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Original Research Article

Self-Reported Presence and Experience of Pain in Adults with Down Syndrome

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Abstract

Objective. The aim was to examine whether the presence of pain (based on physical conditions and participants' report) and self-reported pain experience in adults with Down syndrome (DS) differ from general population controls.

Design. Cross-sectional study of 224 adults with DS (mean age = 38.1 years, mild-severe intellectual disabilities) and 142 age-matched controls (median age = 40.5 years, mean estimated IQ = 105.7) in the Netherlands.

Methods. File-based medical information was evaluated. Self-reported presence and experience of pain were assessed in rest and after movement during a test session (affect with facial affective scale (FAS: 0.04–0.97), intensity assessed with numeric rating scale (NRS: 0–10).

Results. Compared with controls, more DS participants had physical conditions that may cause pain and/or discomfort ($p = .004$, 50% vs 35%), but fewer DS participants reported pain during the test session ($p = .003$, 58% vs 73%). Of the participants who indicated pain and comprehended self-reporting scales ($n = 198$ FAS, $n = 161$ NRS), the DS group reported a higher pain affect and intensity than the controls ($p < .001$, FAS: 0.75–0.85 vs 0.50–0.59, NRS: 6.00–7.94 vs 2.00–3.73).

Conclusions. Not all adults with DS and painful/discomforting physical conditions reported pain. Those who did indicated a higher pain experience than adults from the general population. Research into spontaneous self-report of pain, repeated pain assessment, and acute pain is needed in people with DS for more insight into pain experience and mismatches between self-report and medical information.

Key Words. Down Syndrome; Pain Assessment; Clinical Significance

Introduction

An increased life expectancy [1] for people with Down syndrome (DS) and a greater incidence of indications for premature aging [2] mean that people with DS have a greater risk of developing age-related painful physical conditions, such as cervical arthritis [3,4]. DS itself is already characterized by a vulnerability to painful and discomforting physical conditions, such as middle ear infections [5,6] and skin problems [7,8]. It is unclear whether all people with DS affected by painful conditions also report pain, as some people with intellectual

disabilities underreport their pain [9,10] and people with DS have a low tendency to complain about pain [4]. Detecting pain in people with intellectual disabilities may be complicated by their communication difficulties [11], reduced insight into their own health [11], idiosyncratic pain responses [12–14], the wish not to bother others or to waste their time [9], and being afraid of doctors or the reactions of others [9,15]. Insight into the presence of pain may promote early pain detection by caregivers and medical professionals. This is clinically relevant because undertreatment of pain in adults with intellectual disabilities has been reported [16,17] and pain could negatively influence quality of life [18].

It is also relevant to increase the awareness of health care workers that the pain experience in people with intellectual disabilities may be different than in the general population. According to the most recent review [19], people with DS appear to have a delayed pain expression but could be actually more sensitive to pain. The delayed pain response may be caused by a disturbed sensory transmission due to a slower peripheral [20,21] and/or central processing [22–24]. The higher pain sensitivity may be caused by a magnified nociception and/or an inefficient pain inhibition [19]. This possibility is supported by findings in people with DS of a reduced connectivity in the dorsal prefrontal cortex [25], a reduced gray matter volume in the frontal lobes [26,27], and a reduced white matter volume in the frontal lobes and brain stem [28]. The frontal lobe, especially the dorsal prefrontal cortex, is involved in pain modulation [29]. Because gray matter volume of frontal areas is positively correlated to cognitive functioning in DS [30], the reduced gray matter [26,27] may lead to a decline in cognitive functioning. Therefore, the reduced connectivity in the dorsal prefrontal cortex and reduced gray matter volume in the frontal lobes could result in inefficient pain inhibition. The brain stem is another region involved in pain modulation [31]. It is known that white matter pathology may result in a higher pain experience [32,33], for example, by disrupting the connection between cortical and subcortical brain areas [34]. Therefore, the reduced white matter volume in the frontal lobes and brain stem could disturb the inhibitory control of pain and magnify the nociceptive process.

Empirical evidence for a higher pain experience in DS is limited to two findings: 1) a longer persisting pain response after medical procedures in babies with DS compared with a control group [35] and 2) a lower heat-pain threshold in individuals with unspecified intellectual disabilities or DS compared with a control group after correction for reaction time [21]. The difference in the heat-pain threshold was not statistically significant between the DS participants and the control group ($p = 0.059$) and a lower heat-pain threshold has also been found in DS without correction for reaction time [36].

In contrast, arguments also exist for a lower pain experience in DS. For example, high concentrations of endogenous opioids leu-enkephalin and dynorphin A in the frontal cortex [37] may cause a strong pain inhibition. Further, the reduced volume of the hippocampus, amygdala, insula, and anterior cingulate cortex [26,27] may decrease suffering from pain because these brain areas process the emotional aspect of pain [38,39]. In addition, a lower volume of the hippocampus, insula, and anterior cingulate cortex in DS may directly or indirectly relate to worse cognitive functioning [30,40], suggesting that these brain areas could also function abnormally in the processing of the emotional aspect of pain. Empirical evidence for a decreased pain experience in DS is, however, scarce and should be interpreted cautiously because it may be explained at least partly by a delayed pain expression [19], an impaired verbal expression [4], and unique pain behavior that is difficult to recognize [41].

In short, a hypothesis about pain experience in DS remains unclear because the empirical evidence is not robust, the possible implications of neuropathology are contradictory, and the neuropathology does not necessarily lead to a different pain experience. Both a higher and a lower reported pain experience would be clinically relevant. A higher pain experience could result in behavioral problems and unnoticed suffering from pain (i.e., due to the tendency in DS to express medical problems with problematic behavior instead of complaining about pain) [4], while a lower pain experience increases the risk for unnoticed injury. Important aspects of pain are intensity (i.e., sensory dimension of severity [42]) and affect (i.e., perceived unpleasantness [42]).

The aim of the present study was to examine whether the presence of pain (based on physical conditions and participants' report) and the self-reported pain experience (affect and intensity) in adults with DS differ from those in general population controls.

Methods

Study Design

The design was a cross-sectional study with between-subject comparisons in 224 adults with DS and 142 adults from the general population. Participants were assessed during one test session for both pain (in rest and after movement) and demographic measures (estimated intelligence level in both groups, language comprehension in DS group, and education level in control group).

Ethical Approval

The Medical Ethical Committee of VU University Medical Center Amsterdam (NL33540.029.11) approved the study and informed consent procedure.

Participants of Down Syndrome Group

Participants with DS were recruited from 17 care centers for people with intellectual disabilities in locations throughout the Netherlands. Before the start of the study, the care centers' caregivers and behavioral specialists assessed inclusion and exclusion criteria per client. Other participants with DS were recruited through the Dutch Down Syndrome Foundation Web site. Inclusion criteria were: being 18 years or older, speaking and understanding Dutch, the capability to verbally answer simple questions, and a clinical impression of testability. This latter inclusion criterion implied that adults with DS could participate, regardless of their level of intellectual disability, as long as they could comprehend the instructions for at least some of the tests. Exclusion criteria were: the presence of neurological diseases such as cerebrovascular accidents, tumors, or dementia; the presence of severe visual impairments or hearing loss; and the use of antipsychotics, anticonvulsants, or antidepressants due to possible neuropsychological side effects [43,44].

To screen participants aged 40 years and older for a possible indication of dementia, scores for the Social Functioning Scale for Intellectual Disability (i.e., SRZ or SRZ-P: see paragraph about estimated intellectual disability level) [45,46] and the Dementia Questionnaire for Intellectual Disability [47] were examined for two moments in time (i.e., with data from the current study, and with previously collected data from the participants' files), with at least six months between them to assess deterioration over time. A possible indication of dementia was considered to be present if the decrease in the total scores of the questionnaires was statistically significant according to criteria in the manuals. This procedure resulted in the exclusion of eight people. The final group consisted of 224 adults with DS.

Participants had to provide informed consent to be included in the study. If there was doubt regarding their capacity to provide informed consent, consent was also required from family members or guardians. All tests were performed in a quiet room of the care center or home where participants lived.

Participants of Control Group

Inclusion criteria for the control group were: being age 18 years or older and speaking and understanding Dutch. Exclusion criteria were: the presence of neurological diseases or neuropsychological impairment; the presence of visual impairments or hearing loss that would influence the tests; the presence of depressive symptoms or an anxiety disorder; excessive alcohol use; and the use of anticonvulsants, antidepressants, or antipsychotics. The Mini-Mental State Examination (MMSE) [48] was used to screen for the presence of neuropsychological impairment. All participants scored above the cut-off [49], suggesting that evident neuropsychological impairment was absent.

Inclusion and exclusion criteria were used to recruit potential participants. General practitioners were asked to approach potential participants from their general medical practice, which resulted in five participants. Potential participants who varied in age, gender, and level of education were also recruited in the personal environments of the researchers. An information letter with consent form was sent to potential participants. After the form was signed, the test session took place in the general medical practice or at home. The final group consisted of 160 control participants.

Because the average age was higher in the control group than in the DS group (t (256) = 3.46, $p = 0.001$, $r = 0.21$) and the maximum age of the DS group was 65 years, controls older than 65 years were excluded. The age-matching of groups resulted in an age range of 18–65 years in both groups, a statistically nonsignificant group difference in age ($U = 14613.50$, $p = 0.19$, $r = -0.07$), and a reduction from 160 to 142 participants in the control group.

Sample Size Calculation

According to the statistical program Gpower [50] with $\alpha = 0.05$, $\beta = 0.80$, and a medium effect size, the following sample sizes were required: $N = 88$ for comparing groups on presence of pain according to physical conditions and participants' report (obtained: $N = 366$) and $N = 68$ for comparing groups on pain experience with one covariate (obtained: $N = 156$).

Estimated Level of Intellectual Disability and Intelligence in the Down Syndrome Group

Information on intellectual disability level was obtained from the Social Functioning Scale for Intellectual Disability (i.e., SRZ or SRZ-P). The SRZ and SRZ-P can be used to assess social and cognitive abilities and activities of daily living and is used with those who have been observed to demonstrate a higher level of functioning. Caregivers were asked to identify the scale they believed was most appropriate for the participant's level of functioning. By using the population norms of the manual, the SRZ total score was converted into a standardized score, which was then converted into an estimated level of intellectual disability using the Manual of Psychodiagnostics and Limited Ability [51]. In order to be able to compare the estimated intellectual disability level of the participants, the intellectual disability levels for all participants were based on the SRZ. Participants for whom only the SRZ-P score was available were identified as having a mild level of intellectual disability according to the SRZ.

The level of intelligence was estimated using the subtests Block Design and Vocabulary of the Wechsler Preschool and Primary Scale of Intelligence–Revised Version (WPPSI-R) [52]. Participants had to construct patterns with blocks within a limited time and to

describe the meaning of words. Afterwards, the age equivalents in years and months corresponding to the raw scores of the two subtests were retrieved from the Manual of Psychodiagnostics and Limited Ability [51], and the mean age equivalent was calculated.

Language Comprehension and Vocabulary in the Down Syndrome Group

Language comprehension was screened by the two sample sentences and the first 10 sentences of Sentence Comprehension, a subtest of the Dutch Aphasia Foundation test (Dutch: Zinsbegrip subtest, Stichting Afasie Nederland test [53]). Participants chose drawings corresponding to sentences that were read aloud by the researcher in a neutral tone. When the researcher noticed that the participant chose randomly, then the instructions were repeated. Possible scores in this study ranged from 0 to 10. For vocabulary, the age equivalent of the vocabulary subtest of the WPPSI-R was used.

Medical Information in the Down Syndrome Group

We tried to avoid underestimation of painful conditions in the DS group. People with DS tend to visit physicians less often than people from the general population due to a low tendency to complain about pain. Therefore, we collected current information about physical conditions and pain complaints from caregivers or family members. Caregivers for participants with DS provided the researcher with file-based medical information. Family members used their personal records to provide such information. Physical conditions, complaints, and medication administered for painful/discomforting conditions were used to determine the possible presence of pain or discomfort. Both physical conditions that theoretically could cause pain/discomfort (such as arthrosis) and complaints (such as back pain) were included as "possible pain and/or discomfort." In cases of indefinite diagnoses or doubt, the most certain information was used (e.g., "back problems due to wearing and tearing, possible arthrosis" was coded as "back problems due to wearing and tearing" instead of "arthrosis").

To check that the medical information provided by proxy was accurate and complete, the medical files of 28 (12.5% of 224) randomly chosen participants were collected post hoc from the care center for people with intellectual disabilities or, if the participant was living at home, from the general physician. After comparing the information collected post hoc with the information provided during the study, it was found that 71.4% ($n = 20$) of the files were comparable concerning the physical conditions that may cause pain or discomfort. For the rest of the files, it appeared that the number of painful/discomforting conditions may have been overestimated (10.7%, $n = 3$) or underestimated (17.9%, $n = 5$). In short, this sample suggests that in 89.3% of the cases, the number of physical conditions possibly causing pain/discomfort based on the medical information available during the study was similar or even underestimated in comparison with the medical files from the care center or the general physician.

Because it is somewhat unclear when discomfort transits into pain, no distinction between pain and discomfort was made. Although pain and discomfort are not the same, information regarding both possibilities was therefore collected. One physiotherapist (EJAS), one general physician, and two specialized physicians for people with intellectual disabilities rated whether the physical conditions could be expected to cause pain or discomfort. The two specialized physicians for people with intellectual disabilities first reached a consensus, resulting in one list of ratings from the physiotherapist, one list from the general physician, and one list from the two specialized physicians for people with intellectual disabilities. The raters were blind to the ratings by the other professionals. A Fleiss' kappa of 0.66 was found, indicating a substantial agreement between the three lists [54]. A physical condition was ultimately rated as possibly causing pain or discomfort when at least two of the three professionals indicated that this could be the case.

Only information about analgesics as treatment for the painful/discomforting physical conditions was used because the variety of nonpharmacological treatment (e.g., lotions, physical therapy, special toothpaste, fiber-rich food) was too extensive.

Level of Education in the Control Group

The Verhage Education System is a Dutch seven-point scale for the highest education level completed by an individual, ranging from level 1 ("less than elementary school") up to and including level 7 ("university or technical college") [55].

Estimated Intelligence Level in the Control Group

The Groninger Intelligence Test II is a Dutch intelligence test battery containing 10 different tests (GIT-2) [56]. Its reliability and validity are satisfactory to good [57]. The short form contains six tests: Synonyms, Mental Rotation, Visual Synthesis, Mental Arithmetic, Word Analogies, and Fluency (animals and professions). The correlation of $r = .94$ between IQ scores from the short GIT-2 and the total GIT-2 means that the short GIT-2 IQ is a good estimation of the total GIT-2 IQ [56].

Medical Information in the Control Group

General medical information about the participants was obtained from the medical files of the general physician for the year preceding and up to the time of the test. The procedure to determine the possible presence of pain or discomfort was the same as in the DS group.

Reported presence of pain in the Down Syndrome Group

Pain was assessed during the test session in one rest situation and four movement situations. If participants felt pain in more locations per test situation, then they were asked to indicate which location was the most painful. The rest situation preceded the movement situations to prevent carryover effects of pain due to movement. The movement situations were included for a more representative assessment of daily pain. People with musculoskeletal pain report a higher pain intensity in more physically demanding activities, such as walking compared with sitting [58]. In addition, cognitively impaired people with musculoskeletal pain may forget their pain at rest [59]. Therefore, acute pain or discomfort of the involved musculoskeletal structures (i.e., muscles and joints) was provoked during function by encouraging participants to push the maximum limits of their movement capabilities.

In the rest situation, participants were asked whether they felt any pain at that moment. If this was not the case, then they were asked whether they had felt pain during the day of the test session or in the preceding week. When participants answered affirmative to any of these questions (i.e., reported the presence of pain), then they were asked to point to the painful location on their own body.

Subsequently, participants were asked to imitate four series of active movements as demonstrated by the researcher in a standardized order: 1) movement of the legs and hips (rising from the chair, walking to the end of the room and back, and sitting again), 2) movement of the neck, shoulders, elbows, wrists, and fingers (moving the chin to the ceiling, to the chest, and to the shoulders, stretching the arms upwards and sideways, stretching the arms forward and touching the shoulders with the hands, stretching the arms forwards again to rotate the wrists, and "playing the piano" with fingers), 3) movement of the back (touching the toes with stretched legs and standing up again to rotate the torso), and 4) movement of the jaw (opening the mouth as far as possible). Directly after each series (i.e., four times in total), participants were asked whether they felt any pain during the movements and, if so, where this was. Each series was performed once.

Self-Reported pain Affect and Intensity in the Down Syndrome Group

Self-reported pain experience was only assessed when participants' answers on the comprehension test matched the a priori determined answers. The comprehension test had a least-most extremes format for the first 48 participants with DS and an ordering/magnitude format for the rest of the DS group and the control group. This difference is the result of refining the comprehension test to further increase the reliability because the use of unordered scale items for the test would more accurately represent the comprehension of the scale [60]. "Comprehension" in this context refers to the ability to understand the ordinal position of the scale items such as numbers or faces, not the ability to translate the own pain experience into one of the scale items. The formats of the comprehension test will be described next per self-reporting scale.

For pain *affect*, the facial affective scale (FAS) [61,62] was used. This is an ordinal series of nine drawn faces with expressions ranging from no distress to utter distress, with values from 0.04 (maximum positive affect) to 0.97 (maximum negative affect) printed on the back side [62]. The FAS relates more to pain affect than to pain intensity [63]. The examiner asked: "Which face fits best with how the pain makes you feel inside?"

In the least-most extremes format of the FAS, the nine faces were shown in the original presentation (see Figure 1). Participants were asked which face represents someone with "least pain." The first and second faces (i.e., faces with values 0.04 and 0.17 in Figure 1) were considered to be correct. Participants were then asked which face represents someone with "most pain." The last face and the one before it (i.e., faces with values 0.97 and 0.85 in Figure 1) were considered to be correct. In participants who answered both questions according to the intended answers and who reported pain, pain affect was assessed. The same original presentation of nine faces was shown, and participants were asked which face corresponded to the reported pain.

In the ordering format of the FAS, three faces were presented in the order of severe pain, mild pain, and moderate pain (see Figure 2) while participants were asked to arrange the faces in the correct order. In participants who both chose the intended order (from mild to severe pain) and reported pain, pain affect was assessed by using a set of cards (see Figure 3). During each test situation in which pain was assessed, the original option of choosing between nine faces was modified to the option of choosing two times between three faces. Card A was first shown and participants were asked which face corresponded to the reported pain (choice 1). When the left face of Card A was chosen, Card B was shown and participants were again asked which face corresponded to the reported pain (choice 2). When the middle face of Card A was chosen, Card C was shown and participants were asked which face corresponded to the reported pain (choice 2). When the right face of Card A was chosen, Card D was shown and participants were asked which face corresponded to the reported pain (choice 2). The final chosen face from Card B, C, or D was noted.

For pain *intensity*, the numeric side of the colored analogue scale [61,62] was used. This scale is referred to in the rest of the manuscript as "numeric rating scale (NRS)." It consists of a vertical "ruler" ranging

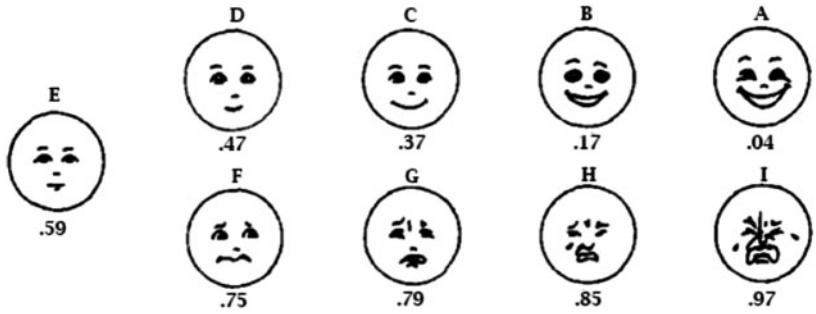

Figure 1 Faces and their corresponding values of the facial affective scale [61]. This is the backside: The front side (faces without letters and numbers) was presented to participants. Photocopy of test material (first author). Patricia A. McGrath, Pain in Children – Appendix: Pain Assessment, Guilford, New York, United States of America, Copyright 1990.

Figure 2 Facial affective scale: comprehension test with ordering format. Three faces were presented in the order of severe pain, mild pain, and moderate pain. Participants were requested to arrange the faces from "least pain" to "most pain." The intended order was from mild to severe pain (corresponding to the McGrath's values of 0.17, 0.75, and 0.85).

continuously from 0 to 10 with a plastic slide. A higher score indicated more pain. The examiner instructed: "Please place the plastic slide on the number that shows how much pain you have."

In the least-most extremes format of the NRS, participants were asked at what level the slide should be positioned when someone has "least pain" and at what level when someone has "most pain" (see Figure 4). Answers that were considered to be correct were 0 or 1 and 9 or 10, respectively. In the ordering format of the NRS, two questions were added that focused on the magnitude of numbers: "What is more: 2 or 8?" and "What is more: 6 or 4?" In participants who answered all questions according to the intended answers and who reported pain, pain intensity was assessed. The NRS was presented with the plastic slide in the middle, and participants were asked to place it on the number corresponding to the reported pain.

For participants who passed the comprehension test according to the intended response but who did not have pain, the FAS value of 0.04 (corresponding to the face with the lowest pain affect) and the value of 0 (corresponding to the lowest pain intensity) were used, respectively.

Assessment of Reported pain in the Control Group

The procedure for assessing the reported presence and experience of pain in the control group was the same as in the DS group, including the comprehension tests of the self-reporting scales.

Statistical Analysis

Statistical analyses were performed using SPSS 21. The level of statistical significance was set at $\alpha = 0.05$ (two-sided). Pain was assessed during the test session in one rest situation and four movement situations. Thirteen participants were not able or willing to perform all four movement series. Because the sum of the FAS scores (Cronbach's $\alpha = 0.65$) and the sum of the NRS values (Cronbach's $\alpha = 0.55$) were highly correlated ($r_s = 0.91$, $p < 0.001$), a domain of pain experience was formed by taking the mean of the FAS and NRS standardized scores (Cronbach's $\alpha = 0.79$). This domain was only used in the multiple linear regression analysis. Measures for pain affect (FAS), pain intensity (NRS), and pain experience (mean of FAS and NRS) were based on participants who comprehended the self-reporting scale. The scale scores for these participants was 0.04 (FAS) or 0 (NRS) in situations with self-reported absence of pain.

The main analyses were: 1) Mann-Whitney U tests (i.e., for continues variables) and Chi-squared tests (i.e., for dichotomous variables) to compare groups on demographic and medical characteristics, 2) Chi-squared tests to compare groups on the presence of pain based on participants' report, and 3) multiple linear regression

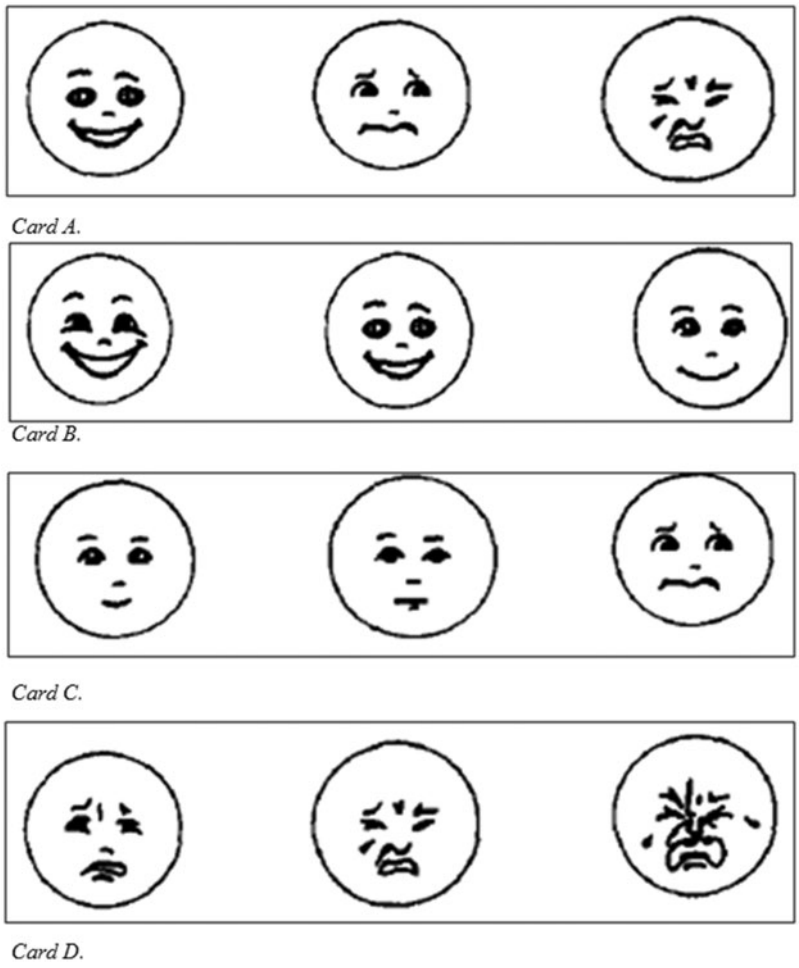

Figure 3 Facial affective scale, divided into three different parts. Card A was first shown, and participants were asked which face corresponded to the reported pain. When the left face of Card A was chosen, the question was repeated while showing Card B. When the middle face of Card A was chosen, the question was repeated while showing Card C. When the right face of Card A was chosen, the question was repeated while showing Card D.

to relate group with self-reported pain experience while taking the presence of physical conditions that may cause pain and/or discomfort into account. All assumptions of the regression analyses were met [64]. Multilevel analysis was not necessary. The dichotomous variable "possible pain/discomfort" was based on medical information (e.g., in relation to physical conditions). The dichotomous variable "presence of pain according to participant's report" and the continuous variable "self-reported pain experience" referred to the presence and ratings (i.e., affect and intensity) of pain as reported by participants during the test session.

Results

Presence of pain According to Medical Information

Group characteristics and group differences were described in Table 1. The number of participants with physical conditions that may cause pain/discomfort was larger in the DS group than in the control group. The categories of physical conditions that may cause pain/discomfort were described in Table 2.

Presence of pain According to participant's Report

Fewer participants in the DS group than the control group reported pain during the test session ($X^2(1) = 8.71$, $p = 0.003$, $Phi = -0.15$, 58% vs 73%), but only at rest ($X^2(1) = 21.54$, $p < 0.001$, $Phi = -0.24$, 44% vs 69%) and not during active movements ($X^2(1) = 0.11$, $p = 0.74$, $Phi = 0.02$, 43% vs 42% pain during at least one series). The most painful locations self-reported by DS participants were the trunk front side in rest and during transfers, the neck during upper body movements, the back during back movements, and the cheek during jaw movement. The most painful locations self-reported by control participants were the trunk back

Figure 4 Colored analogue scale for pain, numeric side [61]. Photocopy of test material (first author). Patricia A. McGrath, Pain in Children – Appendix: Pain Assessment, Guilford, New York, United States of America, Copyright 1990.

side in rest and during transfers (also the head in rest), the neck during upper body movements, the legs during back movements, and the throat/neck during jaw movement.

Of those with physical conditions possibly causing pain/discomfort, 68% ($n = 77$) of the DS participants and 76% ($n = 38$) of the control participants reported pain during the test session (in rest and/or during movement). A mismatch in the presence of pain according to participant's report vs medical information was more prevalent in the control group than in the DS group ($X^2(1) = 8.09$, $p = 0.004$, $Phi = -0.15$, 55% control vs 40% DS).

The question arises whether the participants' report of presence of pain was reliable in participants with DS who did not comprehend any of the scales for self-reported pain experience because these participants may fail to understand the general concept of pain. The association between comprehending self-reporting scales and reporting pain presence during the test session was not statistically significant (see Table 3). However, reporting pain presence was associated with the presence of pain/discomfort according to medical information within participants who comprehended at least one of the self-reported scales ($X^2(1) = 9.05$, $p = 0.003$, $Phi = 0.23$), whereas this was not the case within participants who did not comprehend any of the scales ($X^2(1) = 0.06$, $p = 0.81$, $Phi = 0.04$). Within the DS group, estimated intelligence level was compared between participants with a mismatch in the presence of pain according to participant's report vs medical information and participants without such a mismatch. The difference in estimated intelligence level was statistically significant (t (190.11) $= 2.04$, $p = 0.043$, $r = 0.15$), in which participants with a mismatch ($M = 4.80$) had a lower estimated intelligence level.

Self-Reported pain Experience

More participants in the control group than in the DS group comprehended the scales for pain affect ($X^2(1) = 41.64$, $p < 0.001$, $Phi = -0.34$, 100% vs 75%) and pain intensity ($X^2(1) = 114.96$, $p < 0.001$, $Phi = -0.57$, 99% vs 43%). Of the DS participants, 79% ($n = 173$) comprehended at least one scale. Within the DS group, participants who comprehended a pain scale had a lower age (applied only to NRS), a higher estimated intelligence level, a better vocabulary, and better language comprehension than participants who did not comprehend a pain scale (see Table 3). All analyses on self-reported pain experience in the following paragraphs included only participants who comprehended the self-reporting scale.

The self-reported pain experience of the groups during the test session is described in Table 4 per situation (i.e., rest, transfer, upper body, back, and jaw in only the participants who reported pain in that specific situation) as well as for the entire test session (i.e., summed and averaged pain ratings in all participants who reported pain in at least one situation). In both groups, all participants who used analgesics had possible painful/discomforting conditions. Due to the very small number of participants who both used pain medication and comprehended the self-reporting pain scales, the self-reported pain experience could not be compared between users and nonusers of pain medication.

While controlling for the presence of physical conditions that may cause pain/discomfort, the pain experience was higher in the DS group than the control group (F (1, 153) $= 28.69$, $p < 0.001$, $B = -0.74$, $pn^2 = 0.16$, $n = 156$). The group variances for this analysis were unequal, resulting in a somewhat liberal F-ratio, but that probably had no influence because of the relatively large effect size.

Table 1 Demographic and medical characteristics of the Down syndrome and control groups

Characteristic	Down syndrome group ($N = 224$): N	Control group ($N = 142$): N	Group difference
Age (range is 18–65 y in both groups)	$M = 38.1$ y ($SD = 11.1$)	$Mdn = 40.5$ y ($IQR = 25$)	$U = 14{,}613.50$, $p = 0.19$, $r = -0.07$
Gender: male	118 (53%)	65 (46%)	$X^2(1) = 1.66$, $p = 0.20$, $Phi = -0.07$
Living situation: in care center or with family	197 (88%), 27 (12%)	–	–
Intellectual disability[†]: mild, moderate, severe	56 (25%), 147 (66%), 21 (9%)	–	–
Estimated intelligence level (y age equivalent[‡])	201 (87%), $M = 5.0$ ($SD = 1.5$)	$M = 105.7$ ($SD = 13.3$) IQ	–
Education: most frequent level (level 6)	–	68 (48%)	–
Mini-Mental State Examination score	–	Mdn = 29.0 (IQR = 1)	–
Language comprehension (number of words)	217 (94%), $M = 8.1$ ($SD = 1.6$)	–	–
Vocabulary (y age equivalent)	207 (89%), $Mdn = 4.1$ ($IQR = 2.0$)	–	–
Sleep problems and/or symptoms of depression*	15 (7%): 1 (7%) sleep medication	2 (1%): no medication	$X^2(1) = 5.49$, $p = 0.019$, $Phi = 0.12$
Present analgesics use	10 (5%)	6 (4%)	$X^2(1) = 0.01$, $p = 0.91$, $Phi < 0.01$
Physical conditions possible pain/discomfort*	113 (50%)	50 (35%)	$X^2(1) = 8.17$, $p = 0.004$, $Phi = 0.15$
Number of categories possible pain/discomfort	$Mdn = 1.0$ ($IQR = 1.0$)	$Mdn = 1.0$ ($IQR = 1.0$)	$U = 2{,}448.50$, $p = 0.12$, $r = -0.12$

*Indicates significance $p = 0.05$.

[†]The difference between the three subgroups based on intellectual disability level did not reach statistical significance for age ($H(2) = 0.01$, $p = 1.0$, $r = -0.001$ to -0.01), gender ($X^2(2) = 0.56$, $p = 0.76$, *Cramer's* $V = 0.05$), and presence of possible pain/discomfort ($X^2(2) = 2.97$, $p = 0.23$, *Cramer's* $V = 0.12$).

[‡]Years age equivalent is comparable with mental age (i.e., an average mental age of five years). Physical conditions possible pain/discomfort: number of participants with a possible presence of pain or discomfort according to medical information (physical conditions, complaints, and medication use).

Table 2 Categories of pain/discomfort according to medical information in the Down syndrome group and control group

Category	DS: *N*	CG: *N*	Category	DS: *N*	CG: *N*
Skin condition*	**31**	**15**	Stomach pain or discomfort (e.g., gastric acid)/gastroesophageal reflux disease	9	2
Subcutaneous inflammation/varicose veins	4	0	Constipation/bowel disease/intestine problems/pain abdomen	**27**	4
Headache/migraine	2	**8**	Hip dysplasia/stiff or worn hip joints/ hip pain or complaints	11	0
Eye irritation or inflammation	7	0	Urine tract infection/infection of the bladder/urethral stricture	2	3
Ear pain or inflammation	1	0	Severe period pain	3	2
Sinusitis (causing toothache and headache)	0	1	Vaginitis	0	3
Tooth ache/pain in jaw/pain associated with partial or full dentures	7	1	Knee pain or complaints (e.g., long ligaments)/patella luxation	14	2
Chronic inflammation of the gums	11	0	Toe/foot/ankle/leg pain or discomfort	5	3
Neck deformation/neck pain	3	3	Deviant foot position†	11	1
Shoulder pain (e.g., due to bursitis or lesion)	2	2	Arthrosis	3	**9**
Cervicobrachialgia/Ulnar Neuropathy	0	3	Albers Schönbergs disease	1	0
Dupuytren's contracture/Carpal Tunnel syndrome	1	3	Bone necrosis (knee and/or hip)	2	0
Wrist pain/hand joint pain	2	1	Gout	4	1
Chest pain/syndrome of Tietze/contusion rib	2	1	Fractures	0	2
Back pain (e.g., lumbago)/vack problems due to wearing/scoliosis	**17**	5	Muscle pains/spasm or cramp‡	6	0

The bold numbers in the columns represent the top three most prevalent category per group. Some participants had conditions in several categories or several conditions in the same category.
*Callus, psoriasis, eczema, not healing wounded toe, boils, inflammation/cyst fingertips, abrasive skin irritation, erysipelas, lichen simplex chronicus, piles, hidradenitis suppurativa, open wounds, intertrigo, fungal infection.
†Pes equinus, pes quinovarus adductus, pes cavus, hallux valgus.
‡Spasm/cramp in neck, back, jaw, oesophagus, legs, or foot.

Discussion

Presence of pain

The first main finding of the present study was that more adults with DS than adults from the general population had possible painful physical conditions, but fewer adults with DS reported the presence of pain during the test situation. The relatively high prevalence of possible painful conditions in DS is in line with the syndrome-specific vulnerability to conditions such as neck pain and early-onset arthritis [65,66]. The relatively low prevalence of the reported presence of pain may be explained in several ways. The physical conditions that were mentioned in the medical information could have been based partly on spontaneous pain complaints (i.e., back pain), whereas the presence of pain based on participants' report during the test session was based on questions and evoked pain. The physical conditions may not have caused pain during the test assessment due to the fluctuating nature of symptoms, or the movement series during the test session may not have been severe enough to induce pain. If pain was present, then general explanations for underreporting pain by people with intellectual disabilities may apply: communication difficulties, the wish not to bother others or to waste their time, being afraid of the reactions of others, and being afraid of doctors [9–11,15].

Concerning the aforementioned possible explanations of the difference between the medical information and the test session, it is unsurprising that a mismatch occurred in a subgroup of participants. This was also the case in the control group. Still, clinical awareness for such mismatches should be especially increased for people with DS because these individuals are more likely to have difficulties with reporting the presence of pain during a test session and in daily life. The results show that a lower estimated intelligence level and no comprehension of the self-reporting scales are related to a mismatch. It is possible that these individuals do not comprehend the concept of pain when the presence of pain is asked during the test session or during a medical consult. It is further possible that they have difficulties with expressing spontaneous pain complaints and with nonverbal pain communication, reducing the chance that pain is noticed and included in a medical record.

Table 3 Relationship between comprehending self-reporting scales and other variables in Down syndrome

Variable	Statistic	*p*	Effect size	*N*	Statistic	*p*	Effect size	*N*
Age	t (222) = 2.64 Yes: M = 37.0 y No: M = 41.4 y	0.009	r = 0.18	224	t (218) = 5.48 Yes: M = 34.0 y No: M = 41.7 y	<0.001*	r = 0.35	220
Gender	X^2(1) = 1.17	0.28	*Phi* = -0.07	224	X^2(1) = 1.79	0.18	*Phi* = −0.09	220
Intellectual disability level	X^2(2) = 10.03	0.007	*Cramer's V* = 0.21	224	X^2(2) = 6.83	0.033	*Cramer's V* = 0.18	220
Estimated intelligence	U = 1332.00 Yes: *Mdn* = 5.1 y AE No: *Mdn* = 4.0 y AE	<0.001*	r = 0.44	195	t (193) = -7.45 Yes: *Mdn* = 6.0 y AE No: *Mdn* = 4.1 y AE	<0.001*	r = 0.47	195
Vocabulary	U = 1372.00 Yes: *Mdn* = 5.0 y AE No: *Mdn* = 3.1 y AE	<0.001*	r = −0.48	200	U = 1846.00 Yes: *Mdn* = 5.1 y AE No: *Mdn* = 4.0 y AE	<0.001*	r = -0.52	207
Language comprehension	U = 1956.50 Yes: *Mdn* = 9.0 words No: *Mdn* = 7.0 words	<0.001*	r = 0.38	209	U = 2689.50 Yes: *Mdn* = 9.0 words No: *Mdn* = 8.0 words	<0.001*	r = 0.42	213
Symptoms of autism	Fisher's exact test	0.47	*Phi* = -0.06	224	Fisher's exact test	0.76	*Phi* = −0.03	220
Possible pain/discomfort	X^2(1) = 0.01	0.94	*Phi* = 0.01	224	X^2(1) = 0.41	0.52	*Phi* = −0.04	220
Self-reported presence of pain (during test session)	X^2(1) = 0.61	0.43	*Phi* = -0.05	224	X^2(1) = 1.41	0.24	*Phi* = 0.08	220

Results in gray cells correspond to the facial affective scale; results in white cells correspond to the numeric rating scale. Yes = participants who passed the comprehension test of the pain scale, No = participants who failed the comprehension test of the pain scale.
*Indicates significance (p = 0.006, p = 0.05/9 due to multiple testing).
AE = age equivalent.

Table 4 Pain ratings of participants who reported to be in pain during the test session

Group	Pain affect (scale: 0.04–0.97, substantial pain $\geq$ 0.75)				Pain intensity (scale: 0–10, moderate pain $>$ 4)			
	M	*SD*	Range	*N*	*M*	*SD*	range	*N*
DS (in rest)	*Mdn* = 0.85	*IQR* = 0.22	0.04–0.97	71	7.34	2.58	0.00–10.00	41
DS (transfer movement)	*Mdn* = 0.79	*IQR* = 0.22	0.17–0.97	36	7.94	1.68	5.00–10.00	22
DS (upper body movement)	*Mdn* = 0.75	*IQR* = 0.10	0.04–0.97	31	6.36	2.97	0.25–10.00	20
DS (back movement)	0.78	0.17	0.37–0.97	31	6.00	2.30	2.00–10.00	21
DS (jaw movement)	0.77	0.16	0.47–0.97	12	6.67	2.60	3.00–10.00	9
DS (summary test session)*	0.75–0.85	0.16–0.22	0.04–0.97	12–71	6.00–7.94	1.68–2.79	0.00–10.00	9–41
DS (sum test session)†	*Mdn* = 1.62	*IQR* = 1.15	0.12–4.85	95	*Mdn* = 11.25	*IQR* = 12.75	0.00–45.00	60
DS (average test session)	*Mdn* = 0.33	*IQR* = 0.25	0.04–0.97	95	*Mdn* = 2.40	*IQR* = 2.55	0.00–9.00	60
CG (in rest)	*Mdn* = 0.59	*IQR* = 0.16	0.04–0.97	97	3.73	2.34	0.00–10.00	96
CG (transfer movement)	*Mdn* = 0.59	*IQR* = 0.12	0.17–0.85	20	2.79	1.70	0.75–6.00	19
CG (upper body movement)	0.53	0.17	0.17–0.75	32	3.10	1.81	0.50–7.50	31
CG (back movement)	0.57	0.16	0.17–0.97	28	*Mdn* = 2.00	*IQR* = 1.50	0.50–7.00	28
CG (jaw movement)	0.50	0.16	0.17–0.75	12	2.21	1.97	0.50–7.00	12
CG (summary test session)*	0.50–0.59	0.12–0.17	0.04–0.97	12–97	2.00–3.73	1.50–2.34	0.00–10.00	12–96
CG (sum test session)	*Mdn* = 0.91	*IQR* = 0.71	0.20–3.27	103	*Mdn* = 5.25	*IQR* = 5.00	0.00–22.50	101
CG (average test session)	*Mdn* = 0.18	*IQR* = 0.14	0.04–0.65	103	*Mdn* = 1.05	*IQR* = 1.00	0.00–4.50	101

Self-reported pain experience was only examined in participants who passed the comprehension test of the self-reporting scale.

*For each situation, only participants were selected who reported pain in that specific situation (instead of selecting all participants who reported pain in at least one situation, as is the case for the "sum" and "average" measures): For a global overview, values of *M* were combined with *Mdn* and *SD* with *IQR*.

†Of the DS participants who reported pain during the test session, the difference between the three subgroups based on intellectual disability level did not reach statistical significance for summed pain affect (H (2) = 0.91, p = 0.63, r = -0.01 to -0.09, n = 95) and summed pain intensity (H (2) = 0.17, p = 0.92, r = -0.02 to -0.12, n = 60).

DS = Down syndrome. CG = control group.

Self-Reported pain Experience

The second main finding was that, within the subgroup participants who reported pain and comprehended the self-reporting scales, adults with DS reported a higher pain experience than adults from the general population. During the test session, the pain ratings of the DS group (FAS: 0.75–0.85 and NRS: 6.00–7.94) were above the cut-offs of greater than 0.75 for substantial pain on the FAS [67] and greater than 4 for moderate pain on the NRS [68], whereas this was not the case in the control group (FAS: 0.50–0.59 and NRS: 2.00–3.73). A higher pain experience is in line with the recently suggested magnified nociception and/or inefficient pain inhibition in DS [19] supported by neuropathology: the reduced connectivity in the dorsal prefrontal cortex [25], the reduced gray matter volume in the frontal lobes [26,27], and the reduced white matter volume in the frontal lobes and brain stem [28]. A comparison with literature about pain experience in people with intellectual disabilities is hampered by the scarcity of studies with data on self-reported pain. Indications for pain insensitivity, pain indifference, and an increased pain threshold have been reported [69], but these indications were based on proxy ratings. A higher self-reported pain experience in DS is in contrast to findings that suggest a decreased pain sensitivity in DS, such as in a murine model [70]. One of the possible explanations for the contrast is that the pain threshold is increased and the pain tolerance is decreased: It takes longer before pain is noticed (and reported), but the pain itself is experienced intensely. This is in line with the most recent review on the topic [19] and with recent evidence of a slower pain detection in combination with a slower recovery from pain in neonates with DS compared with healthy neonates [35].

Another possible explanation for the higher pain experience is that the use of the self-reporting scales was not entirely understood. Although pain was only assessed in participants who succeeded on the comprehension test, these participants could still have difficulty reflecting on their own pain experience and choosing the corresponding scale item. Studies in both adults with intellectual disabilities [71] and young children in the general population [72–78] show a tendency to give relatively high ratings on self-reporting scales for pain. Such a tendency may also have occurred in the DS participants of the present study because the average mental age was five years. This could explain the average higher rating on the facial scale, especially since ratings tend to be higher when the anchor is a smiling face, such as in the FAS [75], but it must be noted that the higher average rating was also found on the NRS and it has not yet been examined whether young children have a response bias on the NRS. Still, the NRS correlates highly with the faces pain scale [79] and with the visual analogue scale [80], and younger children give higher pain ratings on those scales than older children [72,73,77,78]. The response tendency could be caused by a cognitive inability to understand the question and/or to quantify an experience [81], but also by less efficient coping with pain, which may increase overall pain experience [78].

Strengths and Limitations

The strengths of the present study are that a relatively large sample of adults with DS were recruited throughout the Netherlands and that a comprehensive approach to assess pain was used (i.e., both presence and experience of pain, both physical conditions and participant's report, both rest and movements, both facial and numeric pain scales). A limitation of the present study is the lack of information about the chronicity and severity of painful conditions as this information may be significant to pain experience and to discriminate between pain and discomfort. The use of a "pain and/or discomfort" category is theoretically inadequate because some discomfort will not transit into pain. Although pain and discomfort are not the same, information regarding both possibilities was collected because it is difficult to discern between the two. The movement series are limited by the use of a standard instead of a random order, which may have resulted in more pain during the first series due to a warm-up effect or in more pain during the last series due to exhaustion. Moreover, the question about the presence of pain at the end of a movement series may have appealed to memory for pain during movements of that series. Another limitation is that the refinement of the comprehension tests for the self-reporting scales to further increase reliability has resulted in the use of two different formats. The only consequence of this procedure is that participants who passed the test with the least-most format may have comprehended the scales less well than those who passed the test with the ordering/magnitude format.

For 12 participants, the choice of the Social Functioning Scale for Intellectual Disability [45] or the Social Functioning Scale for Intellectual Disability Plus [46] appeared to be incorrect according to guidelines in the manuals. However, a comparison with a previous measurement of the same questionnaire was still possible to screen for the presence of dementia. Further, a modified version of the Vocabulary WPPSI-R subtest was used, because our Dutch translation of three of the 12 words differed from forward-backward translation based on guidelines [82] and data collection was too far advanced to make adaptations. Furthermore, for eight participants with DS, the series of movements for the back consisted only of touching the toes: Rotation was not yet included in the study protocol of seven participants and was refused by one participant due to back pain.

Recommendations for Research

Based on our study, we can make several recommendations. First, the average self-reported presence and experience of pain assessed at several points over time would be a more accurate estimation than only one moment of pain assessment. Second, to interpret the

findings of the present study, more information is needed about the response tendencies of people with DS during the use of self-reporting scales. Third, the acute pain experience of DS adults should be examined, for example, by pain assessment before and after a painful medical procedure.

Conclusion

The results of the present cross-sectional study show that physical conditions that could cause pain or discomfort are common in adults with DS. Although the results indicate that adults with DS rate higher pain experience on self-reporting scales than adults from the general population, other results show that self-reported presence of pain does not always correspond to medical information in both groups. This is especially alarming concerning the adults with DS because their mismatch between self-report of pain and medical pain-related information is related to estimated intelligence level and comprehension of the concept of pain (i.e., as represented by self-reporting scales).

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