



<https://openaccess.leidenuniv.nl>

### **License: Article 25fa pilot End User Agreement**

This publication is distributed under the terms of Article 25fa of the Dutch Copyright Act (Auteurswet) with explicit consent by the author. Dutch law entitles the maker of a short scientific work funded either wholly or partially by Dutch public funds to make that work publicly available for no consideration following a reasonable period of time after the work was first published, provided that clear reference is made to the source of the first publication of the work.

This publication is distributed under The Association of Universities in the Netherlands (VSNU) 'Article 25fa implementation' pilot project. In this pilot research outputs of researchers employed by Dutch Universities that comply with the legal requirements of Article 25fa of the Dutch Copyright Act are distributed online and free of cost or other barriers in institutional repositories. Research outputs are distributed six months after their first online publication in the original published version and with proper attribution to the source of the original publication.

You are permitted to download and use the publication for personal purposes. All rights remain with the author(s) and/or copyrights owner(s) of this work. Any use of the publication other than authorised under this licence or copyright law is prohibited.

If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please contact the Library through email: [OpenAccess@library.leidenuniv.nl](mailto:OpenAccess@library.leidenuniv.nl)

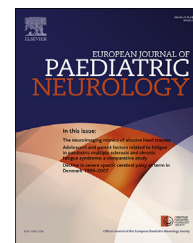
### **Article details**

Markus-Doornbosch F. van, Peeters E., Pas S. van der, Vlieland T.V. & Meesters J. (2019), Physical activity after mild traumatic brain injury: What are the relationships with fatigue and sleep quality?, *European Journal of Paediatric Neurology* 23(1): 53-60.  
Doi: 10.1016/j.ejpn.2018.11.002



ELSEVIER

Official Journal of the European Paediatric Neurology Society



## Original article

# Physical activity after mild traumatic brain injury: What are the relationships with fatigue and sleep quality?



F. van Markus-Doornbosch <sup>a,b,\*</sup>, E. Peeters <sup>c</sup>, S. van der Pas <sup>d</sup>,  
T. Vliet Vlieland <sup>a,b,e</sup>, J. Meesters <sup>a,b</sup>

<sup>a</sup> Sophia Rehabilitation, The Hague, The Netherlands

<sup>b</sup> Leiden University Medical Centre, Department of Orthopaedics, Rehabilitation and Physical Therapy, Leiden, The Netherlands

<sup>c</sup> Haga Teaching Hospital, Juliana Children's Hospital, The Hague, The Netherlands

<sup>d</sup> Leiden University Medical Centre, Medical Statistics, Department of Biomedical Data Sciences, Leiden, The Netherlands

<sup>e</sup> Rijnlands Rehabilitation Centre, Leiden, The Netherlands

## ARTICLE INFO

## Article history:

Received 12 July 2018

Received in revised form

2 November 2018

Accepted 6 November 2018

## Keywords:

Brain injuries

Adolescent

Fatigue

Sleep

Physical activity

Pediatric

## ABSTRACT

**Objectives:** To determine self-reported physical activity (PA) levels and relationships with fatigue and sleep quality in adolescents and young adults after mild traumatic brain injury (mTBI).

**Setting:** Follow-up 6–18 months after visiting the emergency department of one of 2 general hospitals.

**Participants:** Forty-nine adolescents and young adults aged 12–25 years (mean 18.4 years), 22 (45%) male with mTBI.

**Design:** Cross-sectional survey study.

**Main outcome measures:** The Activity Questionnaire for Adults and Adolescents (AQuAA), with results dichotomized into meeting or not meeting Dutch Health Enhancing PA recommendations (D-HEPA), the Checklist Individual Strength (CIS, 4 subscores) and the Pittsburgh Sleep Quality Index (PSQI, total score) were administered.

**Results:** Twenty-five participants (51%) did not meet the D-HEPA recommendations. After adjusting for sex, BMI and age, not meeting the recommendations was associated with a higher CIS Total Score (OR 1.04 95%CI 1.01, 1.07) but not with PSQI Total Score (OR 0.99, 95% CI 0.80, 1.21).

**Conclusions:** In adolescents and young adults with mTBI the level of reported PA is associated with fatigue but not with sleep quality. It remains to be established whether interventions aiming to promote PA should primarily be focused on PA or fatigue or both.

© 2018 European Paediatric Neurology Society. Published by Elsevier Ltd. All rights reserved.

\* Corresponding author. Sophia Rehabilitation, Vrederustlaan 180, 2543 SW, The Hague, The Netherlands.

E-mail address: [f.vanmarkus@sophiarevalidatie.nl](mailto:f.vanmarkus@sophiarevalidatie.nl) (F. van Markus-Doornbosch).

<https://doi.org/10.1016/j.ejpn.2018.11.002>

1090-3798/© 2018 European Paediatric Neurology Society. Published by Elsevier Ltd. All rights reserved.

## 1. Introduction

Traumatic brain injury (TBI) is one of the leading causes of death and disability in adolescents and young adults (AYA), with an estimated yearly incidence of 2.25–2.96 per 100 for the age group 15–25 years in western countries.<sup>1,2</sup> The majority is classified as mild TBI (mTBI), with symptoms often resolving within 4 weeks. However, a significant minority reports persistent symptoms.<sup>3,4</sup> These longer-term consequences of mTBI in adolescents and young adults are often multiple and complex, affecting physical, emotional, cognitive and/or social functioning.<sup>4</sup>

Regarding the physical symptoms, lower PA levels are one of the reported consequences of mTBI in adults.<sup>5–7</sup> In children and adolescents studies on PA levels are often merely focusing on “return to play”,<sup>8</sup> “sports participation”<sup>9,10</sup> or participation in activities<sup>11</sup> or concern advices on rest until symptoms resolve.<sup>12–14</sup> Some of these studies only include selected patients with mTBI related to sport concussions, whereas patients with traffic related injuries and injuries occurring at home or school should be considered as well, to give a complete perspective on activity levels after mTBI.

Regarding factors associated with physical activity, Baque et al. found in a mixed population of children with an acquired brain injury that older age and lower level of gross motor functioning partially explained physical performance, although no distinction was made for TBI severity.<sup>15</sup> In addition, in particular fatigue and sleep quality have been previously identified as relevant in pediatric populations.<sup>16,17</sup>

In pediatric TBI populations fatigue was found at 6–12 months post-injury<sup>18,19</sup> and 24 months post-injury.<sup>20</sup> A recent study by Theadom and colleagues found in a pediatric cohort of mTBI patients sleep difficulties 12 months post-injury.<sup>21</sup>

Interrelationships between physical activity and respectively, fatigue or sleep have been examined in other pediatric conditions including multiple sclerosis<sup>22</sup> and pediatric oncology<sup>23</sup> and adult TBI studies<sup>24–27</sup> but are limited in the pediatric TBI population. One study by Tham et al. found sleep disorders to predict decreased activity participation 24 months post-injury.<sup>28</sup>

Given the lack of knowledge on PA after mTBI in adolescents and young adults, the aim of the current study was to describe the level of physical activity after mTBI and as its relationship with fatigue symptoms and sleep quality 6–18 months post-injury. Better insight into these symptoms will allow clinicians to develop interventions suitable for the pediatric mTBI population and improve health outcomes.

## 2. Methods

### 2.1. Study design

This multicentre, cross-sectional study was executed at the Haaglanden Medical Centre and Haga Teaching Hospital (location Leyweg and Juliana Children's Hospital), both large teaching hospitals in The Hague, The Netherlands.

The study was approved by the Medical Ethics Review Committee of the Leiden University Medical Centre (P12.156)

and all patients and their parents (when patient was under 18 years of age) provided written informed consent.

### 2.2. Participants

Patients were eligible for the study if they met all of the following criteria a) aged 12–25 years at injury; b) registered with the diagnosis mild traumatic brain injury (Glasgow Coma Scale 13–15).<sup>29</sup> c) visited the Emergency Department (ED) of one of the two hospitals between March 1, 2012 and March 1, 2013. Patients were not eligible if they a) visited the ED for brain injuries more than once in the same year; b) underwent surgery related to the trauma; c) had other medical conditions with an impact on functioning (such as congenital disorders, rheumatic disease, chronic fatigue syndrome, epilepsy, psychiatric diagnosis); d) had an intellectual level with an IQ < 70 based on self-report in ED report or school level; e) were non-fluent in the Dutch language (based on ED report or self-report) or lived outside of The Netherlands.

Date of birth, sex, date of ED visit, and location of trauma were extracted from the medical files (all data extracted by the principle investigator, FvM-D). Medical history (reported in categories: congenital disorder, reumatic disorder, neurologic disorder, chronic fatigue syndrome, psychiatric disorder), surgery (yes/no) or multiple ED visits for all potential participants were extracted out of the medical files. Location of trauma was categorized in home, school, work, street/traffic related, sport/field, or other).

When Glasgow Coma Scale (GCS) was not reported but the patient was fully conscious (ie, walked into the Emergency Department, cycled to the hospital) with the diagnosis mild brain injury they were included in the mild TBI group.

### 2.3. Assessments

This study is part of a larger study with a one-time survey comprising five validated Patient Reported Outcome Measures (PROMs), completed by patients (if necessary with help from their parents) at home, either electronically (NetQ, [www.netq.nl](http://www.netq.nl)) or on paper. Those completing the paper version returned the questionnaire in a pre-stamped envelope. The questionnaires were coded to match the medical records and made anonymous. By providing 2 methods for completing the questionnaire the impediment of not having a computer or having computer problems was avoided.

All eligible patients and/or their parents were invited by postal mail 6–18 months post-injury and, if they agreed to participate, asked to return the signed informed consent and to state whether they preferred a paper or electronic questionnaire. Patients and/or their parents who did not respond were contacted once by postal mail 2 weeks after the first mailing, and once again by telephone after 3 months. Patients received an incentive (€10 voucher) for completing the questionnaire.

### 2.4. General and sociodemographic characteristics

Patients were asked to report height and weight; from which body mass index: BMI = weight (kg)/height squared (m<sup>2</sup>) was calculated. For patients aged 12 to 17 underweight was defined

as BMI <17.0 and overweight and obesity.<sup>30,31</sup> For patients 18 years and older cut-off points for underweight, overweight and obesity according to international criteria: <18.5, 25 and > 30 kg/m<sup>2</sup>, respectively, were used.<sup>32</sup> Current age was determined using the date of questionnaire completion; for non-responders the mean date of completion was used (June 1, 2014).

### 2.5. Physical activity

Physical activity was measured using the Activity Questionnaire for Adults and Adolescents (AQuAA), a 5 category self-assessment of physical activity based on the SQUASH (Short QUestionnaire to ASsess Health enhancing physical activity). The AQuAA has been validated in the Netherlands for children and adults.<sup>33</sup> Patients were asked about frequency (number of days per week), duration (time spent) and intensity (low, average, or high) spent on activities in the past 7 days with examples of activities to facilitate questionnaire completion. Each activity has a MET (Metabolic Equivalent of Task) score related to the intensity of the activity, and is reported as milliliter oxygen use per kilogram bodyweight per minute. The METS compendium developed by Ainsworth<sup>34</sup> was used in this study. Activities were further categorized, using the METS for each activity, into low, moderate or vigorous activities,<sup>35</sup> with the total amount of PA being expressed as minutes spent on low, moderate and vigorous activities per week. In addition, the achievement of the Dutch Health Enhancing PA recommendations (D-HEPA) was calculated from the data. In The Netherlands, a healthy PA level has been established for children and adults<sup>35,36</sup>: children (4–17 years of age) should be physically active 60 minutes with moderate to vigorous activities (minimum 5 METS), 7 days a week. Adults meet the criterium if they are physically active (minimum 4 METS) for 30 minutes, 5 days a week. This questionnaire proved to be fairly reliable and reasonably valid for the healthy Dutch population; test-retest reliability ICC (intraclass correlation) ranging from 0.30 to 0.59 for adolescents, and for adults an ICC ranging from 0.49 to 0.60 for sedentary, light and moderate intensity activities and an ICC = –0.005 (poor) for vigorous activities. Similar guidelines have been developed by the American College of Sports Medicine,<sup>37</sup> and the World Health Organization.<sup>38</sup> To obtain a more clinically comparable situation the data was dichotomized into meeting or not-meeting the D-HEPA.

### 2.6. Fatigue

The Checklist Individual Strength (CIS), was used to measure fatigue. It is a 20-item self-report rating scale for assessing fatigue and associated behavior during the past two weeks. Four domains, (1) severity of fatigue (8 items, score range 8–56), (2) concentration problems (5 items, score range 5–35), (3) reduced motivation (4 items, score range 4–28), and (4) reduced physical activity (3 items, score range 3–21) are measured. Each item is scored on a seven point Likert scale. The Total Score is calculated by the sum of the 20 items (range 20–140). Higher scores indicate higher levels of fatigue, higher levels of concentration problems, decreased motivation, and lower levels of physical activity.<sup>39</sup> The CIS has been validated for use in the adolescent and adult Dutch population.<sup>40</sup>

### 2.7. Sleep quality

To evaluate sleep quality the Pittsburgh Sleep Quality Index (PSQI)<sup>41</sup> was administered. It is a self-rated questionnaire which evaluates sleep quality and disturbances over a 1 month interval. Seven items (subjective sleep quality, sleep latency (the time from lying down for sleep to the start of actual sleep), sleep duration, habitual sleep efficiency (the proportion of actual sleep time spent in bed), sleep disturbances, use of sleep medication and day time dysfunction) are scored on 4 point Likert scales (0–3, low to high), with a total score ranging from 0 to 21 with higher scores representing poorer sleep quality. The PSQI has been used in pediatric<sup>42</sup> and adult TBI studies.<sup>43</sup>

### 2.8. Statistical analysis

Descriptive statistics were used for the sociodemographic and injury characteristics of all eligible patients and compared between participants and non-participants by means of independent sample t-tests or Chi square test, where appropriate.

Due to non-normal distribution of the data, medians and interquartile ranges (IQR, i.e. the 25th – 75th percentile) were calculated for physical activity levels (AQuAA) in minutes per week, CIS total and subscores and PSQI total score. The associations between, respectively fatigue (CIS) and sleep quality (PSQI) scores of participants (independent variables) and meeting or not meeting the Dutch norm for healthy PA (yes/no; dependent variable) were calculated by unadjusted logistic regression analyses. Subsequently, adjusted regression analyses were performed with the same dependent and independent variables while adjusting for sex, BMI and age. Results are reported as Odds ratios and 95% confidence intervals.

For the comparison of characteristics the level of statistical significance was defined as  $p < 0.05$ .

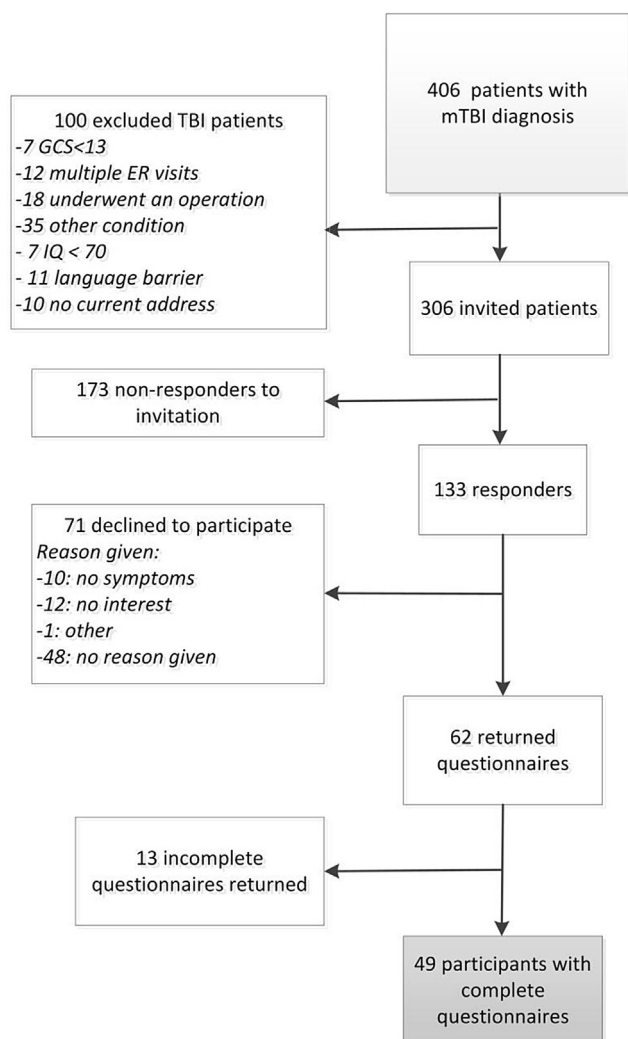
All analyses were performed using SPSS 22.0 for Windows.<sup>44</sup>

## 3. Results

Of the 406 patients identified from the registry, 100 were excluded based on the information in the medical records; 7 had a GCS below 13, 12 had multiple visits to the ED in the same year, 18 underwent surgery for their injuries, 35 had a congenital, neurological or psychiatric condition, 7 had an IQ below 70, 11 did not speak the Dutch language or lived outside of The Netherlands and 10 envelopes were returned by the postal service. Of the 306 invited patients, 133 responded with 49 returning a complete questionnaire (37%) (see Fig. 1)

Baseline characteristics of the patients who did ( $n = 49$ ) and did not participate in the study ( $n = 257$ ), were significantly different regarding sex ( $p = 0.04$ ), with more female patients among participants (55%, 38%, respectively) and time since injury (1.6 years (SD 0.5), 1.8 years (SD 0.3), respectively,  $p < 0.01$ ), with no significant differences in age at injury (mean 16.8 years (SD 3.6), 17.7 years (SD 3.6), respectively,  $p = 0.10$ ), or current age (18.4 years (SD 3.6), 19.5 years (SD 3.6),





**Fig. 1 – Flowchart of participants with mild traumatic brain injury.**

respectively,  $p = 0.06$ ). Forty-nine percent of participating patients had a sports injury, whereas 51% were injured at home, school, work or traffic related, compared to 56% sport related and 44% home, school, work or traffic related in the non-participant group ( $p = 0.72$ ).

Within the group of non-participants, sex, age at injury and current age of responders who chose not to participate ( $n = 71$ ) did not differ significantly from the non-responders ( $n = 173$ ).

Within the participant group, 24 were aged 12–17 years and 25 were 18 years or older. Participants had a mean BMI of 22.2 (SD 2.7) with 74% having a normal weight. Twenty-five out of the 49 participating patients did not meet the D-HEPA recommendations (51%); 13 of which were adolescents aged 12–17 years (54% of the adolescent group) and 12 were 18 years or older (48% of the young adult group). Nine (41%) were male and 4 (44%) had overweight with a BMI greater than 25. Age, sex and BMI were not significantly different between those meeting or not meeting the D-HEPA recommendations (see [Table 1](#)).

Participants performed general physical activity (METs > 2) on average 1350 min/week (IQR 755–2250 min/week). Moderate to vigorous activities were performed on average 793 min/week (IQR 248–1133 min/week) and sedentary activities

2670 min/week (IQR 1750–4405 min/week). In the unadjusted analyses not meeting the D-HEPA was associated with time spent on general activities (OR 0.23, 95%CI 0.08, 0.62) but no association was found with time spent on sedentary activities (OR 0.40, 95%CI 0.15, 1.08).

The median CIS Total Score was 64.0 (IQR 48.5–85.5); when dichotomized between those meeting the D-HEPA and those not meeting the D-HEPA, not meeting the D-HEPA was associated with a higher CIS Total Score (OR 1.03, 95%CI 1.00, 1.06). The median CIS subscore Fatigue was 26.0 (IQR 16.5–37.0) with not meeting the D-HEPA being associated with higher fatigue scores (OR 1.07, 95%CI 1.01, 1.13). The subscore Physical Activity (median 7.0 IQR 4.0–11.5) was associated with not meeting the D-HEPA (OR 1.15, 95%CI 1.00, 1.33). The subscores Concentration and Motivation were not significantly associated with meeting or not meeting D-HEPA recommendations (OR 1.04, 95%CI 0.97, 1.12; OR 1.10, 95%CI 0.98, 1.23, respectively). The median PSQI Total Score was 4.5 (IQR 4.0–6.0) for the total group with no significant association with meeting or not meeting the D-HEPA recommendations (OR 0.99, 95%CI 0.82, 1.19) (see [Table 2](#)).

After adjusting for potential confounders sex, BMI, and current age, the association between the CIS Total Score and subscore Fatigue on the one side and not meeting D-HEPA recommendations on the other side remained significant (OR 1.04, 95%CI 1.01, 1.07; OR 1.09 95%CI 1.02, 1.17, respectively) (see [Table 3](#)).

#### 4. Discussion and conclusions

This study comparing PA, fatigue and sleep in AYA with mild TBI 6–18 months post-injury, found that 51% had activity levels lower than recommended by the D-HEPA. Not meeting public health recommendations for PA was associated with fatigue symptoms but not sleep quality.

Concerning the amount of PA and the percentage of patients meeting D-HEPA recommendations observed in the mTBI group, comparisons with the literature are difficult to make. Previous studies on pediatric TBI populations report outcomes in terms of return to play,<sup>8</sup> general activity patterns<sup>11</sup> or PA capacity<sup>15</sup> instead of amount of PA. A previous study, from our own research group, included AYA with TBI who had taken part in a rehabilitation program, found that 50% of the AYA with mTBI met D-HEPA recommendations<sup>45</sup> which is comparable to the current study with 49% of AYA with mTBI meeting the D-HEPA recommendations. Although no direct comparisons can be made, the results in the mTBI and OI groups observed in our study are similar to results found in the general Dutch population. National Dutch data, also acquired with the AQuAA during the same time period, reported the total amount of PA ranging from 966 to 1414 min/week, with 45% of adolescents and 69% of adults meeting the D-HEPA recommendations.<sup>46</sup>

Regarding fatigue, in the current study fatigue reported by the AYA with mTBI is similar to data collected earlier in The Netherlands in the general population where a mean CIS Total Score of 59 for school-aged female adolescents and 51 for school-aged males was reported.<sup>40</sup> The data in the current study support previous studies with pediatric populations

**Table 1 – Characteristics of participants and non-participants in a cohort of adolescents and young adults (AYA) with mild traumatic brain injury (mTBI).**

	Participants n = 49	Non-participants n = 257	p value
Sex, male; no. (%)	22 (45)	159 (62)	0.04
Age at injury, years; mean (SD)	16.8 (3.7)	17.7 (3.6)	0.10
Time since injury, years; mean (SD)	1.6 (0.5)	1.8 (0.3)	<0.01
Current age, years; mean (SD)	18.4 (3.6)	19.5 (3.6)	0.06
Under 18 years, no. (%)	24 (49)	93 (36)	
18 years and older, no. (%)	25 (51)	164 (64)	
Location of injury; no. (%)			
home	6 (12)	35 (14)	
school	1 (2)	5 (2)	
work	5 (10)	17 (7)	
street/traffic related	11 (23)	39 (15)	0.72
sport/field	24 (49)	146 (56)	
other	2 (4)	16 (6)	
BMI (kg/m <sup>2</sup> <sup>a</sup> ; mean (SD)	22.2 (2.7)		
Underweight, no. (%)	3 (6)		
Normal weight, no. (%)	36 (74)		
Overweight, no. (%)	9 (18)		
Obesity, no. (%)	0		
Missing	1 (2)		
Does not meet D-HEPA recommendations <sup>b</sup>			
No. (%)	25 (51)		
Under 18 year (n = 24)	13 (54)		0.67
18 years and older (n = 25)	12 (48)		
Male sex (n = 22)	9 (41)		0.20
Female sex (n = 27)	16 (59)		
BMI under 25 (n = 39)	21 (54)		0.61
BMI boven 25 (n = 9)	4 (44)		
Missing (n = 1)			

\* Significance ( $p < 0.05$ ) between participants and non-participants were carried out by means of Independent samples t-tests for continuous variables and Chi square test for categorical variables.

<sup>a</sup> Body Mass Index (BMI; weight (kg)/height squared (m<sup>2</sup>)). Underweight is BMI under 18.5 above 18 years of age and under 17.0 for young adults under 18 years of age, normal weight 18.5–25.0, overweight 25.1–30.0, obesity above 30.0.

<sup>b</sup> D-HEPA: children ( $\leq 17$  years) meet the recommendation if they perform moderate to vigorous (minimum 5 METS) activities for a minimum of 60 minutes, 7 days a week. Adults ( $\geq 18$  years) meet the recommendation if they perform moderate to vigorous (minimum 4 METS) activities for a minimum of 30 minutes, 5 days a week.

showing higher fatigue scores with lower activity levels (children with mild to moderate physical disabilities<sup>16</sup>; pediatric multiple sclerosis<sup>22</sup>). Whereas in a study on cerebral palsy the relationship between fatigue and physical activity was not found.<sup>47</sup> In adult TBI studies it is suggested that increasing demands on participation<sup>24,48</sup> and muscular deconditioning<sup>49</sup> contribute to post-injury fatigue symptoms.

In the current study sleep quality was not associated with physical activity levels 6–18 months post-injury. PSQI Total Score was similar to the scores found by Theadom<sup>21</sup> at 12 months post-injury for the mTBI group. Studies on sleep problems after mTBI are contradictory, with several studies finding less sleep disturbances over time<sup>50,51</sup> while others studies<sup>52</sup> indicate sleep problems 3 years post-injury. The relationship between physical activity and sleep in adolescents and young adults is questionable. One pediatric study with healthy children found no relationship between sleep and PA<sup>53</sup> while in pediatric cancer patients a positive relationship between improved PA and better sleep quality was reported.<sup>54</sup>

#### 4.1. Limitations and directions for future research

There are several limitations in this study. We collected only post-injury data and have no data concerning PA levels,

fatigue or sleep before the trauma. In TBI research collection of pre-injury data is not possible unless registry data or similar data are available. Due to the cross-sectional design of this study no causal relationship can be established.

The response rate of 43% is moderate, but is similar to studies concerning TBI in children and adolescents.<sup>55</sup> Specifically, the results reflect a hospital based population and excludes those with a mild TBI that consulted only ambulance personnel, a general practitioner or sought no care at all. Many telephone numbers were disconnected or unavailable. A higher response rate can be expected when approaching patients shortly after their injury. On the other had we approached an unselected hospital population with a diversity of trauma's identifying important aspects, i.e. PA, fatigue and sleep quality, in this patient population.

Identification of patients with mild TBI was based on GCS. Due to incomplete registration in the medical files, further classification was not possible. Consequent classification and registration of individuals presenting to the ED is needed.

Regarding the assessments, measuring PA and sleep with only subjective measures, i.e. questionnaires, may have given rise to report bias. Use of accelerometers or other objective measures to quantify PA and sleep after TBI have been suggested and implemented in TBI studies<sup>7,56,57</sup> although exact

**Table 2 – Physical activity, fatigue and sleep quality in adolescents and young adults with mild traumatic brain injury (mTBI), comparing those meeting the Dutch Health Enhancing Physical Activity recommendations (D-HEPA) to those not meeting the D-HEPA recommendations. Raw scores reported as medians and interquartile ranges (IQR). Unadjusted analyses reported as odds ratios (OR) and 95% confidence intervals (95%-CI).**

	Total Group n = 49, median (IQR)	Not meeting D-HEPA recommendations <sup>b</sup> n = 25, median (IQR)	Meeting D-HEPA recommendations n = 24, median (IQR)	Unadjusted OR, (95%-CI)
AQuAA <sup>a</sup> (minutes/week)				
General activities >2 METS	1350 (755–2250)	920 (505–1580)	1918 (1221–3244)	0.23 (0.08, 0.62)*
Moderate-vigorous activities > 5 METS	793 (24–133)	225 (113–438)	1065 (871–1348)	
Sedentary activities < 2 METS	2670 (1750–4405)	2420 (1538–3438)	3413 (2010–4789)	0.40 (0.15, 1.08)
CIS <sup>c</sup>				
Total Score (range 20–140)	64.0 (48.5–85.5)	78.0 (54.5–89.5)	57.5 (41.3–67.0)	1.03 (1.00, 1.06)*
Fatigue (range 8–56)	26.0 (16.5–37.0)	32.0 (21.0–43.0)	22.5 (14.3–28.9)	1.07 (1.01, 1.13)*
Concentration (range 5–35)	20.0 (13.0–24.0)	20.0 (14.0–28.0)	19.5 (12.3–22.5)	1.04 (0.97, 1.12)
Motivation (range 4–28)	11.0 (7.5–15.0)	13.0 (9.0–16.0)	8.0 (6.3–14.8)	1.10 (0.98, 1.23)
Physical Activity (range 3–21)	7.0 (4.0–11.5)	10.0 (5.0–12.5)	6.0 (4.0–8.8)	1.15 (1.00, 1.33)*
PSQI <sup>d</sup>				
Total Score (range 0–21)	4.5 (4.0–6.0)	4.5 (4.0–6.0)	4.5 (4.0–7.8)	0.99 (0.82, 1.19)

\*p < 0.05.

<sup>a</sup> Activity Questionnaire for Adults and Adolescents (AQuAA): 5 category self-assessment containing questions in the domains of commuting activities, household activities, leisure time and sport activities, activities at school and/or work, and sedentary activities.

<sup>b</sup> D-HEPA: children (<17 years) meet the recommendation if they perform moderate to vigorous (minimum 5 METS) activities for a minimum of 60 minutes, 7 days a week. Adults (≥18 years) meet the recommendation if they perform moderate to vigorous (minimum 4 METS) activities for a minimum of 30 minutes, 5 days a week.

<sup>c</sup> Checklist Individual Strength (CIS): higher scores represent higher levels of fatigue.

<sup>d</sup> Pittsburgh Sleep Quality Index (PSQI): higher scores represent poorer sleep quality.

**Table 3 – Multivariate regression analysis assessing the relationship between fatigue and sleep quality (independent variables) and not meeting Dutch Health Enhancing Physical Activity recommendations (D-HEPA) (dependent variable) while correcting for sex, BMI, and age in a cohort of adolescents and young adults with mild traumatic brain injury (mTBI).**

		Not meeting D-HEPA recommendations <sup>a</sup> Odds ratio, (95%-CI)
Checklist Individual Strength <sup>b</sup>	Total Score (range 20–140)	1.04 (1.01, 1.07)*
	Female sex	1.60 (0.41, 6.27)
	BMI	1.13 (0.86, 1.49)
	Age	0.84 (0.69, 1.03)
	Fatigue (range 8–56)	1.09 (1.02, 1.67)*
	Female sex	1.17 (0.27, 5.04)
	BMI	1.12 (0.84, 1.48)
	Age	0.82 (0.67, 1.02)
	Concentration (range 5–35)	1.05 (0.97, 1.14)
	Female sex	2.55 (0.70, 9.25)
	BMI	1.18 (0.91, 1.54)
	Age	0.89 (0.74, 1.08)
	Motivation (range 4–28)	1.10 (0.97, 1.25)
	Female sex	2.15 (0.58, 7.90)
	BMI	1.17 (0.90, 1.52)
Age	0.88 (0.72, 1.06)	
Physical Activity (range 3–21)	1.17 (0.99, 1.38)	
Female sex	1.64 (0.42, 6.31)	
BMI	1.14 (0.88, 1.48)	
Age	0.86 (0.70, 1.04)	
Pittsburgh Sleep Quality Index <sup>c</sup>	Total Score (range 0–21)	0.99 (0.80, 1.21)
	Female sex	2.25 (0.60, 8.45)
	BMI	1.18 (0.92, 1.53)
	Age	0.89 (0.74, 1.08)

\*p < 0.05.

<sup>a</sup> D-HEPA: children (<17 years) meet the recommendation if they perform moderate to vigorous (minimum 5 METS) activities for a minimum of 60 minutes, 7 days a week. Adults (≥18 years) meet the recommendation if they perform moderate to vigorous (minimum 4 METS) activities for a minimum of 30 minutes, 5 days a week.

<sup>b</sup> Checklist Individual Strength (CIS): higher scores represent higher levels of fatigue.

<sup>c</sup> Pittsburgh Sleep Quality Index (PSQI): higher scores represent poorer sleep quality.

measurements for physical activity and rest are limited. Further research should explore the use of objective measures in addition to subjective measures when studying physical activity<sup>7</sup> and sleep.<sup>57</sup>

Future research should explore other pre- and post-injury factors that can influence activities and participation in adolescents and young adults after mTBI such as deconditioning, increasing demands on participation, or psychosocial issues.

## 5. Conclusions

Six to 18 months post-injury, adolescents and young adults with mTBI report fatigue and reduced PA but not decreased sleep quality. Higher fatigue levels are associated with activity levels lower than recommended by the D-HEPA recommendations. The causal relationship between fatigue symptoms and physical activity is unknown and requires longitudinal research. Enhancing physical activity in the general youth population is an accepted principle and further specification for the adolescent and young adult population with mTBI is needed.

## Conflicts of interest and source of funding

The authors declare no conflicts of interest or financial gains.

## Acknowledgements

We would like to thank all the participants that participated in this study. Further we would like to thank the Brain Power study group: Haaglanden Medical Centre, The Hague, The Netherlands: prof. M. Taphoorn MD PhD, S. Rhemrev MD PhD, S. Keizer MD; Haga Hospital, The Hague, The Netherlands: G. Zijp MD, H. van der Meulen MD, S. de Bruijn MD PhD and colleagues that have supported the study at different stages: Cedric Kromme, Gerard Volkers, Laurika Kraaij and Hanneke Kranenborg.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ejpn.2018.11.002>.

## REFERENCES

- McKinlay A, Grace R, Horwood L, Fergusson D, Ridder E, MacFarlane M. Prevalence of traumatic brain injury among children, adolescents and young adults: prospective evidence from a birth cohort. *Brain Inj* 2008;Feb;22(2):175–81.
- de Kloet A, Hilberink S, Roebroek M, et al. Youth with acquired brain injury in The Netherlands: a multicenter study. *Brain Inj* 2013;27:843–9.
- Barlow K, Crawford S, Stevenson A, Sandhu S, Belanger F, Dewey D. Epidemiology of postconcussion syndrome in pediatric mild traumatic brain injury. *Pediatrics* 2010;126:e374–81.
- Barlow K. Postconcussion syndrome: a review. *J Child Neurol* 2014;Jan;31(1):57–67.
- Fleming J, Braithwaite H, Gustafsson L, Griffin J, Collier M, Fletcher S. Participation in leisure activities during brain injury rehabilitation. *Brain Inj* 2011;25(9):806–18.
- Driver S, Ede A, Dodd Z, Stevens L, Warren A. What barriers to physical activity do individuals with a recent brain injury face? *Disabil Health J* 2012;5(2):117–25.
- Hassett L, Moseley A, Harmer A, van der Ploeg H. The reliability, validity and feasibility of physical activity measurement in adults with traumatic brain injury: an observational study. *J Head Trauma Rehabil* 2015;30(2):E55–61.
- Cancelliere C, Hincapié C, Keightley M, et al. Systematic review of prognosis and return to play after sport concussion: results of the international collaboration on mild traumatic brain injury prognosis. *Arch Phys Med Rehabil* 2014;Mar;95(3 Suppl):S210–29.
- Howell D, Osternig L, Chou L. Adolescents demonstrate greater gait balance control deficits after concussion than young adults. *Am J Sports Med* 2015;43(3):625–32.
- Gagnon I, Swaine B, Friedman D, Forget R. Exploring children's self-efficacy related to physical activity performance after a mild traumatic brain injury. *J Head Trauma Rehabil* 2005;20(5):436–49.
- Anaby D, Law M, Hanna S, Dematteo C. Predictors of change in participation rates following acquired brain injury: results of a longitudinal study. *Dev Med Child Neurol* 2012;54(4):339–46.
- Sawyer Q, Vesce B, Valovich McLeod TC. Physical activity and intermittent postconcussion symptoms after a period of symptom-limited physical and cognitive rest. *J Athl Train* 2016;51(9):739–42.
- McCrorry P, Meeuwisse W, Dvorak J, et al. Consensus statement on concussion in sport—the 5th international conference on concussion in sport held in Berlin, October 2016. *Br J Sports Med* 2017;51(11):1–10.
- Grool A, Aglipay M, Momoli F, et al. Association between early participation in physical activity following acute concussion and persistent postconcussive symptoms in children and adolescents. *JAMA* 2016;316(23):2504–14.
- Baque E, Barber L, Sakzewski L, Ware R, Boyd R. Characteristics associated with physical activity capacity and performance in children and adolescents with an acquired brain injury. *Brain Inj* 2017;31(5):667–73.
- Maher C, Crettenden A, Evans K, et al. Fatigue is a major issue for children and adolescents with physical disabilities. *Dev Med Child Neurol* 2015;57(8):742–7.
- Saunders T, Gray C, Poitras V, et al. Combinations of physical activity, sedentary behaviour and sleep: relationships with health indicators in school-aged children and youth. *Appl Physiol Nutr Metabol* 2016;41:S283–93.
- Crichton A, Anderson V, Oakley E, et al. Fatigue following traumatic brain injury in children and adolescents: a longitudinal follow-up 6 to 12 months after injury. *J Head Trauma Rehabil* 2018 May/June;33(3):200–9.
- Crichton A, Babl F, Oakley E, et al. Prediction of multidimensional fatigue after childhood brain injury. *J Head Trauma Rehabil* 2017;Mar/Apr;32(2):107–16.
- Starkey N, Jones K, Case R, Theadom A, Barker-Collo S, Feigin V. Post-concussive symptoms after a mild traumatic brain injury during childhood and adolescence. *Brain Inj* 2018;32(5):617–26.
- Theadom A, Starkey N, Jones K, et al. Sleep difficulties and their impact on recovery following mild traumatic brain injury in children. *Brain Inj* 2016;30(10):1243–8.
- Yeh E, Kinnett-Hopkins D, Grover S, Motl R. Physical activity and pediatric multiple sclerosis: developing a research agenda. *Mult Scler* 2015;21(13):1618–25.



23. Braam K, van der Torre P, Takken P, Veening M, van Dulmen-den Broeder E, Kaspers G. Physical exercise training interventions for children and young adults during and after treatment for childhood cancer. *Cochrane Database Syst Rev* 2016;**3**, CD008796.
24. Ponsford JLZC, Parcell DL, et al. Fatigue and sleep disturbance following traumatic brain injury-their nature, causes, and potential treatments. *J Head Trauma Rehabil* 2012;**27**(3):224–33.
25. Ponsford J, Schönberger M, Rajaratnam S. A model of fatigue following traumatic brain injury. *J Head Trauma Rehabil* 2015;**30**(4):277–82.
26. Driver S, Ede A. Impact of physical activity on mood after TBI. *Brain Inj* 2009;203–12.
27. Jankowski L, Sullivan S. Aerobic and neuromuscular training: effect on the capacity, efficiency, and fatigability of patients with traumatic brain injuries. *Arch Phys Med Rehabil* 1990;**71**(7):500–4.
28. Tham S, Palermo T, Vavilala M, et al. The longitudinal course, risk factors, and impact of sleep disturbances in children with traumatic brain injury. *J Neurotrauma* 2012;Jan 1;**29**(1):154–61.
29. Teasdale G, Jennett B. Assessment of coma and impaired consciousness: a practical scale. *Lancet* 1974;**13**:81–4.
30. Cole T, Flegal K, Nicholls D, Jackson A. Body mass index cut offs to define thinness in children and adolescents: international survey. *BMJ* 2007;**335**(7612):19.
31. van Buuren S. Body mass index cut-off values for underweight in Dutch children. *Ned Tijdschr Geneesk* 2004;**148**(40):1967–72.
32. WHO. *World database on body mass index [internet]*. World Health Organization; 2017. [http://apps.who.int/bmi/index.jsp?introPage=intro\\_3.html](http://apps.who.int/bmi/index.jsp?introPage=intro_3.html). [Accessed 13 April 2018].
33. Wendel-Vos G, Schuit A, Saris W, Kromhout D. Reproducibility and relative validity of the short questionnaire to assess health-enhancing physical activity. *J Clin Epidemiol* 2003;**56**(12):1163–9.
34. Ainsworth B, Haskell W, Leon A, et al. Compendium of physical activities: classification of energy costs of human physical activities. *Med Sci Sports Exerc* 1993;**25**:71–80.
35. Kemper H, Ooijendijk W, Stiggelbout M. Consensus over the Dutch health recommendation for healthy physical activity. *Tijdschr Soc Gezondheidsz* 2000;**78**:180–3.
36. Ooijendijk W, Hildebrandt V, Hopman-Rock M. Physical activity in The Netherlands 2000–2005. In: *Trend report Physical activity and health 2004/2005*. Hoofddorp/Leiden: TNO; 2007.
37. Garber C, Blissmer B, Deschenes M, et al. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. *Med Sci Sports Exerc* 2011;**43**(7):1334–59.
38. *Global recommendations on physical activity for health*. Switzerland: WHO Press; 2010.
39. Vercoulen J, Swanink C, Fennis J, Galama J, van der Meer J, Bleijenberg G. Dimensional assessment of chronic fatigue syndrome. *J Psychosom Res* 1994;383–92.
40. ter Wolbeek M, van Doornen L, Kavelaars A, Heijnen C. Severe fatigue in adolescents: a common phenomenon? *Pediatrics* 2006;**117**(6):e1078–86.
41. Buysse D, Reynolds Cr, Monk T, Berman S, Kupfer D. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatr Res* 1989;**28**(2):193–213.
42. Theadom A, Starkey N, Barker-Collo S, et al. Population-based cohort study of the impacts of mild traumatic brain injury in adults four years post-injury. *PLoS One* 2018;**13**(1), e0191655.
43. Ponsford J, Parcell D, Sinclair K, Roper M, Rajaratnam S. Changes in sleep patterns following traumatic brain injury: a case controlled study. *Neurorehabilitation Neural Repair* 2013;**27**(7):613–21.
44. IBM Corp. *SPSS statistics for Windows, version 22.0*. 2015 [Armonk, NY].
45. van Markus-Doornbosch F, Meesters J, Kraaij L, Wolterbeek R, Vliet Vlieland T. Fatigue and its relationship with physical activity in adolescents and young adults with traumatic brain injury. *Eur J Phys Rehabil Med* 2017;**53**(6):900–9.
46. *TNO monitor physical activity and health 2000-2013*. Leiden: TNO; 2013.
47. Balemans A, van Wely L, Becher J, Dallmeijer A. Longitudinal relationship among physical fitness, walking-related physical activity, and fatigue in children with cerebral palsy. *Phys Ther* 2015;**95**(7):996–1005.
48. Mollayeva T, Kendzerska T, Mollayeva S, Shapiro C, Colantonio A, Cassidy J. A systematic review of fatigue in patients with traumatic brain injury: the course, predictors and consequences. *Neurosci Biobehav Rev* 2014;**47**:684–716.
49. Chaudhuri A, Behan P. Fatigue in neurological disorders. *Lancet* 2004;**363**(9413):978–88.
50. Hooper S, Alexander J, Moore D, et al. Caregiver reports of common symptoms in children following a traumatic brain injury. *NeuroRehabilitation* 2004;**19**:175–89.
51. Necajauskaite O, Endziniene M, Jureniene K. The prevalence, course and clinical features of post-concussion syndrome in children. *Medicina (Kaunas)* 2005;**41**(6):457–64.
52. Kaufman Y, Tzischinsky O, Epstein R, Etzioni A, Lavie P, Pillar G. Long-term sleep disturbances in adolescents after minor head injury. *Pediatr Neurol* 2001;**24**(2):129–34.
53. Soric M, Starc G, Borer K, et al. Associations of objectively assessed sleep and physical activity in 11-year old children. *Ann Hum Biol* 2015;**42**(1):31–7.
54. Orsey A, Wakefield D, Cloutier M. Physical activity (PA) and sleep among children and adolescents with cancer. *Pediatr Blood Cancer* 2013;**60**:1908–13.
55. de Kloet A, Lambregts S, Berger M, van Markus F, Wolterbeek R, Vliet Vlieland T. Family impact of acquired brain injury in children and youth. *J Dev Behav Pediatr* 2015;**36**(5):342–51.
56. Baque E, Barber L, Sakzewski L, Boyd R. Randomized controlled trial of web-based multimodal therapy for children with acquired brain injury to improve gross motorcapacity and performance. *Clin Rehabil* 2017;**31**(6):722–32.
57. Berger I, Obeid J, Timmons B, DeMatteo C. Exploring accelerometer versus self-report sleep assessment in youth with concussion. *Global Pediatr Health* 2017;**4**:1–9.