatigue; DMFS-C = subscale of the DMFS measuring coping with fatigue.

* $p < .05$ ** $p < .001$.

Correlations between Fatigue, Coping and Mood

Table 5 presents the correlation coefficients between coping and mood measures and fatigue. In the mild TBI group, self-reported anxiety, depression, and passive coping highly positively correlated with impact of fatigue, consequences of fatigue, mental fatigue, and

physical fatigue. Active coping highly negatively correlated with impact of fatigue and physical fatigue, and moderately negatively correlated with consequences of fatigue. In the moderate-severe TBI group, self-reported level of depression was found to be moderately positively correlated with impact of fatigue. Passive coping was moderately positively correlated with consequences of fatigue. In this group, no significant correlations were found between self-reported anxiety and active coping and the reported levels of fatigue.

Table 5

Correlations Between Mood and Coping Measures and Fatigue

Variable	1. Mild TBI <i>n</i> = 55					2. Mod-Sev TBI <i>n</i> = 25				
	DMFS-I	DMFS-Con	DMFS-M	DMFS-Ph	DMFS-C	DMFS-I	DMFS-Con	DMFS-M	DMFS-Ph	DMFS-C
Anxiety and depression questionnaire										
HADS-A	.64**	.64**	.50**	.60**	.13	.28	.28	.31	.24	.32
HADS-D	.63**	.64**	.52**	.54**	.22	.50*	.28	.48	.23	.33
Coping questionnaire										
UCL-A	-.38**	-.32*	-.27	-.45**	-.09	-.06	-.13	-.39	-.07	.15
UCL-P	.44**	.45**	.43**	.44**	.00	.24	.39	.41	.25	.51*

Note. HC = healthy controls; TBI = traumatic brain injury; Mod-Sev = moderate to severe; DMFS-I = subscale of the Dutch Multifactor Fatigue Scale (DMFS) measuring impact of fatigue; DMFS-Con = subscale of the DMFS measuring direct consequences of fatigue; DMFS-M = subscale of the DMFS measuring mental fatigue; DMFS-Ph = subscale of the DMFS measuring physical fatigue; DMFS-C = subscale of the DMFS measuring coping with fatigue. HADS-A = subscale of the Hospital Anxiety and Depression Scale (HADS) measuring anxiety; HADS-D = subscale of the HADS measuring depression; UCL-A = subscale of the Utrechtse Copinglijst (UCL) measuring active coping; UCL-P = subscale of the UCL measuring passive coping.

* $p < .05$ ** $p < .01$.

Multiple Linear Regression

Tables 6 and 7 present the linear model of predictors of mental fatigue for the mild and moderate-severe TBI group, respectively. In the mild TBI group, sex and education were significant predictors of mental fatigue. Self-reported levels of depression (HADS-D) nearly reached significance ($p=0.9$). In the moderate-severe TBI group, an objective measure of information processing speed (Digit Span forwards), was a significant predictor of mental fatigue.

Table 6

Linear Model of Predictors of Mental Fatigue (DMFS-M) in the Mild TBI Group, n = 55

	<i>b</i>	<i>SE B</i>	β	<i>p</i>
Constant	8.99	6.34		$p = .164$
Educational level	2.17	.91	.34	$p < .05$
Gender	3.47	1.39	.31	$p < .05$
Age in years	-.03	.05	-.07	$p = .584$
Digit Span forwards	-.55	.47	-.15	$p = .249$
HADS-A	.23	.32	.14	$p = .474$
HADS-D	.43	.25	.29	$p = .090$
UCL-P	.74	1.01	.12	$p = .467$

Note. Adjusted $R^2 = .36$ ($p = .001$).

Table 7

Linear Model of Predictors of Mental Fatigue (DMFS-M) in the Moderate-Severe TBI Group, n = 25

	<i>b</i>	<i>SE B</i>	β	<i>p</i>
Constant	45.46	13.52		<i>p</i> = .005
Educational level	1.21	1.36	.20	<i>p</i> = .392
Gender	-4.42	2.84	- .33	<i>p</i> = .142
Age in years	-.22	.11	-.48	<i>p</i> = .069
Digit span forwards	-1.82	.68	-.66	<i>p</i> < .05
HADS-A	-.10	.60	-.06	<i>p</i> = .874
HADS-D	.46	.36	.31	<i>p</i> = .225
UCL-P	.27	2.47	.04	<i>p</i> = .915

Note. Adjusted $R^2 = .30$ (*p* = .09).

Discussion

The objective of the present study was primarily to investigate the relationship between information processing speed and fatigue, in mild and moderate-severe TBI patients. Furthermore, it was examined whether anxiety, depression, and coping style were related to fatigue in both groups. The results showed that in the moderate-severe TBI group, from multiple information processing speed measures, a significant negative association was found between attention span and levels of mental fatigue. However, in the mild TBI group, no significant associations were found between information processing speed and fatigue. In the mild TBI group however, subjectively reported levels of anxiety, depression, and coping style were strongly associated with almost all aspects of fatigue.

Information processing speed tests revealed that, in the current study, mild as well as moderate-severe TBI patients showed lower performance on several basic and complex information processing speed tests when compared to healthy controls. Mild and moderate-severe TBI patients did not significantly differ from one another on information processing speed measures. The impaired information processing speed found in the moderate-severe TBI group is in line with previous findings (Rakers et al., 2018; Spencer et al., 2017; Spikman, Timmerman, Milders, Veenstra & Van der Naalt, 2012), and can be interpreted as a consequence of the diffuse axonal injury (DAI) (Rabinowitz, Hart, Whyte & Kim, 2019). A possible explanation for the lower performance on information processing speed measures in the mild TBI group could be that, in addition to possible mild sequelae of a reduced processing speed, the psychological distress commonly experienced in this group has negatively influenced performance on the information processing speed measures. A patient's perceived control over emotionally stressing situations can negatively influence performance (Scheenen et al., 2017; Whittaker, Kemp & House, 2017).

In this study, lower performance on an information processing speed test (specifically measuring attention span) was associated with higher levels of mental fatigue in the moderate-severe TBI group. Moreover, it was a significant predictor for mental fatigue in this group explaining 8 % of the variance. This finding is in line with the hypothesis that there is a significant relationship between performance on information processing speed measures and reported fatigue in this group, and could be interpreted as a consequence of the higher level of compensation that is needed in the moderate-severe TBI group in order to function at their premorbid level, resulting in higher levels of fatigue. However, based on the existing literature suggesting higher levels of fatigue in the more severely injured patients (Beaulieu-Bonneau & Ouellet, 2017), one might expect even more and stronger associations between more processing speed measures and fatigue in the moderate-severe TBI group. An explanation for this finding could be the underreporting of fatigue by the moderate-severe TBI patients, as a consequence of impaired self-awareness in the more severely injured patients (Prigitano, 2005), since in the current study fatigue is measured through a self-report questionnaire.

In the mild TBI group, no association was found between performance on information processing speed tests and fatigue. Subjectively reported anxiety, depression, and coping style however, were strongly associated with almost all aspects of fatigue in this group. Higher levels of anxiety, depression, and more use of passive coping were related to more impact and consequences of fatigue for daily life, and higher levels of mental and physical fatigue. On the other hand, higher levels of active coping were related to less impact and consequences of fatigue for daily life, as well as less physical fatigue. A higher level of education and being female were significant predictors of mental fatigue in this group. Furthermore, a self-report questionnaire measuring depression was nearly significant in predicting mental fatigue in the mild TBI group. In contrast, in the moderate-severe TBI group there were limited to no

associations between fatigue and the psychological factors. In the mTBI group, higher levels of reported fatigue can partly be interpreted as a consequence of psychological distress influencing illness perception and through this, reported complaints (Scheenen et al., 2017; Whittaker, Kemp & House, 2017).

Several limitations of this study have to be mentioned. Fatigue was assessed through self-report measures, on which the outcome is influenced by severity of impairment. Both psychological distress in the mTBI group, as well as impaired self-awareness in the more severely injured patients can influence the levels of fatigue reported by these patient groups (Prigitano, 2005; Scheenen et al., 2017; Whittaker, Kemp & House, 2017). This should be taken into account when interpreting the results. In addition, the generalizability of the results is limited by the fact that all patients that participated in the current study were recruited on emergency department admission, excluding a group of patients who do not consult a medical centre. Further studies, taking these factors into account, are necessary to help map and concretize the (long-term) consequences of experiencing a TBI.

In conclusion, associations were found between information processing speed and mental fatigue in the moderate-severe TBI group, while in the mild TBI group no such association was found. Additionally, fatigue was strongly associated with anxiety, depression, and passive coping in the mild TBI group, whereas in the moderate-severe TBI group little to no association seems to be present between the psychological factors and fatigue. When approaching these two patient groups in clinical practise, healthcare professionals should be aware of the fact that fatigue can arise from various causes, demanding a different approach when aiming to treat or minimize the fatigue, thereby providing the most suitable care for each individual patient.

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