Self-reported presence and experience of pain in adults with Down syndrome

This chapter is under revision as:
ABSTRACT
The aim of the present study was to examine whether the presence of pain (based on physical conditions and participants' report) and self-reported pain experience (affect and intensity) in adults with Down syndrome (DS) differ from general population controls. Participants were 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. File-based medical information was evaluated. Self-reported presence and experience of pain were assessed (affect with Facial Affective Scale (FAS: .04 - .97), intensity with Numeric Rating Scale (NRS: 0 - 10)). Compared to controls, more DS participants had physical conditions that may cause pain and/or discomfort ($p = .004$, 50% versus 35%), but fewer DS participants reported pain during the test session ($p = .003$, 58% versus 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 $Mdn = 0.32$ versus 0.18, NRS $Mdn = 2.40$ versus 1.05). Not all adults with DS and painful/discomforting physical conditions reported pain, but those who did indicated a higher pain experience than adults from the general population (although the average scale values were still relatively low). More research into spontaneous self-report of pain, repeated pain assessment, acute pain, pain threshold, and pain tolerance is needed in people with DS.

Key words: Down Syndrome, pain assessment, clinical significance.
An increased life expectancy [25] for people with Down syndrome (DS), and a greater incidence of indications for premature aging [53] mean that people with DS have a greater risk of developing age-related painful physical conditions, such as cervical arthritis [22,66]. DS itself is already characterized by a vulnerability to painful and discomforting physical conditions, such as middle ear infections [10,65] and skin problems [56,59]. It is unclear whether all people with DS affected by painful conditions also report pain, as some people with intellectual disabilities under-report their pain [6,20] and people with DS have a low tendency to complain about pain [66]. Detecting pain in people with intellectual disabilities may be complicated by their communication difficulties [64], reduced insight into their own health [64], deviant pain responses [32,44], the wish not to bother others or to waste their time [20], and being afraid of doctors or the reaction of others [20,21]. Insight into the presence of pain may promote early pain detection by caregivers and medical professionals. This is clinically relevant, because under-treatment of pain in adults with intellectual disabilities has been reported [8,51] and pain could negatively influence quality of life [71].

It is also relevant to increase the awareness of health care workers that the pain experience (i.e., motivational-affective pain aspect) in DS may be different than in the general population. Based on neuropathology of brain areas involved in pain processing, we have argued that pain experience in DS may either be increased or decreased compared to the general population [33]. A higher pain experience in DS might be explained by small frontal lobes and a lower white matter volume in the frontal lobes and brain stem [12,29,55,73]. The pain inhibiting function of these brain areas [15,42] may be disturbed and white matter pathology could increase pain experience [63,74]. A lesser pain experience in DS might be caused by high concentrations of endogenous opioids leu-enkephalin and dynorphin A [58], and small volumes of the hippocampus, amygdala, insula, and anterior cingulate cortex [29,73]. These brain areas process the emotional aspect of pain [41,69], and researchers have suggested that atrophy of these brain areas [11,24,61] may explain the finding that the experience of pain (i.e., affect and intensity) is lower in people with Alzheimer’s disease than elderly people without dementia [63]. Although the risk for developing Alzheimer’s disease
neuropathology is increased in DS, possibly due to the overexpression of the amyloid protein precursor [28,62], this does not mean that the pain experience in DS is the same as in Alzheimer’s disease.

In short, a hypothesis about the motivational-affective pain component in DS remains unclear, because 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 behavioural problems and unnoticed suffering from pain (i.e., due to the tendency in DS to express medical problems with problematic behaviour instead of complaining about pain) [66], while a lower pain experience increases the risk for unnoticed injury.

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.

MATERIAL AND 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.

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 centres for people with intellectual disabilities in locations throughout the Netherlands. Before the start of the study, the care centres’ caregivers and behavioural specialists assessed inclusion and exclusion criteria per client. Other participants with DS were recruited through the Dutch Down Syndrome Foundation website. Inclusion criteria were: being 18 years of age 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 [27,67]. A previously described method [31] was used to screen for the presence of dementia. This 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 centre or home where participants lived.

**Participants of control group**

Inclusion criteria for the control group were: being 18 years of age 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) [23] was used to screen for the presence of neuropsychological impairment. All participants scored above the cut-off [68], 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 \( t (256) = 3.46, \ p = .001, \ r = .21 \) and the maximum age of the DS group
was 65, controls aged 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 non-
significant group difference in age ($U = 14613.50$, $p = .19$, $r = -.07$), and a reduction
from 160 to 142 participants in the control group.

**Sample size calculation**
According to the statistical program Gpower [18] with $\alpha = .05$, $\beta = .80$, 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: $N = 161 - 198$).

**Estimated level of intellectual disability and intelligence in the
Down syndrome group**
The level of intellectual disability was estimated by using a previously described
method [31]. The level of intelligence was estimated by using the subtests Block
Design and Vocabulary of the Wechsler Preschool and Primary Scale of Intelligence
- Revised version (WPPSI-R) [72]. 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' [37], 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 ten sentences of Sentence Comprehension, a subtest of the Dutch Aphasia
Foundation test (Dutch: Zinsbegrip subtest, Stichting Afasie Nederland test; [16]).
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 commonly 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 osteoarthrosis” was coded as “back problems due to wearing and tearing” instead of “osteoarthrosis”).

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 centre 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 to the medical files from the care centre or the general physician.

Because it is somewhat unclear when discomfort transits into pain, no distinction between pain and discomfort was made. One physiotherapist (E.J.A.S.), 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 .66 was found, indicating a substantial agreement between the three lists [40]. 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 non-pharmacological 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”) [70].

**Estimated intelligence level in the control group**

The Groninger Intelligence Test II is a Dutch intelligence test battery containing ten different tests (GIT-2) [43]. Its reliability and validity are satisfactory to good [17]. 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 [43].

**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**

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 reported pain during any of these questions, then they were asked to point to the painful location on their own body. If participants felt pain in more locations per test situation, then they were asked to indicate which location was the most painful.

Subsequently, participants were asked to imitate four series of active movements as demonstrated by the researcher: 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 forwards and touching the shoulders with the hands, and stretching the arms forwards and “playing the piano”), 3) movement of the back (touching the toes with stretched legs and rotating the torso), and 4) movement of the jaw (opening the mouth as far as possible). By encouraging participants to push the maximum limits of their movement capabilities, pain or discomfort of the involved musculoskeletal structures (i.e., muscles and joints) was provoked during function. Directly after each series, participants were asked whether they felt any pain during the movements and if so, where this was.

Self-reported pain affect and intensity in the Down syndrome group

For pain affect, the Facial Affective Scale (FAS) [49,50] 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 [50]. Pain affect refers to perceived unpleasantness [57], and is related to pain tolerance and suffering from pain [63]. The examiner asked: “Which face fits best with how the pain makes you feel inside?” For pain intensity, the numeric side of the Coloured Analogue Scale [49,50] 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 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 feel.”

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.

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 face (i.e., faces with values .04 and .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 .97 and .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.

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: “Which is larger: 2 or 8?” and “Which is larger: 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 .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 $\alpha = .05$ (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. For each participant, the number of situations in which pain was reported and the number of painful locations that were reported during the test session were divided by the number of situations completed. The sum of the FAS scores (Cronbach's $\alpha = .63$) was divided by the number of test situations in which the FAS was used. Similarly, the sum of the NRS values (Cronbach's $\alpha = .53$) was divided by the number of test situations in which the NRS was used. Because these measures of average pain affect and average pain intensity were highly correlated ($r = .75$, $p < .001$), a domain of Pain Experience was formed by taking the mean of the standardized scores (Cronbach's $\alpha = .89$). This domain was only used in the multiple linear regression analysis.

The main analyses were Chi-squared tests, Mann-Whitney U tests, and multiple linear regression analyses. All assumptions of the regression analyses were met [19]. Multilevel analysis was not necessary. “Possible pain/discomfort”
FIG. 1
Faces and their corresponding values of the Facial Affective Scale [49]. This is the backside: the front side (faces without letters and numbers) were 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.

FIG. 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 .17, .75, and .85).
FIG. 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.

FIG. 4
was based on medical information (e.g., in relation to physical conditions). “Presence of pain according to participant’s report” and “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, both at rest ($\chi^2(1) = 21.54, p < .001, \Phi = .24, 44\%$ versus $69\%$) and during active movements ($\chi^2(1) = 8.71, p = .003, \Phi = .15, 58\%$ versus $73\%$ pain during at least one series). DS and control participants who reported pain during rest also reported pain during active movements. 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.

The question arises whether the self-reported 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 during the test session was not statistically significant (see Table 3). However, reporting pain was associated with the presence of pain/discomfort according to medical information within participants who comprehended at least one of the self-reported scales ($\chi^2(1) = 9.05, p = .003, \Phi = .23$), while this was not the case within participants who did not comprehend any of the scales ($\chi^2(1) = 0.06, p = .81, \Phi = .04$).
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Down syndrome group (N = 224): n</th>
<th>Control group (N = 142): n</th>
<th>Group difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years (range is 18-65 years in both groups)</td>
<td>$M = 38.1 (SD = 11.1)$</td>
<td>$Mdn = 40.5 (IQR = 25)$</td>
<td>$U = 14613.50, p = .19, r = -.07$</td>
</tr>
<tr>
<td>Gender: male</td>
<td>118 (53%)</td>
<td>65 (46%)</td>
<td>$\chi^2(1) = 1.66, p = .20, \Phi = -.07$</td>
</tr>
<tr>
<td>Living situation: in care centre, or with family</td>
<td>197 (88%), 27 (12%)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Intellectual disability: mild, moderate, severe</td>
<td>56 (25%), 147 (66%), 21 (9%)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Estimated intelligence level</td>
<td>$201 (87%), M = 5.0 (SD = 1.5) AE$</td>
<td>$M = 105.7 (SD = 13.3) IQ$</td>
<td>-</td>
</tr>
<tr>
<td>Education: most frequent level (level 6)</td>
<td>-</td>
<td>68 (48%)</td>
<td>-</td>
</tr>
<tr>
<td>Mini-Mental State Examination score</td>
<td>-</td>
<td>$Mdn = 29.0 (IQR = 1)$</td>
<td>-</td>
</tr>
<tr>
<td>Language comprehension</td>
<td>217 (94%), $M = 8.1 (SD = 1.6)$</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Vocabulary (years age equivalent)</td>
<td>207 (89%), $Mdn = 4.1 (IQR = 2.0)$</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Symptoms of autism</td>
<td>11 (5%)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Sleep problems and/or symptoms of depression*</td>
<td>15 (7%): 1 (7%) sleep medication</td>
<td>2 (1%): no medication</td>
<td>$\chi^2(1) = 5.49, p = .019, \Phi = .12$</td>
</tr>
<tr>
<td>Thyroid disorder*</td>
<td>76 (34%): 75 (99%) medication</td>
<td>4 (3%): 4 (100%) medication</td>
<td>$\chi^2(1) = 49.25, p &lt; .001, \Phi = .37$</td>
</tr>
<tr>
<td>Diabetes</td>
<td>7 (3%)</td>
<td>2 (1%)</td>
<td>$Fisher's Test, p = .49, \Phi = .05$</td>
</tr>
<tr>
<td>Present analgesics use</td>
<td>10 (5%)</td>
<td>6 (4%)</td>
<td>$\chi^2(1) = 0.01, p = .91, \Phi &lt; .01$</td>
</tr>
<tr>
<td>Physical conditions possible pain/discomfort*</td>
<td>113 (50%)</td>
<td>50 (35%)</td>
<td>$\chi^2(1) = 8.17, p = .004, \Phi = .15$</td>
</tr>
<tr>
<td>Number of categories possible pain/discomfort</td>
<td>$Mdn = 1.0 (IQR = 1.0)$</td>
<td>$Mdn = 1.0 (IQR = 1.0)$</td>
<td>$U = 2448.50, p = .12, r = -.12$</td>
</tr>
</tbody>
</table>

* = statistically significant. *a* = the difference between the three subgroups based on intellectual disability level did not reach statistical significance for age ($H (2) = 0.01, p = 1.0, r = -.001$ to -.01), gender ($\chi^2(2) = 0.56, p = .76, Cramer's V = .05$), and presence of possible pain/discomfort ($\chi^2(2) = 2.97, p = .23, Cramer's V = .12$). AE = years age equivalent. 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>
<thead>
<tr>
<th>Category</th>
<th>DS: n</th>
<th>CG: n</th>
<th>Category</th>
<th>DS: n</th>
<th>CG: n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin condition(^{a})</td>
<td>31</td>
<td>15</td>
<td>Stomach pain or discomfort (e.g., gastric acid) / Gastroesophageal reflux disease</td>
<td>9</td>
<td>2</td>
</tr>
<tr>
<td>Subcutaneous inflammation / Varicose veins</td>
<td>4</td>
<td>0</td>
<td>Constipation / Bowel disease / Intestine problems / Pain abdomen</td>
<td>27</td>
<td>4</td>
</tr>
<tr>
<td>Headache / Migraine</td>
<td>2</td>
<td>8</td>
<td>Hip dysplasia / Stiff or worn hip joints / Hip pain or complaints</td>
<td>11</td>
<td>0</td>
</tr>
<tr>
<td>Eye irritation or inflammation</td>
<td>7</td>
<td>0</td>
<td>Urine tract infection / Infection of the bladder / Urethral stricture</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Ear pain or inflammation</td>
<td>1</td>
<td>0</td>
<td>Severe period pain</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Sinusitis (causing toothache and headache)</td>
<td>0</td>
<td>1</td>
<td>Vaginitis</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Tooth ache / Pain in jaw / Pain associated with partial or full dentures</td>
<td>7</td>
<td>1</td>
<td>Knee pain or complaints (e.g., long ligaments) / Patella luxation</td>
<td>14</td>
<td>2</td>
</tr>
<tr>
<td>Chronic inflammation of the gums</td>
<td>11</td>
<td>0</td>
<td>Toe / foot / ankle / leg pain or discomfort</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Neck deformation / Neck pain</td>
<td>3</td>
<td>3</td>
<td>Deviant foot position(^{b})</td>
<td>11</td>
<td>1</td>
</tr>
<tr>
<td>Shoulder pain (e.g., due to bursitis or lesion)</td>
<td>2</td>
<td>2</td>
<td>Osteoarthrosis</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>Cervicobrachialgia / Ulnar Neuropathy</td>
<td>0</td>
<td>3</td>
<td>Albers Schönbergs disease</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Dupuytren's contracture / Carpal Tunnel Syndrome</td>
<td>1</td>
<td>3</td>
<td>Bone necrosis (knee and/or hip)</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Wrist pain / Hand joint pain</td>
<td>2</td>
<td>1</td>
<td>Gout</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Chest pain / Syndrome of Tietze / Contusion rib</td>
<td>2</td>
<td>1</td>
<td>Fractures</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Back pain (e.g., lumbago) / Back problems due to wearing / Scoliosis</td>
<td>17</td>
<td>5</td>
<td>Muscle pains / Spasm or cramp(^{c})</td>
<td>6</td>
<td>0</td>
</tr>
</tbody>
</table>

\(^{a}\) = 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.  
\(^{b}\) = pes equinus, pes quinovarus adductus, pes cavus, hallux valgus.  
\(^{c}\) = spasm/cramp in neck, back, jaw, oesophagus, legs, or foot. The bold numbers in the columns represent the top 3 most prevalent category per group. Some participants had conditions in several categories or several conditions in the same category.
### TABLE 3
Relationship between comprehending self-reporting scales and other variables in Down syndrome

<table>
<thead>
<tr>
<th>Variable</th>
<th>Statistic</th>
<th>( p )</th>
<th>effect size</th>
<th>( n )</th>
<th>Statistic</th>
<th>( p )</th>
<th>effect size</th>
<th>( n )</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>( t(222) = 2.64 )</td>
<td>.009</td>
<td>( r = .18 )</td>
<td>224</td>
<td>( t(218) = 5.48 )</td>
<td>&lt;.001*</td>
<td>( r = .35 )</td>
<td>220</td>
</tr>
<tr>
<td></td>
<td>Yes: ( M = 37.0 ) years</td>
<td></td>
<td></td>
<td></td>
<td>Yes: ( M = 34.0 ) years</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No: ( M = 41.4 ) years</td>
<td></td>
<td></td>
<td></td>
<td>No: ( M = 41.7 ) years</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td>( \chi^2(1) = 1.17 )</td>
<td>.28</td>
<td>( Phi = -.07 )</td>
<td>224</td>
<td>( \chi^2(1) = 1.79 )</td>
<td>.18</td>
<td>( Phi = -.09 )</td>
<td>220</td>
</tr>
<tr>
<td><strong>Intellectual disability level</strong></td>
<td>( \chi^2(2) = 10.03 )</td>
<td>.007</td>
<td>( Cramer's V = .21 )</td>
<td>224</td>
<td>( \chi^2(2) = 6.83 )</td>
<td>.033</td>
<td>( Cramer's V = .18 )</td>
<td>220</td>
</tr>
<tr>
<td><strong>Estimated intelligence</strong></td>
<td>( U = 1332.00 )</td>
<td>&lt;.001*</td>
<td>( r = .44 )</td>
<td>195</td>
<td>( t(193) = -7.45 )</td>
<td>&lt;.001*</td>
<td>( r = .47 )</td>
<td>195</td>
</tr>
<tr>
<td></td>
<td>Yes: ( Mdn = 5.1 ) years AE</td>
<td></td>
<td></td>
<td></td>
<td>Yes: ( Mdn = 6.0 ) years AE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No: ( Mdn = 4.0 ) years AE</td>
<td></td>
<td></td>
<td></td>
<td>No: ( Mdn = 4.1 ) years AE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Vocabulary</strong></td>
<td>( U = 1372.00 )</td>
<td>&lt;.001*</td>
<td>( r = -.48 )</td>
<td>200</td>
<td>( U = 1846.00 )</td>
<td>&lt;.001*</td>
<td>( r = -.52 )</td>
<td>207</td>
</tr>
<tr>
<td></td>
<td>Yes: ( Mdn = 5.0 ) years AE</td>
<td></td>
<td></td>
<td></td>
<td>Yes: ( Mdn = 5.1 ) years AE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No: ( Mdn = 3.1 ) years AE</td>
<td></td>
<td></td>
<td></td>
<td>No: ( Mdn = 4.0 ) years AE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Language comprehension</strong></td>
<td>( U = 1956.50 )</td>
<td>&lt;.001*</td>
<td>( r = .38 )</td>
<td>209</td>
<td>( U = 2689.50 )</td>
<td>&lt;.001*</td>
<td>( r = .42 )</td>
<td>213</td>
</tr>
<tr>
<td></td>
<td>Yes: ( Mdn = 9.0 ) words</td>
<td></td>
<td></td>
<td></td>
<td>Yes: ( Mdn = 9.0 ) words</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No: ( Mdn = 7.0 ) words</td>
<td></td>
<td></td>
<td></td>
<td>No: ( Mdn = 8.0 ) words</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Symptoms of autism</strong></td>
<td>Fisher's exact test</td>
<td>.47</td>
<td>( Phi = -.06 )</td>
<td>224</td>
<td>Fisher's exact test</td>
<td>.76</td>
<td>( Phi = -.03 )</td>
<td>220</td>
</tr>
<tr>
<td><strong>Possible pain/ discomfort</strong></td>
<td>( \chi^2(1) = 0.01 )</td>
<td>.94</td>
<td>( Phi = .01 )</td>
<td>224</td>
<td>( \chi^2(1) = 0.41 )</td>
<td>.52</td>
<td>( Phi = .04 )</td>
<td>220</td>
</tr>
<tr>
<td><strong>Self-reported presence of pain (during test session)</strong></td>
<td>( \chi^2(1) = 0.61 )</td>
<td>.43</td>
<td>( Phi = -.05 )</td>
<td>224</td>
<td>( \chi^2(1) = 1.41 )</td>
<td>.24</td>
<td>( Phi = .08 )</td>
<td>220</td>
</tr>
</tbody>
</table>

Results in grey cells correspond to the Facial Affective Scale; results in white cells correspond to the Numeric Rating Scale. * = statistically significant \( p = .006 \) (\( p = .05 / 9 \) due to multiple testing). AE = age equivalent. Yes = participants who passed the comprehension test of the pain scale, No = participants who failed the comprehension test of the pain scale.
Self-reported pain experience

More participants in the control group than in the DS group comprehended the scales for pain affect ($\chi^2(1) = 41.64, p < .001, \ Phi = -.34, 100\% \text{ versus } 75\%$) and pain intensity ($\chi^2(1) = 114.96, p < .001, \ Phi = -.57, 99\% \text{ versus } 43\%$). 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 is described in Table 4. 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 non-users 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 ($F (1, 153) = 31.11, p < .001, B = -0.76, \eta^2 = .17, n = 156$). 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.

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 [14,60]. The paradoxical combination with a relatively low prevalence of the reported presence of pain confirms clinical observations in DS [66] and may be explained in several ways. The physical conditions may not have caused pain
SELF-REPORTED PAIN IN DOWN SYNDROME

During the test assessment due to the fluctuating nature of symptoms. If pain was present, then general explanations for under-reporting 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 reaction of others, and being afraid of doctors [6,20,21,64]. Possible explanations that are more specific to DS suggest that the presence of pain may not have been experienced adequately: high concentrations of endogenous opioids leu-enkephalin and dynorphin A have been found in the frontal cortex [58], as well as a small mediodorsal thalamic nucleus [30], which is a nucleus that projects sensory information to the prefrontal cortex [48]. Prefrontal and frontal brain areas are important in the conscious perception of pain [34,42].

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. This is in line with the data shown in Table 4:

<table>
<thead>
<tr>
<th>Group</th>
<th>Pain affect (scale values: .04 - .97)</th>
<th>Pain intensity (scale values: 0 - 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mdn</td>
<td>IQR</td>
</tr>
<tr>
<td>DS</td>
<td>0.15</td>
<td>0.33</td>
</tr>
<tr>
<td>DS: self-reported presence of pain a</td>
<td>0.32</td>
<td>0.25</td>
</tr>
<tr>
<td>CG</td>
<td>0.15</td>
<td>0.22</td>
</tr>
<tr>
<td>CG: self-reported presence of pain</td>
<td>0.18</td>
<td>0.14</td>
</tr>
</tbody>
</table>

Self-reported pain experience was only examined in participants who passed the comprehension test of the self-reporting scale. a = 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 average pain affect ($H(2) = 2.05, p = .36, r = -.10 to -.21, n = 95$) and average pain intensity ($H(2) = 0.12, p = .94, r = -.02 to -.09, n = 60$).
with growing evidence for white matter neuropathology in DS, such as early myelin degeneration [47], low white matter integrity [55], and low white matter volumes [12,73], because white matter neuropathology could increase pain experience [63,74]. 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 [7], 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 [46]. 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 recent evidence of a slower pain detection in combination with a slower recovery from pain in neonates with DS compared to healthy neonates [1].

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 [9] and young children in the general population [2,5,13,26,38,39,45] 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 about 5 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 [13], 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 [52] and with the Visual Analogue Scale [4] and younger children give higher pain ratings on those scales than older children [2,26,38,39]. The response tendency could be caused by a cognitive inability to understand the question and/or to quantify an experience [3], but also by less efficient coping with pain [38].
It should be noted that, despite the group difference, the self-reported pain experience in the DS group was relatively low (i.e., a median pain affect of 0.32 on a scale from 0.04 to 0.97 and a median pain intensity of 2.40 on a scale from 0 to 10). This may also be related to the tendency of young children to use the ends of a self-reporting scale [2,3]. Even if the average rating is no response bias, then the pain experience of adults with DS does not seem alarmingly high (e.g., an NRS rating is considered to be clinically relevant from a value of 3 [4]).

**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, since this information may be significant to pain experience and for discriminating between pain and discomfort. The use of a “pain and/or discomfort” category is theoretically inadequate, because some discomfort will not transit into pain. However, it remains difficult to determine which medical conditions cause pain in a clinical population with a possibly disturbed pain experience. 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 [36] or the Social Functioning Scale for Intellectual Disability Plus [35] 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 3 of the 12 words differed from forward-backward translation based on guidelines [54] 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 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 average pain scale values are low, the pain experience of adults with DS could be higher than adults from the general population. This is clinically relevant to daily functioning, quality of life, and pain management in the DS population and indicates a need for further research.

**REFERENCES**


[40] Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics 1977;33:159.


