Chronic pain, fatigue, and depressive symptoms in adults with spastic bilateral cerebral palsy

WILMA M A VAN DER SLOT1,2 | CHANNAH NIEUWENHUIJSEN1 | RITA J G VAN DEN BERG-EMONS1 | MICHAEL P BERGEN2 | SANDER R HILBERINK1 | HENK J STAM1 | MARIJ E ROEBROECK1

1 Department of Rehabilitation Medicine and Physical Therapy, Erasmus MC, University Medical Center, Rotterdam; 2 Rijndam Rehabilitation Center, Rotterdam, the Netherlands.

Correspondence to Dr Wilma van der Slot at Rijndam Rehabilitation Center, Westersingel 300, 3015 LJ Rotterdam, the Netherlands. E-mail: w.vanderslot@erasmusmc.nl

This article is commented on by Belew. To view this paper visit http://dx.doi.org/10.1111/j.1469-8749.2012.04374.x

PAIN AND FATIGUE ARE COMMON SYMPTOMS IN ADULTS WITH CEREBRAL PALSY (CP).1–4 In CP, pain often begins at an early age and frequently becomes a chronic condition.1,2,4 At least 67% of adults with CP in the USA experience chronic pain.4

Fatigue is a well-known symptom in various neurological disorders, but is rarely studied in CP.5–6 In a Norwegian study5,7 the prevalence of fatigue was higher in adults with CP (30%) than in the general population (22%).

Pain and fatigue are also common symptoms in the general population8,9 and often co-occur, especially when they are severe.8 In the general population, pain and fatigue have been shown to have an impact on daily activities2 and to be associated with psychological distress, negative mood, and depression.8,10 For the impact of pain and fatigue on daily activities in CP, Schwartz et al.4 found that adults with CP tended to report only minor interference from pain on their activity level and social or work functioning, whereas Jahnsen et al.11 demonstrated that one-third of their CP sample reported a moderate to extreme impact of pain in daily life and an association of fatigue with limitations due to physical health problems. In a study among children with CP, pain and fatigue were associated with lowered school functioning and, in some cases, partly explained the association between severity of CP and performance at school.5

Very little has been reported about depression in adults with CP. Jensen et al.11 found that in adults with CP experiencing chronic pain at least 42% had depressive symptoms and that average pain intensity was associated with depressive symptoms.12

To our knowledge, co-occurrence of chronic pain, fatigue, and depressive symptoms has not been investigated in adults with CP and objective information on these symptoms in subtypes of CP is scarce. According to Jahnsen et al.,2,3 musculoskeletal pain in the back, knee, foot, and ankle, as well as fatigue, tended to be more prevalent in bilateral than unilateral CP. In our opinion, studying subgroups is a prerequisite for handling the heterogeneity of CP, therefore we focused on adults with spastic bilateral CP (SBCP) because we expected them to be particularly at risk for chronic pain and fatigue.

The present study aimed to investigate the prevalence and co-occurrence of chronic pain, fatigue, and depressive symptoms in a sample of adults with SBCP without severe cognitive impairment, aged 25 to 45 years. Persons with SBCP were compared with Dutch reference samples and differentiated...
into condition-severity subgroups using the Gross Motor Function Classification System (GMFCS). In addition, we explored the associations of chronic pain and fatigue with depressive symptoms and daily functioning.

**METHOD**

**Participants**

This study was part of a larger study on daily functioning and physical fitness in adults with SBCP. Participants were recruited from 10 rehabilitation centres in the western and central regions of the Netherlands and through the Association of Physically Disabled Persons and their Parents (BOSK). In addition to registers of adult rehabilitation, historical registers of paediatric rehabilitation were used to trace adults with CP, because in the Netherlands only part of the adult CP population receives rehabilitation care. The inclusion criteria were a diagnosis of SBCP and age 25 to 45 years. Exclusion criteria were any multimorbidity with lasting effects on physical activity or contraindicated for a progressive maximal ergometer test (e.g. severe cardiopulmonary disease), full dependence on electric wheelchair propulsion, inadequate Dutch language proficiency, legal inability, and severe cognitive impairment according to medical files. The last criterion excluded persons who could not understand study instructions and questionnaires. Of 152 eligible persons who received the study invitation, 138 replied. Six persons were excluded because of multimorbidity. Seventy-six persons declined to participate for several reasons: a lack of time or burden of the measurement (n=27), personal reasons (n=6), inadequate language proficiency (n=2), and no clear reason (n=41). Fifty-six persons (35 males, 21 females; mean age 36y 5mo, SD 5y 10mo) participated in the study. Characteristics of the study sample are presented in Table I.

A non-response study showed that, on average, participants were older than non-participants (mean difference 2y 6mo; p<0.01). There was no difference in sex or distribution of limb impairment.

All participants received oral and written information about the study and gave their written consent to participate. The Medical Ethics Committee of the Erasmus Medical Center and the participating rehabilitation centres approved the study.

**Procedures**

Data were collected in face-to-face interviews, which included questions on chronic pain. Self-report instruments administered in the presence of a trained researcher included demographics, Fatigue Severity Scale (FSS), Multidimensional Fatigue Inventory (MFI-20; mean age 41y 5mo, SD 1y 5mo, n=67), and CES-D (age group 25–44y from a total sample of n=255).

**Measures**

**Demographic and CP-related characteristics**

Participants were asked to report their age, sex, and level of education. Gross motor functioning was classified according to the GMFCS, which is a five-level classification system grading severity of gross motor limitations and valid in adults with CP. Neuromotor abnormality, distribution of limb impairment (diplegia or quadriplegia), and spasticity were determined. Spasticity was assessed in four muscle groups of the lower limbs (hip adductors, hamstrings, rectus femoris, and gastrocnemius) using the Tardieu Scale. The number of spastic muscle groups of the more affected lower limb has been reported.

**Pain**

We asked whether a person currently had pain. In participants with current pain, we assessed per localization information on duration, frequency, and possible causes. Chronic pain was

<table>
<thead>
<tr>
<th>Table I: Characteristics of study participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample (n=56)</td>
</tr>
<tr>
<td>Age, mean (SD) y:mo</td>
</tr>
<tr>
<td>Males/Females, n</td>
</tr>
<tr>
<td>Educational level&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Low</td>
</tr>
<tr>
<td>Medium</td>
</tr>
<tr>
<td>High</td>
</tr>
<tr>
<td>GMFCS level</td>
</tr>
<tr>
<td>I</td>
</tr>
<tr>
<td>II</td>
</tr>
<tr>
<td>III</td>
</tr>
<tr>
<td>IV</td>
</tr>
<tr>
<td>Limb distribution</td>
</tr>
<tr>
<td>Diplegia</td>
</tr>
<tr>
<td>Tetraplegia</td>
</tr>
<tr>
<td>Spasticity in most affected lower extremity&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Two muscle groups</td>
</tr>
<tr>
<td>Three muscle groups</td>
</tr>
<tr>
<td>Four muscle groups</td>
</tr>
<tr>
<td>Life-habits: difficulty in performance</td>
</tr>
<tr>
<td>Daily activities subdomain&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Social participation subdomain&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Values n (%) except where otherwise stated. <sup>a</sup>Low: no education or pre-vocational theoretical education and upper secondary vocational education (vocational high school); medium: pre-vocational theoretical education and upper secondary vocational education (vocational high school); high: secondary education, higher education, and university. <sup>b</sup>Spasticity was assessed in 50 of the 56 participants. <sup>c</sup>Participants reporting difficulty in daily activities or social roles (mean score <8.0). GMFCS, Gross Motor Function Classification System.

---

What this paper adds

- In adults with SBCP, there is a high prevalence and relatively frequent co-occurrence of chronic pain, fatigue, and depressive symptoms.
- Severity of fatigue was associated with depressive symptoms.
- Chronic pain and fatigue were not associated with limitations in daily functioning.
defined as continuous or intermittent musculoskeletal or neuromuscular pain lasting longer than 3 months. Possible causes were self-reported and defined as (1) a diagnosis made by a medical doctor or (2) pain in muscles or muscle cramps. We reported on localization, the number of sites, and possible causes of chronic pain, as well as pain lasting more than 1 year.

**Fatigue**

Severity of fatigue was assessed by the FSS. Participants rated their agreement with nine statements about the severity and impact of fatigue on daily life on a scale of 1 to 7. Severe fatigue was defined as an FSS score more than 2SDs above the mean score in healthy individuals (FSS≥5.1) and fatigue as a score at least 1SD above the mean score in healthy individuals (FSS≥4.0). The Multidimensional Fatigue Inventory is a 20-item self-report instrument designed to assess the nature of fatigue during the previous 2 weeks. Scale scores range from 4 to 20, higher scores indicating greater fatigue.

**Depressive symptoms**

The CES-D is a widely used self-report instrument to screen current depressive symptoms. In the present study, the originally determined cut-off score of at least 16 (out of a maximum of 60) was used to indicate depressive symptoms based on international literature.

**Daily activities and social participation**

The Assessment of Life Habits 3.0 was used to assess performance in daily activities and social participation. A mean score of less than 8.0 (maximum=9) on it indicated performance with difficulty.

More information on the questionnaires, including psychometric properties, and reference samples is presented in Data S1, supporting online information.

**Statistical analysis**

To compare the prevalence of chronic pain, fatigue, and depressive symptoms between persons with SBCP and reference samples, one-sample t-tests (for means) or binomial tests (for proportions) were used. Differences between subgroups (i.e. sex, GMFCS in three subgroups [I, II, and III/IV]) were analysed by t-tests or analysis of variance (for means) and χ² test (for proportions). For scores with a skewed distribution, the Mann–Whitney U test or Kruskal–Wallis test were used. Associations of chronic pain, fatigue, and depressive symptoms with demographic and CP-related characteristics were explored with univariable logistic regression analyses. For multivariable logistic regression analyses, each symptom was used as a dichotomized variable (no/yes). To study fatigue as a determinant, raw sum-scores of the FSS were transformed into z-scores to allow better comparison of the strength of the determinant. Multivariable logistic regression analyses were performed to study associations of chronic pain and severe fatigue with depressive symptoms, daily activities, and social participation (the last two were dichotomized as with or without difficulty). In addition, interrelationships among chronic pain, fatigue, and depressive symptoms were explored. In all these analyses we corrected for sex and GMFCS level (categorized in three subgroups: I, II, III/IV) based on clinical and scientific data. Correcting for the distribution of limb impairment instead of GMFCS level showed comparable results. Sex and GMFCS were entered in the first block (basic model), and one of the symptoms was entered in a second block (extended model). For the multivariable models, odds ratios (OR) with 95% confidence intervals (95% CI) and p values are reported. All models were validated using bootstrap analysis, generating 1000 bootstrap samples from the original data, refitting the logistic regression model to each sample, and computing the mean ORs and corresponding bias-corrected 95% CI from the bootstrap estimates. Data analysis was performed using SPSS for Windows (version 16.0; SPSS Inc, Chicago, IL, USA). The bootstrap procedure was performed with Stata 12 (StataCorp, College Station, TX, USA).

**RESULTS**

**Chronic pain**

Seventy-five per cent of the adults with SBCP reported chronic pain (>3mo) compared with 39% of the Dutch reference group in the same age range (p=0.001; Table II). Occurrence of chronic pain did not differ between males and females (p=0.15) or between GMFCS levels (p=0.47). Chronic pain lasting more than 1 year was reported in 68% of the adults with SBCP and was more frequent in females than males (85% vs 58%, p=0.04).

Localization and the number of sites of chronic pain in adults with SBCP and the Dutch reference sample are presented in Table II. Forty-five per cent of the sample described pain related to the muscles or muscle cramps and 18% reported osteoarthritis. Other self-reported causes of pain included tendinitis, arthritis, bursitis, hip dysplasia, carpal tunnel syndrome, and physical overuse.

**Fatigue**

Mean scores for severity of fatigue (FSS) and nature of fatigue (Multidimensional Fatigue Inventory) were higher in persons with SBCP than the Dutch reference samples (p<0.01; Table II). Twenty per cent of the sample was fatigued and a further 41% were severely fatigued. Subgroup analysis showed no effect of sex (p=0.72) on severity of fatigue, whereas a trend was found for GMFCS level (p=0.08).

**Depressive symptoms**

Adults with SBCP had significantly more depressive symptoms than a Dutch reference sample aged 25 to 44 years (25% vs 12%, p=0.004; Table II). No differences were found between males and females for the depressive symptoms scale (p=0.63) or its subscales. Participants in GMFCS level III or IV had a higher total score, as well as higher dimension scores of somatic retarded affect and interpersonal affect (p=0.004, p=0.013, and p=0.009, respectively) than participants in GMFCS level I or II.
Chronic pain, severe fatigue, and depressive symptoms were not related to age or level of education (p values >0.05).

**Co-occurrence and associations of chronic pain and fatigue with depressive symptoms**

Results of analyses of co-occurrence of chronic pain, severe fatigue, and depressive symptoms are presented in Figure 1. Chronic pain and severe fatigue co-occurred in 34% and in combination with depressive symptoms in 16% of the study sample. In the 42 persons with chronic pain, the prevalence of severe fatigue was 45% and depressive symptoms 29% and in those without chronic pain it was 29% and 14%, respectively. Corrected for sex and GMFCS level, chronic pain was not significantly associated with reporting severe fatigue (OR 1.76, 95% CI 0.46–6.79) or depressive symptoms (OR 1.94, 95% CI 0.35–10.64; Table III). In the 23 persons with severe fatigue, 83% had chronic pain and 44% depressive symptoms, compared with 70% and 12% in persons without severe fatigue. Those with more severe fatigue tended to report chronic pain (OR 2.26, 95% CI 1.08–4.72) or depressive symptoms (OR 3.38, 95% CI 1.38–8.30; Table III) more often, after correcting for sex and GMFCS level. Additional bootstrap analyses showed similar results, except for no significant association between severity of fatigue and chronic pain (bootstrap OR 2.26, 95% CI 0.97–10.87).

**Associations of chronic pain and fatigue with daily activities and participation**

Almost two-thirds of the sample reported difficulty in performing daily activities, and one-third in social participation (Table I). Chronic pain or severe fatigue was not significantly associated with difficulty in daily activities or social participation, after correcting for sex and GMFCS level (OR 0.59, 95% CI 0.15–2.39 and OR 0.86, 95% CI 0.18–3.99 for
chronic pain, and OR 0.82, 95% CI 0.43–1.55 and OR 1.12, 95% CI 0.56–2.24 for more severe fatigue). These results seemed to be robust as verified by bootstrap analyses.

**DISCUSSION**

In this study, adults with SBCP without severe cognitive impairment, aged 25 to 45 years, showed a high prevalence of chronic pain, fatigue, and depressive symptoms compared with healthy reference samples. Prevalence of these symptoms was not age or sex specific, nor associated with GMFCS level or level of education, except for more depressive symptoms in persons in GMFCS level III or IV.

The high level of chronic pain observed in the present study is in accordance with the studies of Schwartz et al.\(^4\,_{11}\) The number of pain sites was higher in SBCP than in the general Dutch population of the same age.\(^9\,_{22}\) As with previous studies in adults with CP,\(^1\,_{2,4}\) most pain sites were localized in the back, hips, or lower extremities, which matches the bilateral distribution of CP. In accordance with Murphy et al.,\(^29\) the present sample reported a variety of assumed causes of pain. These may be consequences of spasticity, musculoskeletal deformities, and pathological movement patterns, possibly in combination with overuse of affected areas.

For fatigue severity, similar levels were reported by Opheim et al.,\(^7\) which emphasizes the seriousness of fatigue in adults with SBCP. Three factors may affect fatigue in this population. First, low levels of physical activity and physical fitness may play a role; in fact, in the present sample physical fitness in males was weakly associated with fatigue.\(^2\,\,^{13}\) Second, for CP-related fatigue, central sensitization, psychological
characteristics, or brain damage, such as observed after stroke, may be of influence; however, their role is not yet clear. The present study showed similar levels of physical and mental fatigue in SBCP, whereas Jahnsen et al. found higher levels of physical fatigue, but not mental fatigue, in those with CP than in the general population. Third, pain medication, anti-spastic medication, and anti-depressants may have fatigue as a side effect.

The relatively high prevalence of depressive symptoms in the present sample, especially in persons with lower gross motor functioning, suggests that their lifelong disability may coincide with feelings of depression. Other factors, such as psychological characteristics or brain damage, may also play a role, but were not studied.

Co-occurrence of chronic pain, severe fatigue, and depressive symptoms seemed higher in adults with SBCP than the general Dutch population, reporting 42 to 48% chronic pain and 12% depressive symptoms in persons with fatigue and 8% depressive symptoms in those with chronic pain. The reliability of the co-occurrence rates in the present study might be limited by the small sample size.

Although associations between chronic pain and fatigue have previously been shown in adults with CP, in other diagnoses, and in the general population, our findings did not support this. In the bootstrap analyses the association between chronic pain and fatigue was not confirmed, which might be explained by the small sample size. Contrary to our expectations, chronic pain and depressive symptoms were not related. In addition to the small sample size, this might be due to the relatively young age of the study sample, or to their apparent acceptance of pain as part of their lifelong disability. However, other aspects of the lifelong disability, like deterioration of body functions, might contribute to the development of depressive symptoms. Severity of fatigue and depressive symptoms were associated in our study. This association has been described previously in various populations and is complex. It is unlikely that it can be explained solely by the assessment methods, because fatigue (FSS) and depressive symptoms (CES-D) have been shown to be distinct entities in persons with and without chronic diseases. Owing to the cross-sectional design, as well as the scarce knowledge of the complex mechanisms that might occur between the three symptoms studied, causal interpretation is limited.

In the study sample, neither chronic pain nor fatigue was associated with difficulty in daily functioning. In persons with SBCP these symptoms might not affect functioning as much as they would in able-bodied persons, because activities and participation could have been limited or adapted from an early age. In addition, persons with CP may cope with or become accustomed to pain and fatigue, which may desensitize them to any detrimental effects. Furthermore, the assessment method, which addresses the degree of difficulty and not the frequency of daily activities and participation, might have obscured any association.

Other limitations of the study include the low study participation and some aspects of the assessment methods used. First, the low participation should be mentioned. In the Netherlands there is no national CP register, and less than one-third of the adults with CP are under the regular control of a rehabilitation physician. In fact, only 5% of the present study sample was currently receiving rehabilitation treatment. Consequently, adults with CP are difficult to trace back and may not be inclined to participate in research. Other reasons for the low study participation were a lack of time and burden of the research, including a 48-hour registration with accelerometry for another part of the study. In comparable diagnoses, such as in former polio patients, similar problems in tracing persons and low study participation have been encountered.

Our non-response study identified age (mean difference of 2 years, 6 months) as the only significantly different variable between participants and non-participants; however, because age was not associated with the symptoms studied, no bias for this parameter is expected. In addition, sex, level of education, and GMFCS level were comparable to the subgroup of adults with SBCP without severe cognitive impairment in a representative cohort from the same geographic region, adding to the likelihood of a representative sample.

Finally, some aspects of the methods of assessment should be addressed. The prevalence of chronic pain, fatigue, and depressive symptoms in general populations is relatively high. Therefore, to avoid overestimation of the problem of these symptoms in SBCP, we compared our sample to Dutch reference samples. Depressive symptoms could be over-diagnosed in a population with chronic disease owing to their physical complaints. However, inclusion or exclusion of physical items of the CES-D is known to have a minimal effect on the validity of the dimension scores on this scale. Moreover, physical symptoms are part of the DSM-IV diagnostic criteria of depression and should therefore be taken into account.

Despite some limitations, we believe the present results fill a gap in the literature and contribute to understanding the clinical status of persons with SBCP without severe cognitive impairment at adult age. Future research should focus on developing preventive measures and more effective interventions to reduce chronic pain, fatigue, and depressive symptoms in adults with SBCP.

ACKNOWLEDGEMENTS
We thank all the participating adults with CP. We acknowledge Helen Luiting for her contribution to the data collection and Sten Willemse for statistical advice (Department of Biostatistics, Erasmus Medical Center, Rotterdam). This work was supported by the Johanna Children’s Fund, the Children’s Fund Adriaanstichting (grant number 2003/0047-063), and the Foundation Erasmus Pain Fighting Fund, the Netherlands. Members of the Transition
Additional material and supporting information for this paper may be found online.

Data S1: Questionnaires and reference samples.

REFERENCES


Appendix SI: Members of the Transition Research Group.

Please note: This journal provides supporting online information supplied by the authors. Such materials are peer reviewed and may be re-organized for online delivery, but may not be copy-edited or typeset. Technical support issues or other queries (other than missing files) should be addressed to the authors.