Review:
Pain in adults with intellectual disabilities

This chapter has been published as:
During the last two decades, the number of studies focusing on the experience, assessment, and treatment of pain in older people with dementia has increased considerably [38]. One major conclusion of those studies [38] is that pain is still undertreated in this population due to the complexity of reliable pain assessment, which is a prerequisite for effective pain treatment. Unfortunately, these pain studies do not address other groups of people who have intellectual disabilities (IDs) such as Down syndrome. The scarcity of knowledge about the experience, assessment, and treatment of pain in IDs is more remarkable still for three reasons: 1) people with IDs may suffer from more painful conditions than controls do [37]; 2) the prevalence of age-related painful conditions is increasing, due to increases in estimated life expectancy [7]; and 3) the neuropathology of IDs affects pain-related grey and white matter (Table 1), which may alter pain experience.

The goal of the present review is, therefore, to gain more insight into the experience of pain in adults with IDs by (1) addressing epidemiological studies on the presence of musculoskeletal disorders, in relation to clinical pain in people with IDs; (2) discussing the available experimental human studies on pain in IDs; and (3) presenting theoretical considerations about possible alterations in pain experience in IDs, based on the neuropathology characteristic of the various subtypes.

**EPIDEMIOLOGICAL STUDIES ON MUSCULOSKELETAL DISORDERS AND CLINICAL PAIN EXPERIENCE IN INTELLECTUAL DISABILITIES**

The proportion of older adults with IDs who suffer from arthritis and who use analgesics is considerably larger than the comparable proportion of younger adults with IDs [13]. In addition to age, the aetiology of IDs is a factor in the prevalence of musculoskeletal disorders.

Cerebral palsy is a neurological condition primary characterised by motor impairment that frequently coincides with IDs [20,26,47]. In adults with cerebral palsy, disorders of the hips, back, and lower extremities are common [43] and related to pain experience [40,43]. The pain is caused by arthritis, contractures, spasticity, deformities, and weakness [35]. Female carriers of the Fragile-X mental
retardation gene may suffer from neuropathy and chronic muscle pain, related to fibromyalgia [12]. Scoliosis and excessive laxity of joints have been observed in fragile-X syndrome [14], but have not been examined in relation to pain experience.

Individuals with Down syndrome have a higher risk of musculoskeletal disorders than the general population [2,24,37,41]. Instability and other degenerative changes in the cervical spine occur at a much earlier age in individuals with Down syndrome than they do in the general population, and these problems increase with age [1]. Arthritis develops in 1% to 2% of adolescents with Down syndrome [37], and it occurs more often in individuals with Down syndrome than it does in the general population [37]. Hip instability [24] and osteoporosis, which results in fractures [2], are also common in people with Down syndrome. It is worth noting that the extent to which people with Down syndrome suffer from pain from one or more of these conditions has not been described in literature. Rett syndrome is characterized by scoliosis, joint deformities, spasticity, and kyphosis [18]. Whether these conditions are related to pain experience remains unknown. The same applies to the 22q11.2 Deletion syndrome, the Prader-Willi syndrome, and Williams syndrome. The 22q11.2 Deletion syndrome is characterized by scoliosis, patella dislocation, and disc disease [5], Prader-Willi by scoliosis, osteoporosis, and hip dysplasia [10], and Williams syndrome by radioulnar synostosis, kyphosis, lordosis, and scoliosis [35].

Taken together, in most subtypes of IDs, the presence of musculoskeletal disorders has not been examined in relation to the experience of clinical pain. Experimental studies on pain in IDs may provide more insight.

EXPERIMENTAL STUDIES ON PAIN IN INTELLECTUAL DISABILITIES

In one study, 65% of adults with IDs receiving intramuscular injections were able to report pain using the Coloured Visual Analogue Scale [27]. The frequency and intensity of facial activity did not differ between subjects who were able to self-report and those who were not. This leads to the question whether adults with IDs experience more or less pain compared to those without IDs. On the one hand, individuals with IDs rate pain experiences depicted in photographs of simulated painful situations as more intense according to a coloured analogue scale.
NEUROPATHOLOGY IN INTELLECTUAL DISABILITIES AFFECTS GREY AND WHITE MATTER INVOLVED IN THE PROCESSING OF PAIN; THEORETICAL CONSIDERATIONS

The intralaminar and medial thalamic nuclei, the insula, the parietal operculum, the hypothalamus, the prefrontal cortex, the anterior cingulate cortex, the amygdala, and the hippocampus are involved in the motivational-affective aspects of pain, and the cognitive-evaluative aspects of pain. The latter two areas are also involved in the memory of pain, and the hypothalamus in the autonomic responses to pain.
Sensory-discriminative aspects of pain are processed by the lateral thalamus, the primary and secondary somatosensory cortex, the parietal operculum, and the insula [39].

The neuropathology of the above mentioned pain-related brain regions (Figure 1) and white matter (Table 1) may alter pain experience. This appears to be the case in dementia [39], a neurodegenerative disease that, in contrast to most subtypes of IDs (Table 1), is not characterized by painful conditions such as musculoskeletal disorders. For example in Alzheimer’s disease, degeneration of pain-related areas may explain the observed increase in pain tolerance and hence the reduction in pain experience. The white matter lesions (de-afferentiation) that are characteristic of vascular dementia, by contrast, may produce a lowering of pain tolerance and hence an intensification of the pain experience [39].

This same line of reasoning may be true of those subtypes of IDs that show neuropathology in pain-related grey matter and white matter (Table 1). For example in Down syndrome, the smaller volumes of the hippocampus, amygdala, insula, and the anterior cingulate cortex [25,45] may on the one hand lead to a decrease in the various aspects of pain experience while on the other hand smaller volumes of the frontal lobe [25] and of white matter [45] may enhance pain experience. The smaller volumes of the hippocampus, thalamus, and white matter volume in Williams syndrome [29] may lead to a similar hypothesis. Concerning Prader-Willi syndrome, the higher pain threshold seems unrelated to insular pathology [32] but may be related to hypothalamic pathology [9,36]. The reduced frontal white matter [46] may however lower the pain tolerance in Prader-Willi syndrome. In Fragile-X syndrome, the smaller volume of white matter is a neuropathological hallmark [19] and may cause an increase in suffering from pain (lower pain tolerance). The same line of reasoning may hold for patients with 22q11.2 Deletion Syndrome [3].

RECOMMENDATIONS FOR PAIN ASSESSMENT IN INTELLECTUAL DISABILITIES

Since clinical pain studies in people with IDs are limited, recommendations for pain assessment in this population may emerge from clinical studies on pain in dementia. For a summary of pain assessment instruments for non-verbal older
<table>
<thead>
<tr>
<th>Adults with IDs/dementia</th>
<th>Musculoskeletal disorders</th>
<th>Clinical pain studies</th>
<th>Exp. pain studies</th>
<th>Neuropathology in pain-related grey and white matter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebral palsy</td>
<td>Spasticity, scoliosis, arthritis, hip displacement, orthopaedic deformity, patella alta, cervical stenosis, instability of the cervical spine, disc degeneration, and severe osteoporosis [43].</td>
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<td>+</td>
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<tr>
<td>Rett syndrome</td>
<td>Scoliosis, joint deformities, spasticity, and kyphosis [18].</td>
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<tr>
<td>Down syndrome</td>
<td>Instability and other degenerative changes in the cervical spine, arthritis [2], hip instability [24].</td>
<td></td>
<td>+</td>
<td>Frontal cortex (including anterior cingulate cortex), amygdala, hippocampus, and insula [25,45]. Decreasing number of cells of locus coeruleus with increasing age and dementia [28]. Reduced white matter volume in the brainstem [45].</td>
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<tr>
<td>Fragile-X syndrome</td>
<td>Excessive laxity of joints and scoliosis [14].</td>
<td></td>
<td></td>
<td>Frontal lobe, thalamus [31]. Hyperaroused hypothalamic-pituitary-adrenal axis [23]. Reduced white matter in brainstem (extending into pons), frontal lobe (extending into prefrontal cortex), reduced white matter in frontostriatal and parietal sensory-motor tracts [4,19].</td>
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<tr>
<td>Prader-Willi syndrome</td>
<td>Scoliosis, osteoporosis, hip dysplasia [10].</td>
<td></td>
<td>+</td>
<td>Insula [33]. Hypothalamus (smaller paraventricular nucleus and physiological disturbance) [34,42]. Reduced right and left frontal white matter [46].</td>
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<tr>
<td>Williams syndrome</td>
<td>Radioulnar synostosis, kyphosis, lordosis, and scoliosis [35].</td>
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<td>Hippocampus, thalamus. Reduced white matter volume [29].</td>
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<tr>
<td>Alzheimer's disease</td>
<td></td>
<td>+</td>
<td>+</td>
<td>Secondary somatosensory cortex, anterior cingulate cortex, amygdala, hippocampus, thalamus, hypothalamus, insula, locus coeruleus, parabrachial nucleus, periaqueductal grey; white matter lesions [39].</td>
</tr>
<tr>
<td>Frontotemporal dementia</td>
<td></td>
<td>+</td>
<td></td>
<td>Middle frontal gyrus, right medial prefrontal cortex, orbitoprefrontal cortex, insula, anterior cingulate cortex, hypothalamus [39].</td>
</tr>
</tbody>
</table>

*Note.* + = one or more clinical and/or experimental (Exp.) pain studies.
FIG. 1
people with dementia, see [22]. Most of these instruments include the observation of pain, as expressed in the face or body for example. When using these scales, one should realize that typical facial expressions shown spontaneously by some individuals with IDs might be confused with facial expressions of pain [15]. Moreover, the level of the IDs affects pain behaviour. For example, before the application of an acute pain stimulus (vaccination), individuals with severe-profound IDs display a higher level of facial and body expressions than individuals with mild-moderate IDs. In the presence of acute pain (during vaccination), assessment of facial pain expression in individuals with severe-profound IDs becomes less reliable due to a lack of facial movements (“freezing”). In contrast, individuals with mild-moderate IDs show an increased level of both facial and body expressions during vaccination [15]. When using visual analogue pain scales, one should take the visual impairments of this population into account [17]. Even limited verbal communication with people with IDs, such as giving instructions for the use of visual analogue pain scales, requires a special conversation style. Open questions and simple language should be used. To check whether the person understands the question, rephrasing the question by changing the sequence of words should lead to the same answer. The reason for this is that people with IDs tend to answer ‘yes’ to every closed question and to repeat the final option in questions with multiple answers [44].

CONCLUSIONS

• In most subtypes of IDs, the presence of musculoskeletal disorders has not been examined in relation to the experience of clinical pain. In other words, clinical pain studies with people with IDs are lacking. This is remarkable, since adults without IDs rate chronic musculoskeletal disorders such as arthritis as severe or extremely painful [30].

• As far as we know, alterations in the processing of acute painful and thermal stimuli have only been examined in experimental studies including individuals with Down syndrome and Prader-Willi syndrome. Individuals with Down syndrome react relatively slowly when expressing a verbal response to cold and hot stimuli, have difficulty in localizing cold stimuli, and experience heat as painful at a lower temperature. These findings are quite alarming: they
could implicate that a person could experience intense pain from a hot object while being less able to express a verbal response quickly enough to avoid burns.

- The neuropathology in pain-related brain regions and white matter suggests that pain experience may either decrease or increase in Down syndrome, Williams syndrome, and Prader-Willi syndrome. Patients with Fragile-X syndrome and 22q11.2 Deletion Syndrome may suffer from an increase in pain experience. Clinical studies are needed to confirm or reject these hypotheses.

- Because the hippocampus, anterior cingulate cortex, prefrontal cortex, and other brain areas are also involved in cognitive functioning, future studies should address the question whether any positive or negative relationship actually exists in IDs between cognitive functioning and various aspects of pain, such as the motivational/affective aspects of pain. If there is such a relationship, irrespective of its nature, neuropsychological examination might contribute to pain assessment in this population.

REFERENCES


[28] Mann DMA, Royston MC, Ravindra CR. Some morphometric observations on the brains of patients with Down's syndrome: Their relation-


