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## Pain, fatigue, depressive symptoms and sleep disturbance in young adults with cerebral palsy

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### ABSTRACT

**Purpose:** Investigate pain, fatigue, depressive symptoms and sleep disturbance in young adults with cerebral palsy compared to references.

**Materials and methods:** Young adults with cerebral palsy ( $n=97$ , aged 21–34 years) and age-matched references from the general population ( $n=190$ ) rated pain using a numeric rating scale and fatigue, depressive symptoms, sleep disturbance and global health using Patient-Reported Outcomes Measurement Information System® short forms. Scores were compared between cerebral palsy subgroups and the reference population. Correlation coefficients and linear regression analyses assessed interrelationships of health issues and associations with global health.

**Results:** Individuals with Gross Motor Function Classification System level I had less pain, fatigue and depressive symptoms, while individuals with levels II and III–V had more pain (53% and 56%,  $p < 0.001$ ) and those with levels III–V more fatigue (39%,  $p = 0.035$ ) than references (pain: 26%, fatigue: 14%). Pain and fatigue were more interrelated (correlation coefficients: 0.71 vs. 0.41) and stronger associated with global mental health in individuals with cerebral palsy.

**Conclusions:** Young adults with Gross Motor Function Classification System levels II–V report more pain and those with levels III–V report more fatigue than references. Pain and fatigue are highly interrelated and specifically relate to mental health in individuals with cerebral palsy.

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### KEYWORDS

Cerebral palsy; young adult; pain; fatigue; depressive symptoms; sleep disturbance

### ► IMPLICATIONS FOR REHABILITATION



- Except for those in the highest level of motor function, young adults with cerebral palsy report higher levels of pain and fatigue compared to the general population of the same age.
- Pain and fatigue are strongly interrelated and associated with mental health in young adults with cerebral palsy.
- The present study recommends to monitor pain and fatigue in young adults with cerebral palsy with low levels of gross motor function.
- We advise rehabilitation professionals to consider combined treatment for both pain and fatigue.

## Introduction

Cerebral palsy (CP) is the most common childhood-onset physical disability [1]. Much of the past research on CP focused on children and physical problems, but in recent years attention has broadened towards functioning and health of adults with CP [2]. Pain and fatigue are reported in children with CP and increase with age, as these children become adults [3–5]. Depressive symptoms and sleep disturbance are associated to pain and fatigue in other populations, but this is not known for adults with CP. Knowledge of health issues is especially relevant in individuals in their twenties, since at that age they have to

develop adult roles, which includes managing their health and healthcare [6]. Thus, in order to identify possible healthcare needs, more insight should be attained in health issues in young adults with CP.

Pain and fatigue are often studied, found to be highly prevalent and to occur more often in adults with CP than in the general population [2,4,7–10]. The literature is inconclusive on differences between subgroups of severity of motor impairment: some found no differences in subgroups [5,9,11], while others indicated that more severely impaired individuals have more pain and fatigue [10,12,13]. Moreover, for specific subgroups of

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individuals with CP health issues were not compared to reference values. Therefore, studying pain and fatigue in individuals with CP in their twenties by level of gross motor functioning in comparison to a reference population could provide valuable new insight.

Depressive symptoms and sleep disturbance have been studied less often in individuals with CP, but may be relevant issues as well and are assumed to correlate with pain and fatigue [9,14]. There is some evidence that adults with CP are at increased risk of depressive symptoms compared to the general population [15]. Also, depressive symptoms were more prevalent in a sample of adults with CP [9]. In this sample, pain, depressive symptoms and fatigue were described as a symptom cluster, similar to the clustering that is observed in individuals with other chronic conditions [9,16,17]. A recent study confirmed these associations in adults with CP, and also found associations with sleep disorders [18]. Furthermore, sleep disturbance is recognized as an underemphasized health issue in individuals with disabilities and occurs frequently in children with CP [19,20], but has amply been studied in adults with CP. Knowledge of depressive symptoms and sleep disturbance may establish the relevance of these health issues in treatment of young adults with CP.

Individuals' overall health and wellbeing is reflected in their perceived global health. Global health is known to be associated with pain and fatigue in adults with CP [21–23], but the association with depressive symptoms and sleep disturbance is unknown. Moreover, it is unknown whether associations between health issues and global health differ between individuals with CP and the general population. Insight in these associations may inform health professionals on the impact of health issues and can help to prioritize treatment goals.

Thus, knowledge gaps exist regarding levels of depressive symptoms and sleep disturbance in young adults with CP and the clustering of these health issues with pain and fatigue. In addition, levels of health issues and their impact on global health of individuals with CP have not been studied for specific subgroups, in comparison to the general population. We therefore aimed to assess whether pain, fatigue, depressive symptoms and sleep disturbance levels in young adults with CP differ between GMFCS subgroups from those of the general population of the same age. Second, we aimed to study how these health issues interrelate and their association to global physical and mental health compared to the general population.

## Methods

### Design

This is a cross-sectional study in young adults with CP. Participants were former participants of the Pediatric Rehabilitation Research in the Netherlands program that recruited cohorts of children with CP between 2002 and 2007 in the Netherlands for a prospective cohort study.

### Participants

Participants of the previous 9–16 and 16–24 years cohort studies [6,24] were invited to participate in the current cross-sectional study (current age: 21–34 years). Exclusion criteria for the present study were additional disorders affecting motor functioning or having an intellectual disability, which was classified as having attended special education for children with intellectual disability [24]. Of all 211 participants of the previous 9–16 years and 16–24 years cohort studies, 176 participants were eligible and 167 were invited to participate (Figure 1). The study was approved by

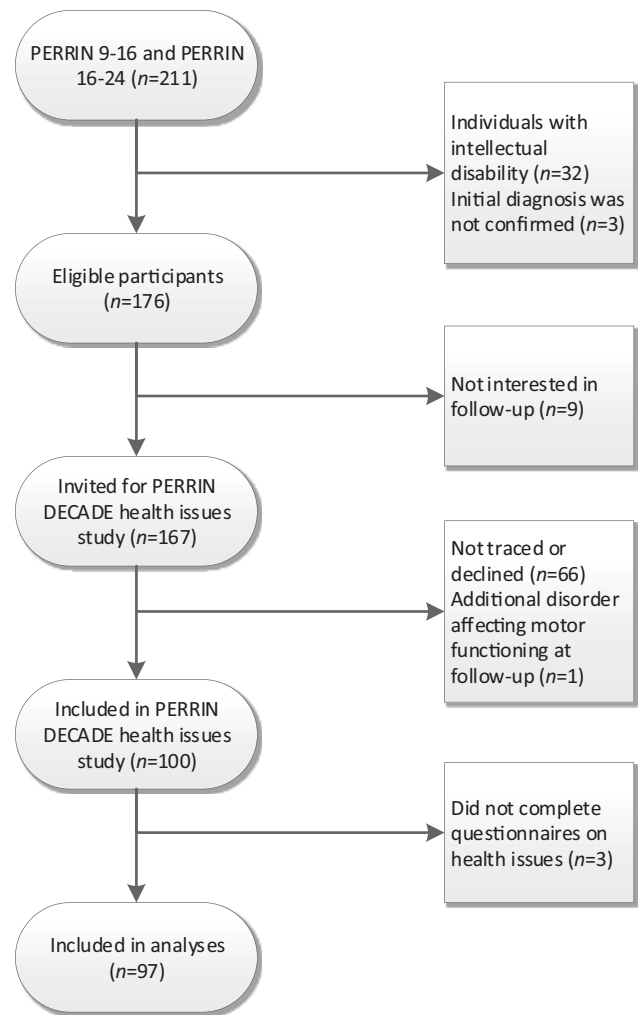


Figure 1. Flow chart of inclusion of study participants.

the medical ethical committees of VU University Medical Center and Erasmus MC University Medical Center.

In addition, reference values of two samples representative of the Dutch population were available from an online panel (Desan Research Solutions; [www.desan.nl](http://www.desan.nl)), assessed for validation studies of the Dutch-Flemish PROMIS instruments. These samples were composed to be representative of the general population with a maximum of 2.5% deviation from the distributions of gender, age, education, ethnicity and region, based on data from Statistics Netherlands in 2016 or 2013. From these samples, observations of individuals aged 21–34 years were selected [25,26].

### Outcome measures

Pain, fatigue, depressive symptoms, sleep disturbance and global physical and mental health were assessed using self-report questionnaires in online surveys. CP characteristics were classified in a face-to face interview by a trained physical or occupational therapist in participants with CP [27].

Type of CP was classified as unilateral spastic CP, bilateral spastic CP or non-spastic CP [28]. The level of functional ability was classified using the Gross Motor Function Classification System (GMFCS), Manual Ability Classification System (MACS) and Communication Function Classification System (CFCS), ranging from I (most able) to V (least able) [29–31]. Highest level of

education of individuals with CP was classified as primary, secondary or tertiary according to the international standard classification of education [32].

Pain was assessed as the average pain severity over the past week using an 11-point numeric rating scale ranging from 0 (no pain) to 10 (worst pain imaginable), which is one of the items of the Global Health Version 1.2 scale (Global07r) of the PROMIS® (Patient-Reported Outcomes Measurement Information System) [25]. Pain scores 1–3 were considered mild, scores 4–7 moderate and scores 8–10 severe [33]. This item was found valid and reliable to assess pain intensity in adults with CP [34].

Fatigue, depressive symptoms and sleep disturbance were assessed using the Dutch-Flemish translations of the PROMIS v1.0 short forms 8a in the CP sample [25,26,35–37]. These PROMIS short forms consist of eight items that are 7-day recall statements, scored on 5-point Likert scales. Physical and mental health were assessed using the PROMIS Global Health Version 1.2 scale [38]. Psychometric properties of PROMIS measures for Fatigue, Depression, Sleep Disturbance and Global Health have been studied extensively and show acceptable to excellent reliability and validity across several United States (US) and Dutch (clinical) populations [36,37,39–43]. In reference samples, the Fatigue (95 items) and Sleep Disturbance item banks (27 items) and Global Health Version 1.2 scale (including the pain item) were answered by one sample ( $n = 190$ , aged 21–34), while the Depression item bank (28 items) was answered by another sample ( $n = 202$ , aged 21–34). Response pattern scoring was used to transform the PROMIS short form (adults with CP) or full item banks (reference populations) and global health scale scores into a  $T$ -score [40,43]. A  $T$ -score of 50 (with a SD of 10) represents the average of a representative sample from the US general population. Higher scores indicate more of the concept being measured (i.e., more fatigue, better physical health). In line with the PROMIS guidelines, scores for fatigue, depressive symptoms and sleep disturbance of 55–60 were considered mild issues, 60–70 moderate issues and  $>70$  severe issues [44]. Global mental and physical health scores were classified “poor” ( $<34$  for physical,  $<28$  for mental health) to “excellent” ( $>58$  for physical,  $>57$  for mental health), based on US population estimates [44,45].

### Statistical analysis

SPSS for Windows was used for analyses and a  $p$ -value  $<0.05$  was considered statistically significant (SPSS 22, IBM SPSS Statistics, Armonk, NY, USA). The median and interquartile range of pain severity, and means and standard deviations of fatigue, depressive symptoms and sleep disturbance, physical health and mental health were computed for the total CP sample, GMFCS subgroups and reference samples. Additionally, frequencies of mild, moderate and severe issues were calculated. To study differences between subgroups, scores of individuals with CP (total sample and GMFCS subgroups I, II and III–V) and reference groups were compared using logistic regression for pain (dichotomized for scores 0–2 versus scores  $>3$ ) and linear regression analyses for fatigue, depressive symptoms and sleep disturbance ( $T$ -scores). Because the distribution of gender differed between the CP sample and reference samples, and health issues are known to be associated to gender [7,10], gender was expected to be a confounder in these analyses. We therefore corrected the analyses for gender.

To study clustering of health issues, associations were determined between pain, fatigue, depressive symptoms and sleep disturbance for individuals with CP and references using Spearman (for associations with pain) and Pearson correlation coefficients, except for associations with depressive symptoms in references

Table 1. Characteristics of study participants.

	Participants with CP without intellectual disability ( $n = 97$ )
Mean age (SD)	28.5 years (3.8 years)
Age range	21.6–34.3 years
Male/female, $n$ (%)	59/38 (61/39)
Highest educational level, $n$ (%)	
Primary education	6 (6)
Secondary education	41 (42)
Tertiary education	50 (51)
CP type, $n$ (%)	
Unilateral spastic CP	39 (40)
Bilateral spastic CP	44 (45)
Non-spastic CP	14 (15)
GMFCS level, $n$ (%)	
I	49 (51)
II	30 (31)
III	5 (5)
IV	10 (10)
V	3 (3)
MACS level, $n$ (%)	
I	49 (51)
II	41 (42)
III	4 (4)
IV	3 (3)
V	–
CFCS level, $n$ (%)	
I	78 (80)
II	17 (18)
III	2 (2)
IV	–
V	–

SD: standard deviation; CP: cerebral palsy; GMFCS: Gross Motor Function Classification System; MACS: Manual Ability Classification System; CFCS: Communication Function Classification System.

because these were assessed in another sample. The 95% confidence intervals (CIs) of the estimated correlation coefficients indicated whether correlation coefficients were significantly different between groups.

To study associations of pain, fatigue, depressive symptoms and sleep disturbance with global physical and mental health, linear regression analyses were conducted separately for individuals with CP and references (except for depressive symptoms in the reference population). Then, analyses were performed on the combined data of both groups, including a group\*health issue interaction for pain, fatigue, and sleep disturbance, to determine whether associations differed between individuals with CP and the general population.

### Results

Participant characteristics are presented in Table 1; 97 young adults with CP (no intellectual disability) completed the measurements (58% response rate, mean age: 28.5 years [SD: 3.8 years], 59% male). Individuals in the reference sample for pain, fatigue and sleep disturbance ( $n = 190$ ) had a mean age of 28.1 years (SD: 3.7 years) and 56 (30%) were male, for depressive symptoms ( $n = 202$ ) they had a mean age of 28.1 years (3.9 years) and 76 (38%) were male.

Figure 2(a) shows the occurrence of mild, moderate and severe health issues in the GMFCS subgroups and references. Of those with GMFCS levels II and III–V 53% and 56% reported pain, respectively, and of those with GMFCS levels III–V 39% reported fatigue. In the reference samples 26% reported pain and 15% reported fatigue. No differences between individuals with CP and references were found in pain occurrence (defined as NRS  $> 3$ ), and fatigue and sleep disturbance scores. Depressive symptoms were less severe (lower scores) in individuals with CP (Tables 2 and 3).

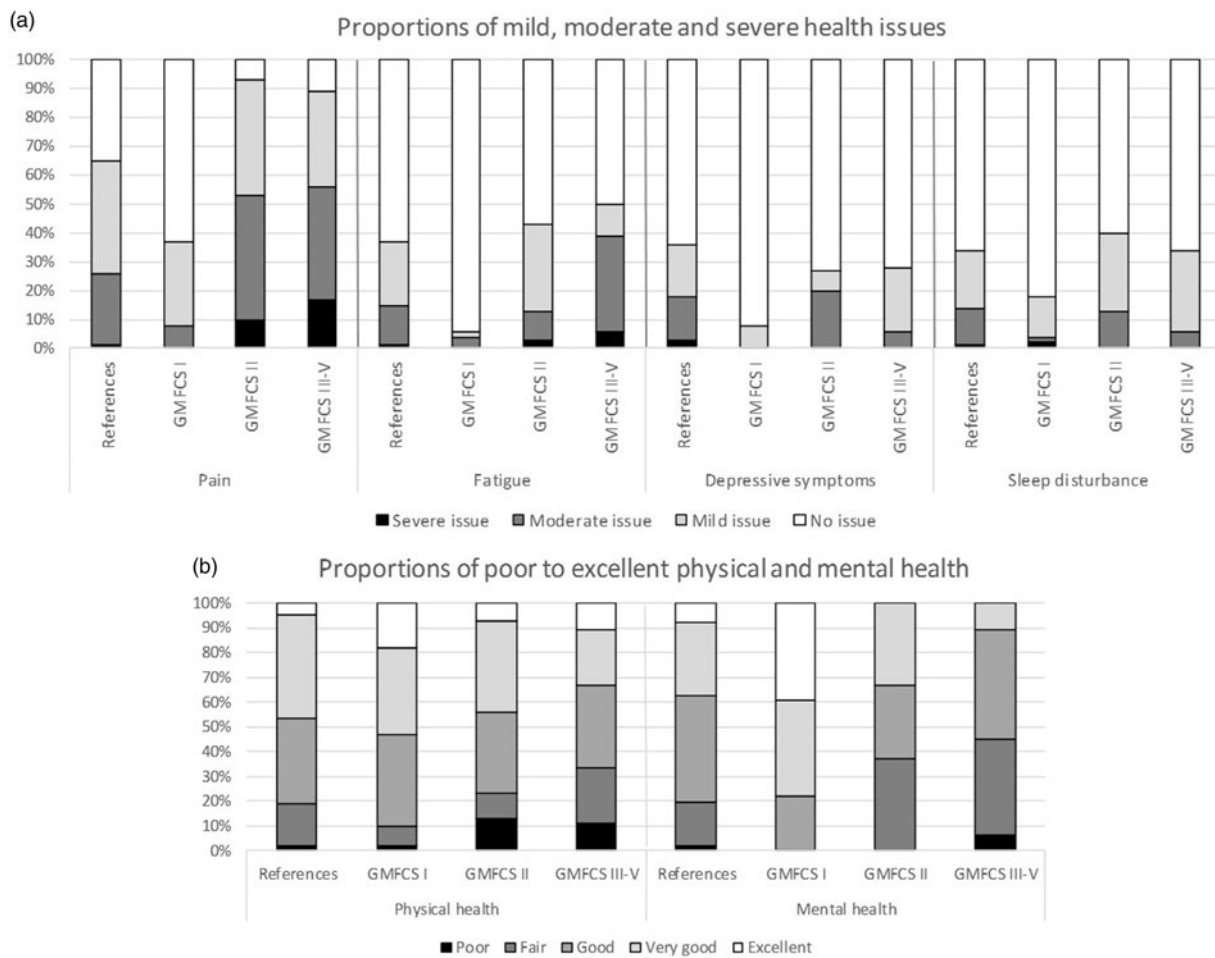


Figure 2. Proportions of health issues (a) and physical and mental health (b) of references ( $n = 190$  for pain, fatigue, sleep disturbances and global health,  $n = 202$  for depressive symptoms), individuals with GMFCS level I ( $n = 49$ ), GMFCS level II ( $n = 30$ ) and GMFCS levels III–V ( $n = 18$ ).

Table 2. Descriptives of perceived health outcomes of young adults with CP without intellectual disability and an age-matched reference population.

	CP (all)	GMFCS level I	GMFCS level II	GMFCS levels III–V	Reference population
Health issues	Mean (SD); $n = 97$	Mean (SD); $n = 49$	Mean (SD); $n = 30$	Mean (SD); $n = 18$	Mean (SD); $n = 190/202^a$
Pain <sup>b</sup> , NRS-scale, range 0–10	2 (0–4.5)	0 (0–2)	4 (2–6)	5 (2–7)	1 (0–4)
Fatigue, PROMIS, $T$ -score	48.6 (9.9)	44.3 (8.0)	52.2 (8.2)	54.3 (12.3)	50.5 (9.5)
Depression, PROMIS, $T$ -score	46.7 (8.6)	43.9 (6.7)	49.5 (10.6)	49.4 (7.3)	51.5 (9.4)
Sleep disturbance, PROMIS, $T$ -score	50.1 (7.8)	48.1 (8.0)	51.8 (8.0)	52.8 (5.8)	50.9 (8.3)
Global health	Mean (SD); $n = 97$	Mean (SD); $n = 49$	Mean (SD); $n = 30$	Mean (SD); $n = 18$	Mean (SD); $n = 190$
Physical health, PROMIS, $T$ -score	49.0 (8.6)	51.6 (7.7)	46.4 (9.0)	46.0 (8.7)	48.7 (7.1)
Mental health, PROMIS, $T$ -score	47.9 (9.9)	54.3 (7.3)	42.5 (7.3)	39.3 (8.1)	45.7 (7.9)

CP: cerebral palsy; SD: standard deviation; GMFCS: Gross Motor Function Classification System; NRS: Numeric Rating Scale; PROMIS: Patient-Reported Outcomes Measurement Information System.

<sup>a</sup>Reference population for depression,  $n = 202$ .

<sup>b</sup>Median (interquartile range).

However, when individuals with GMFCS levels I, II and levels III–V were analyzed separately, those with GMFCS level I had less severe pain, fatigue and depressive symptoms compared to references. Those with GMFCS levels II and III–V had higher odds of pain (OR [CI]: 3.84 [1.69–8.74] and 4.32 [1.55–12.02]) and those with GMFCS levels III–V had somewhat more severe fatigue (beta [SE]: 4.61 [2.31]) compared to references (Table 3).

Figure 3 shows the correlation coefficients between the health issues in individuals with CP and the reference group. There were positive associations between all health issues in both the individuals with CP and references (see Figure 3). Pain and fatigue

correlated more strongly in individuals with CP compared to references ( $r = .71$  vs.  $r = .41$ ).

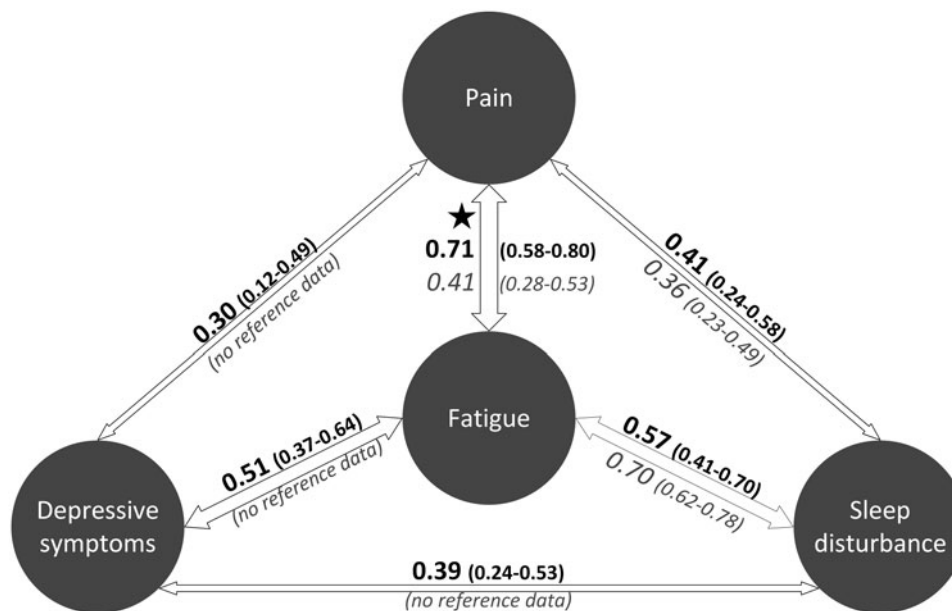
Table 4 describes the associations between pain, fatigue, depression, sleep disturbance and physical and mental health for individuals with CP and references. All health issues related negatively to global physical and mental health in individuals with CP and references with standardized betas ranging from  $-0.25$  to  $-0.84$ . In individuals with CP pain and fatigue had a stronger association with mental health, and a weaker association with physical health compared to references, as indicated by significant interactions (see Table 4).

**Table 3.** Regression coefficients for the differences in pain, fatigue, depression and sleep disturbance between individuals with CP and references.

	Dependent	Pain	Fatigue	Depressive symptoms	Sleep disturbance
	Independent	Odds ratio; 95% CI; <i>p</i> -value	Beta (SE); std beta; <i>p</i> -value	Beta (SE); std beta; <i>p</i> -value	Beta (SE); std beta; <i>p</i> -value
Crude analysis	CP (versus references)	1.25; 0.73 to 2.15; <i>p</i> = 0.410	-1.87 (1.20); -0.09; <i>p</i> = 0.121	-4.78 (1.14); -0.24; <i>p</i> < 0.001**	-0.78 (1.02); -0.05; <i>p</i> = 0.448
Adjusted for gender	CP (versus references)	1.50; 0.85 to 2.67; <i>p</i> = 0.163	-1.03 (1.25); -0.051; <i>p</i> = 0.412	-4.87 (1.11); -0.24; <i>p</i> < 0.001**	-0.35 (1.07); -0.02; <i>p</i> = 0.742
Crude analysis	GMFCS I (versus references)	0.25; 0.09 to 0.73; <i>p</i> = 0.011*	-6.17 (1.49); -0.24; <i>p</i> < 0.001**	-7.51 (1.45); -0.30; <i>p</i> < 0.001**	-2.78 (1.30); -0.13; <i>p</i> = 0.033*
	GMFCS II (versus references)	3.20; 1.46 to 7.03; <i>p</i> = 0.004**	1.74 (1.83); 0.06; <i>p</i> = 0.343	-1.97 (1.78); -0.06; <i>p</i> = 0.268	0.89 (1.59); 0.03; <i>p</i> = 0.578
	GMFCS III-V (versus references)	3.50; 1.31 to 9.37; <i>p</i> = 0.013*	3.81 (2.30); 0.10; <i>p</i> = 0.098	-2.05 (2.23); -0.05; <i>p</i> = 0.360	1.92 (2.00); 0.06; <i>p</i> = 0.331
Adjusted for gender	GMFCS I (versus references)	0.30; 0.10 to 0.89; <i>p</i> = 0.030*	-5.32 (1.54); -0.21; <i>p</i> = 0.001**	-7.62 (1.48); -0.30; <i>p</i> < 0.001**	-2.35 (1.34); -0.11; <i>p</i> = 0.081
	GMFCS II (versus references)	3.84; 1.69-8.74; <i>p</i> = 0.001**	2.43 (1.85); 0.08; <i>p</i> = 0.190	-2.06 (1.79); -0.07; <i>p</i> = 0.252	1.24 (1.62); 0.05; <i>p</i> = 0.445
	GMFCS III-V (versus references)	4.32; 1.55 to 12.02; <i>p</i> = 0.005**	4.61 (2.31); 0.12; <i>p</i> = 0.047*	-2.15 (2.25); -0.06; <i>p</i> = 0.339	2.33 (2.03); 0.07; <i>p</i> = 0.252

CP: Cerebral Palsy; GMFCS: Gross Motor Function Classification System; SE: standard error; std beta: standardized beta.

\**p* ≤ 0.05; \*\**p* ≤ 0.01.



★ Indicates that correlations significantly differed (*p* < 0.05) between individuals with CP and references

**Figure 3.** Correlations among pain, fatigue, depressive symptoms and sleep disturbance of individuals with CP and references (in grey and italics).

## Discussion

This study provided insight into the health issues in individuals with CP in their twenties. Young adults with CP with GMFCS levels II and III-V more often reported moderate to severe pain (53% and 56%) and those with GMFCS levels III-V more often reported moderate to severe fatigue (39%) than a reference group (pain: 26%, fatigue: 15%). In contrast, those with GMFCS level I had lower levels of pain, fatigue and depressive symptoms. Pain and fatigue showed a stronger inter-relationship in individuals with CP, and correlated more strongly to mental health compared to a reference group.

Pain in subgroups of GMFCS levels have not been previously compared to reference populations. Our result of much higher moderate to severe pain occurrence in individuals with GMFCS levels II-V compared to GMFCS level I is in line with a recent

meta-analysis that found more pain in individuals with CP with GMFCS levels II and IV compared to GMFCS level I [10]. Some other studies did not identify this difference, which may be explained by lower numbers of individuals with GMFCS level I in these populations, and therefore they may not have had enough power to determine the difference [9,11]. Furthermore, these populations had a slightly higher age than the present sample which may explain the different results. In conclusion, pain occurs often in young adults with GMFCS levels II-V and we therefore advise professionals to monitor pain in these individuals.

Regarding fatigue, we found somewhat higher severity levels in individuals with CP with GMFCS levels III-V (mean *T*-score: 54.3) compared to those in the reference population (mean *T*-score: 50.5). Previous studies did not compare subgroups of GMFCS to reference values, but did find that individuals with lower motor

**Table 4.** Regression coefficients for the relations between pain, fatigue, depression, sleep disturbance and physical and mental health for individuals with CP and references.<sup>a</sup>

Dependent	Physical health			Mental health		
	beta (SE); std beta; <i>p</i> -value			beta (SE); std beta; <i>p</i> -value		
Independent	CP	References	Interaction	CP	References	Interaction
Pain	-1.05 (0.31); -0.33; <i>p</i> = 0.001**	-1.98 (0.17); -0.64; <i>p</i> < 0.001**	0.93 (0.32); 0.24; <i>p</i> = 0.004**	-3.04 (0.21); -0.84; <i>p</i> < 0.001**	-0.86 (0.24); -0.25; <i>p</i> < 0.001**	-2.18 (0.34); -0.50; <i>p</i> < 0.001**
Fatigue	-0.34 (0.08); -0.39; <i>p</i> < 0.001**	-0.49 (0.04); -0.65; <i>p</i> < 0.001**	0.15 (0.08); 0.47; <i>p</i> = 0.067	-0.73 (0.07); -0.73; <i>p</i> < 0.001**	-0.44 (0.05); -0.53; <i>p</i> < 0.001**	-0.29 (0.09); -0.78; <i>p</i> = 0.001**
Depressive symptoms	-0.63 (0.08); -0.63; <i>p</i> < 0.001**			-0.52 (0.11); -0.45; <i>p</i> < 0.001**		
Sleep disturbance	-0.44 (0.10); -0.40; <i>p</i> < 0.001**	-0.48 (0.05); -0.57; <i>p</i> < 0.001**	0.04 (0.10); 0.14; <i>p</i> = 0.676	-0.60 (0.12); -0.47; <i>p</i> < 0.001**	-0.42 (0.06); -0.44; <i>p</i> < 0.001**	-0.18 (0.12); -0.51; <i>p</i> = 0.130

CP: cerebral palsy; SE: standard error; std beta: standardized beta.

<sup>a</sup>Correcting analyses for gender provides very similar results and are therefore not presented.

\**p* ≤ 0.05; \*\**p* ≤ 0.01.

function experience more fatigue compared to those with higher motor function [9,12]. Therefore, our results emphasize that fatigue is an issue in individuals with GMFCS levels III–V in their twenties. We therefore suggest to monitor fatigue in young adults with CP during their transition from adolescence into adulthood.

Young adults with CP did not have higher levels of depressive symptoms and sleep disturbance compared to an age-matched reference group. This is in contrast with the literature that found individuals with CP at higher risk of depression compared to reference values [9,14]. A possible explanation for this may be a floor effect in the assessment of depressive symptoms. This floor effect was observed in other studies as well [42], and is more pronounced in the short form that was used for individuals with CP than in the item bank that was used in the reference population [46]. Because of this, the Depression short form does not seem to adequately cover low scores on the depressive symptoms short form [46], which may have led to an underestimation of the average level of depressive symptoms in individuals with CP. Still, this only affects the scores of those with low levels of depressive symptoms, the scores of individuals with moderate to severe depressive symptoms were not affected. Therefore, since depressive symptoms and sleep disturbance were not more severe in individuals with CP compared to the general population in their twenties they may not require specific attention in rehabilitation care.

Remarkably, we did not find a difference in pain and fatigue between the total sample and the reference population, contrasting other studies [4,7–9]. This can be explained by the large proportion of individuals with GMFCS level I in our sample, who had very low levels of pain and fatigue. These low levels may be related to the lifelong aspect of their disability. Similar to the response shift theory, individuals with CP are accustomed to functioning with their disability, may have struggled with health issues in the past, and therefore rate their health more positively [47].

As expected, all health issues in individuals with CP and the general population were associated, in line with the literature [9,16–18]. Moreover, our results support the idea that there is a clustering of pain and fatigue in individuals with CP [8,48], which was also found in individuals with stroke [16]. Because of the low occurrence of depressive symptoms we did not confirm a triad of pain, fatigue and depressive symptoms that was previously found in a population of individuals with bilateral CP and in individuals after stroke [9,16]. Furthermore, the association between fatigue and sleep disturbance tended to be less prominent in individuals with CP compared to the general population. This may be caused by a stronger correlation in individuals with CP between fatigue and other health complaints, like pain or physical limitations, than

between fatigue and sleep. For the healthier reference group on the other hand, sleep problems could be a major issue causing fatigue. Although the underlying mechanism of the association between pain and fatigue is unclear, health professionals may consider treating pain and fatigue in combination if both issues occur. A lifestyle intervention program may for instance be fitting, since this has previously found to reduce both fatigue and pain [49].

All health issues had a negative association with global health. This is in line with previous studies that found associations between pain and fatigue with global health in children with CP and associations of pain and fatigue with health concerns of adults with CP [21,23]. In addition, pain and fatigue were more strongly associated to mental health, but weaker to physical health in young adults with CP compared to the general population. Pain and fatigue therefore seem to affect mood and quality of life, which determine the PROMIS global mental health score. Global physical health was less affected by pain and fatigue in individuals with CP compared to the reference population in our study. This may be explained by their physical disabilities that may be dominant in rating their global physical health. In conclusion, our results suggest that pain and fatigue should be intervened on timely in young adults with CP to prevent reduced mental health. In addition, in line with a recently developed patient-centered research agenda for CP, future research may aim to determine which variables, in addition to GMFCS level predict the occurrence of pain and fatigue in young adulthood [50].

### Strengths and limitations

Strengths of this study are studying four health issues and global health simultaneously, thus allowing to disentangle associations between them and directly comparing the results to a reference population of the same age. Limitations mainly concern representativeness of the used samples. First, we checked that non-response of participants from the previous representative CP cohorts for this study was not selective regarding gender, GMFCS level and type of CP, and the distribution of these factors was similar to population-based studies in CP when excluding those with intellectual disability [51]. Despite this, we cannot rule out that other specific factors may have caused individuals to not respond to this study. Second, the reference groups were representative of the Dutch population within the age range 18–40 years [25]. Since we selected an age subgroup from this sample, deviations from norm data distributions may exceed 2.5%. Deviations in distributions were observed for gender (reference samples had an overrepresentation of women). We therefore

corrected our analyses for gender to allow conclusions on differences in health issues between individuals with CP and samples from the general population. Third, the relatively small size of the population of individuals with CP limited the study. We combined subgroups of individuals with GMFCS levels III–V to have adequate group sizes for the analyses, because of low numbers of individuals with GMFCS levels III and V. Future studies are needed to confirm our results in separate groups of individuals with GMFCS levels III–V.

## Conclusions

Young adults with CP and GMFCS levels II–V report higher levels of pain and those with GMFCS levels III–V report higher levels of fatigue compared to age-matched individuals from the general population, while those with GMFCS level I report lower levels of pain, fatigue and depressive symptoms. Pain and fatigue are strongly interrelated and are specifically associated with mental health in young adults with CP. Therefore, we recommend that health professionals monitor pain and fatigue in young adults with GMFCS levels II–V and consider combined treatment for both health issues. Depressive symptoms and sleep disturbance do not seem to be more prominent in young adults with CP compared to the general population of the same age.

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No potential conflict of interest was reported by the authors.

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