The SID Pain App

Korving, Helen

2025

DOI (link to publisher)
10.5463/thesis.976

document version
Publisher's PDF, also known as Version of record

citation for published version (APA)
Korving, H. (2025). *The SID Pain App: Design, development and testing of a pain measurement application for use in the care for adults with a severe or profound intellectual disability*. [PhD-Thesis - Research and graduation internal, Vrije Universiteit Amsterdam]. https://doi.org/10.5463/thesis.976

This dedication is dedicated to all the children and adults
with a severe or profound intellectual disability
who have participated during the phases of this project.

In memory of Andy & Flint.

Because I could not stop for Death,

He kindly stopped for me;

The carriage held but just ourselves

And Immortality.

- Emily Dickinson

The SID Pain App

Design, development and testing of a pain measurement application for use in the care for adults with a severe or profound intellectual disability

Helen Korving

This research was financially and organizationally supported by the academic research lab ‘Affect-us’: a collaboration between Bartiméus, Stichting Ons Tweede Thuis, Odion and Vrije Universiteit Amsterdam.
www.affect-us.nl

This research was also supported by Eindhoven University of Technology.

All research described in this dissertation was funded by ZonMw (grant number 8084 5009 8345).

ISBN: 978-90-83448-51-0
DOI: https://doi.org/10.5463/thesis.976
Cover Design: Amy Vermeer-van Reede | RAD Drukkerij
Layout: Paul Korving
Printing: RAD Drukkerij Dordrecht

VRIJE UNIVERSITEIT

The SID Pain App

Design, development and testing of a pain measurement application for use in the care for adults with a severe or profound intellectual disability

ACADEMISCH PROEFSCHRIFT

ter verkrijging van de graad Doctor aan
de Vrije Universiteit Amsterdam,
op gezag van de rector magnificus
prof.dr. J.J.G. Geurts,
in het openbaar te verdedigen
ten overstaan van de promotiecommissie
van de Faculteit der Gedrags- en Bewegingswetenschappen
op woensdag 22 januari 2025 om 11.45 uur
in een bijeenkomst van de universiteit,
De Boelelaan 1105

door

Helen Korving

geboren te Leidschendam

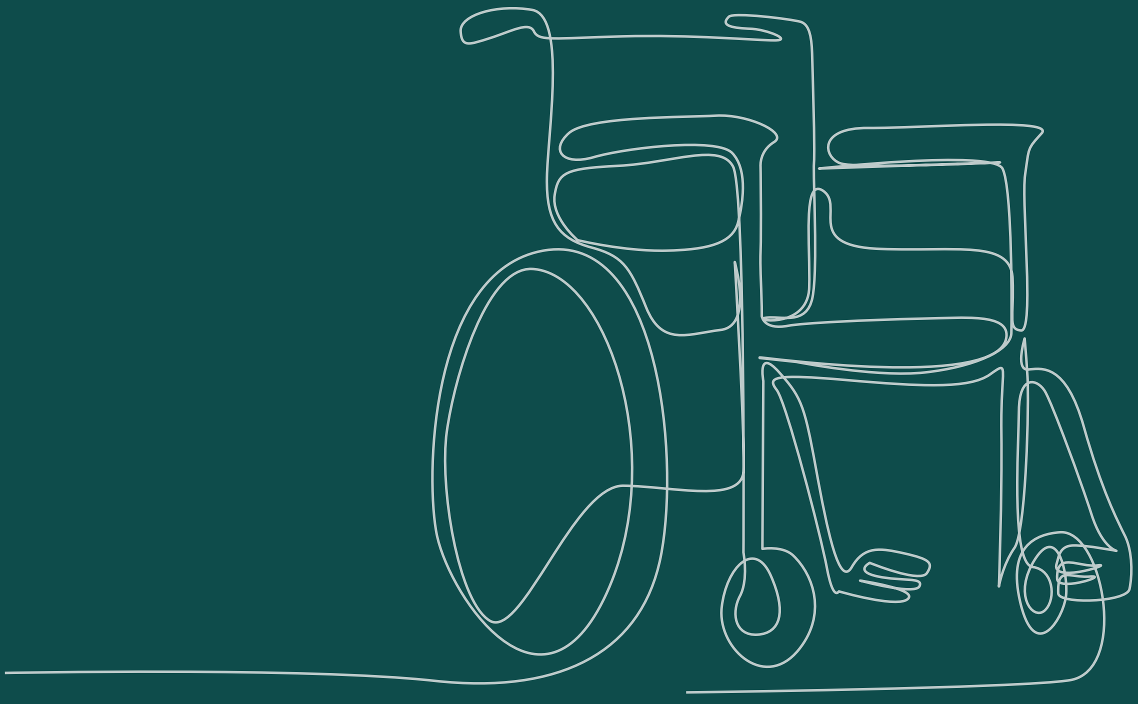
promotoren: prof.dr. P.S. Sterkenburg
prof.dr. P. Markopoulos

copromotor: dr. E.I. Barakova

promotiecommissie: prof.dr. P.J. Beek
prof.dr. I. Malagon
prof.dr. B. Maes
dr. D. Festen
dr. J. Liang

paranimfen: Edwin Korving
René Korving

Table of Contents



Chapter 1

Introduction

Andy enjoys the company of his family, especially his favourite older brother. He is fond of parties and the presence of company. His own birthday is his favourite moment, not for the gifts but for the many people surrounding him and the amounts of good food. He will walk around in a party hat from morning till night. The Dutch celebration of 'Sinterklaas' will fill Andy with joy for weeks after. Other pleasures Andy takes in life revolve primarily around food. Around dinnertime, you will find him in the kitchen, or he will be baking, frying, or cooking something or other in his toy kitchen. He has a big appetite, preferring fried meat, lasagna, and pie with whipped cream, but there are only a few things Andy does not like to eat. His family is convinced that Andy could have become a chef.

When Andy was six years old, he was diagnosed with the metabolic disease 'Syndrome of Sanfilippo'. This is a rare genetic disorder affecting the brain and spinal cord due to buildup of large sugar molecules. Children affected by Sanfilippo generally have a few normative years after which their development slows, and they may show behavioural problems. The following intellectual and motor decline is progressive, which means the children do not acquire complete skills and lose skills they have acquired, such as walking and speaking (Medline, 2017).

Andy has lived at home his entire life, and his parents feel he enjoys it there. They do often struggle to determine whether Andy is in pain, because Andy will not show any sign of pain or being uncomfortable. Often, he will get an infection to his urinary tract and his parents need to use all their senses to determine whether this is the case. He ended up in hospital, having to need a surgery to remove part of his femoral head which slid against his hip socket: a very painful situation. But to his family no clear signs of pain were shown and Andy's need for medical care was only discovered when it was specifically searched for.

1.1. General introduction

In the care for children and adults with a severe or profound intellectual disability (SID) many challenges arise. These are individuals with an IQ under 40 and a developmental age under 36 months who often have limitations in motor skills, communication, and expression, and can suffer from a multitude of chronic and/or painful medical disorders (DSM-V, 5th ed.; American Psychiatric Association, 2013; National Institute of Public Health and the Environment, 2022). They need caregivers to attune to their most basic needs such as health, food and hygiene, but also for psychological wellbeing, emotion regulation and developmental opportunities (e.g., Doodeman, Schuengel & Sterkenburg, 2023; Van der Putten & Vlaskamp, 2011; Van Tuyll van Serooskerken et al., 2022).

The Netherlands Institute for Social Research has estimated that in 2018 68.000 people had a moderate to profound intellectual disability (IQ<55; Sociaal Cultureel Planbureau, 2013). Those with a severe or profound intellectual disability (IQ<40) in the Netherlands are divided into two main groups: the group with severe or profound intellectual and motor disability and those with a severe or profound intellectual disability and challenging behaviour. Dutch organisations for the care of people with a disability estimated that there are 4,000 – 15,000 people with a severe or profound intellectual disability living in The Netherlands, of which 95% are being cared for by professionals in home care facilities (Cello, 2022; HandicapNL, 2022; 's Heerenloo, 2022). At least 2,000 individuals in the Netherlands have a profound intellectual and motor disability (IQ unmeasurable or under 25; Kennisplein Gehandicaptensector, 2021).

The International Association for the Study of Pain recognises that in individuals with intellectual disability (ID) many factors contribute to their increased risk of experiencing both chronic and acute pain (IASP, 2019). The vulnerability of people with a severe or profound intellectual disability to experience pain starts with an increased risk of accidental injury, and continues with physical and medical comorbidities (IASP, 2019; Van der Putten & Vlaskamp, 2011). Over 50% of people with a severe or profound intellectual disability suffer from seizure disorders, such as epilepsy (Arts, 1999), and an estimated 70% from gastroesophageal reflux (Böhmer, 1999), of which the latter can lead to respiratory disorders (Evenhuis, 2002). Furthermore, infections in the neuroskeleton, facial cavities, teeth, lungs, and bladder are more prevalent, either because of physical deformities (Cuvertino et al., 2017; Rodriguez, 2014) or a lower-than-average immune response to bacterial or viral pathogens combined with a higher infection risk with living together in close quarters (Dworkin et al., 2006; Van Schrojestein Lantman–de Valk & Noonan Walsh, 2008). The exact number of people with ID in pain is difficult to assess, because especially for those with a severe or profound intellectual disability self-report is impossible. At an evaluation, caregivers reported a certainty of daily pain in 13% of clients with ID, approximately equal to the amount in the general population (IASP, 2019).

Both regarding general everyday aspects and psychological and developmental aspects of life, an experience of pain causes a disruption (e.g., Attridge et al., 2015; Crombez et al., 1996). And since the genetic disorder leading to a severe or profound intellectual disability often also causes painful medical disorders, such as deformities in the skeleton and urinary tract, pain will exist in the lives of those with SID (Van Timmeren et al., 2016; Poppes, Van der Putten & Vlaskamp, 2010). The existence of pain will likely cause disruptions in development and daily life, which creates a challenge for caregivers to keep attuned to their clients' arousal, behaviour, and general wellbeing to become aware of possible pain they experience as well as accurately find and treat its cause (Evenhuis, 2002; Heslop & Houghton, 2019; World Health Organisation, 2024).

Out of the list of common painful medical conditions of people with a severe or profound intellectual disability, only neuroskeletal defects cannot be easily treated with well-known and commonly used medication (e.g., fibre-supplements for obstipation, Podzemny, Pescatori & Pescatori, 2015; calcium carbonate for reflux, Tran, Lowry & El-Serag, 2007; physician general knowledge, 2023). Where treatments are varied, common and low risk, such as those for infections, reflux and obstipation, recognising the existence of these disorders is paramount to provide relief, while with medical disorders where treatments are uncommon or possibly risky, pain relief treatment needs to be provided as soon as possible (Evenhuis, 2002). In both instances there lies a challenge for caregivers to timely identify signals of pain in their clients (e.g., McGuire, Daly & Smyth, 2010). For when any painful medical disorder runs its course for too long, for example a bladder infection, the risk of hospital stays, operations and even death due to renal failure increases (e.g., Mencap, 2013; World Health Organisation, 2024; York et al., 2022).

1.2. Pain and behaviour

There is a growing body of research concerning pain, its causes and effects, and the manners in which it is experienced (e.g., EFIC, 2022; IPRCC, 2019). The two leading descriptions of what pain is are from the IASP (2020; p. 1976): ‘an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage’, and pain expert Margo McCaffery (1968; p. 95): ‘whatever the experiencing person says it is’. Despite the difference regarding physical evidence of pain in these two descriptions, there is general agreement on pain’s disruptive nature and the necessity for pain relief and treatment (IASP Acute Pain, 2021).

Pain comes in many forms, which medical theory has categorised into three variations: acute pain, subacute pain, and chronic pain (Van Tulder et al., 1997). The main difference between these categories is the duration of the pain experience, but other differences also apply. Pain is considered acute if it lasts no more than six weeks (Bonica, 1953; Merskey & Bogduk, 1994). Pain that lasts longer than six weeks and no more than three months is subacute (Van Tulder et al., 1997). More serious injuries cause subacute pain, but the pain duration is not the same as the duration of healing. Complete healing of an injury can last longer than three months, but the maximum pain duration corresponds to how long the healing should hurt. When pain lasts longer than three months it is considered chronic (Merskey & Bogduk, 1994) and may not be linked to actual tissue damage or the healing of an injury anymore.

Among medical and behavioural professionals, there is consensus that not displaying pain in either expressions, behaviour, sounds or otherwise does not necessarily mean pain is not felt (IASP Pain in Intellectual Disability, 2021). So far, very little conclusive evidence has shown that non-communicative people that can hardly or not show their pain have an alternate pain tolerance threshold, but the studies that examined this report a lower pain tolerance and baseline, depending on the sensory test and aetiology of the intellectual disability (Defrin et al., 2004; Valkenburg, Tibboel & Van Dijk, 2015). The lack of self-reporting ability of, for example, people with a severe and profound intellectual disability makes it difficult to evaluate their pain experience (e.g., Evenhuis, 2002; Van der Putten & Vlaskamp, 2011), let alone design an experiment in which it can be tested. It seems that further research is needed to gain insight into the pain experience of persons who are unable to communicate (IASP factsheet, 2019).

1.2.1. Pain model

Loeser (1980) presented a pain model consisting of four levels, displayed in simple circles (Figure 1.1). Where the basic levels of nociception and perception do not require conscious thought, the greyed-out circles of experience and especially behaviour do so. Though there are many expressions that are considered universal, among which the reaction to pain, many pain behaviours such as seeking help and changing posture are learned and sometimes mimicked. However, the ability of people with a severe or profound intellectual disability to learn and mimic behaviours is limited (DSM-V, 2013).

Regarding what we know of pain and Loeser's model, a detection of a noxious stimulus travels through the body to the brain in several ways for several reasons (Basbaum et al., 2009; Chen et al., 2023). Just reflexively removing the painful stimulus from the body or removing the body from the painful stimulus does not solve all problems (Morrison, Perini & Dunham, 2013; Chen et al., 2023). The situation which led to the pain needs to be understood and tissue that was broken needs to be healed. The brain contains a 'pain library' where experiences causing pain are stored with their subsequent emotional response (e.g., Garland, 2012).

The emotional response is a matter in itself: The limbic system regulates emotions in the brain. Here it will be decided whether a painful experience makes a person cry out or not. Physiological responses, stemming from the activation of the autonomic nervous system and the arousal of the hypothalamic-pituitary-adrenal system, also originate in the limbic system (Catani, Dell'Acqua & Thiebaut De Schotten, 2013; Garland, 2012; Tennant, 2013). In other words, the limbic system creates an emotional response and causes the heart to start pounding, the body temperature to go up and stress hormones to release when someone is in pain.

It has been shown that the existence of an intellectual disability does not necessarily interrupt or interfere with the automated limbic processes (e.g., Aguilar Cordero, Mur Villar & García García, 2015; Benromano et al., 2017). Understanding pain, on the other hand, is something the ‘pain library’ helps realise for it is a warning system for behavioural change, to not repeat behaviour that led to pain (e.g., Melzak, 1961; Nay & Fetherstonhaugh, 2012). It may require a level of cognition which cannot be expected for people with a severe or profound intellectual disability, as it would not be expected for children up to 3 years old. This means that any behaviour related to an experience of pain, whether it is a behavioural change or a behavioural expression, may also surpass the ability of a person with a severe or profound intellectual disability (e.g., Baldridge & Andrasik, 2010; Dubois et al., 2010; Herr et al., 2006; Millard & de Knegt, 2019).

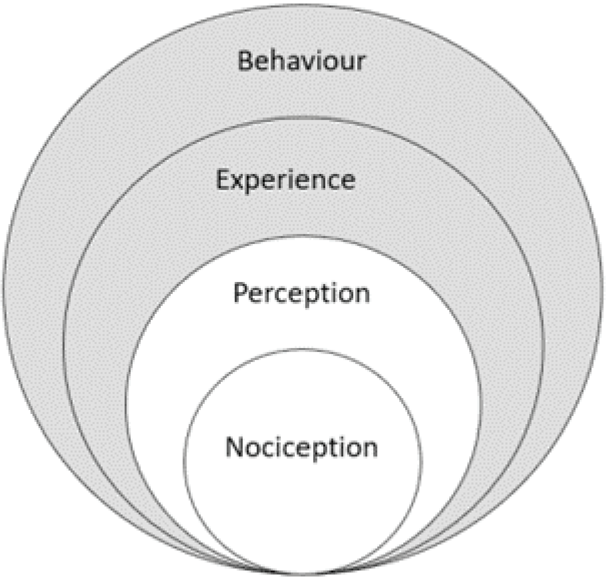


FIGURE 1.1. The four levels of pain, based on the pain model by Loeser (1980).

1.2.2. Pain Behaviour

Even though pain is a personal and often subjective experience, a person can usually tell when another person experiences pain. It is either communicated verbally or non-verbally by vocalising, grimacing or pain-specific movements (e.g., Visser & Davies, 2009). A large portion of a person's pain behaviour is learned behaviour, which has been reinforced and/or modified by their environment (Hart, 1988; Visser & Davies, 2009). Where a young child will loudly cry or scream, thought of as preprogrammed behaviour (Bowlby, 1973), most adolescents and adults will have modified this behaviour to a moderate whine and a grimacing face. Of course, for children and adults able to communicate their painful experience will be part of their narrative, their verbal expression of the type and intensity of pain they are experiencing. But when a severe or profound intellectual disability prevents a person to cognitively develop beyond the age of a toddler, an experience of pain can be quite difficult to understand let alone communicate to others (e.g., Enninga, 2023; Millard & de Knegt, 2019; Nay & Fetherstonhaugh, 2012).

Research on pain observations of children and adults with an intellectual disability show interesting results. Defrin, Lotan and Pick (2006) found that behaviours vary between children and adults in a way that a non-communicating pain checklist can be applied to assess pain in children, but not in adults with an intellectual disability. This same study also showed that the extent of the intellectual disability influences pain behaviour: We see more idiosyncratic pain behaviour in adults with a severe or profound intellectual disability, compared to adults with a mild to moderate intellectual disability.

1.3. Pain measurement

Within the study of pain, which can encompass anything from determining pain thresholds for different groups to the effectiveness of certain pain relief strategies, self-report is considered the gold standard (Von Baeyer, 2013; McCaffery, 1968; McCaffery et al., 2011). Certainly, when a pain patient is coherent and can self-report it would not be logical to use any other type of pain assessment method. On the other hand, if a patient is unable to communicate and self-report it is up to the environment to assess the pain and react to it (Moulster, 2020). This by-proxy assessment is possible in several ways, such as checking physiological responses and observing behaviour, but specifics for each method can differ per group, per setting and even for each person. It makes a difference if a person has an intellectual disability or not, or if the person is recovering from an operation or trauma in a hospital setting, or when they are in a residential setting going about their day.

Furthermore, the assessment of acute or subacute pain differs from that of chronic pain (Bonica, 1953; Merskey & Bogduk, 1994).

When a person stubs a toe or gets a cut on their hand, the pain they perceive is acute. It is close in time to the cause of the pain and usually does not last very long, a few hours to a few weeks (Van Tulder et al., 1997). Furthermore, the autonomous nervous system can respond heavily to a situation of acute pain, putting the body in a state of readiness to either fight or flee, to make sure the action that caused pain is not prolonged or repeated. This is why the heart starts beating more rapidly and sweat erupts, to make sure everything is ready to bring the body back to safety and away from whatever has caused it physical trauma. This automatic system does not distinguish between harmless and harmful situations, because that is what the brain does, and the assessment the brain makes is much slower than the speed of the nervous system (e.g., Morrison, Perini & Dunham, 2013).

If the physical trauma is more extensive, such as a broken bone, pain can last longer than weeks and up to a few months (Merskey & Bogduk, 1994). Pain that lasts longer than three months and has stopped being related to physical trauma, where the trauma has healed, is called chronic pain. Chronic pain is the most difficult of the pains to assess, evaluate and combat, because there is no physical cause to treat and the body usually stops responding to the pain (e.g., Coppetiers et al., 2016). However, the body will react once again when a noxious stimulus causes an acute pain experience. For chronic pain, unfortunately, there is no maximum time it can last and no single form of treatment has been discovered that can heal chronic pain (NIH, 2023).

The recognition of pain signals in people with severe or profound intellectual disability is considered a challenge since these people do not always show responses to pain that those without intellectual disability consider natural (Abu-Saad, 2000; Defrin, Lotan & Pick, 2006; Lotan et al., 2009a; Lotan et al., 2009b). Though pain is often shown in the face, the response is not always with the contortion of the brow and mouth. Laughing or relaxing all facial muscles also occurs. When a bodily response to pain is shown, it can vary from freezing to moving the limbs more rapidly, and groaning as well as becoming silent. Parents and professional caregivers of people with severe or profound intellectual disability report all these behaviours when their child or client is in pain (Enninga et al., 2023, Kreukniet et al., 2016). These contradictions in possible pain responses increase the challenge to observe and recognise signs of pain by caregivers.

1.3.1. Pain observation via a systematic observation list

Although the existence of pain can be a regular worry for caregivers of people with SID (Korving, Enninga et al., 2021; Van der Putten & Vlaskamp, 2011) and this target group has a very limited ability or inability to self-report (Abu-Saad, 2000; Defrin, Lotan & Pick, 2006), until recently no systematic observation list was specifically validated for adults with a severe or profound intellectual disability in a residential setting (Enninga et al., 2023). Parents and caregivers would try to read their child or client, often checking off a list of possible causes for the behavioural change they noticed. Causes such as hunger, stress, exhaustion, overstimulation, a need for intimacy, or a dirty diaper would have to be ruled out before a physician was contacted. Since the result of this search could be delayed diagnosis and management of medical disorders, setbacks in hospitalisation and increased death rates (Jancar & Speller, 1994; Roy & Simon, 1987; World Health Organisation, 2024; York et al., 2022), several research studies were performed to attempt to provide an adequate observation list.

The Face, Legs, Activity, Cry, Consolability (FLACC; see Table 1.1) Behavioural Pain Assessment Scale (Merkel et al., 1997) has been developed to assess postoperative pain in young children (in the ages between 2 months and 7 years) or those unable to communicate their pain. The scale was shown to also be useful for adults on intubation machinery, offering a similar evaluation as the Checklist of Nonverbal Pain Indicators which is used in Intensive Care Units. Nonetheless, postoperative circumstances are dissimilar to residential circumstances so that this scale is inadequate to be used in daily care for individuals with a severe or profound intellectual disability.

TABLE 1.1. The FLACC Behavioural Pain Assessment (Merkel et al., 1997).

Category	**Scoring**		
	1	**2**	**3**
Face	No particular expression or smile	Occasional grimace or frown, withdrawn, disinterested	Frequent to constant quivering chin, clenched jaw
Legs	Normal position or relaxed	Uneasy, restless, tense	Kicking, or legs drawn up
Activity	Lying quietly, normal position, moves easily	Squirming, shifting back and forth, tense	Arched, rigid or jerking
Cry	No cry (awake or asleep)	Moans or whimpers; occasional complaint	Crying steadily, screams or sobs, frequent complaints
Consolability	Content, relaxed	Reassured by occasional touching, hugging or being talked to, distractible	Difficult to console or comfort

The Numeric Rating Scale (NRS-11; see Figure 1.2) is most often used by caregivers and medical personnel for non-communicative adults or children (Chiarotto et al., 2019; Von Baeyer & Hicks, 2000). The scale runs from zero to ten, or from no pain to worst possible pain, and is filled out according to observations of pain expressions in the patient's face. The NRS provides facial pictographs that correspond to different numbers on the scale but provides no other information for observers. Considering this scale is not specifically designed for pain expression of people with a severe or profound intellectual disability, it may not be sensitive enough to provide insight in their pain experience.

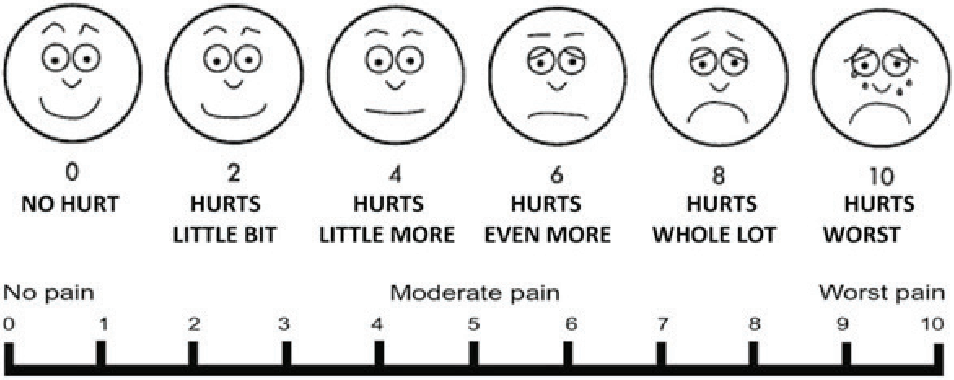


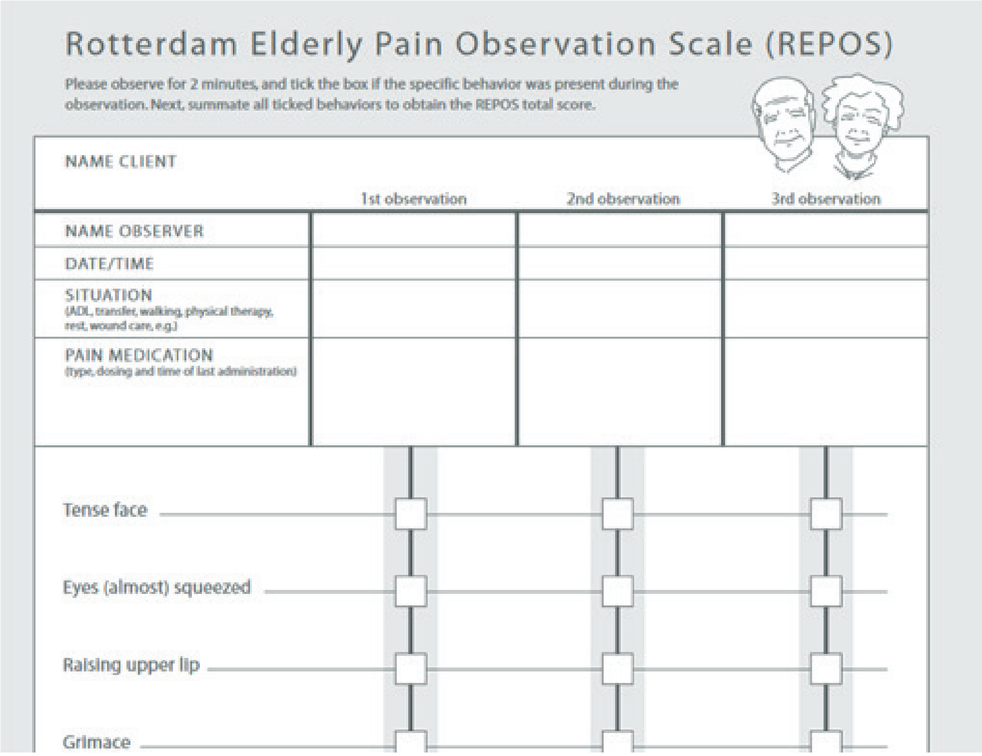
FIGURE 1.2. The Numeric Rating Scale with faces (e.g., Von Baeyer & Hicks, 2000).

The Non-Communicating Adult Pain Checklist (NCAPC; see Table 1.2) is specifically developed for adults with various levels of intellectual and developmental disability in a clinical setting (Defrin, Lotan & Pick, 2006; Lotan et al., 2009a). This checklist showed a sensitivity to pain responses across all levels of intellectual and developmental disorders during either an influenza vaccination or a dental hygiene treatment. However, it has not been researched whether adults with a severe or profound intellectual disability will respond the same way to pain in their home setting where we assume that they experience less stress

TABLE 1.2. The first seven items of the non-communicating adults pain checklist (NCAPC; e.g., Defrin, Lotan & Pick, 2006).

Item	**Score**			
	Not at all	Just a little	Fairly often	Very often
Vocal reaction				
Moaning, whining, whimpering (fairly soft)	0	1	2	3
Crying (moderately loud)	0	1	2	3
Screaming or yelling (very loud)	0	1	2	3
Emotional reaction				
Not cooperating, cranky, irritable, unhappy	0	1	2	3
Agitated, being difficult to distract, not able to satisfy or pacify	0	1	2	3
Facial expression				
Furrowed eyebrows, raising eyebrows	0	1	2	3
A change in eyes including (squinting of eyes, eyes opened wide, eye frowning)	0	1	2	3

The Rotterdam Elderly Pain Observation Scale (REPOS; see Figure 1.3) was developed for use in residents of nursing homes who are incapable of self-reporting pain (Boerlage et al., 2008). It appears to be sensitive to pain responses of people with various levels of cognition, which makes it possibly useful for people with a severe or profound intellectual disability in a residential setting, although it has not yet been validated in adults born with ID. Considering that pain behaviours are learned, via positive reinforcement throughout life, a difference can be expected between those born with an intellectual disability and those experiencing cognitive decline later in life (e.g., Cordier & Diers, 2018; Linton & Shaw, 2011).



Rotterdam Elderly Pain Observation Scale (REPOS)

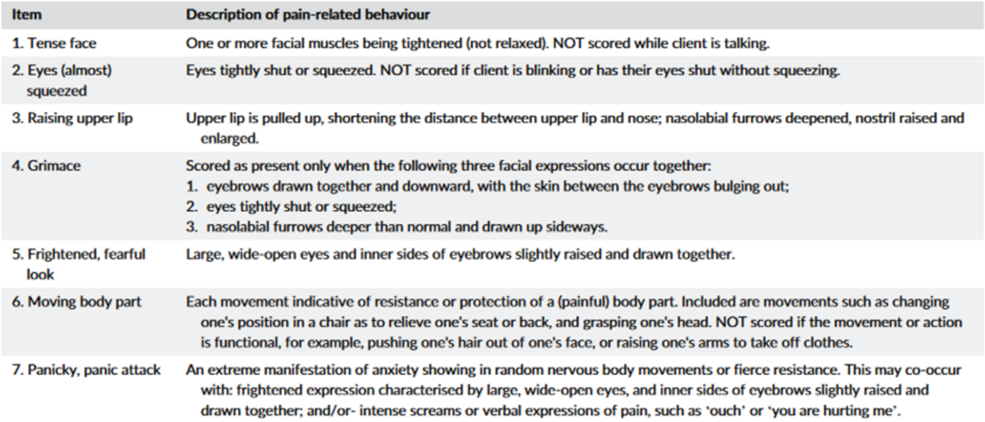
Please observe for 2 minutes, and tick the box if the specific behavior was present during the observation. Next, summate all ticked behaviors to obtain the REPOS total score.

NAME CLIENT

	1st observation	2nd observation	3rd observation
NAME OBSERVER			
DATE/TIME			
SITUATION (ADL, transfer, walking, physical therapy, rest, wound care, e.g.)			
PAIN MEDICATION (type, dosing and time of last administration)			
Tense face	☐	☐	☐
Eyes (almost) squeezed	☐	☐	☐
Raising upper lip	☐	☐	☐
Grimace	☐	☐	☐

FIGURE 1.3. An example of a REPOS scoring card with the first four items (Boerlage et al., 2008).

The Pain Observation Scale for Adults with profound Intellectual Disability (POSAID; see Figure 1.4) is a pain observation list currently being developed for adults with severe and profound intellectual and multiple disabilities in a residential setting. The items that make up this list are a combination of items from the REPOS-scale and literature, and they were tested on video material of more than 100 adults with a severe or profound intellectual disability. Reliability and validity testing is still underway though results so far look promising (Kreukniet, Bruns & Van der Putten, 2016).



Item	Description of pain-related behaviour
1. Tense face	One or more facial muscles being tightened (not relaxed). NOT scored while client is talking.
2. Eyes (almost) squeezed	Eyes tightly shut or squeezed. NOT scored if client is blinking or has their eyes shut without squeezing.
3. Raising upper lip	Upper lip is pulled up, shortening the distance between upper lip and nose; nasolabial furrows deepened, nostril raised and enlarged.
4. Grimace	Scored as present only when the following three facial expressions occur together: 1. eyebrows drawn together and downward, with the skin between the eyebrows bulging out; 2. eyes tightly shut or squeezed; 3. nasolabial furrows deeper than normal and drawn up sideways.
5. Frightened, fearful look	Large, wide-open eyes and inner sides of eyebrows slightly raised and drawn together.
6. Moving body part	Each movement indicative of resistance or protection of a (painful) body part. Included are movements such as changing one's position in a chair as to relieve one's seat or back, and grasping one's head. NOT scored if the movement or action is functional, for example, pushing one's hair out of one's face, or raising one's arms to take off clothes.
7. Panicky, panic attack	An extreme manifestation of anxiety showing in random nervous body movements or fierce resistance. This may co-occur with: frightened expression characterised by large, wide-open eyes, and inner sides of eyebrows slightly raised and drawn together; and/or- intense screams or verbal expressions of pain, such as 'ouch' or 'you are hurting me'.

FIGURE 1.4. The first seven items of the POSAID with description (Kreukniet et al., 2016).

In sum, caregivers of adults with SID cannot yet use a specialised pain observation checklist for their target group in a residential setting. Besides this lack, using a systematic pain observation list is time-consuming, burdensome, and difficult. When pain is experienced during a caregiving moment, a second caregiver will be needed to observe the client. The daily practice of caregiving often conflicts with the filling out of an observation list and professional caregivers that know a client well have been shown to differently assess their client's behaviour than an objective observer would. Furthermore, even when pain behaviours correlate well with a patient's verbal report '[…] external observers tend to 'underestimate' pain intensity' (Visser & Davies, 2009, p. 35). Therefore, a continuous, automated, and objective manner of pain detection is certainly desired.

1.3.2. Physiological pain measurement via a wearable

The fact that the body responds physiologically to pain means these responses can be measured. We can measure an increased heart rate, a change in heart rate variability, a change in the need for oxygen, increased sweat production, brain activity and blood pressure, and even changes in hormonal levels (e.g., Bentley et al., 2016; De Knegt et al., 2013; Koenig et al., 2014). All these changes are either measurable on the inside or outside of the body and are found in both healthy and sick adults, children, and neonates (Arbour & Gélinas, 2014; Coppetiers et al., 2016; Kyle & McNeil, 2014). Most of the physiological reactions can be measured constantly without caregiver input by wearable sensors (e.g., Kim et al., 2019).

Such wearable sensors, or wearables, have been used as early as 1956 to provide information on patient’s health status, athlete performance, risks of certain diseases and more (Kim et al., 2019). A wearable biosensor has two main functions: a ‘bio-receptor’ which targets a specific bio-organic process, such as sweating, temperature increase or decrease, or enzyme production, and a ‘physico-chemical transducer’ which transforms the bio-receptor’s response to useful chemical, electrical, or mechanical output (e.g., Naresh & Lee, 2021; Smith, Lee & Tse, 2023). The first of the bio-optic devices, which were one-time use sensors that were assessed in a lab setting, were eventually further developed to incorporate ‘on the body’ testing and assessment, or in other words, the first wearables. From 2010 onwards several advanced and reusable wearable biosensors have been developed (Kim et al., 2019).

Since the transition from in vitro to in vivo measurements, care has been taken to limit the invasiveness of wearables, specifically when the target group has a vulnerability, such as an illness or chronic pain (Kim et al., 2019). The comfort of the person using a wearable to assess their health status is deemed just as important as that health status itself. Wearables have become invisible and unnoticeable, embedded in crowns or mouthguards, or at the very least as non-invasive as possible, such as sensors in contact lenses or temporary tattoos.

When we want to assess a physiological change as a response to pain, we require a non-invasive assessment for the quite simple reason that an invasive measurement could elicit a stress response in the wearer. Such a stress response leads to a physiological change, to a comparable change as the one the biosensor is trying to assess. This, in turn, leads to the entanglement of measurements: Does the biosensor measure the stress response to pain or the stress response to the invasiveness of the biosensor? Therefore, the biosensor’s measurement needs to be clean from any possible confounding influences (Smith, Lee & Tse, 2023).

To assess pain in people with a severe or profound intellectual disability, the need to have a non-invasive measurement is essential, since these people are hardly able to communicate about their stress level (e.g., Doodeman, Schuengel & Sterkenburg, 2023; Evenhuis, 2002; Van der Putten & Vlaskamp, 2011). With their limited capacity to understand their surroundings, stability and predictability are deemed important for their sense of safety. Introducing a wearable, even a non-invasive one, can upset their structure. With that in mind, the choice was made to convert regular cotton socks into wearable smart socks (Bremmer, Croes & Sterkenburg, 2014). The inside sole of the socks could house several fabric biosensors, which would not be felt by the wearer, and the sock itself was quite similar to regular socks. Also, for people with a severe or profound intellectual disability, the process of getting dressed in the morning and undressed whenever necessary would not change with the introduction of the smart sock. Therefore, the structure of their day and their sense of safety would not be altered.

Another aspect of the wearable and its use is the interpretation of the measurement's signal. As described before, a physico-chemical transducer translates the biosensor's information to a signal that can be sent to an interpretative device. It is this device that determines the value of the received signal, for example whether that signal is a reason for alarm. The trustee of the interpretative device can either be the wearer of the wearable, or another party, such as a parent, medical professional, or caregiver. No matter who is trusted with the interpretation, the result should be clear and unambiguous.

Those who interpret the results of the pain detection method will need a clear and intuitive illustration of what the measurement provides. Both in a hospital setting and a residential caregiving setting, several professionals with varying points of view tend to care for one patient or client. These are professionals with varying degrees of experience, education, intelligence and various cultural and personal backgrounds. Therefore, the information provided on the physiological response cannot be too complex, in any way vague or multi-interpretable, which is a challenge that should be addressed in the design and development stages already.

Despite their differences on multiple aspects, the group of professional caregivers of children and adults with a severe or profound intellectual disability also has something in common. They spend their working day caring for those who need help in daily care, for clients that have limited communicative and expressive skills. It is a group of caregivers devoted to give an extremely vulnerable group of people developmental possibilities and a good quality of life. That commonality in professional choice may mean the group has an important common insight for the design of a caregiving aid.

Therefore, the group of professional caregivers and parents of people with SID should be candidates for cocreating the aid they will use in daily practice. Cocreation in industry has become popular since 2000 and the work of Prahalad and Ramaswamy (2000). When cocreation is implemented, industry profits and customers' engagement grow (Huang & Rust, 2017; Kotler, Kartaya & Setiawan, 2010). Within research, cocreation is considered to move universities from just translating knowledge to society to collaborative knowledge production, which results in a higher impact of the research (Greenhalgh et al., 2016).

1.4. Research Approach

This study combines several quantitative and qualitative research methods in a Research-Through-Design approach (Stappers & Giaccardi, 2012; Figure 1.5). In this approach, theory and research are used as a foundation from which to develop prototypes based on practical needs and constraints. Insights from the use and testing of prototypes is fed back into the research for further development (Stappers, 2007). The design phases are as much part of the research as the experiments and systematical observations.

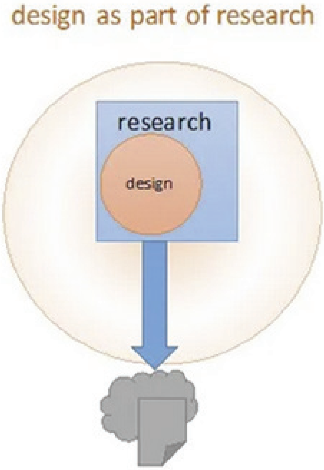


FIGURE 1.5. Research-Through-Design, where design activities create tools or stimuli from theory and research.

The initial phase of this study will be a comprehensive systematic literature review, to examine what is already known and has been done in the field of physiological pain measurements. The results will form a basis for the pain measurement system to be developed and tested. The review will look at the methods that are feasible and ethical to be used on people unable to give informed consent, by not only looking at the sensitivity and functionality of the researched methods, but by also assessing their invasiveness and technology readiness level (United States Department of Defense, 2010). The knowledge gained will be used to create the first prototype of the pain measurement system.

In a series of experiments the first prototype of the pain measurement system will be tested. These tests will combine the usability of the system itself, and the outcome the system is supposed to provide. The target group will be healthy adults without intellectual disability, who can be well-informed and give consent, but also will provide feedback on how easy and intuitive the system is in use. Quantitative measures, physiological data and a demographic questionnaire, will be used to provide the input to further develop a pain measuring technique, while qualitative data, video observations and usability input, will contribute to the improvement of the system's user friendliness.

In a next step, eventual users of the system will be invited to contribute to the design and the research. These will be the parents and caregivers of adults with a severe or profound intellectual disability, as they will be the ones connecting their child or client to the system and assessing the system's output. This part of the study will focus on the design of a mobile application for output of the system and will be based on theoretical knowledge and practical needs and constraints. Again, quantitative research methods, such as questionnaires, and qualitative methods, e.g., interviews, workplace walk-throughs and design focus groups, will be combined to provide a thorough overview of what a practical pain measurement system needs for it to be used in daily caregiving. Unlike a user friendliness study, this phase will have input from eventual users during the development of the system's output application, which will need to be adjusted to what the eventual user can focus on while performing daily tasks and what they need the system to provide for them to decide to use it.

Simultaneously to the cooperative design phase, data from the pain experiments with healthy adults without ID will be used to create a pain classification algorithm. Because physiological data creates a lot of data points to process, machine learning will be used. Physiological responses to induced pain will be compared to physiological responses to a similar, pain-free experience, and classified accordingly in a model. Then, new data will be introduced, and the model will try to classify these data as either pain or no pain. Preferably, the model should have a success rate of more than 90%, which means both positive (pain) and negative (no pain) classifications should be correct in over 90% of data points, but the study continues when the success rate is at least 80%.

The following step is the usability phase, where the user friendliness of the system is tested as a whole. Both the system's hardware, that gets input from the wearer, as the software, that provides output for the user, are tested on practicality, intuitiveness, desirability, and perspicuity. Again, quantitative measurements, via a questionnaire providing benchmark data, and qualitative measures in the form of interviews during workplace use, are combined to provide thorough insight into the needs and wishes of the user for a pain measurement system. In this phase, clients with a severe or profound intellectual disability will wear the system only to test its usability, not to provide physiological data. The use of a validated usability questionnaire will make sure the system will adhere to ISO standards (ISO 9241-11: 2018).

In the final phase of the study, clients with a severe or profound intellectual disability will again be the wearers of the system and provide pain data. They will be observed during a physical therapy session, a wound treatment, or a vaccination, and both their physiological and behavioural response to the expected pain moment will be recorded. The pain moments will be coded using systematic observation lists for pain in non-communicating adults with a severe or profound intellectual disability. The speed with which the physiological measurement system records a pain moment will be compared to the speed with which a systematic observer can code a pain moment.

The described research approach is graphically displayed in Figure 1.6. It displays the study’s design process of divergent thinking using results from the systematic review to co-create a system with the eventual users, to converge to focused action by making a version of the system for a testing phase (the left blue diamond). Then, in the testing phase (the right blue diamond), theoretical information and user needs, wants, and constraints are gathered to investigate how the system can and will be used in daily practice. This phase is concluded by providing a solution based on the users’ feedback (Double Diamond Model; Banathy, 1996).

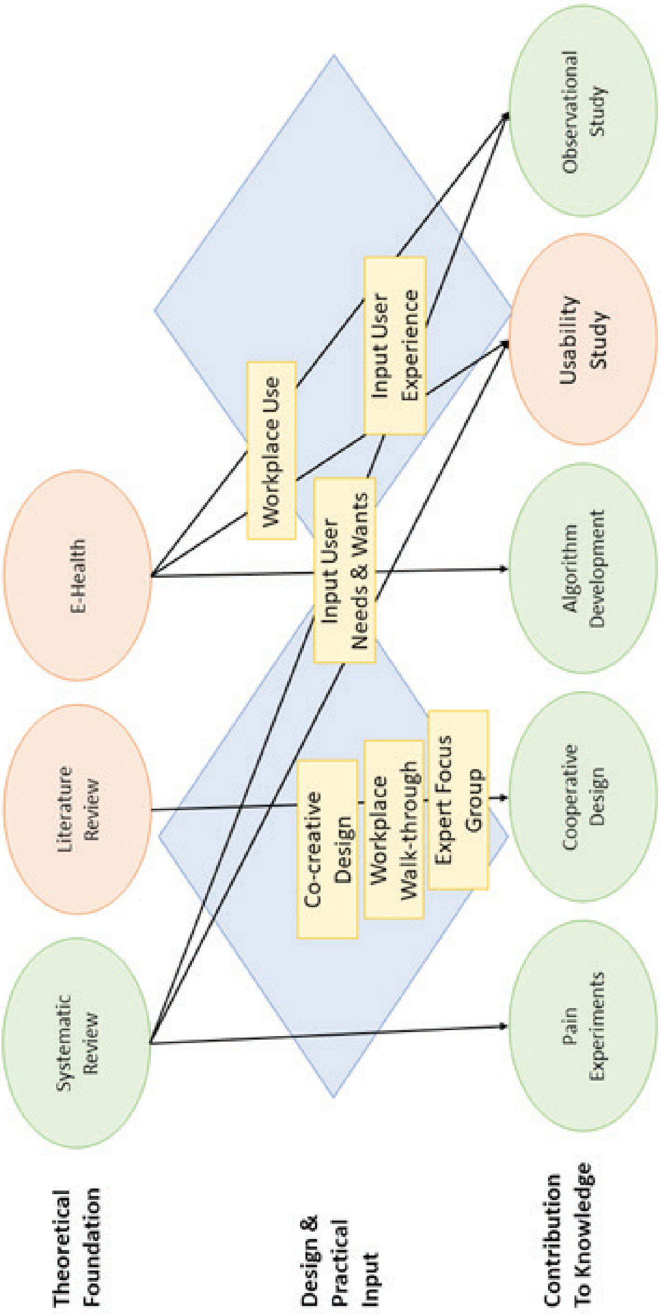


FIGURE 1.6. The study's research approach on three levels: Theory, Design & practice, and Contribution to knowledge. The green circles are chapters in the dissertation.

1.5. Testing the Pain app in the target group with a severe or profound intellectual disability

Considering little is known about the pain experience of adults with a severe or profound intellectual disability, or the physiological responses that pain elicits in this group, an important phase of this study is to test whether the pain signalling system works the same in adults with a severe or profound intellectual disability as it would work on those without an ID. The algorithm that classifies the incoming signal in the SID Pain App as either pain or no pain will be trained on healthy adults without ID, therefore expecting similar results in the target group that has several medical disorders and an intellectual disability is not feasible. And even though the experiment in the target group of the SID Pain App will look very different than the one that was conducted to train the algorithm, without this important step, the system cannot be brought out to be used in daily caregiving.

Since the ability to self-report pain in the target group is limited or non-existent, whether a pain experience is present needs to be systematically observed or reported by others. As no experimental condition can be tested with persons with a severe or profound intellectual disability, this limits the situations in which the pain detection algorithm can be tested. However, predictable and necessary moments of pain are present during physical therapy, wound care or when given a vaccination. Having a client with a severe or profound intellectual disability wear a smart sock connected to the SID Pain App in these situations will give the necessary data to evaluate the system's wanted functionality.

The experimental observations in the target group will provide not only data about whether the system works on a person with a severe or profound intellectual disability, but it will also provide information about the speed of a physiological pain signal compared to a systematic observation of pain behaviour, as well as the sensitivity of the physiological measurement compared to a systematic observation. It will be possible to synchronise the skin conductance data with video data, which will enable a comparison of the moment the SID Pain App signals pain and the moment a systematic observation list codes pain based on its cut-off score – the number of pain-related behaviours that are observed within a certain observation-time. The data from the observations in the target group will also show whether physiological pain signals are sometimes unaccompanied by observable pain-related behaviour.

1.6. Scope and content of the thesis

The goal of this project is to create a reliable and specific way to physiologically measure pain in adults with a severe or profound intellectual disability (SID) in a residential setting. These adults suffer from a multitude of painful medical disorders, some of which are easily treated; they often show unique and idiosyncratic pain behaviour, and caregivers do not always have the time or skills to recognise these signals or fill out pain observation checklist. The creation of a mobile physiological pain detection system, non-invasive and easily integrated in daily caregiving, was a necessary addition to residential settings of adults with a severe or profound intellectual disability.

1.6.1. The aims of this thesis are:

1. To evaluate several physiological pain detection methods on usability, invasiveness and technological readiness;
2. To develop a reliable, valid, and specific physiological pain detection algorithm to be programmed into a mobile application;
3. To test this mobile pain detection application on adults with SID and to assess the user experience of the caregivers using the mobile application.

1.6.2. Relevance of the research

This manuscript describes the development of a system for the physiological assessment of pain in adults with a severe or profound intellectual disability. The system uses wearable sensors in a smart sock to measure skin conductance and can therefore constantly evaluate the wellbeing of the wearer, even when there is no caregiver close-by. The sock contains a transmitter unit that uses Bluetooth® to send the appraisals to a mobile device, which assesses the skin conductance signals and will indicate whether the wearer is in pain or not.

Technology is all around us and constantly in development. Its use in caregiving is not only desirable to decrease caregivers' responsibilities and workload, but also necessary to improve clients' independence, self-efficacy, and quality of life. When technology is used in a client-focused, relational, and innovative manner, there are many benefits for people with a severe or profound intellectual disability. Technology that is used to attune to the needs of a client, to provide information about their wellbeing, to give opportunities for decision making, or to enhance their experiences, can improve health and mobility, increase developmental opportunities, explain and decrease problem behaviour and self-harm, and severely limit the consequences of any type of pain. The question is not if technology should be used in caregiving, but when and how.

Especially considering their increased risk of painful medical disorders and their inability to communicate with language about their wellbeing, people with a severe or profound intellectual disability can suffer from several serious consequences of pain on a behavioural, developmental, and social level. Pain that goes unrecognised and untreated leads to a severely limited quality of life and can result in illness, hospital stays and death. What this manuscript will show, is that recognising pain in the behaviours of people with a severe or profound intellectual disability can be quite challenging. Even parents or caregivers that have known them for a long time can be uncertain about when and whether their child or client is in pain. Pain behaviours can be subtle or fleeting, unexpected and idiosyncratic, or there may appear to be nothing wrong with the person with SID until a serious injury or illness is discovered.

This manuscript provides an overview of the development and testing of an automatic pain detection system to be used in daily caregiving. The study was co-founded by parents and caregivers of adults with a severe or profound intellectual disability, the eventual users of the system. In every step of development, they were invited to advise on, co-create, and test all aspects of the system, in order to bring about a pain signalling aid that is intuitive, useful, and practical to be used with and around all tasks and distractions of daily caregiving.

1.6.3. Structure of the thesis

Chapter 2 reviews physiological pain assessment methods used on several target groups. Using 29 review studies on physiological pain measurement methods, which included 540 unique articles published between 1973 and 2019, function, invasiveness, and technological readiness of 18 measurement methods and vulnerability of seven target groups were assessed. Vulnerability of the target group has an inverse correlation to the invasiveness of the measurement method, and many of the most-used pain measurement methods have the highest or second-highest technological readiness. Their function is very varied, which was related to small participant groups, outside influences on the measurement, and unreliability of the method to detect pain.
Design: Systematic search using PRISMA-guidelines and quality assessment using CASP.

Chapter 3 describes a pilot study where an existing physiological measurement method, for detecting electrodermal activity in a sensor sock, is tested as a pain assessment method on four healthy adults without intellectual or physical disability. Pain was elicited by asking each participant to submerge the non-dominant hand in a tub of ice-water at least

once until the pain tolerance threshold was reached. Each participant wore a smart sock and self-reported pain on a seven-point Likert scale, from ‘no pain’ to their pain threshold. Results indicate that each pain experience gives a clear physiological response, this response is unique for each person, and physiological response to a second pain experience happening within five minutes to the first experience is smaller.
Design: Pilot with a multiple case study visual assessment of physiological data.

Chapter 4 describes the process of creating a pain detection algorithm and the subsequent programming of the mobile pain signalling application. With pain data from 28 healthy adults between 19 and 52 years of age without intellectual or physical disabilities 68,900 data points were created. Models were made using the classification method Random Forest Prediction, which led to a disbalanced model. Using the Synthetic Minority Oversampling Technique, classes were balanced by increasing the data of pain moments based on the nearest neighbours. With 50% interpolated pain data, weighted averages of reliability, precision, recall and F1-score increased to over 0.80.
Design: Single-blind experimental design with two conditions for data gathering, and random forest prediction modelling for developing the classification algorithm.

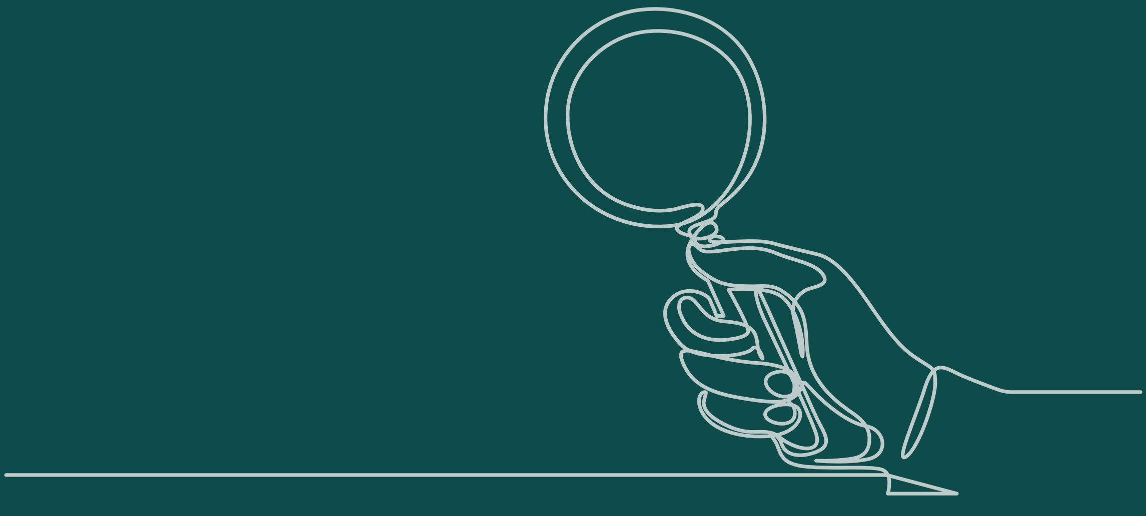
In **Chapter 5** a description is given of the design-research for the visualisation of the pain signalling application. Several groups of professional caregivers and parents of adults with a severe or profound intellectual disability have collaborated in this research in either focus groups, interviews, questionnaires, and workplace walk-throughs, to assess the needs of the eventual users. In three sub-studies, all needs and possibilities mentioned by the caregivers involved were considered for the design of a visualisation that would attract a caregiver’s attention without being a visual burden.
Design: Three-phase multi-modal design research, using both quantitative and qualitative methods for data gathering and collation.

Chapter 6 examines alternative methods to create a pain prediction algorithm and assesses the user friendliness of the system. Different modelling techniques are presented and discussed, as well as an opportunity to combine three to five models and involve ChatGPT. User friendliness of the system is evaluated with the User Experience Questionnaire in twenty participants’ native language. The findings are discussed on six subscales, and these are benchmark compared to other systems.
Design: Machine learning for further algorithm development and seven-point Likert questionnaire design for user experience.

Chapter 7 describes the testing of the SID Pain App in the target group of adults with a severe or profound intellectual disability. Fourteen clients (50% female) have worn the pain app system during a physical therapy treatment of fifteen to thirty minutes, while their facial expressions and behaviour was videotaped. Video-material was coded with the Non-communicating Adult Pain Checklist and the Pain Observation Scale for Adults with Intellectual Disabilities, and physiological data was added and synchronised.
Design: Observational research, gathering both physiological and video data to be compared.

Chapter 8 discusses the main findings and conclusions of this thesis, divided per chapter. Implications for theory, practice and design are discussed as well as lessons learned and further research possibilities. The thesis ends with a discussion of plans for this pain signalling system.

Lastly, in five appendices, references, easy-to-read English and Dutch summaries, author contributions, a word of thanks, and information about the author are provided.



Chapter 2

Physiological Measures of Acute and Chronic Pain within Different Subject Groups: A Systematic Review[1]

---

[1] Published as: Korving, H., Sterkenburg, P. S., Barakova, E. I., & Feijs, L. M. G. (2020). Physiological measures of acute and chronic pain within different subject groups: A systematic review, *Pain Research and Management, vol. 2020*, Article ID 9249465, 10 pages. Doi: 10.1155/2020/9249465.

Abstract

Background and objective: The most frequently used methods for assessing pain are self-reports and observation. However, physiological methods could improve accuracy and reliability for those with communicative difficulties. This review's objective is to analyse methods used to physiologically assess pain, to rank them by invasiveness per method and vulnerability per subject group, and to assess their technological maturity. Databases and data treatment: Six international databases were searched for review papers between 2007 and 2019. Inclusion criteria were as follows: at least one physiological method for acute or chronic pain in humans; languages were as follows: English, French, Dutch, German, and Spanish. Quality of reviews was assessed using the CASP checklist. Results: The methods' heart rate variability and electroencephalogram show clear and consistent results as acute pain assessment. Magnetic resonance imaging can measure chronic pain. Ordered by invasiveness and vulnerability, a trend shows that invasive methods are used more with less vulnerable subjects. Only instruments used for skin conductance and automatic facial recognition have a lower-than-average technological maturity. Conclusions: Some pain assess¬ment methods show good and consistent results and have high technological maturity; however, using them as pain assessment for persons with ID is uncommon. Since this addition can ameliorate caregiving, more research of assessment methods should occur.

2.1. Introduction

When a person is unable to communicate that he or she has pain, for example those with severe or profound intellectual disability (S/PID), this may cause unnoticed suffering. They might receive less pain relief medication or receive it too late, and not knowing whether there is pain creates doubt in caregivers. A verbal person without disabilities can be asked to self-report about their pain, but this is impossible in persons with S/PID. Observations seem like a good alternative, but they have been shown to miss subtle signs of pain specific in adults with S/PID (Van der Putten, & Vlaskamp, 2011). The assessment of physiological signs of pain can be a good alternative for persons unable to communicate about pain. Furthermore, physiological assessment might be more accurate than observations for this group.

Pain research among persons with intellectual disabilities is scarce (De Knegt, et al., 2013), and research focusing on physiological signs of pain in this group even more so. De Knegt, et al. (2013) conclude that specific behavioural indicators are often and consistently mentioned as indicators for pain in people with intellectual disabilities, but also indicated that there are physiological responses clues that can be examined to measure pain. This indicates that physiological assessment of pain can be introduced as an addition in caregiving for persons with S/PID. This provides an incentive for researchers to add physiological assessments to pain research among persons with intellectual disabilities.

While reliability is a very important aspect of instruments used to physiologically assess pain, aspects of instrument invasiveness and patient vulnerability should also be considered. Not all physiological pain-detection instruments are equally (non-)invasive and not all patients are equally able to express and communicate emotions or give consent. For example, when deciding which instrument to use for pain assessment for a comatose patient, a physician and the patient's legal representative might decide to use the less invasive method, until that time that the patient is able to give consent. This stems from the Universal Declaration of Human Rights, which recognizes the 'inherent dignity' of every human being (World Health Organisation, 2019) and thus the responsibility to consider the invasiveness of methods.

When using a technical instrument to assess physiological signals that can indicate pain, technological maturity is a factor which relates to the instrument's reliability. Technological maturity can be assessed using technology readiness levels (TRLs), as first conceptualized in 1974 by The United States National Aeronautics and Space Administration (Banke, 2010; Mihaly, 2017). TRLs were adopted by the US Department of Defense in their Defense Acquisition Guidebook (US DoD, 2010) and are rated on a scale which corresponds to the reported fundamental and practical steps for to development and testing of instruments (Banke, 2010). Using TRLs to assess the maturity of instruments used to detect physiological signals of pain gives additional information to make comparisons between assessment methods and instruments.

Thus, there is a need to use physiological methods to detect pain in subject groups. In this review the relationship between instrument invasiveness and patient vulnerability will be examined, as well as the technological maturity of most-used pain assessment instruments. The research questions are as follows: 1) Which physiological methods to detect pain are used with which subject groups?; 2) Which methods with which subject groups indicate that pain assessment is possible and reliable, and are these results consistent among studies?; 3) Which pattern concerning physiological assessment of pain can be identified when we compare the invasiveness of the physiological measure and the vulnerability of the subject groups?; 4) What are the technology readiness levels for physiological instruments used to measure pain?

2.2. Materials and Methods

2.2.1. Included Articles.

This systematic review was conducted following PRISMA-guidelines (Moher, et al., 2009). In Table 2.1, the inclusion and exclusion criteria are reported. The included articles had to be reviews or meta-analyses, which described original research articles. These research articles had to describe research using at least one physiological method to detect pain in humans. The pain studied in the research articles could be present already, or it could be induced by either a medical procedure (e.g., a vaccination) or a scientific method (e.g., a deliberate painful experience). Authors were contacted when a full text of the review was unavailable online. The reviews were published in Dutch, English, French, German and Spanish between January 2007 and March 2019. This 12-year period was chosen to get a well-rounded image of the use of physiological methods for pain in the late 20th and early 21st century.

A systematic search of review articles was conducted on Worldcat, Wiley Online Library, Springerlink, IEEE Publications Database, ScienceDirect and Cochrane Library between December 1st, 2018, and March 31st, 2019, via the University LibSearch on Worldcat.org. The search strategy consisted of a combination between free-text and title words, which is shown in Figure 2.1. This search gave 1.984 results.

Of the 1.984 results, 200 (10,1%) were randomly selected. The first author (HK) and two other researchers (SD & GK) independently coded the title and abstract of the 200 articles on inclusion and exclusion criteria. There was a 100% agreement on the inclusion and exclusion of these 200 articles (Cohen’s Kappa = 1.00). The first author (HK) then conducted a title and abstract screening of the remaining 1.784 articles. After this screening, 63 reviews were included in the full-text coding.

Of these 63 reviews, 13 (20,6%) were randomly selected. The first author (HK) and another independent researcher (LW) screened the full text on inclusion and exclusion criteria. Both researchers agreed 100% on which of those articles should be included and which should be disregarded (Cohen’s Kappa = 1.00). In this phase, reviews were excluded when physiological methods were used, but not to assess pain, or when pain was experimentally induced, but not assessed. After this second phase, 29 reviews remained. A flow chart of the entire search strategy is shown in Figure S2.1.

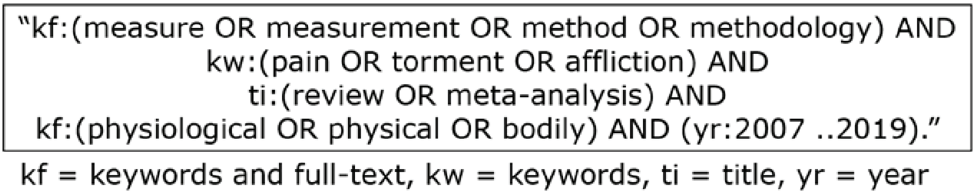
2.2.2. Quality Assessment.

Of the 29 reviews, a random subset of 6 (20,7%) was assessed on quality by HK and GK. For this quality assessment the CASP checklist (Critical Appraisal Skills Programme, 2018) was used. This checklist assesses reviews with ten questions on three aspects: A) validity of results, B) precision of results, and C) usefulness of results. After discussion of results and compromise on when an aspect could be considered adequately conducted, HK assessed the remaining 23 reviews according to the agreement made.

For each question it was assessed whether this element was adequately conducted (noted by a plus sign (+)) or inadequately carried out (noted by a minus sign (-)). Moderately adequate elements were noted by a slash sign (/) and when it was unclear whether an element was adequately carried out, this was noted by a question mark (?). As the CASP checklist was designed for educational purposes, a scoring system is not suggested. The number of adequately carried out elements was counted, and it was noted whether each review was carried out according to a systematic method. Results of the quality assessments are given in the supplementary material (Table S2.1).

TABLE 2.1: Inclusion and exclusion criteria.

Criteria	**Inclusion**	**Exclusion**
Population	(i) Human study	(i) Animal study
Instruments	(ii) At least one physiological measurement	(ii) No physiological measurement
Outcome	(iii) A clinical pain measure physiologically obtained	(iii) No clinical pain measures
		(iv) Only a self-report measure
Report	(iv) Review, systematic review, meta-analysis	(v) Article, letter to the editor
	(v) Full-text available	(vi) Full-text not available
Period	(vi) 2007 - 2019	(vii) All other years
Language	(vii) Dutch, English, French, German, Spanish	(viii) All other languages



"kf:(measure OR measurement OR method OR methodology) AND
kw:(pain OR torment OR affliction) AND
ti:(review OR meta-analysis) AND
kf:(physiological OR physical OR bodily) AND (yr:2007 ..2019)."

kf = keywords and full-text, kw = keywords, ti = title, yr = year

FIGURE 2.1. Search terms used in all database searches.

2.2.3. Literature Taxonomy.

A taxonomy was developed using the 540 articles described in the 29 reviews. The taxonomy comprised of the physiological method used to detect pain (modality) for each subject group. The first step in this taxonomy was to list all modalities used and all subject groups included in the reviews. The modalities were then scored on invasiveness and the target group on vulnerability. The first two authors (HK and PS) and an independent researcher (GK) scored the modalities independently. Scores on invasiveness could vary between 0 and 6 and scores on vulnerability between 0 and 5 (Table 2.2) and when needed half points were given. Subsequently averages were calculated for each modality and each subject group.

The three researchers (HK, PS & GK) scored the invasiveness of modalities and the vulnerability of subject groups according to an agreed-upon scoring model (Table 2.2). Invasiveness was based on two aspects: 'How drastic is the method?' which considered both the patient's physical integrity and their privacy on a scale from 0 to 3 and how long would analysis of results take?' on a scale from 0 to 3. Half points were given when a modality's physical invasiveness was more than moderate but less than very drastic. A higher score indicates a more invasive modality. The modalities started at the least invasive 'respiratory rate', which is not at all drastic for the patient and fast, to 'conducting genetic research', which both uses bodily fluids and takes generally more than 1 day to analyse.

Vulnerability was based on three aspects: 'What are the communicative capabilities of the group?' on a scale from 0 to 2; 'How competent is the group?' on a scale from 0 to 2; and 'Does the group have a (medical) condition (including an intellectual disability)?' on a scale from 0 to 1. Higher scores indicate more vulnerability. Non-verbal (comatose) patients, who have limited non-verbal expressivity, cannot decide their own fate, and have an illness or injury were considered the most vulnerable group, closely followed by people with severe ID. Healthy adults were considered the least vulnerable group. This way an average score was calculated for 18 physiological modalities for pain and 7 subject groups on which those modalities were used. The average scores are shown in Table 2.3.

Most assessment methods are used to measure pain at the moment of measurement. They are monitored during surgical procedures, during vaccinations, or during experimentally induced pain. During these procedures heart rate, pupillometry, and needle-based EMG can give information about the existence of pain. Other methods, such as (f) MRI, PET and genetics, are most often used to assess changes in the brain or the genes as a result of long-term chronic pain. An MRI can show the density of different brain regions and is used to search for differences between chronic pain patients and healthy controls. Genetic research can look for inherent changes in genes in chronic pain patients, or for damage in DNA.

A random subset of 6 reviews (20,7%) was made and HK and another independent researcher (SC) independently assessed the used modality for pain and the subject group on which this modality was used. This assessment was done as follows: if a study assessed pain with both heart rate variability and skin conductance on both healthy adults and verbal patients (e.g., four unique combinations: heart rate variability and healthy adults, heart rate variability and verbal patients, skin conductance and healthy adults, and skin conductance and verbal patients), this led to four unique codes in the taxonomy. If a study utilized three modalities on three subject groups, this was coded as 9 combinations and so on. After both researchers coded the 6 reviews, they held a meeting to discuss terminology. Agreement before the meeting was high (Cohen's Kappa = 0.88), and in the meeting, the researchers reached consensus on aspects that were still unclear, such as when an infant is a neonate, and when a patient is comatose. HK assessed the remaining 23 reviews and removed duplicate articles. The assessment resulted in 1.054 unique combinations of article, modality and target group.

The coded combinations of modality and target group were then visualized in a scatter plot with target group on the y-axis and modality on the x-axis. The modalities and subject groups were ordered according to their averages on invasiveness or vulnerability, according to the model previously described (see also Table 2). The point where the two axes come together is the place of least invasive modality and most vulnerable group, point 0, 0. On this point on the scatter plot the measurement of pain via respiratory rate connects with (non-communicative) comatose patients. The point where least vulnerable group (healthy adults) meets the most invasive pain assessment method (genetics) is point 6, 5.

2.2.4. Pain Assessment per Method.

For each review, the evidence of pain measurement methods was assessed, and results were gathered. The results will be displayed per review further on in this article. Where this is specified in the review, the used instruments to measure pain and the subjects the instrument was used on will also be mentioned.

TABLE 2.2. Scoring for invasiveness of modalities and vulnerability of patient groups.

Invasiveness physiological modality			Vulnerability subject group		
Drastic	0	Not drastic or privacy invading	**Communicative capability**	0	Both verbal and non verbal
	1	Mildly drastic		1	Limited verbal
	2	Moderately drastic		2	Limited non-verbal and not verbal
	3	Very drastic or privacy invading	**Competence**	0	Normative competence
Duration	0	Up to 1 hour		1	Limited competence
	1	From 1 up to several hours		2	No or very little competence
	2	From several hours up to 1 day	**Illness**	0	No illness injury or disability
	3	More than 1 day		1	Illness injury or disability

TABLE 2.3. Average scores for invasiveness of modalities (left side of the table) and vulnerability of subject groups (right side of the table).

Method	Average score	Subject Group	Average score
Respiratory rate	0.00	Comatose patients	0.17
Respiratory analysis	0.33	People with severe ID	0.33
Heart rate	0.67	Neonates	1.83
Muscle tension	0.83	Children patients	3.00
Body temperature	1.00	People with moderate ID	3.50
Skin conductance	1.17	Verbal patients	3.83
Heart rate variability	1.33	Healthy adults	5.00
Blood pressure	1.50		
Pupillometry	1.67		
Cerebral BFV	1.83		
Facial recognition	2.00		
ECG	2.67		
EEG	3.00		
(f)MRI	3.83		
PET/SPECT	4.00		

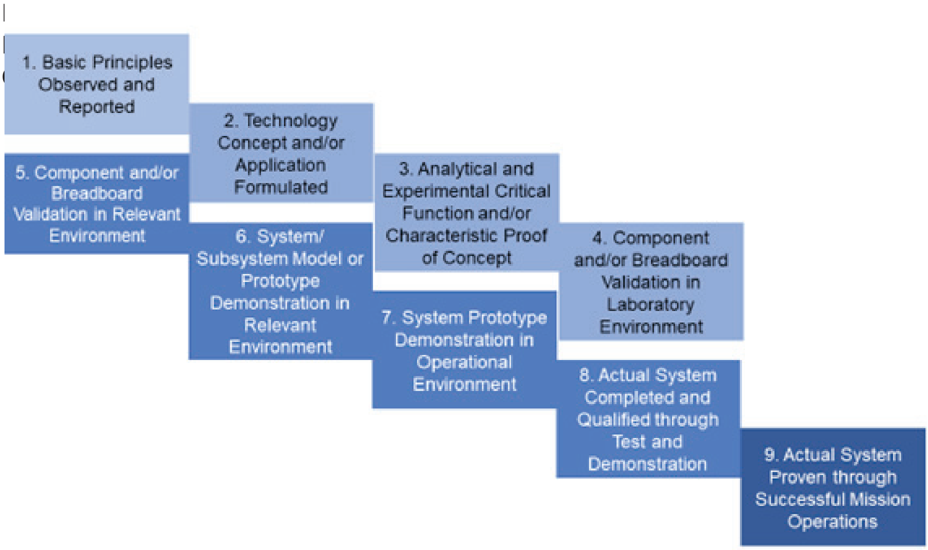


FIGURE 2.2. Technology readiness level descriptions used by the United States Department of Defense (US DoD, 2020). The figure is adapted from a figure used by the European Association for Research and Technology Organizations (EARTO, 2014) to improve legibility.

2.2.5. Technology Readiness Level.

All methods to measure pain with physiological signals were then ordered according to their technology readiness level (TRL). The United States Department of Defense has published their version in 2010, which was adapted for this assessment (Figure 2.2). The translation from each level was done in accordance with the evaluation of technological instruments to physiologically measure pain in a clinical setting and is included in the supplemental material (Figure S2.2).

For each method of measuring pain physiologically, one technical instrument was chosen to assess its TRL. This instrument represents the most used technical method to measure that particular physiological signal; for example, skin conductance is more often measured with stick-on electrodes, and less often with wearable electrodes. When more than one method is used frequently or the most used method could not be determined, a choice was made. With two or more equal methods, based on TRL, a random choice was made between the methods. When the methods differed much on TRL, the most mentioned method in the articles reviewed was chosen.

2.3. Results and Discussion

2.3.1. Quality Assessment.

The quality of each of the 29 reviews was assessed with the checklist of the Critical Appraisal Skills Programme (2018). The quality score of the reviews was generally high (median = 7/10). The reviews scored mostly well on their validity and their usefulness but lacked precision in their results. It was not always clear whether the authors took enough steps to ensure that all relevant studies were included in the reviews. Also, the generalizability of the articles was sometimes limited, which also limited the generalizability of the reviews. Out of the 29 reviews, only ten (34.5%) mentioned making use of a systematic method for conducting the review and fifteen of the reviews (51,7%) assessed the quality and risk of bias of the articles included.

2.3.2. Literature Taxonomy.

There were 1,054 combinations of modality and subject group, from 540 articles (published between 1972 and 2017) reported in 29 reviews (published between 2007 and 2019). Each review described more than one article on physiological measures for pain. Only articles where the physiological modality and the subject group were clearly described were used to create the taxonomy. The modalities are ordered on the x-axis according to invasiveness (with the more invasive measures further to the right) and the subject groups on the y-axis according to vulnerability (with the least vulnerable groups further to the top). The taxonomy shows that the more invasive modalities are more often used on the least vulnerable subjects, while less invasive measures are used on subject groups of all vulnerability levels (Figure 2.3). The lack of studies that looked at physiological measures for pain in subject groups with mild or severe intellectual disability can also be seen in the taxonomy. This is not an effect of studies on pain. There is very little research done on subjects with intellectual disabilities in general (De Knegt, et al., 2013). The search for this review only uncovered one review discussing studies on subjects with moderate or severe intellectual disability.

Verbal patients were most often studied with physiological measures for pain (375 combinations), followed by healthy adults and neonates (262 and 205, respectively). The physiological method most used to measure pain is the (f) MRI (193 combinations), followed by heart rate variability (184) and heart rate (169). Both (f) MRI and heart rate variability were most often measured for pain in verbal patients (in 193 studies) and healthy adults (in 141 studies), while heart rate was most often measured for pain detection in neonates (in 80 studies). Heart rate was also the most found method for measuring pain in children (in 32 studies) and non-verbal patients (in nineteen studies).

With people with moderate or severe intellectual disability as subject group, respiratory rate was measured for pain in four studies, while only one study with healthy adults as a subject group used respiratory rate to measure pain. The relatively new way to detect pain with automated facial recognition was used in four studies and only with verbal patients.

2.3.3. Pain Assessment per Method.

Among the 540 studies discussed, different subject groups participated, and the focus of studies also varied greatly. Care was made to look for similarities and material to compare among studies. Results per measurement method are displayed in Table 2.4. Table 2.4 shows that pupillometry, cerebral blood flow velocity (CBFV), respiratory and muscular measures were among the low invasive measures that showed both the ability to measure pain and consistency in results among pain studies. Both pupillometry and CBFV have not yet been researched as a pain assessment method often but show promise in this category. The two respiratory measures and muscle tension all showed inconsistent or no results among one certain subject group, but it is unclear whether this is due to the measurement method or the study design.

Among the promising, yet more invasive pain assessment methods are magnetic resonance imaging (MRI), hormonal analyses, electromyogram, and genetic research. MRI and hormones can measure both acute and chronic pain responses, while genetics can only measure changes as a result of chronic pain and the electromyogram is only used for acute pain measurement. Few studies were found that used either hormonal analyses, electromyogram, or genetics as pain measurement method, so this may limit the scope of these results. Electromyogram, MRI, and genetics were most often used to compare chronic pain patients to healthy adults, so results among other subject groups are based on few studies.

The remaining methods show inconsistent results among at least one subject group, which makes the results difficult to generalize, or show doubtful results as a pain measurement method. Skin conductance responses to pain were only consistently found in healthy adults, and the promising new technique of automatic facial recognition is still influenced by too many personal and environmental factors.

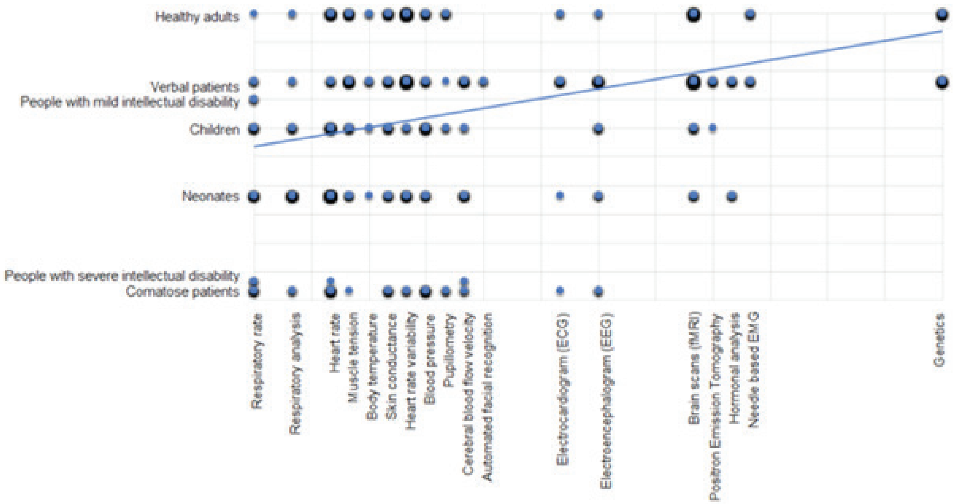


FIGURE 2.3. Taxonomy with measurement methods on the x-axis, ordered from least to most invasive, and subject groups on the y-axis, ordered from most to least vulnerable.

2.3.4. Technology Readiness Levels.

Technology readiness levels indicate the technological maturity of an instrument. This can range from (1) only theoretical knowledge to (9) certified and used daily. Per modality shown in the taxonomy above one technological instrument was chosen, based on most use or most described in the articles in the taxonomy. Of course, the instrument had to be technical in order to determine a TRL. Heart and respiratory rate are often observed and computed manually by a nurse, but the determination of a TRL was based on a technical instrument that computes this automatically. Technology readiness levels per modality are reported in Table 2.5.

The average TRL of all (most used or most described) instruments together was eight, which is not surprising, considering that the instruments used in hospitals (such as an MRI-scanner or a fingertip pulse oximeter) are certified and used daily. The newest method, automated facial recognition, has the lowest TRL (four). The software has been validated in a lab, but not yet in a relevant environment with a patient group. The skin conductance measurement also has a moderate TRL (six). This is based on the fact that there has been a validation of a prototype in a hospital or clinic, but the demonstration of a GSR-measurement for pain in an operational way has not yet been done. There are certified instruments and software to use with GSR-electrodes, but these need to be adjusted to measure pain.

2.4. Summary of Evidence

In this systematic review, the physiological methods to assess pain in humans were made. From 29 reviews found, 540 articles described 1054 unique combinations of physiological assessment method and subject group. When these combinations were presented in a graph it showed a clear trend that the more invasive methods are most commonly used to assess pain in the least vulnerable groups. Moreover, in some of the vulnerable subject groups (those with mild or severe intellectual disability), there is hardly any research done on a physiological assessment method for pain. Since the review by De Knegt, et al in 2013, only two studies were conducted concerning physiological measurements of pain in persons with ID (Symons, et al., 2015; De Knegt, et al., 2016). Since people with severe intellectual disability are mostly unable to express their pain and show different non-verbal signs of pain than expected (e.g., freezing of face and/or body), a consequence is that their caregivers do not easily recognize their pain. Therefore, there is a great need for research examining the precision and reliability of physiological assess¬ment of pain in persons with severe intellectual disability.

This study shows that half of the most often used instruments reached the maximum level of technological maturity and another quarter of the instruments reached the penultimate level. Technology readiness of instruments used to measure physiological indications of pain is generally high. The only exception is the relatively new method of automated facial recognition software. Although facial recognition in general is making real strides, the automated recognition of emotions and facial expressions still needs to be developed further in order for it to be able to be used in the assessment of pain. Although when this technology reaches the point when it can be used accurately and reliably, there is still the question of whether it can be used on all subject groups, seeing as expressions of pain differ in persons with ID.

TABLE 2.4. Pain assessment results per measurement method.

Method	Subjects	Able pain measure	Consistent across studies	Limitations
Electro-encephalogram (EEG)	Neonates, infants, CPPs, ICU patients	Yes	Moderate	Influenced by opioids, not consistently found in neonates
Cardiovascular measures				
Heart Rate	Neonates, infants, TBI patients, ICU/ OR patients, CPPs, people with SID, healthy adults	Doubtful	No	Variable results among brain injured patients, reduced reaction in CPPs, no reaction in SID
Heart Rate Variability	Neonates, infants, ICU/ OR patients, healthy adults	Yes	Moderate	Inconsistent among infants in the first year of life
Body Temperature	Neonates, infants, healthy adults	Yes	Moderate	Inconsistent among healthy adults
Blood Pressure	Neonates, infants, TBI patients, OR patients, healthy adults	Doubtful	No	Blood pressure responded inconsistently to pain
Respiratory measures				
Respiratory rate	Neonates, infants, TBI patients, people with SID, healthy adults	Yes	Yes	Respiratory ‘irregularities’ were not related to acute pain in persons with SID
Respiratory analysis	Neonates, infants, TBI patients	Yes	Yes	Oxygen saturation was not favored for pain in neonates

		Muscular measures		
Muscle tension	Infants, ICU/ OR patients, healthy adults	Yes	Yes	In healthy adults muscle tension response was only found with intense and prolonged pain
Electromyogram	CPPs, healthy adults	Yes	Yes	Few studies
		Electrodermal activity		
	TBI patients, OR patients, healthy adults	Doubtful	No	Only consistently found in healthy adults
		Pupillometry		
	Infants, OR patients, CPPs, healthy adults	Yes	Yes	Few studies
		Brainscan		
MRI	CPPs, healthy adults	Yes	Yes	Different studies focused on different areas
NIRS	Neonates, infants	No	Yes	Presence of pain on a cortical level was not found
CBFV	Infants, CPPs, OR patients, people with SID	Yes	Yes	Few studies
(S)PE(C)T	Infants, CPPs	Yes	No	Activity varied greatly across studies
		Hormonal analysis		
	Neonates, CPPs	Yes	Yes	Few studies
		Genetics		
	CPPs, healthy adults	Yes	Yes	Not yet validated in large human cohorts
		Automatic facial recognition		
	CPPs	Doubtful	Yes	Influenced by gender, age, ethnicity, movement, & lighting

Note. CPPs = Chronic Pain Patients, ICU = Intensive Care Unit, OR = Operating Room, TBI = Traumatic Brain Injury, (S)ID = (Severe) Intellectual Disability, MRI = Magnetic Resonance Imaging, NIRS = Near-infrared Spectroscopy, CBFL = Cerebral Blood Flow Velocity, PET = Positron Emission Tomography, SPECT = Single-photon Emission Computer Tomography.

2.4.1. Limitations.

For this study a thorough and systematic search was made for published reviews between 2007 and 2019. Reviews that were primarily unavailable to the researchers, were searched for by addressing the authors and for hand selection reference lists of the included reviews were examined. However, there may have been eligible reviews that were not added such as unpublished reviews or those published before 2007. On the other hand, great efforts were made to include as many reviewed articles as possible by adding English, Spanish, Dutch, German and French reviews. Therefore, the vast majority of review articles was examined.

The searches for articles included in the reviews could also result in articles missed, due to unavailability or language barriers. Even so, the amount of articles assessed (540) is deemed sufficient to give an overview of the trend in research and the results shown in the taxonomy. Therefore, this study gives an overview of research trends that should be quite similar to all research conducted.

Of the 29 reviews discussed in this review, only a third used a systematic method and half assessed the quality and risk of bias in the included articles. When the risk of bias was assessed, it was generally scored as moderate or high by the authors of the reviews and the quality of evidence was usually moderate or low. Therefore, when studies selectively report their findings, this is copied by the reviews describing those studies and ultimately also in this review.

The taxonomy that shows the trend in physiological pain assessment methods and subject groups is based on the number of combinations of method and group discussed per article. The taxonomy is not ordered according to the sizes of participant groups the methods are used on, but on the number of articles where that certain combination was discussed. The trend, therefore, might be different if the combinations were ordered on participant group sizes. Nonetheless, the way the taxonomy was ordered gives a clear overview of research trends in pain assessment. Otherwise, the trend would mostly show which participants are more easily reached by researchers, rather than which combinations of method and subject group are more worthwhile for being studied.

TABLE 2.5. Technology Readiness Levels (TRL) determined for one technological instrument (most used or most described) per detection method, ordered according to invasiveness.

Method	Instrument	TRL
Respiratory rate	Respiratory measure instrument	8
Respiratory analysis	Fingertip pulse oximeter	9
Heart rate	Visual stethoscope with oximeter probe	9
Muscle tension	Skin electrodes and EMG-monitor	8
Body temperature	Tympanic (ear) thermometer	9
Skin conductance	Skin electrodes, transmitter and display-software	6
Heart rate variability	Photo plethysmograph	7
Blood pressure	Digital sphygmo¬manometer	9
Pupillometry	Pupilometer	8
Cerebral BFV	Transcranial Doppler	9
Facial recognition	Facial recognition software	4
ECG	Skin electrodes and ECG-monitor	8
EEG	EEG cap and monitor	8
f (MRI)	MRI-scanner	9
PET/SPECT	PET-scanner	9
Hormonal analysis	Clinical centrifuge	9
Needle-based EMG	Needle electrode and monitor	7
Genetics	Genetic analysis instrument	9

2.5. Conclusions

Technology readiness of instruments used to assess pain is generally high. Some new and less used technologies, such as facial recognition and skin conductance, still need to be developed further. In general, it can be said that instruments used in hospitals and clinics to assess pain in patients physiologically are technologically mature.

Whether all proposed methods of pain assessment can be used specifically to measure the existence of pain is another matter. In general, the examined studies show evidence that respiratory measures, muscle tension, MRI, CBFV, hormonal analysis, and pupillometry can reliably indicate acute pain, although not all of these methods were often studied, and if they were, often on the same two subject groups (chronic pain patients and healthy adults). Cardiovascular methods were studied among many different subject groups, but do not seem to give a clear indication that they respond to pain or nociception. There is little evidence also for electrodermal activity and near-infrared spectrometry as pain assessment methods. Brain scan techniques and genetics on the other hand seem to be useful in finding anomalies in chronic pain patients compared to healthy controls. The use of computer-based facial recognition software to detect pain needs to be further developed to be viable. In general, there is a need to find further evidence on the ways to measure pain physiologically, especially for those that are unable to communicate or express their pain. And specifically, there may be a task for (medical) engineers to be involved in instrument development and improvement.

The taxonomy shows a trend that the more invasive pain assessment methods are often only used on the less vulnerable subjects, while on the more vulnerable patients, less invasive pain assessment methods are used. As a result, this could suggest that researchers are hesitant to use more invasive pain assessment methods with subjects where informed consent is difficult to obtain. Very little research on physiological pain assessment is done with persons with intellectual disabilities. Participants with intellectual disability should generally be included more in scientific research, especially on subjects as pain, for pain relief will have a positive impact on their general wellbeing.

2.6. Acknowledgements

This project is funded by The Netherlands Organization for Health Research and Development ZonMw, Den Haag, the Netherlands [project number 8084 5009 8345]. The authors would like to thank Gloria Kempelmann MSc (GK), Lucia Willems MSc (LW), Suzanne Derks MSc (SD) and Sara Colijn MSc (SC) for collaborating as independent researchers on this systematic review.

2.7. Supplementary Materials

Figure S2.1. Flowchart for inclusion into the review. Table S2.1. Results of quality and transparency assessment for the 29 reviews (alphabetically). Figure S2.2. Technology readiness levels as described by the United States Department of Defense in accordance with instruments for physiological measurements for pain. (Supplementary Materials).

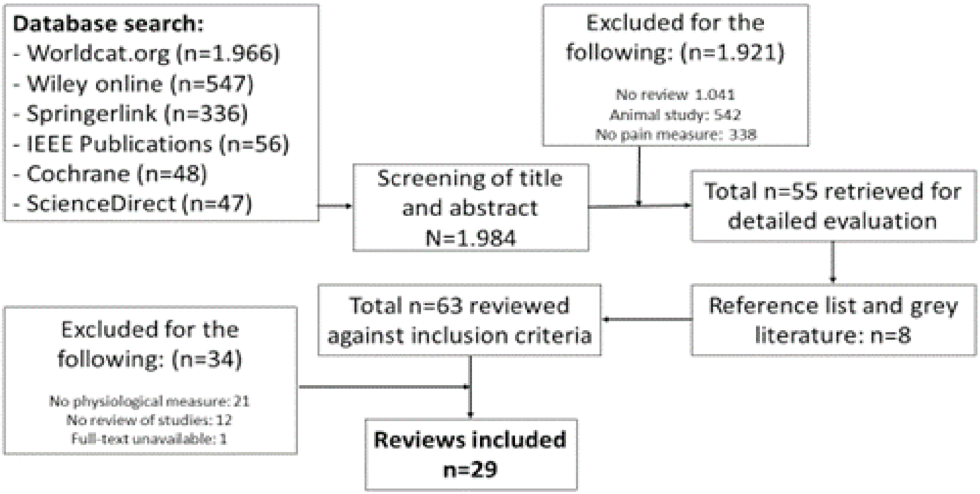


FIGURE S2.1. Flow chart for inclusion into the review.

TABLE S2.1. Results of quality and transparency assessment for the 29 reviews (alphabetically).

Review	A)Validity					B)Precision		C)Usefulness			Adequate answers	Systematic guidelines
(first) Author and year	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**		
Arbour, & Gélinas, 2014	+	+	+	+	+	+	/	+	?	+	8/10	no
Benoit, et al., 2017	+	+	+	?	+	+	-	?	+	+	7/10	yes
Bentley, et al., 2016	+	+	+	-	+	/	-	-	+	+	6/10	no
Bonan, et al., 2014	+	+	?	-	?	+	-	?	+	+	5/10	no
Cagnie, et al., 2014	+	+	+	+	+	+	-	-	+	+	8/10	no
Choon Wyn Lim, et al., 2011	+	+	+	+	+	+	+	?	+	+	9/10	no
Coleman, et al., 2015	+	+	+	-	+	+	/	-	?	+	6/10	no
Coppetiers, et al., 2016	+	+	+	+	+	+	/	-	?	+	7/10	yes
De Jonckheere, et al., 2015	+	+	?	-	+	+	/	+	+	+	7/10	no
De Knegt, et al., 2013	+	+	+	+	+	/	/	+	+	+	8/10	yes
Dorfman, et al., 2014	+	+	+	+	+	+	/	+	+	+	9/10	no
Hatfield, & Ely, 2015	+	+	+	+	+	+	+	?	+	+	9/10	no
Heales, et al., 2016	+	+	+	+	+	/	+	?	+	+	8/10	no
Hecke, van, et al., 2015	+	+	+	+	+	/	/	-	+	+	7/10	no
Henry, et al., 2011	+	+	?	-	+	/	-	?	+	+	5/10	no
Koenig, et al., 2014	+	+	+	-	+	+	-	+	+	+	8/10	yes
Koenig, et al., 2016	+	+	+	-	+	+	+	+	+	+	9/10	yes
Kyle & McNeil, 2014	+	?	+	+	+	/	-	-	+	+	6/10	no
Manocha, & Taneja, 2016	+	-	+	-	+	/	-	-	+	+	5/10	no
Meeus, et al., 2013	+	+	+	+	-	+	/	?	+	+	7/10	yes
Parker, et al., 2016	+	+	+	+	+	+	+	?	+	+	9/10	no
Pudas-Täkhä, et al., 2008	+	+	?	+	+	+	/	-	+	+	7/10	yes
Raeside, 2011	+	+	+	+	+	+	-	-	+	+	8/10	no
Relland, et al., 2019	+	+	+	+	+	+	+	?	+	+	9/10	yes
Roulin, & Ramelet, 2012	+	+	+	?	+	/	/	?	+	+	6/10	yes
Schmidt, & Martin, 2017	+	+	+	-	-	/	-	-	+	+	5/10	no
Subramaniam, et al., 2018	+	+	?	?	+	+	-	?	-	?	4/10	no
Waxman, et al., 2015	+	+	+	+	+	+	/	?	+	+	8/10	yes
Zamzmi, et al., 2018	+	+	?	-	+	+	+	-	+	+	7/10	no

NB. + = adequate, - = inadequate, / = moderately adequate, ? = unclear

1) Did the review address a clearly focused question?
2) Did the authors look for the right type of papers?
3) Do you think all the important, relevant studies were included?
4) Did the review's authors do enough to assess quality of the included studies?
5) If the results of the review have been combined, was it reasonable to do so?
6) What are the overall results of the review?
7) How precise are the results?

8) Can the results be applied to the local population?
9) Were all important outcomes considered?
10) Are the benefits worth the harms and costs?

1 Basic principles observed and reported: Theoretical knowledge on the physiological method and how it relates to other measurements. There are ideas on how this could be measured in humans, but no instrument or design schematics.

2 Technology concept and/or application formulated: Ideas about the application of the physiological method, for example about the best place on the human body to assess this measurement, the best time of day, or the best posture for the patient assessed.

3 Analytical and experimental critical function and/or characteristic proof of concept: A raw prototype of the physiological measurement instrument, for example a big and unfinished way to measure (breadboard) is present. The parts of the instrument are there, but they have not yet been satisfactorily integrated.

4 Component and/or breadboard validation in laboratory environment: A validation of the measurement in a controlled environment with healthy subjects (in a lab). Proof that the physiological measurement can be independently measured and is not influenced by other physical processes.

5 Component and/or breadboard validation in relevant environment: A validation of the measurement in the patient group. Proof that the measurement in non-healthy subjects also gives reliable results and is not influenced by physical processes pertaining to the disease/affliction.

6 System/subsystem model or prototype demonstration in relevant environment: A demonstration of an alpha prototype in the environment for which it is developed (a hospital or clinic). For an alpha test a small group of experts checks the instrument for common errors and overload. An integrated circuit and a compact/least invasive way to measure.

7 System prototype demonstration in operational environment: Beta-test. This test is done on a large group of users. Final quirks will be removed from the system. A comparison with what is currently used and discussion on how this instrument is better/an addition.

8 Actual system completed and qualified through test and demonstration: An adjustment of the system to the patient group and their wishes and necessities. Validated for patient group. A working system in a variation of circumstances.

9 Actual system proven through successful mission operations: System is certified and used in daily practice.

FIGURE S2.2. Technology Readiness Levels as described by the United States Department of Defense in accordance with instruments for physiological measurements of pain.

Chapter 3

Pain signalling with physiological data for persons with communication difficulties: A pilot study of the Pain App[1]

---

[1] Published as: Korving, H., Peters, P., Barakova, E., Feijs, L., & Sterkenburg, P. (2020). Pain signalling with physiological data for persons with communication difficulties: A pilot study of the pain app, *11th IEEE International Conference for Cognitive Infocommunications (CogInfoCom)*, Mariehamn, Finland, 23-25 September 2020.

Abstract

Pain is a common occurrence in life. For some groups of people expressing, communicating, and seeking pain relief is not possible, due to age, illness, disability, or unconsciousness. To support caregivers, pain detection through physiological measures can be a solution. Currently, an algorithm for an application indicating arousal according to electrodermal changes has been developed and tested. Pain is unique to every person, so new research and algorithm development are necessary to assess which measurable signals coincide with pain. A mobile application utilising such algorithms would allow caregivers to better attend to the patients' needs in daily practice. This study aims to develop an application that can signal pain for caregivers of persons with communication difficulties and examine whether utilizing this software solution, pain can be reliably detected in an experimental setting. Visual analysis of plotted results from a pilot study indicates that within the same person pain shows significant deviation from relaxation and neutral experiences. Further research is needed to examine the reliability of pain detection.

3.1. Introduction and related work

For caregivers (e.g., parents, professional caregivers, nurses) it is challenging to understand the needs of people with communication difficulties. These people may display subtle, idiosyncratic behaviours to express their state of wellbeing (Defrin, Lotan & Pick, 2006). Consequently, caregivers may be uncertain about what their client is feeling, or whether they experience pain, the absence of which is one of the most important aspects of being well (De Knegt et al., 2013). The experience of pain can be common in certain groups of people, such as patients in intensive care, individuals with severe or profound intellectual disability, and premature neonates (Doody & Bailey, 2006; Walsh, Morisson & Mc Guire, 2011). Both acute and chronic pain are frequently experienced by several groups of people with difficulty to communicate (Breau, McGrath & Zabalia, 2006; Van der Putten & Vlaskamp, 2011). When we cannot rely on self-report, we need to look for other ways to help these individuals communicate about their pain, so that caregivers can support them adequately and contribute to their wellbeing.

When a self-report of pain is not feasible, systematic observation is often used. This is a good alternative for some, but when someone displays idiosyncratic behaviours, observation lists are not sensitive enough to capture pain (Defrin, Lotan & Pick, 2006; Lotan et al., 2010). In that case, the measurement of physiological signals is a good alternative. Physiological signals, such as heart rate, blood pressure, or brain signals have previously been used to assess attention, stress or mental effort (Gazdi et al., 2016; Katona & Kovari, 2018; Taelman et al., 2009). When used to assess pain, it can measure a reaction to acute pain but not always long-term pain, because habituation causes the body's responses to diminish and disappear over time. A physiological method is therefore unable to assess chronic pain via most methods unless the body responds to a sudden aggravation of the pain (Korving et al, 2020b).

A systematic review of physiological pain assessment methods and subject group combinations showed that more invasive techniques were mostly used with less vulnerable subjects (Korving et al., 2020b). The review rated 18 different physiological assessment methods on invasiveness, from breath analysis to magnetic resonance imaging. Invasive assessment methods were those that are uncomfortable (blood pressure cuff, breast band) or physically demanding (pupillometer), pierce the skin (needle-based muscle tension), and enter the body (rectal thermometer). Like most other methods, skin conductance can be measured outside the body. It does not need a separate machine, such as for brain imaging measures, or a separate analysis, such as that for hormones and genetics. It can be measured on different places on the body, unlike respiratory measures, and is unrelated to blood flow, unlike body temperature and cerebral blood flow velocity. This makes skin conductance a good pain assessment method for the more vulnerable subject group with communication difficulties, who may suffer from a variety of medical conditions (Breau, McGrath & Zabalia, 2006; Van der Putten & Vlaskamp, 2011).

To get more insight in the stress experienced by people with communication difficulties, a system was developed consisting of a smart sock with sensors that measure skin conductance and a small transmitter that sends the physiological data via Bluetooth® to an application (hereafter app) on a mobile device (Frederiks, et al., 2015). This system makes use of sensor-bridging communication via inter-cognitive communication (Baranyi & Csapo, 2012). To visualize arousal in people with severe intellectual disability, Frederiks et al. developed the Flower App (Frederiks et al., 2019; Sterkenburg et al., 2017). The goal of this system was to trigger responses from parents to signals from their child and to aid in parent-child interaction. Positive results were found for the use of a skin conductance sensor and the evaluation of the measurement system on children with Prader-Willi syndrome. The arousal level in the child and its reaction to a parent was measurable with physiological signals.

When using skin conductance to measure pain, care should be made to distinguish the pain response from a stress response. Research on healthy adults in a laboratory setting (Günther, 2016) showed the possibility to display skin conductance variability (a component of skin conductance) to assess pain without the influence of stress and emotions related to pain. Examples of research on the use of skin conductance variability measurements for pain on people with communication difficulties is limited (O’Leary et al., 2015). So, new software is needed to visualize pain and not arousal.

The current study aims to test whether a system that measures skin conductance, in combination with an app in which the physiological data is processed, can be used as an assistive caregiving tool to assess possible acute pain in persons with communicative difficulties (Iszó, 2015). The system and the outcomes of tests on four healthy participants who receive a painful stimulus are presented. The scope of this article is a description of the system, the design of the pilot study, and observational analysis of the test results in a laboratory setting.

3.2. Methods

In this study, a system for measuring skin conductance is used. This section describes the components of this system and the design of the pilot study in which the assessment of acute pain with skin conductance is tested on healthy volunteers.

3.2.1. The Pain App System

To gather the skin conductance data, a system called the Pain App System is developed. This system’s components measure, transmit, and translate physiological data to a visual of pain for caregivers. The components are the smart sock, the Shimmer™ transmitter, and a mobile application (Pain App).

The smart sock (Korving et al., 2020a) is a sock, made from a cotton and elastane blend, enhanced with fabric sensors on the inside soles. One sensor touches the ball of the foot and the other the heel. The fabric sensors contain silver fabric, which makes them both conductive and anti-bacterial. The smart sock also contains a thread of silver-coated conductive yarn, which connects each of the sensors to one metal push button on the ankle of the sock. The yarn is threaded through the fabric of the sensors but goes only around the outside of the sock to the metal pushbutton.

The Shimmer™ transmitter is the Shimmer3 GSR+ model; GSR stands for galvanic skin response or skin conductance. The Shimmer transmitter has two connecting wires. The transmitter sends a current of max 5 μA from one sensor to the other via the snap fasteners on the smart sock. The transmitter then sends the collected data on the magnitude of the return current via a Bluetooth® connection to an app on a mobile device.

The Pain app is developed by researchers from the Eindhoven University of Technology. It is an adaptation of the Shimmer Capture app provided by Shimmer Sensing. The general workings of the app will be explained in the next section.

3.2.2. Data Analysis in Mobile Application

The mobile application used to receive, store, and analyse the skin conductance data was adapted from an earlier developed application (Frederiks et al., 2019; Sterkenburg et al., 2017). In this previous application, the Shimmer Capture app collected data, visualized it in a graph and created a data file with timepoints, skin resistance, and skin conductance. A typical file contains 51 data points per second. The Pain app used in the pilot study is based on the workings of the Shimmer Capture app. Additionally, it establishes skin conductance variability based on a baseline measure during a relaxing experience. The app then analyses new data points to see how these deviate from baseline. A signal is given when the deviation is large enough to indicate pain.

Furthermore, the pain app shows a visualization of the expected experience of the person wearing the smart sock. This visualization indicates whether the experience is painful or not. This visualization is designed with caregivers for caregivers to provide simple, unambiguous, and intuitive information about the experiences of patients and clients (Korving et al., 2020a).

3.2.3. Pilot Study

To test whether an app with skin conductance measures is applicable to measure pain, four healthy volunteers (all female, age range 29 – 52) without disabilities participated. The inclusion criteria were: healthy adults, 18 to 55 years of age, without cardio-vascular or anxiety disorders, no disorder to the nervous system, and not pregnant. The procedure follows a very strict protocol approved by the medical ethical committee of the Vrije Universiteit Amsterdam Medical Centre (NL 69815.029.19). Because volunteers endure painful moments during the procedure, the sample size (n=4) is limited.

The study starts with a relaxing experience to establish a baseline (watching a relaxing video of ±5 minutes). After the baseline measurement, the participant experiences a painful stimulus (<4 minutes), created by submerging the non-dominant hand in a tub of ice-cold water of ±6° Celsius and a neutral experience (±2 minutes). If the participant decides to repeat the process a total of two painful and two neutral moments are alternated. The study process takes ±20 minutes.

Ice-cold water has been used multiple times in previous pain research and was chosen in this pilot due to its ease and the possibility to precisely regulate water temperature, so the pain condition is equal among different participants (von Baeyer et al., 2005; Mitchell, MacDonald & Brodie, 2004). The temperatures used in this cold-pressor test usually lie between 0 and 10° Celsius, and water is kept moving to minimize hot pockets in the water, caused by the submersed hand.

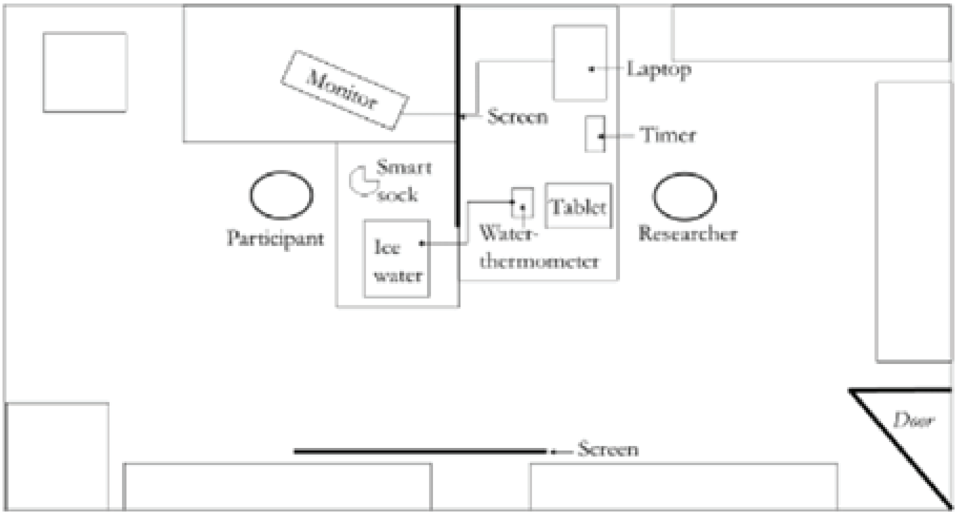


FIGURE 3.1. Map of the space where the experiment was conducted.

The experiment is conducted in a laboratory space with noise and temperature insulation, graphically displayed in Figure 3.1. It is set up to minimize participant movement. A screen is placed partly between participant and researcher, to give privacy during the relaxing experience, but the researcher can supervise during the painful stimulus. Another screen holds a 7-point pictographic Self-Assessment Manikin of arousal (Bradley & Lang, 1994), to self-report pain levels during the submersion of their hand in ice-cold water. During the experiment, the room temperature and the water temperature are regulated, and participant health is checked regularly.

3.2.4. Visual inspection of data

The collected data points are divided into separate parts for relaxation, pain, and no pain. The first 100 seconds of the experiments are to be considered a period of settling in, so these data points are not considered in the analysis. The plotted data are visually inspected to look for similarities within participants among the painful moments and the moments without pain (in oscillations and deviations). Between participants, the data plots are inspected to see whether moments of pain elicit similar skin conductance deviations from the baseline measurements.

For each of the four participants, a graph is made for the duration of skin conductance measurements (approximately 900 seconds = 15 minutes). Vertical lines are added to the graph to distinguish the different moments in the study (baseline, pain, and no pain). The scale of the x-axis (time in seconds) is similar in all graphs, while the y-axis, displaying skin conductance in μS, is normalized to reflect the range of dynamics in the data.

3.3. Results

The current study was conducted to test whether a system for skin conductance measurements can be used to measure pain in a laboratory setting with healthy participants. Four volunteers received a painful stimulus (a hand in ice-cold water) while the pain app system was monitoring skin conductance response. The skin conductance changes during different experiences (relaxation, acute pain, and no pain) were visually analysed.

With all volunteers, the entire study process was followed and three out of four repeated the painful stimulus once. The resulting four graphical displays of skin conductance during relaxation, pain, and no pain are displayed in Figure 3.2.

Results show that variation in skin conductance levels between participants is high, with a participant varying between 0 and 9 μS, another between 1 and 5 μS, a third between 1 and 2.5 μS, and one between 0 and 0.7 μS. Results also indicate that all participants show a pain stimulus response, between 400 and 550 seconds, and that these differ between participants.

When looking at the responses to painful stimuli within participants, the results show that the reaction to a pain stimulus was indicated with a rise and abrupt changes in skin conductance for participants A, C and D. The result from participant B shows abrupt changes to the painful stimulus, but no overall rise in skin conductance. The reaction to the first pain stimulus is stronger than the second. Two consecutive pain experiences could either elicit relatively similar responses (participants A and C) or dissimilar responses (participant D). And although we do see a reaction in skin conductance during the second painful stimulus in participant D, there is little difference in oscillations between the ‘no pain’ moments and the second painful moment (see a summary in Table 3.1).

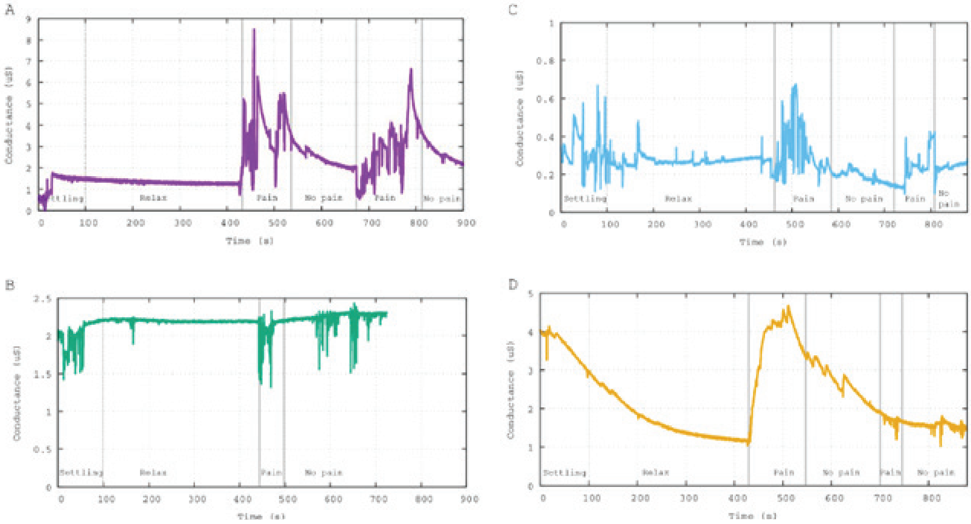


FIGURE 3.2. Results of skin conductance measurements during a meditation exercise (relax), a painful stimulus (pain), and a neutral stimulus (no pain) for participants A, B, C, and D.

TABLE 3.1. Summary of study results per participant.

Participants	Skin conductance response to pain		
	Range in μS	Deviation from baseline	Similarity in response
Participant A	0 – 9.0	Yes	Yes
Participant B	1 – 2.5	Yes	-
Participant C	0 – 0.7	Yes	Yes
Participant D	1 – 5.0	Yes	No

3.4. Discussion

This pilot study was conducted to examine whether the Pain app system, containing a smart sock with skin conductance sensors and mobile app, can be used to measure acute pain in healthy participants. The mobile application of the Pain app system analyses the skin conductance data. The system was developed to help caregivers recognize pain in persons with communication difficulties, who are unable to self-report their pain and seek pain relief themselves.

The study shows promising results on the use of skin conductance to measure acute pain in healthy volunteers. Skin conductance responses of participant A were similar during consecutive pain experience, and the skin conductance range for this participant was the largest of all four. Participant C also shows similarities between the first and second pain moments, and the skin conductance range is the smallest of all four. This indicates that the range of skin conductance does not necessarily represent the magnitude of the reaction. Participant D shows little relation between the reaction to the first painful stimulus and the second, which could be due to habituation to the painful stimulus. Overall, skin conductance could be reliably used to measure the physiological responses to acute pain, as long as no habituation has developed.

Furthermore, visual inspection of the skin conductance data shows that pain responses deviate from baseline but are unique for each person. Baseline measurements vary in magnitude and amount of oscillation, but in each participant, the baseline measure shows less skin conductance oscillation than during pain. This indicates that a deviation from baseline in whatever magnitude could indicate pain. And while we expected skin conductance to go up during pain, this was not the case in all participants (see participant B). Alternative explanations for this effect are the different smart socks that were used for hygienic reasons, or that physiological responses to external stimuli are unique for each person.

When we look at moments of ‘no pain’, participants A and C show more oscillation in pain moments compared to moments of no pain, but this is not seen in the other two participants. This can be due to general arousal, although none of the participants reported being stressed during the experiment. A more likely explanation is movement. Although the lab was set up to reduce any movement of the participants, while wearing a sock with GSR-sensors, feet movements can create skin conductance oscillations unrelated to arousal.

The results of this study indicate that skin conductance as a physiological measurement method could assess pain-related signals, as long as a baseline can be established. This result is promising, because not only can skin conductance be measured in a non-invasive way, the use of a smart sock allows for the system to be integrated into a general caregiving routine for people with communication difficulties.

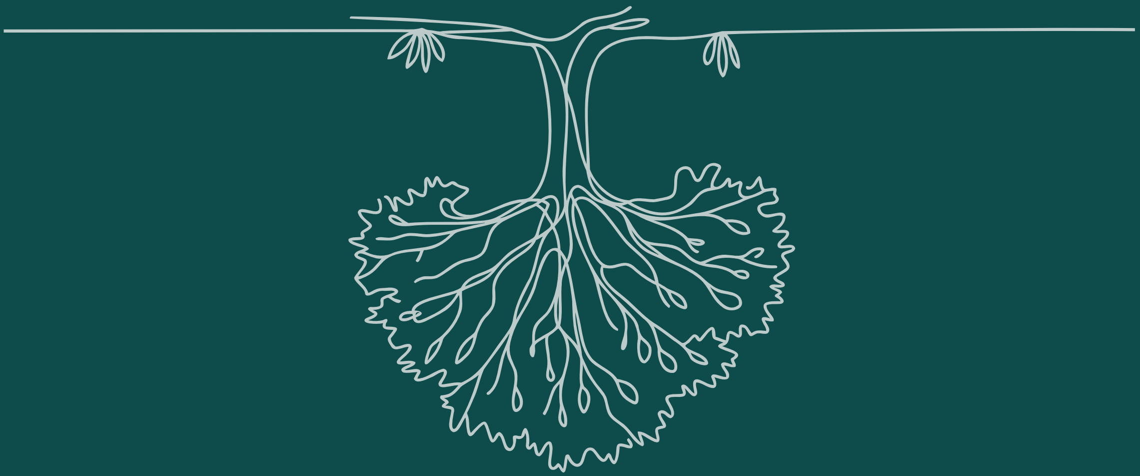
Compared to other assessment methods, where finger clips, wristbands, breast bands, or head caps are needed, putting on a sock will in itself not cause extra stress on the patient. And while a combination of physiological sensors may give a more reliable indication of wellbeing, the pain measurement system is not intended to be used as a diagnostic tool, but as a caregiving aid. Combined with attentive caregivers the pain app system will help people with communication difficulties communicate their pain.

3.5. Conclusion

Initial results on skin conductance measurements during pain with a smart sock on healthy volunteers are mixed but promising. Due to the prevalence of pain in persons with communication difficulties, the development of a system to measure physiological signals of pain will be a welcome aid in caregiving. Further steps will test the Pain app on another larger group of healthy persons before testing will commence on a group of persons with severe or profound intellectual disability, who are in pain due to medical reasons.

3.6. Acknowledgements

We would like to extend special thanks to the volunteers who received a painful stimulus during this pilot study for further development of the pain app. We also thank The Netherlands Organization for Health Research and Development ZonMw, Den Haag for the grant received to conduct this study.



Chapter 4

Development of an AI-enabled system for pain monitoring using skin conductance sensoring in socks[1]

---

[1] Published as: Korving, H., Zhou, D., Xiang, H., Sterkenburg, P. Markopoulos, P. & Barakova, E., (2022). Development of an AI-enabled system for pain monitoring using skin conductance sensoring in socks. *International Journal of Neural Systems, 32*(10), 2250047 (11 pages). Doi: 10.1142/S0129065722500427.

Abstract

Background Where self-report is unfeasible, or observations are difficult, physiological estimates of pain is needed. Methods Pain-data from thirty healthy adults was gathered to create a database of physiological pain responses. A model was then developed, to analyse pain-data and visualize the AI-estimated level of pain on a mobile app. Results The initial low precision and f1-score of the pain classification algorithm was resolved by interpolating a percentage of similar data. Discussion This system presents a novel approach to assessing pain in non-communicative people with the use of a sensor sock, AI predictor and mobile app. Performance analysis and the limitations of the AI algorithm are discussed.

4.1. Introduction

Many studies have focused on ways to physiologically detect pain, with methods having varying degrees of reliability and technological maturity (Korving et al., 2020a; Novak, 2019; Werner et al., 2019). Some approaches, such as magnetic resonance imaging or heartrate variability show great promise for physiological pain detection, but the measurement manner can be deemed invasive and to significantly curtail a patient's freedom of movement. Therefore, a system is needed to detect pain through physiological, non-invasive, and mobile methods and display results to caregivers.

The mobile app to be developed is part of a system that consists of a smart sock with fabric sensors for measuring skin conductance, a Shimmer™ unit that transmits those signals via Bluetooth® to a smartphone or tablet pc, and an ML module to determine the level of pain (Figure 4.1; Frederiks et al., 2015; 2019; Sterkenburg et al., 2017). This system is developed to be non-invasive: The fabric sensors in the sock do not irritate the skin as stick-on sensors may do and, when socks are worn daily, no extra material item, such as a wrist or head band, are introduced. Also, the Shimmer unit can be worn around the ankle, over or under the pants, but can also be placed around a rung of a wheelchair or just placed besides the sock for when a client is laying down. The rest of the system is mobile and wireless, silent and responds quick to physiological changes.

The application was developed according to recommendations for the development of e-Health apps which stress the importance of working in multidisciplinary teams and involving the intended users during the development process (Demiris, 2006). The visualization of the pain condition within the app was designed following the Double Diamond design process model (Kochanowska & Weronika, 2022) with the involvement of the target user group, which is described by Korving et al, 2020.

The use of socks to measure physical signals is becoming more common. The baby sock by Owlet measures a baby's heart rate and pulse oximetry during sleep and alerts caregivers in case of distress (http://dream.owletcare.com). Socks are also used to detect diabetic foot ulcers by measuring skin temperature at six key points on the foot sole (Schneider & Severn, 2018) and to monitor gait (O'Flynn & Tedesco, 2020). The smart sock measuring skin conductance has already been used for establishing heightened arousal in children and adults with severe or profound intellectual disability (Frederiks et al., 2015; 2019; Sterkenburg et al., 2017).

Alternative wearable technology has been used to transmit physiological data on motor movement (Burns & Adeli, 2017), to diagnose medical disorders based on physiological data assessed by artificial intelligence (AI; Raghavendra, Acharya & Adeli, 2020) and increasing the accuracy of motor imagery signals in electro encephalograms (Hassanpour et al., 2019). Contrary to movement or skin ulcers that can be objectively compared, pain is an experience that encompasses many different emotions and is mostly deemed unique for each person (Racine et al., 2011). No two persons have a similar pain experience or pain tolerance threshold, therefore, a system to measure pain in many different people needs some sort of AI at its core (Martinez Mozos et al., 2016). The purpose of an AI-enabled algorithm will be to classify a skin conductance signal from a pre-determined length of time as either pain or no pain.

In that light, the aim of this study is to (1) Gather data on physiological skin conductance signals that accompany a pain experience, (2) Ascertain whether the physiological signal during pain can be accurately distinguished from the signal in moments without pain, (3) Create an AI-model that determines whether new skin conductance data can be categorised as pain or not, and (4) Develop a mobile app that uses the algorithm from step three to categorise skin conductance data from a smart sock to give a warning signal when pain is experienced.

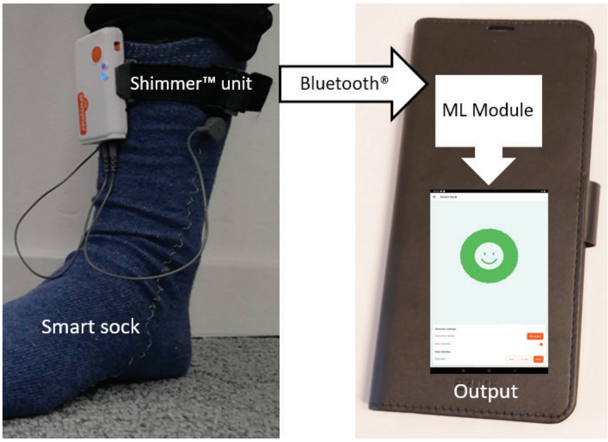


FIGURE 4.1. The process of the pain monitoring system from smart sock, via Shimmer™ unit to the ML module in the mobile app.

4.2. Methods

4.2.1. Experiments with pain moments

In this experiment, healthy participants were exposed to various controlled levels of pain by inserting their hands in cold water. Their skin conductance measured with the sensor sock was recorded and synchronised with the moments when the participants indicated the feeling of pain to create a data set for subsequent use in the algorithm development. The experiment was approved by the medical ethics board of the Vrije Universiteit Medical Centre in 2019 under no. NL69815.029.19.

4.2.1.1. Participants

Psychologically and medically healthy adults were recruited at the Eindhoven University of Technology and the Vrije Universiteit Amsterdam. The exclusion criteria for participation in this study are presented in Table 4.1. Participants were also asked about any other neuropathic or neurologic disorders that may influence skin conductance, as well as the presence of existing pain during the experiment.

Thirty adults participated, with an age range from 19 to 52 years old (M_{age}=32,17, SDAGE=7,30) and self-reported body mass indexes between 17,6 kg/m2 and 40,6 kg/m2 (M_{BMI}=23,83, SD_{BMI}=4,43). The body mass index is a rule of thumb to categorise a person’s weight based on tissue mass and height; a BMI under 20 is categorised as underweight, between 20 and 25 as healthy, between 25 and 30 as overweight, and over 30 as obese (Pi Sunyer et al., 1998).

Out of thirty participants, only one had previously participated in an experiment concerning pain. A third of the participants were experiencing a little pain at the time of the experiments, either an ache in muscles or the back the others reported no pain. None of the participants had taken any pain relief medication for at least six hours before the experiment.

TABLE 4.1. Exclusion criteria for participating in the pain experiments.

#	Criteria
1	Minors or those over 55 years old.
2	Suffering from disorder of the heart or blood vessels.
3	Under treatment for fear, anxiety, trauma, or other related psychological disorder.
4	Pregnancy or a chance thereof.
5	Allergies to materials used in the smart sock (cotton, elastane, silver) or domestic pets.
6	Infections, sores, or wounds on either the hands or the feet.
7	Fracture or existing pain to the limb to be submerged.
8	A history of fainting or seizures.
9	A history of frostbite.
10	Suffering from Raynaud’s disease (decreased blood flow to the fingers).
11	Showing symptoms of COVID-19 (e.g., raised temperature, coughing, runny nose).

4.2.1.2. Procedure

Experiments were conducted according to a standard procedure while keeping to a separate corona-protocol. Participants were invited to visit a lab room where 1,5 meters distance could be maintained throughout the experiment to uphold social distancing rules relating to the Covid-19 pandemic. Hence, they were asked to disinfect their hands and then measure their body temperature with an infrared ear thermometer.

The thermometer would give a beeping warning when the temperature reached 37,5° Celsius or higher. If a beeping warning was heard, the participant could not continue. Results of the body temperatures were neither asked nor stored. All participants followed the protocol, and all were included in the study.

After this, participants were instructed on how to put on their smart sock and attach the Bluetooth™ transmitter around their ankles. They could put their shoe back on or leave it off and were asked to move the foot containing the smart sock as little as possible. A footstool was provided for them to rest their foot on.

The experiment started with a 6:45 minute relaxing video, to establish a skin conductance baseline for each participant. Hereafter, participants were asked whether they wanted to continue with the experiment and to remove any watches or jewellery from their wrist. They were invited to submerge their hand up to the wrist in ice-cold water and note their pain level out loud on a scale of one to seven. Participants were specifically instructed that level seven did not have to be the worst pain participants could imagine and more particularly the moment the feeling had become so uncomfortable they would wish it to stop immediately. Due to a very slight risk of lasting pain or impairment to the hand as a result of the submersion in ice-water, the participants were asked to submerge their non-dominant hand.

Participants alternated the submersion of their hand in ice-cold water, as the pain stimulus, and water of a moderate temperature, as a neutral yet similar stimulus, though they were unaware how cold or moderate the water temperature would be. Each submersion would last for a maximum of four minutes, since from five minutes onwards chances of damage, such as freezer burns could emerge (Godden, Roth & Hines, 1955).

4.2.1.3. Instruments

The pain level scale used was based on the Self-Assessment Manikin (SAM) for arousal (Morris, 1995), shown in Figure 4.2. The original SAM is in black and white, and colours were added (from green for no pain, via orange for discomfort to red for pain) in case it would be easier for participants to name colours instead of the numbers attached to each subsequent level. Level one equalled 'no pain' or the amount of mild pain the participant was in at the start of the experiment. Level four equalled a starting feeling of discomfort, but not yet pain. Level seven equalled their pain tolerance threshold.

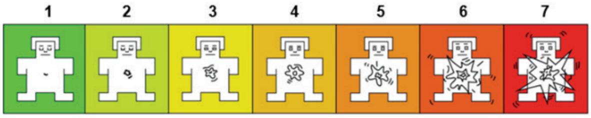


FIGURE 4.2. The seven levels of the self-assessment manikin used during the submersion in ice-cold water.

The tub containing ice water was made from Styrofoam of one-and-a-half centimetres (cm) thick and Polyisocyanurate (pir) insulation sheets of three cm thick. The dimensions of the inside of the tub were 36.5x27x12.5 cm (length x width x height). Tubs containing water of moderate temperature differed for each experiment, though all were at least high and wide enough for a large hand to submerge up to the wrist. The water temperature during the submersion in ice-water ranged from 4.0° Celsius to 9.5° Celsius ($M_{\text{ice water}}$ =6.15°, $SD_{\text{ice water}}$ =0.90°) while the water of moderate temperature ranged between 20.0° Celsius and 26.6° Celsius ($M_{\text{moderate water}}$ =21.2°, $SD_{\text{moderate water}}$ =1.11°).

Data was gathered using a smart sock in the right shoe size, containing two fabric sensors on the inside sole. A Shimmer™3 GSR+ unit worn with an anklet around the ankle connected to the sock and sent a six Ampère current from one fabric sensor to the other. The Shimmer™ unit used Bluetooth to connect to an existing mobile app, where the data was collected, and a text-file was created per participant. The Shimmer™ unit has a sampling frequency of 50 points per second and gathers both raw and standardized skin conductance and skin resistance measures.

4.2.2. Development of the classification algorithm

Although the output included unstandardized raw skin conductance, standardized skin conductance and average skin conductance for each participant, only raw skin resistance was eventually used in the training model because this was the easiest measure to receive and could simply be transformed into galvanic skin response (skin conductance) for output. Raw skin conductance is measured between 0.2 µS and 125 µS, with a sampling rate between 0 and 5 Hertz. An example of the raw skin conductance signal in this research is shown as Figure 4.3.

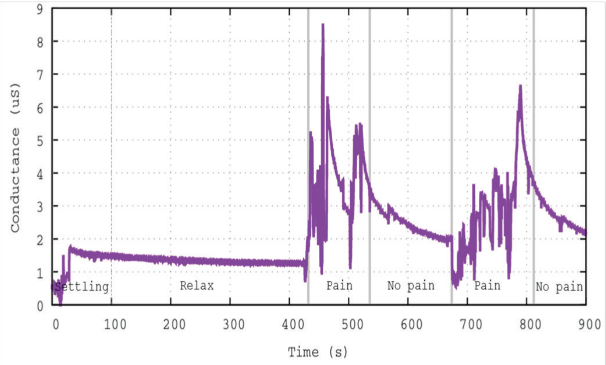


FIGURE. 4.3. An example of a signal from one pain experiment lasting fifteen minutes.

For each participant, an average of 1,378 seconds (SD = 367.4 seconds) was collected, for a total of approximately 68,900 points of raw skin resistance data. These data points were coded according to each participant's self-report. Out of the thirty recruited participants, two showed errors in data and were discarded. From the remaining twenty-eight participants, three participants (P07, P15, and P21) were randomly selected as the testing set, while the remaining were used for training.

Skin conductance data during the relaxing video at the start of the experiment was coded as baseline (BS). The moment right before they submerged their hand in a tub of water was coded as A1, the moment a participant began to feel uncomfortable (number 4 on the SAM scale) was coded as A2, the pain tolerance threshold was coded as B1 and the moment the pain was gone was coded as B2. For each participant, only the data with codes B1 (pain) and B2 (no pain) were extracted for use. Furthermore, to reduce the individual differences, these data were subtracted from each participant's average BS before they were used for training and testing.

As time series data, every 250 data points (nearly 5 seconds) with the same codes B1 or B2 were extracted as a sample. In this way, a total of 5,332 samples labelled B1 and 31,238 samples labelled B2 were obtained respectively for the training set, while a total of 920 samples labelled B1 and 4,350 samples labelled B2 were obtained for the testing set. Eleven time domain features and eleven frequency domain features were used, which are listed in Table 4.2.

The Synthetic Minority Oversampling Technique (SMOTE) was used to balance the classes in the training set by increasing the number of the B1 class based on the k-nearest neighbours. SMOTE could be described with the following steps:

Step 1: Identify the feature vector x_i and identify the k-nearest neighbours xknn.
Step 2: Calculate the difference between the feature vector and k-nearest neighbour.
Step 3: Multiply the difference by a random number between 0 and 1.
Step 4: Add the output number to the feature vector to identify a new point on the line segment.
Step 5: Repeat the process from steps one through four for identifying other feature vectors.

Specifically, we used the imblearn library (Lemaître, Nogueira & Aridas, 2017) to oversample B1 class utterances during training.

TABLE 4.2. Time and frequency domain features.

Time domain feature		Frequency domain feature	
Feature	Equation	Feature	Equation
Mean (Z_1)	$\frac{1}{K}\sum_{k=1}^{K} x(k)$	Mean frequency spectrum (Z_{12})	$\frac{1}{N}\sum_{n=1}^{N} F(n)$
Variance (Z_2)	$\frac{1}{K-1}\sum_{k=1}^{K}(x(k)-Z_1)^2$	Frequency spectrum variance (Z_{13})	$\frac{1}{N-1}\sum_{n=1}^{N}(F(n)-Z_{12})^2$
Standard Deviation (Z_3)	$\sqrt{Z_2}$	Standard deviation frequency spectrum (Z_{14})	$\sqrt{Z_{13}}$
Max (Z_4)	$\max(x(k))$	Max frequency spectrum (Z_{15})	$\max(F(n))$
Min (Z_5)	$\min(x(k))$	Frequency spectrum skewness (Z_{16})	$\frac{1}{N}\sum_{n=1}^{N}(\frac{F(n)-Z_{12}}{\sqrt{Z_2}})^3$
The most common value (Z_6)	$\mathrm{mode}(x(k))$	Frequency spectrum kurtosis (Z_{17})	$\frac{1}{N}\sum_{n=1}^{N}(\frac{F(n)-Z_{12}}{\sqrt{Z_2}})^4$
Peak to peak (Z_7)	$Z_4 - Z_5$	Spectral skewness (Z_{18})	$\frac{\sum_{n=1}^{N}[\left(f(n)-F(n)\right)^3 F(n)]}{\sum_{n=1}^{N}F(n)}$
Zero crossings (Z_8)	$len(x(k) > 0)$	Spectral kurtosis (Z_{19})	$\frac{\sum_{n=1}^{N}[\left(f(n)-F(n)\right)^4 F(n)]}{\sum_{n=1}^{N}F(n)}$
RMS (Z_9)	$\sqrt{\frac{1}{K}\sum_{k=1}^{K} x(k)^2}$	Spectral centroid (Z_{20})	$\frac{\sum_{n=1}^{N}F(n)f(n)}{\sum_{n=1}^{N}F(n)}$
Mean absolute deviation (Z_{10})	$\frac{1}{K}\sum_{k=1}^{K}\lvert x(k)-Z_1\rvert$	Spectral standard deviation (Z_{21})	$\sqrt{\frac{\sum_{n=1}^{N}[(f(n)-Z_{20})^2 F(n)]}{\sum_{n=1}^{N}F(n)}}$
Interquartile range (Z_{11})	$Q_3 - Q_1$	DC component (Z_{22})	DC component in Fourier series

Note. where *x(k)* is the data points in the sample, while *f(n)* and *F(n)* represent the frequency component and the frequency spectrum, respectively.

A Random Forest (RF) algorithm was applied due to its advantages of dealing with unbalanced datasets, fast computation, less parameters than neural networks and good performance (Ho, 1995; Lemaître, Nogueira & Aridas, 2017). In RF, each tree randomly selects a subset of the dataset to build an independent decision tree. Each tree makes the classification of the features and the target variable independently and votes for the final tree class. RF decides the final overall classification based on the majority obtained trees voting.
On the training set, the grid search strategy was applied to identify optimal hyperparameters by using Random Forest. The five-folded cross validation was applied to determine the optimal tree number by grid searching in the range of {50, 100, 150, 200, 250, 300}. The optimized random forest classifier was found with 200 trees, Gini-Index, log2 for the number of features considered for splitting a given node.

To further protect the wearer of the sensor sock and reduce the risk of missing pain, all predicted results with label B2 (no pain) confidence lower than .6 were reported as B1 (pain). As a pilot study with only 28 participants, we generated new training samples with some similarities with those in the testing set by interpolation. We did this to simulate participants in the training set with a similar pain response pattern as the participants in the testing set.

4.2.3. Development of the pain monitoring app

Before starting on the source code for the Pain App, a short online study was conducted among 32 end-users (care professionals). They were asked to assess different user interface and input options which could later be added to the mobile application. This way, the programmers could prepare the app's source code for the additions deemed most desirable by end-users.

Participants were presented with possible additions on three aspects of app development: five possibilities for input (the app user can input information themselves), five possible ways of signalling (the manner in which the mobile app gives a warning when the wearer of the sensor sock has pain) and five possibilities regarding the app's interface (the way the app appears to the user), see Table 4.3. They were asked to order each of the five possibilities by desirability.

Table 4.3 gives the percentage of participants ordering each possibility on first or second place. For example, almost 83% of possible end-users found the addition of a possibility to input information about what happens around a client a desirable addition, more desirable than inputting the client's painful medical conditions (as possible cause of pain) and whether the caregiver thinks the wearer of the sensor sock experiences pain. Concurrently, 83% of participants desired to also receive a warning signal when the physiological data implies a rise in arousal in the wearer, while nearly 66% of end-users would like the mobile app to show them results of physiological responses in their client for the previous fifteen minutes.

Based on the results of this online rating questionnaire, the source code for the SID Pain App was adjusted to in the future incorporate multiple functions. Hereafter the algorithm was introduced into the app, with the goal of triggering the right responses to incoming data.

TABLE 4.3. Possible additions to the pain monitoring app and the percentage of caregivers who put the option either in first or second place.

Input	Score	Signals	Score	Interface	Score
Caregiver thinks client is in pain	34.3%	A sound for pain	28.6%	Changes in pain experience for the last 12 hours	51.4%
What happens around the client	82.9%	A haptic response for pain	17.1%	Changes in pain experience for the last 15 minutes	65.8%
Name of caregiver	2.9%	A combination of visual, sound and haptic at pain	40.0%	Show pain experience for multiple clients	31.4%
Name of client	25.7%	A signal at heightened arousal	82.9%	Overview of client's information on home screen	8.6%
Client's painful medical disorders	54.3%	A signal when pain ends	31.5%	Ability to connect pain app's result to client's electronic file	42.9%

4.3. Results

4.3.1. Pain classification

The classification model that came out of random forest modelling was trained using datasets from twenty-five randomly chosen participants and validated with the other three datasets. The resulting pain classification algorithm ranged from 80-93% AOC.

If the training data is balanced, the metrics of accuracy, precision, recall, f1-score are usually very close to each other. Since the dataset collected from the participants was imbalanced, testing the model with other predictors, (precision, recall, f1-score) showed high accuracy but low precision. Adding balancing strategies and using LSTM instead of Random Forest Modelling did not improve precision. Therefore, we applied SMOTE and ClusterCentroids which resulted in improved F1-scores, as can be seen in Table 4.4.

TABLE 4.4. Results of RF-model with 50% interpolated data and the change (between brackets) from the imbalanced model.

	Precision	**Recall**	**f1- score**	**support (# samples)**
0	0.81 (-.11)	0.97 (+.09)	0.89 (-.01)	3649
1	0.88 (+.67)	0.50 (+.23)	0.64 (+.40)	1621
Accuracy			0.83 (=)	5270
Macro avg	0.85 (+.29)	0.74 (+.16)	0.76 (+.19)	5270
Weighted avg	0.83 (-.02)	0.83 (=)	0.81 (-.03)	5270

Seven experiments were conducted on the training set, by adding different percentages of similar data from the testing set into the training set. In each experiment, K% data (K = 0, 10, 20, 30, 40, 50, 60, 70) were randomly selected from the testing set. After interpolation, the same percentage of similar data as those K% were added in the training set. The classifier was trained on this expanded training set.

The training was run ten times for each experiment, and the average f1-score and precision of the classifier are reported in Table 4.5. It shows that both the average f1-score and precision were 0.54 without any added interpolated data. But when interpolated data were introduced, the performance of the classifier significantly improved. The higher the percentage of interpolated data, the better the classifier performed.

TABLE 4.5. Average f1-score and precision for different percentages of interpolated data (K%).

K (%)	0	10	20	30	40	50	60	70
f1-score	.54	.69	.72	.75	.76	.77	.78	.79
precision	.54	.71	.77	.81	.83	.85	.87	.88

4.3.2. Development of the pain monitoring app

Caregivers suggested in the online questionnaire to add more contextual information about the client, and they considered that adding a client's medical condition would be a valuable feature, that can be added to our model. Most caregivers would not only appreciate to have an indication/signal when their client has pain, but also when the client's arousal level rises. Regarding the interface of the application; caregivers would appreciate being able to look back fifteen minutes in the possible pain experience of their client and in the changes in pain experience over the past twelve hours would also be welcomed (for nighttime use).

Simple solutions, such as noting when the caregiver thinks a client is in pain, were implemented in the app from the first iteration (shown in Figure 1). The possibility to look back fifteen minutes was visualised in a separate screen, where a graph showed the changes in skin conductance for the last five minutes. Signalling for heightened arousal would mean integrating two separate measuring systems and was postponed until after the pain app could be tested on the target group.

The features of the mobile app are as follows: autonomic search for Bluetooth-capable systems, connection, and disconnection to Shimmer sensor, start and stop of data collection, labelling data as either ‘Pain’, ‘No Pain’ or ‘None’, graphical display instead of visualization, and storage of CSV datafiles. The features are kept simple, and a click of one button often features several steps, such as the search and connection to specific Shimmer sensor units or the disconnection to the Shimmer unit and the storage of a datafile. Datafiles can be shared using the features of the mobile device which runs the application.

4.4. Discussion

This study was conducted with the goal of creating a system consisting of a wearable skin conductance sensor, an AI predictor, and a mobile application to process physiological data and categorise that data as either indicating pain or no pain. The app that was created uses a Random Forest algorithm to respond to the data collected from a skin conductance sensor integrated with a smart sock (wearable) and a sensor that transmits via Bluetooth™ to the mobile device. The algorithm resulting on Random Forest Prediction was trained on skin conductance data collected during moments of pain and moments of no pain for 28 healthy participants.

4.4.1. General discussion

The current study uses a physiological signal to detect and classify a pain response. This is similar to earlier studies, where different machine learning algorithms were used on physiological and sometimes social cues to classify stressful and calm or neutral situations, with similar accuracy results as were found in this study (Avila et al., 2021; Chen, Abbod & Shieh, 2021; Korving et al., 2020b; Martinez Mozos, et al., 2016; Sánchez-Reolid et al., 2020; Tamizi, Zawawi & Adzemin, 2021;

Werner et al., 2019). Electrodermal activity, or skin conductance, was also shown to be the preferred physiological method used on wearables and to detect emotional responses to stimuli (Rao Veeranki, Ganapathy, & Swaminathan, 2021). Furthermore, in another study RFP was proposed to be the most accurate to handle medical applications (Kaur et al., 2019).

Results from this study build on previous results, either on the use of an electrodermal activity to measure emotional responses (Aslanidis et al., 2018; Bari et al., 2018), but also on developing a mobile application to display and visualize the emotional state of clients with a severe or profound intellectual disability (Frederiks et al., 2015; 2019; Sterkenburg et al., 2017). With an accuracy between 80 and 93% and precision of 0.88 the app will provide a useful tool to, for example, aid caregivers of those unable to communicate or express their pain, providing more certainty and decreasing possible work stress. But most important, speedy pain signalling for those unable to communicate will make sure a patient’s pain will not go unrecognized and he/she will receive the pain relief and medical treatment needed.

Electrodermal activity has been shown to increase in response to noxious stimuli, such as stress and pain (Aslanidis et al., 2018; Bari et al., 2018; Frederiks et al., 2015; 2019; Korving et al., 2020a; Sterkenburg et al., 2017), but responses can vary between people (Korving et al., 2020b). Circumstances, such as room temperature and time of day, and personal differences, such as race, age, and BMI also influence skin conductance responses (Cagnie et al., 2014). Therefore, the creation of a pain assessment algorithm will offset the imbalance of pain response data coming from a diverse group of people, in a first step towards a pain assessment system with the capability to reliably measure pain in a heterogenous group.

Compared to other physiological pain measurement methods, the use of fabric sensors detecting electrodermal activity in a sock is reliable and non-invasive (Korving et al., 2020a). Equally reliable pain measurement methods, such as real-time brain scans using cerebral brain flow velocity or magnetic resonance imaging, need expensive medical equipment and specialized medical knowledge to be used (Cagnie et al., 2014; Hatfield & Ely, 2015). Other measurements, such as respiratory and muscle tension measurements showed inconsistency among results, namely no results among certain subject groups, i.e., healthy adults and adults with intellectual disability (Dorfman et al., 2014; Heales et al., 2015).

4.4.2. Limitations and strengths

While the goal of the pain app is to classify pain in a physiological manner to be used for persons unable to communicate about their pain, the data gathered for the classification algorithm was not collected from this target group. Skin conductance data was gained from thirty healthy participants well able to communicate and express their experience of pain. This was done for two very important reasons. First, the healthy participants could clearly and timely report the painful moments. Second, the healthy participants could give full informed consent to participate in this experiment with an induced pain experience.

The performed experiment did not take into account differences in pain tolerance and gender differences. Since the goal of the study was to establish physiological responses to the moment the pain tolerance threshold is reached, it was deemed unimportant to establish whether that threshold was low or high. Similarly, differences between men and women were not deemed important, since there is no reason to assume physiological responses to pain differ between males and females.

The current mobile pain monitoring app can classify data on the level of pain or no pain, but it is not (yet) clear whether pain can be reliably distinguished from an extreme emotional reaction. The need to develop this pain classification app was more pressing than examining the full range of emotional responses from skin conductance. And, as both pain and an extreme emotional response reactions require the attention of care staff, they reported that a signal to both pain and an extreme emotional reaction would be welcomed.

Since pain is part of the sympathetic nervous system, it regulates the body's unconscious actions (Brodal, 2004; Knudsen et al., 2019). Research has shown that this reaction can be influenced by emotions, ambient temperature, as well as immune reactions and other bodily processes (Cardinali, 2018; Knudsen et al., 2019). Therefore, using electrodermal activity to assess a pain state may be influenced by processes inside and outside the client. However, as far as invasiveness goes, a skin conductance system has been shown to be of preferred use by very vulnerable clients, like those with intellectual disability (Korving et al., 2020a).

Although the pain classification algorithm created in this study had high accuracy, the severe imbalance of the training data caused for low precision and f1-score. We balanced the dataset by creating more data using established AI techniques, however this still can be seen as a shortcoming of the study. The training set only comes from 25 different people, which may not represent pain experienced by all. New data was generated by interpolation from randomly selected test data and then added to the training data. With similar data added, the performance of the model significantly improved. Thus, it is expected that for healthy adults the pain will classify pain correctly.

Another limitation is the embedding of the algorithm in the mobile application. Although there are fourteen different versions of raw data coming from the Shimmer™ unit, only raw skin resistance was used to generate features and detect a pain signal. The use of more than one measurement feature (e.g., heart rate variability), though necessitating more computational power and making an eventual algorithm more complex, may lead to more accurate and specific pain detection.

4.4.3. Further steps and future work

The first steps were taken to generate a working pain classification algorithm and a mobile app was created that incorporates such an algorithm. When new pain experience data is collected and a model with higher precision and f1-score can be generated, this can easily replace the model that is currently in the app.

In future research the new mobile pain monitoring app should be tested in the target group, namely adults with a severe or profound intellectual disability. This could be done in a naturalistic setting such as during scheduled physical therapy treatments, with both clients who receive physical therapy for rehabilitation, where predicted moments of pain may occur, and with clients who receive physical therapy for maintaining a certain skill, where no moments of pain are expected. The ability of the app to distinguish pain from no pain in the target group can then be examined.

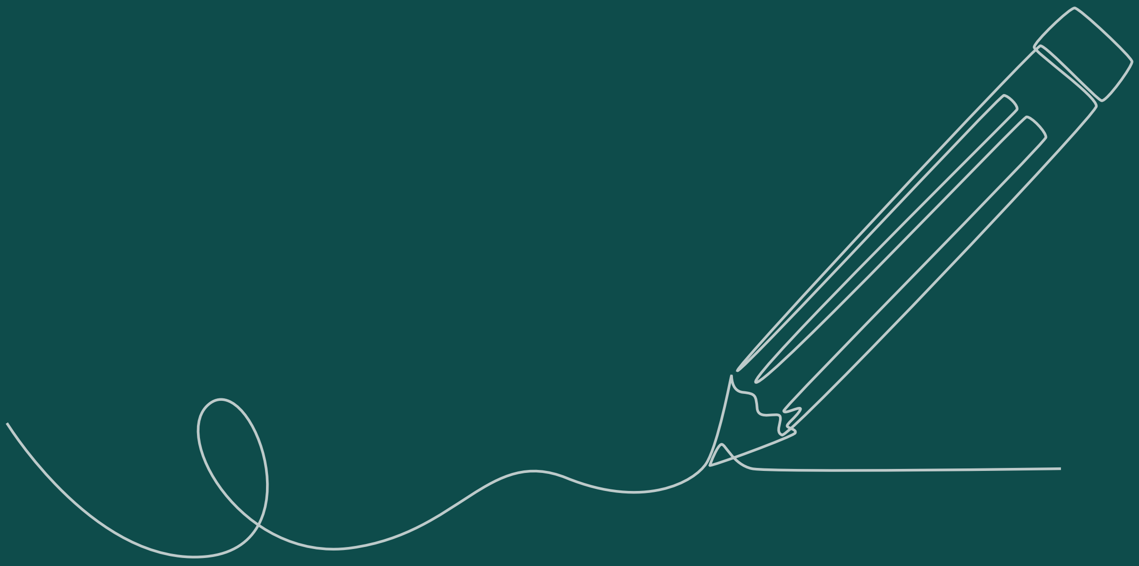
As mentioned before, this study has not yet focused on distinguishing pain from an extreme emotional response, such as stress and anxiety. For future applications in other target groups, this distinction could be a good addition to a mobile pain detection app. Furthermore, the addition of pain experience data from other target groups unable to communicate about pain and stress (e.g., neonates, persons suffering from dementia, persons undergoing an operation) would increase general knowledge on using electrodermal activity to measure pain.

4.5. Conclusion

This article describes a three-tier process of developing a pain classification algorithm using data from 28 experiments in which pain was induced and physiological measurements collected by a wearable sock. The pain classification algorithm was developed using Random Forest Prediction. Initially, the accuracy was adequate, but precision and f1-score were low. The imbalance of the training data was corrected by adding randomly generated data similar to the testing set. The resulting mobile pain monitoring app provides caregivers with a non-invasive and reliable pain detection method, which can be integrated into daily caregiving work without much training or specified medical knowledge.

4.6. Acknowledgements

The authors would like to acknowledge the work of Ir. Bart van Dijk and Ir. Paul van Beek on programming the SID Pain App.



Chapter 5

Designing Pain Visualisation for Caregivers of People with Special Needs: A co-creation approach[1]

---

[1] Published as: Korving, H., Sterkenburg, P., Barakova, E. & Feijs, L. (2022). Designing pain visualisation for caregivers of people with special needs: A cocreation approach. *Heliyon, 8*(12), e11975, DOI: 10.1016/j.heliyon.2022.e11975.

Abstract

Recognizing pain in people with communicative disabilities is challenging. A support system detecting pain signals provides caregivers with information to intervene adequately. This study aims to develop a design for a user interface visualizing pain experiences for a signalling system intended for caregivers. Caregivers receive alerts, indicating the presence or absence of pain experienced by a disabled individual. The design process included the use of value proposition, a brainstorm, a mood board with basic design elements, and multiple questionnaires and focus groups. During the multi-disciplinary design process end-users were extensively involved. The final design was deemed intuitive, clear, and recognizable, and usable in daily caregiving. This article describes the creation process for a non-hedonistic visualization for this niche end-user group.

Highlights

- In this article a complex, hard to recognize and challenging concept (pain) is visualized.
- A multi-disciplinary co-creation approach was used, involving end-users in each aspect.
- The end-users consist of a niche user group on which very few studies have focused.
- The resulting design is intuitive to the end-user and can be implemented in a real-life setting.

5.1. Introduction

When a person is unable to express pain, as is the case for those with severe or profound intellectual disabilities (SID), this poses a challenge for caregivers (Griffiths, & Smith, 2016). Especially when a genetic disorder also brings about a multitude of painful medical afflictions, which is often the case (e.g., Doody & Bailey, 2006; Walsh, Morrison & McGuire, 2011), the necessity to spot the pain timely and adequately increases. Due to SID, clients often display subtle or idiosyncratic signs of distress (e.g., freezing, laughing) and they depend on caregivers for pain and stress relief (Van der Putten & Vlaskamp, 2011). Some of the most frequent painful disorders, such as gastro-oesophageal reflux and obstipation, are easily treatable, which makes inaccurate or absent pain recognition all the more poignant. Caregivers could use aids to help them become aware of pain among those unable to clearly express it.

To provide caregivers with information about the existence of pain in their clients with SID, a system was developed that uses physiological signals to measure possible pain (Korving et al., 2020b). The system utilises a sock with sensors for skin conductance, a transmitter sending and receiving information from the sock sensors and sending it via

Bluetooth™ to a mobile application on phone or tablet (Frederiks et al., 2015; 2019; Korving et al., 2020b). The mobile application contains an AI-enabled algorithm that was trained to distinguish physiological pain signals from other signals. This article focuses on the development of the visualization accompanying the warning in the mobile application.

5.1.1. Related work

The use of technology in healthcare is growing and data is routinely collected, which becomes valuable for use in the design for new care solutions (e.g., Bughin, 2016). Transforming the available data to understandable, timely, and meaningful information for users is of crucial importance. The transformation of data is especially challenging when there are multiple users with different perspectives and a multitude of experiences which shape the appraisal and managing of other's pain (Craig, 2009, p. 24). In terms of phenomenology, the philosophical study of experience and consciousness (Price et al., 2002; Thacker & Moseley, 2012; Zahavi, 2003), the first-person perspective of pain is the person who is experiencing pain, in this case, an individual with SID, who is unable to clearly express this. Those who interact with the individual in pain have a second-person perspective on the pain experience. This will be the caregivers of the individual with SID. Those that do not interact with the client, but observe an interaction, for example researchers and other care professionals, have a third-person perspective on the experience of pain. The application to be developed translates the first-person experience and displays that to someone with a second- or third-person perspective (Figure 5.1).

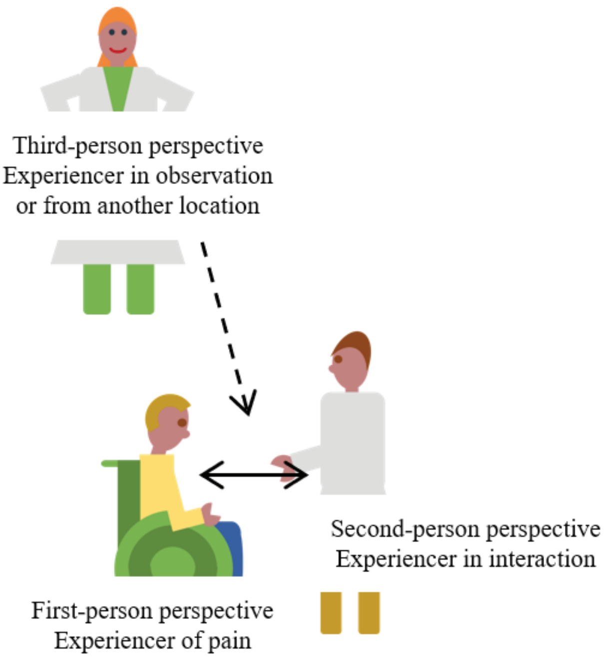


FIGURE 5.1. A graphical representation of the three perspectives correlated in the visualization developed this study.

To signal this first-person pain perspective to another a visualization can be used. The use of technology in aid only emanated in the past half-century, but information has been visualized since there was a need to share it (Birx, 2006). The underlying data might change, but the need to visualize information remains. Considering a limited amount of data can be stored in working memory at one time (Van den Berg et al., 2014), when more data are presented, receivers get confused, make errors and forget items (Maehara, & Saito, 2007). When compacted data is shown in drawings or charts, not only does information become clearer, drawings are "[…] more effortless to recognize and process than words, but also easier to recall" (Dewan, 2015, p. 2). In a busy and distracting caregiving environment, caregivers have limited time to perform a variety of tasks for a variety of clients and simultaneously attend to many aspects of their wellbeing: A simple and intuitive aid to help with one of these aspects will be invaluable.

Visualization of information is also preferred when it provides ambiguous or pre-analysed information. An example of this is data on physical processes. Especially when the goal of physical measurement is information on health status or the presence of an illness, more information can enhance interpretation, but more data may reduce clarity (Bughin, 2016). A dynamic and simple visualization gives sufficient information to a health care provider, without requiring too much cognition or providing too much information for understanding.

5.1.2. Gaps in knowledge

An experience of pain is difficult to capture with standardized numeric measurement tools, such as the Numeric Pain Rating Scale (Jensen, et al., 1986; Gooberman-Hill, et al., 2007; Wylde, et al., 2012). Thus, over time, several colour- and shape-based tools were developed and used for assessment of pain in children, pain from burn wounds and chronic pain (e.g., Grossi, et al, 1983; Machata, et al., 2009; McGrath, et al., 1996). These non-numeric pain assessment tools were validated and compared to numeric scales and results indicated that patients preferred the former to describe a pain experience over the latter. However, studies validating non-numeric based assessment tools used pre-determined colours and shapes/figures without examining whether these accurately represent the pain experience for users. Therefore, it is unknown if visualizations used in these scales are intuitive for the pain experience. The current study bridges this gap by describing a process to ascertain the intuitive colours, figures, shapes, and characteristics associated with pain in the user group.

In the Netherlands, a caregiver usually cares for more than one person with SID, and a person with SID is cared for by more than one caregiver. Since caregivers want to provide high-quality care and attend to the needs and challenges of persons with SID, interpretation of the information in the app should be accurate and easy to understand. Furthermore, since multiple caregivers care for one disabled individual, interpretation of the data should be user independent (Jansen, Van der Putten & Vlaskamp, 2013; Kruithof et al., 2020). Above all, a caregiver’s workplace provides challenges to incorporate a system, therefore one design challenge addressed in this article is converting numerical data to a visualization that is recognizable by many different users with different levels of cognition which corresponds to pain experienced by adult clients with SID, which is practical to use within a distracting working environment.

5.1.3. Study objectives

The aim of the current study was to develop a visual design of pain, which changes in colour, shape and/or characteristic to indicate whether pain is, or is not, present. The design was developed in co-creation with persons from second- and third-person perspectives, meaning that the visualization is co-developed with caregivers who experience the pain of the person with SID by interaction as by care professionals and other persons who observe the interaction. This study addresses the following questions: (1) What are visual associations with pain with respect to shapes, colours, figures and characteristics?, (2) What are factors to be considered when designing visualizations to be used in the workplace?, (3) What design for pain can be made based on a literature search of visual associations of pain from patients with (chronic) pain?, (4) What are preferred characteristics of visualizations with respect to clarity, distinguishability, intuitiveness and pain association?

5.2. Design process

The goal of the design co-creation process was to create a concept for a user interface that visualizes pain applicable in daily caregiving. Accuracy and intuitiveness of the visualization was tested, as well as its usefulness in caregiving situations. Caregivers of persons with SID, the intended end-users of the app in which the visualization is shown, were included in every aspect of the research, and collaborated throughout the design process up to and including the creation of the final concept.

The process consisted of three phases, displayed in Figure 5.2. Phase one included three experimental approaches, performed in parallel, each containing at least two rounds of consultations, in order to create three different designs. The reason for this choice was to keep the involvement of individual caregivers as brief as possible and keep the design aspects to which they had to contribute as simple as possible. Design A was based on end-user preferences regarding basic form aspects, which address their associations to pain. Design B was based on workplace criteria, which address the challenge of designing for tasks in daily caregiving. Design C was based on peer-reviewed literature on qualitative data from (chronic) pain patients, which address the need for simplicity and intuitiveness. The involvement of end-users in every step of the design process has been immensely valuable and has aided into making the design process intuitive and attuned to the end-users' needs.

In phase two, an online questionnaire to evaluate the three designs created in phase one was administered among the user group. Users evaluated each of the three designs on a variety of usability aspects, such as clarity, distinguishability, intuitiveness, and pain association. The challenges of phase one were addressed once more with the addition that designs were mutually compared regarding usability. In phase three an expert focus group was presented with the results of the questionnaire from phase two and a final design was selected which encompassed all aspects from phases one and two. This elaborate design process was used on account of the lack of user research in this very specific target group and the unique needs and challenges professional caregivers for clients with SID face in daily caregiving (Van Timmeren et al, 2017a; Van Timmeren et al., 2017b).

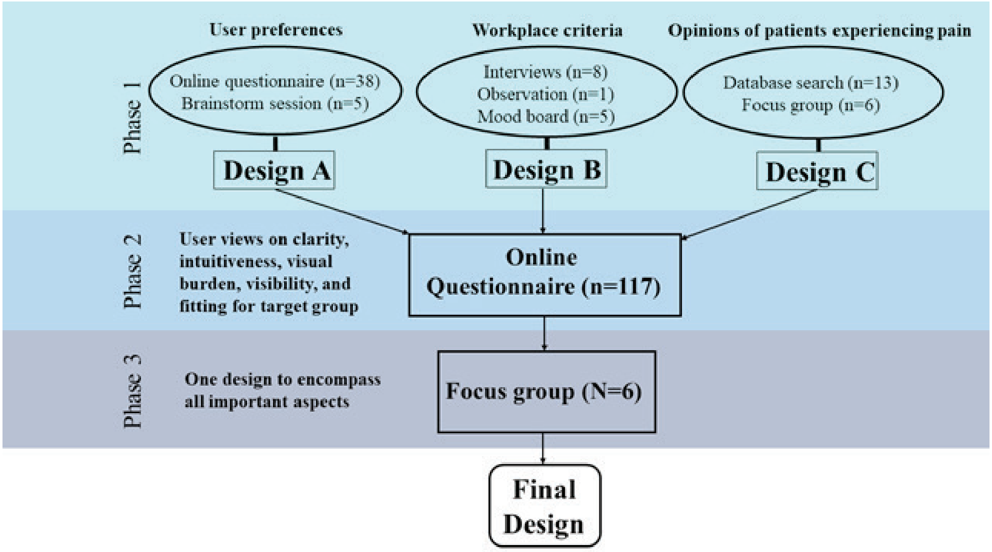


FIGURE 5.2. A visual display of the design process; showing the sub-steps leading to three initial designs and the three phases of the development to one final design.

The design study described in this article is part of a larger study to develop a system to physiologically measure pain in adults with severe or profound intellectual disability. The overall study was approved by the medical ethics board of the Vrije Universiteit Medical Centre in 2019 under no. NL69815.029.19.

5.2.1. Participants

In this study different experts were asked to contribute their opinion, expertise, and ideas on a possible pain design. Most of these experts will eventually also serve as end-users for the system which will contain the visualization. Experts that will possibly not be end-users were the design students and professor, who participated in the brainstorm session of phase 1.1.2 and the researchers with expertise in research among people with severe and profound intellectual disability (SID). Other experts ranged from parents of children and adults with SID to speech therapists and medical personal working with people with SID. Table 5.1 gives an overview of the experts and their respective fields of expertise per phase of the process.

TABLE 5.1. Description of expertise per expertise group for each part of the design process.

Phase	Subphase	Part	Expertise	#
1	1.1	1 1.1.1 (N=38)	Parent of SID	8
			Daily care for SID	30
		1.1.2 brainstorm (N=5)	Design	4 students, 1 prof
		1.1.2 value points	Research in SID	2
	1.2	Design criteria (N=9)	Daily care for SID	5
			Research in SID	3
			Medical personnel	1
		Mood board (N=4)	Daily care for SID	2
			Research in SID	2
		Evaluation	Daily care for SID	3
	1.3	Review	Research in SID	1
		Focus group (N=6)	Daily care for SID	3
			Research in SID	2
			Medical personnel	1
2		Questionnaire (N=117)	Parent of SID	15
			Daily care for SID	33
			Behavioural therapist	24
			Physical therapist	24
			Speech therapist	6
			Medical personnel	6
			Other experts in care	9
3		Focus group (N=6)	Daily care for SID	3
			Research in SID	2
			Medical personnel	1

Due to COVID-19 restrictions, most of the recruitment and execution of the study were done online. For recruitment, the project sent out newsletters to interested parties with an appeal to fill out online questionnaires. Participants for focus groups and design criteria parts were recruited through the network of first and second author;

two national organizations for the care of people with (visual and) intellectual disability collaborate as partners. The design students were recruited through the network of first and last author at Eindhoven University of Technology.

5.2.2. Phase 1.1: From user preferences to design A

Design A was based on user preferences regarding the relation of shapes, colours, figures, and graphical features to an experience of pain. These associations were selected by end-users using visuals in an online questionnaire. The results from the questionnaire were then presented to a group of Industrial Design students in a brainstorm-design-session. Designs made in the brainstorm session were then assessed on aspects from the Value Proposition Tower from Road2Results (Road2Results, 2020; Figure 5.4). Based on their value scores consensus was reached on the best-scoring designs and Design A was created.

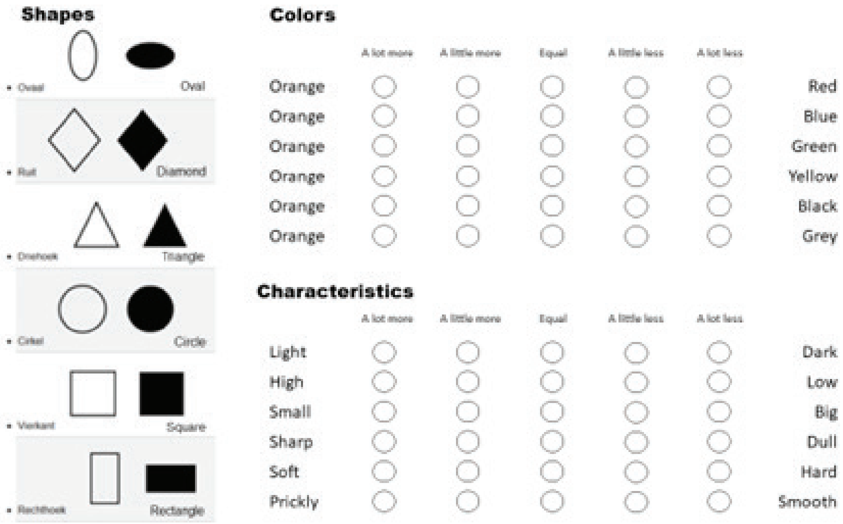
5.2.2.1. Subphase 1.1.1. Online questionnaire to assess user preferences

Phase 1.1.1. Methods

A comprehensive online questionnaire was distributed among those providing care for persons with SID in the Netherlands, using Qualtrics survey software (Version XM of Qualtrics. Copyright © 2020 Qualtrics, Provo, UT, USA). In the questionnaire, participants compared several items on their association with the experience of pain or 'no pain'. Again, this design process, which might seem superfluous, was adopted to correct the overall lack of user research in this niche target group.

The questionnaire items were divided among four categories: "shapes", "colours", "figures" and "characteristics". End-users were asked to either order different items from least to most associated with pain or to individually compare one item to another of a similar category. Figure 5.3 shows an ordering system for six different shapes and a comparison system for the colour orange and six characteristics. All categories and the items within were presented in random order.

In the categories "shapes" and "figures", participants were asked to order six shapes and seven figures from the highest association to pain at the top to the lowest association at the bottom. In the "colour" category, every colour was compared to all other colours in the questionnaire, via a semantic differential method (Osgood et al., 1957). The participant decided whether a colour was 'a lot more', 'a little more', 'equally', 'a little less' or 'a lot less' associated with pain compared to the other colour (for an example, see Figure 5.3). The category "characteristics" consisted of fifteen comparisons between pairs of polar opposites, such as 'light' and 'dark' and 'smooth' and 'prickly'. These were shown in a grid horizontally opposite each other. Participants scored these pairs on the same 5-point scale as colours (Figure 5.3). For each item, a z-score was then calculated, using Microsoft Excel, based on averages and standard deviations of all items in that category. High positive z-scores signify a higher association to pain by participants compared to items with lower positive or negative z-scores. Negative z-scores signify an association with ‘no pain’.



Colors

	A lot more	A little more	Equal	A little less	A lot less	
Orange	○	○	○	○	○	Red
Orange	○	○	○	○	○	Blue
Orange	○	○	○	○	○	Green
Orange	○	○	○	○	○	Yellow
Orange	○	○	○	○	○	Black
Orange	○	○	○	○	○	Grey

Characteristics

	A lot more	A little more	Equal	A little less	A lot less	
Light	○	○	○	○	○	Dark
High	○	○	○	○	○	Low
Small	○	○	○	○	○	Big
Sharp	○	○	○	○	○	Dull
Soft	○	○	○	○	○	Hard
Prickly	○	○	○	○	○	Smooth

FIGURE 5.3. An example of two different assessment methods presented in the online questionnaire of basic aspects. The six provided shapes on the left were ordered from highest association with pain (top) to lowest (bottom) and the colours and characteristics were compared to counterparts on a five-point scale.

Phase 1.1.1. Results

For each category in the questionnaire, both the highest scoring two items and the lowest scoring two items are presented in Table 5.2. Results from z-score calculations indicate that the triangle shape was most associated with pain, while rounded shapes were not. This result is mirrored in the characteristics category. Red was most associated with pain and green with ‘no pain’. From the list of seven possible figures, the ‘sad face’ was chosen as most associated with pain. Participants that gave their own suggestions of shapes associated with pain mentioned the spiked shape/star (7 participants, 23%) and the lightning bolt (6 participants, 20%).

TABLE 5.2. Items in the questionnaire that had the highest and lowest associations with pain from z-score calculations for 30 participants.

Shapes				Colours			
High		Low		High		Low	
Triangle	2.49	Circle	0.62	Red	1.42	Green	-0.91
Diamond	2.37	Oval	0.62	Orange	0.44	Blue	-0.58

Figures				Characteristics			
High		Low		High		Low	
Sad face	2.44	Heart	0.32	Prickly	1.14	Smooth	-1.14
Cross	2.19	Flower	0.48	Rough/Hard	1.09	Fluffy/Soft	-1.09

Note. The categories shapes and figures were only given positive scores, so the score zero represents more association with 'no pain', while the categories colours and characteristics were given positive or negative scores, so negative higher scores represent more association with 'no pain'.

5.2.2.2. Subphase 1.1.2. Brainstorm session and value calculation based on questionnaire results

Subphase 1.1.2. Methods
To interpret and expand on results from the online questionnaire, a creative brainstorm session was held with students and a professor from a bachelor's program in Industrial Design. During the 60-minute session the 'designing for extreme scenarios' and 'designing for extreme characters' (Djajaniningrat, et al., 2000) methods were followed, led by an experienced session leader. These 'extreme' forms use fictional situations and end-users in an excessive manner to let designers consider, among other things, the social role of their designs and how end-users will physically interact with the eventual product.

The design experts were asked to assess the results from the questionnaire in terms of their design ideas, keeping in mind three design requirements:

(1) The visualization should clearly distinguish between a 'pain' and a 'no pain' level;
(2) The design should be visually clear for those with vision impairments and mono-chromatic vision; and
(3) The design should demonstrate when data is being received (e.g., by moving).

Participants in the brainstorm were first asked to freely associate pain-related concepts. They were then asked to design a visualization for a man of around 80 years old, as an example of an extreme character. Next, they were asked to design regarding possibilities that may be possible ten years in the future, as an extreme scenario. Finally, participants presented their designs and were asked to build upon each other's ideas (Design Kit, Ideo.org, 2020). A discussion was initiated about the usefulness of all design ideas generated in the brainstorm in practice now and in the future. First author attended the brainstorm, and collected and categorized all ideas.

First and second author evaluated the design ideas from the brainstorm one by one using a value proposition tower from Road2Results (Road2Results, 2020). This evaluation process, shown in Figure 5.4, aided in developing a viable value proposition in a structured way. Each design idea presented in the brainstorm session was initially evaluated on four basic criteria: Product & Service, Costs, User Needs, and Gains. Product and Service entailed what can realistically be offered by a designer in terms of services. It established the function and constraints of the product. The User Needs were constraints of the design possibilities based on needs of the end-users, for example constraints of a caregiver's working environment (noisiness) or their attention span. Costs were aspects that make an idea less viable to be used or appreciated by end-users, and Gains were idea-aspects that increased its value as a concept. Costs and Gains were assessed based on the outcome of Product & Service and User Needs in an iterative process.

An example of a design's cost is a general negative association with the visual, something that may be perceived as insensitive due to personal beliefs, or something that is open to interpretation. Examples of gains are multiple modality changes for better visibility, clear difference between the negative and the positive poles and recognizability. Of course, a design can both have costs and gains, meaning it can be recognizable as well as culturally insensitive. The final value of each design idea (Value at the top of Figure 5.4) was based on the combined result of the four criteria mentioned before (Value idea at step 2 in Figure 5.4), augmented by how feasible the idea was to become a product (Feasibility).

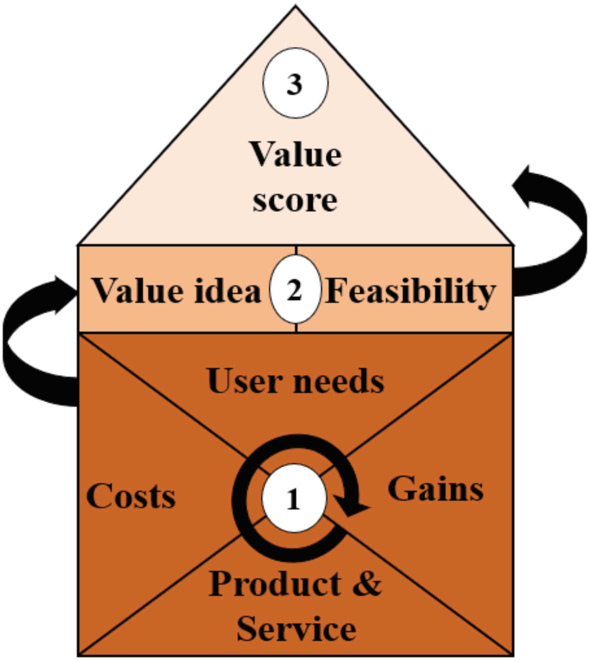


FIGURE 5.4. This Value Proposition Tower shows a process by which each idea is assessed on two levels, starting at the bottom (1) with an iterative route through design possibilities (Products & Service, Costs, User Needs and Gains), which are combined in each idea's initial 'value' (2), which, combined with its feasibility, results in an eventual value score (3).

Subphase 1.1.2. Results

Each participant in the brainstorm session created three to five designs, some of which were interchangeable or unfeasible, which resulted in thirteen ideas, presented in Table 5.3 as simplified descriptions. Scores in the table are based on the value proposition assessment described above. Each cost received a score of -1, when present, or 0, when absent and each gain received either a 1 or 0. An idea's Value score is the total score, evaluated on five possible costs, from -5 to 0, and seven possible gains, 0 to 7.

TABLE 5.3 List of ideas generated in the brainstorm and their results from the value proposition.

Idea	Content	Costs*	Gains≠	Value score (sum)
#1	Happy face -> sad face	0	6	6
#2	Whole body in pain	-2	6	4
#3	Graphical display	-2	4	2
#4	Small dot -> large circle	-1	3	2
#5	Religious characters	-4	2	-2
#6	Military aspects	-4	2	-2
#7	Shapeless blob -> spikes	-1	3	2
#8	Good -> bad weather	0	6	6
#9	Smooth oval -> spiky diamond	0	3	3
#10	Moving line	-2	4	2
#11	Spiral -> spikey graph	-1	3	2
#12	Bubble -> lightning sparks	0	3	3
#13	Low -> high saturation	-3	0	-3

* Such as negative associations, culturally impractical, similar, open to interpretation, etcetera.

≠ Such as clear, intuitive, easy to recognize, distinguishable, usable in colour blindness, etcetera.

With the result from the value proposition, two ideas came out as best scoring: 'the happy and sad face' (#1) and 'good to bad weather' (#8). Authors decided to combine the two ideas in one design, with a shape that transforms from a round sun to a storm cloud and a colour change based on weather conditions: Yellow for good weather/sunshine and grey for bad weather/storm and lightning. The face alters from smiling to sad, as shown in Figure 5.5.

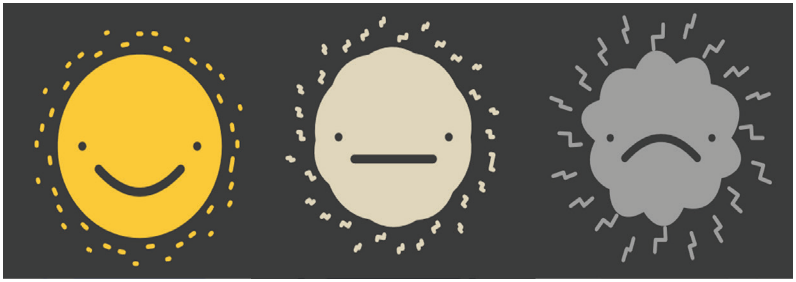


FIGURE 5.5. Design A: the result of subphase 1.1. A yellow and smiling sun represents 'no pain' and a sad storm cloud represents 'pain. The visual in the middle shows in what way the visualization transfigures from a sun to a storm cloud.

5.2.2.3. Phase 1.2. From workplace criteria provided by caregivers to design B

Phase 1.2. Methods

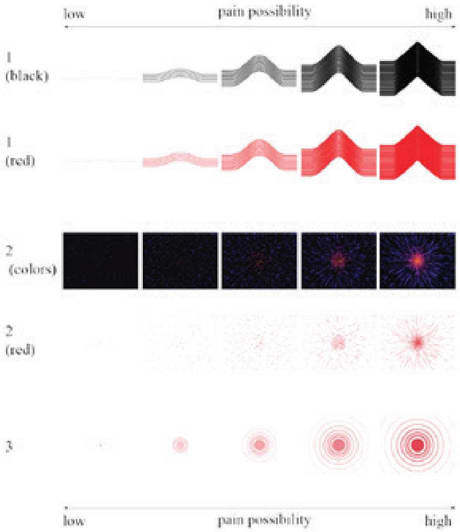


FIGURE 5.6. The mood board created for evaluation in the process to create design B displays three basic design ideas, which were assessed by caregivers, therapists and researchers (Zhang et al., 2021).

Design B was created in collaboration with caregivers in their daily workplace environment. Caregivers from different care organizations were either interviewed or observed at work by a research assistant to assess work-related needs for the visualization. Afterwards, an expert group meeting was organized to translate these needs into design criteria. Based on these first steps, a mood board with nine pain-related basic design images was created to study experts' mental models on perceiving pain from visual elements. The mood board was presented to caregivers, therapists and pain researchers, who were asked to rate the design images on two axes: 'comfortable-painful' and 'attention drawing-easy to ignore'. In addition, experts assessed three basic designs, shown in Figure 5.6 (lines in red or black, spreading dots in red or various colours and growing circles in red), on provisions necessary to integrate the system into caregivers' workplace. Design B was created based on aal the preceding steps. To assess its usefulness, the design was then evaluated in two interviews and assessed through a workplace walkthrough. The design sub-process is displayed in Figure 5.7.

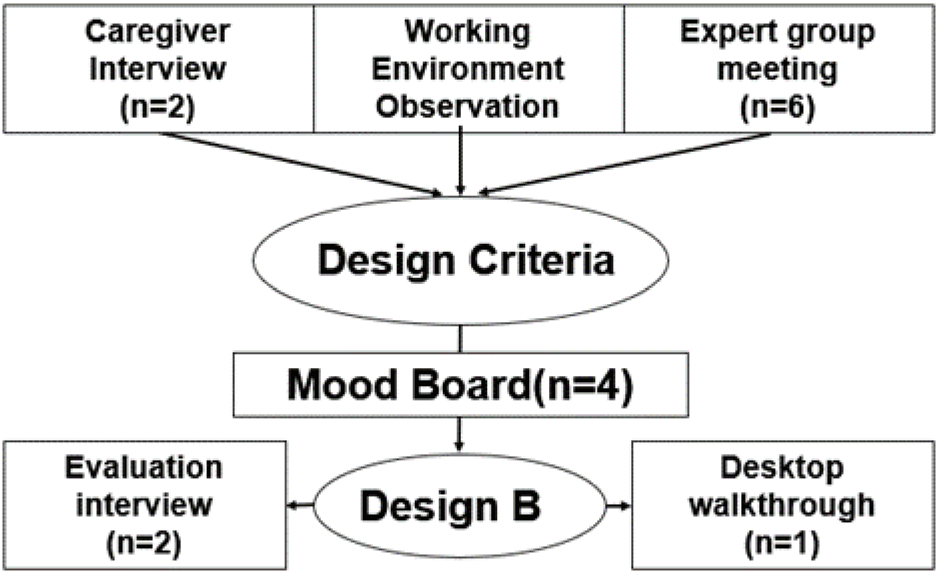


FIGURE 5.7. The process for design B includes two caregiver interviews, an observation in the workplace and an expert group meeting, followed by a mood board with basic design criteria. The final sub-design is evaluated in two interviews and a workplace walkthrough (Zhang et al., 2021).

Phase 1.2. Results

Experts who evaluated basic designs had similar opinions on the association with pain. They believed the first concept (number 1 in Figure 5.6) was 'hardly' associated with pain. Half the experts could not decide when to take action. The second concept (number 2 in Figure 5.6) was most associated with pain, though difficult to understand and found to have the highest mental burden. Experts found the third concept (number 3 in Figure 5.6) simple and easy to understand. It reminded them of alertness, not pain. This design would succeed to attract caregivers' attention most. Half the experts had concerns with the use of the colour red, and one believed it would help understanding. The multi-colour scheme of the second concept received the most positive feedback. This second concept in the multi-colour scheme was then chosen as design B, in a simplified and improved iteration, resulting in Figure 5.8.

The evaluation of this design by two caregivers showed that the design had an association with pain but would not create (extra) stress in a caregiver. After a short explanation, caregivers found the design easy to use. Awareness of the design was mixed, with one caregiver being very sensitive to changes in the display, while the other was less sensitive. Both evaluated the design in its 'no pain' state as not distracting them from computer-related tasks.

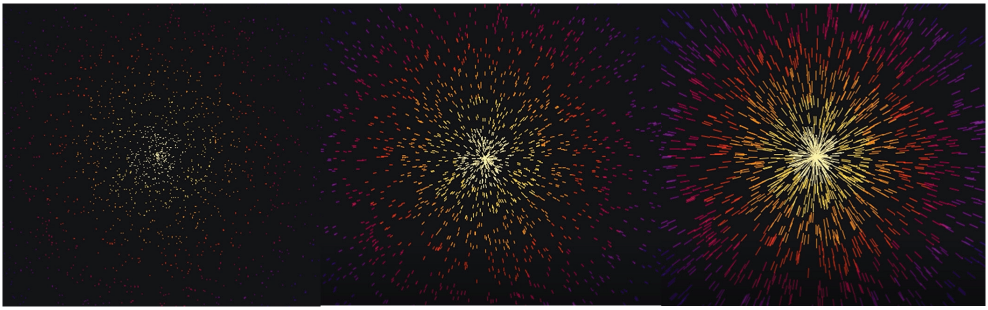


FIGURE 5.8. Design B is the result from subphase 1.2. From a focal point in the middle of the design, multi-coloured dots spread out into lines when the pain-level rises.

5.2.2.4. Phase 1.3. From opinions of patients experiencing pain to design C

Phase 1.3 Methods

The third design was created based on results of peer-reviewed literature following a search on colours and visuals associated with pain in different databases (i.e., Worldcat.org, PsycINFO, Wiley Online Library, ScienceDirect, & ABI/INFORM). Search terms were "pain or nociception or burden or distress" and "colour or colour or visual or vision" in title and keywords. The words "shape" and "figure" were omitted on purpose, for these are commonly used as verbs in titles. The results of the search were ordered and checked on eligibility for the study. Original articles and reviews were included if they: (1) Focused on pain experiences of pain patients, (2) Discussed visual associations of pain, and (3) Results were systematically analysed.

Articles were ordered according to the type of visualization and then on methodology and participant size. Results were categorized in a table presenting the amount of consensus of participants, free associations (if asked), and limitations and implications of the results mentioned by authors. With the result of the literature search, first author chose basic design aspects that were most commonly found in literature and had few limitations, with the aim of creating a third design to be assessed in phase two.

The design based on literature was presented to a focus group of experts in the care for persons with intellectual disabilities. This expert group consisted of six persons: one general practitioner specialized in the care for persons with an intellectual disability, a professional caregiver, a scientist practitioner, a behavioural therapist and coordinator of a national platform for research on persons with severe intellectual disability, a researcher on arousal in persons with an intellectual disability and a behavioural therapist and professor on research in persons with visual or visual and intellectual disabilities.

The group members were asked to relay their personal experience in their working environment and discuss possible implications of using the design as a visual display of pain in daily practice.

Phase 1.3 Results

The literature search generated 2,133 results, of which titles and abstracts were reviewed based on inclusion criteria, resulting in 11 useful articles. Reference lists of relevant articles were scanned, after which a discussion with a design expert took place, leading to the inclusion of two additional articles. Of these 13 articles, ten (77%) evaluated pain associations based on colour, or colour and another aspect. The other three evaluated free pain associations: participants were asked to mention any aspect they could conceive.

Red was most often associated with pain (e.g., Altan et al., 2019), while Wylde et al., 2013, found black/grey associated with persistent pain and red with intense pain. Colours associated with no pain varied from light pink (Grossi et al., 1983) to yellow (Machata et al., 2009) and cool colours such as green (Palmer & Schloss, 2010), although these were also associated with illness (Elliot, 2015). Light and saturated colours were more positive than dark and muted colours (Palmer & Schloss, 2010). Other aspects used to indicate pain were wideness (wider equals more pain; McGrath et al., 1996), size (bigger equals more pain; Jackson et al., 2007) and sharpness (sharper equals more pain; Lootens, & Rapoff, 2011). No pain was represented by a happy or neutral face and pain by a sad or crying face (Machata et al., 2009; McGrath et al., 1996). In the study by Lalloo, et al (2014) forms of pain were associated with sharp edged items, such as needles. The study by Lor et al (2019) resulted in objects and animals as metaphors associated with pain.

First author chose to use red for pain and green for no pain, partly to create a stop-and-go association in caregiving: A caregiver's action can continue as is at green, while red means the caregiver should stop and assess the client's wellbeing. Since sharpness was also intuitive for pain, this character was added. The design based on these results is displayed in Figure 5.9. An expert group evaluated this design as intuitive and understandable. The experts were content with its limited complexity, one visual for pain and one visual for no pain, which would make responses from caregivers upon seeing the visualization most reliable.

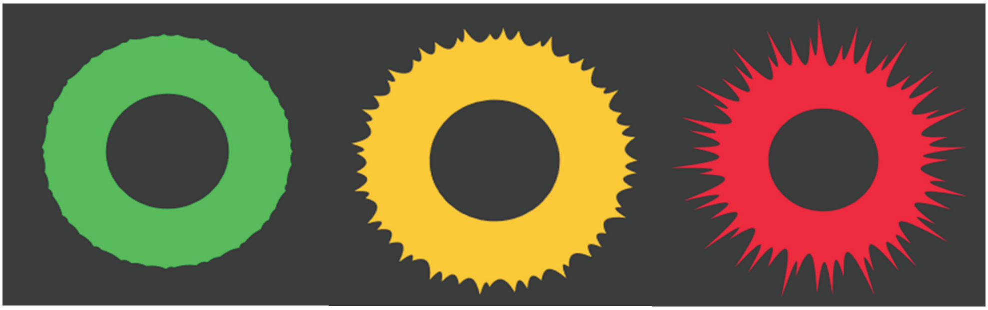


FIGURE 5.9. Design C is the result from subphase 1.3. The visualization shows a green circle with a rounded edge, slowly waving, which represents ‘no pain’, whereas a red circle with sharp spikes represents pain. The colours are adapted to those of a traffic light.

5.2.3. Phase Two: Comparison of the three designs on several important aspects

Phase 2 Methods

In phase two, the three designs (A, B and C) were compared by a group of end-users. The visuals were played as moving gif-images varying from ‘no pain’ to pain, by changing shape, colour and/or property. The designs were distributed in a network of parents and professional caregivers of persons with SID through an online questionnaire. To avoid order effects in the results, the designs were presented in a random order to each participant. Participants were asked to assess each design on several criteria on a scale from 0 to 10. Examples of those criteria are: “this is an accurate representation of pain”, “it is clear what this means”, “this is suitable for the user group” and “it is difficult to understand”. Participants were also asked to evaluate whether each design was suitable for people with many distractions, vision impairments, and mono-chromatic vision. All questions are shown in Supplementary Table 1.

As each new design was presented, participants were first asked to freely associate their thoughts on the aspects of the design. If participants responded that they did not think the design visualized pain well, they were asked to elaborate. Results of these open-ended questions were grouped into a word cloud. For the multiple-choice questions either percentages per answer (nominal or ordinal) or averages (interval or scale) were calculated, using Microsoft Excel.

The online questionnaire was completed by 117 participants, with an average age of 45.1 years (SD 11.8, range 21 – 67) and 95% women. In the Netherlands, 85% of professional caregivers of persons with SID and approximately 95% of primary caregivers at home are women (CBS, 2019). Professional caregivers had on average 16.2 years of experience (SD 10.3 years, range 0.5 – 40 years) in the care for persons with severe or profound intellectual disability.

Phase 2 Results

TABLE 5.4. Numerical results from the online questionnaire in phase two of the design process.

	Clarity				**Understanding**				
Design	Good	Difficult	Intuitive	Fitting	Pain	No pain	Action	Stress	Change
A (n=111)	57%	3.43	5.58	6.05	6.79	5.47	5.71	3.28	74%
B (n=116	19%	5.93	2.21	2.31	2.67	2.63	2.61	2.61	95%
C (n=112)	71%	3.76	5.29	5.67	6.72	6.17	5.73	5.73	61%

As indicated in Table 5.4, 71% of respondents found design C a good way to display pain, making this design the best received. Together with Design A, respondents thought this design was intuitively clear, fitting for the target group, not difficult to understand and would prompt them into action more than design B. Design C also was found to best contrast between pain and no pain. Respondents thought design B was unintuitive and difficult to understand, but it created the least (visual) stress. Most participants desired all three designs to be changed. For design C they wanted another shape and movement, but similar colours. Design B needed a simpler shape, more contrast and less movement. For design A respondents recommended a different shape, more movement and other colours.

Respondents were also asked for their first thought when seeing the design and why they thought this design was not a good visualization for pain. Responses to these open questions are displayed in Word clouds per design in Figures 5.10.(A), (B), and (C). Results indicate that design A reminded the respondents most of emotions but not pain. They saw happiness and distress, anger, tension, unhappiness, and sadness. The positive to negative change was clear and the design reminded them of their clients, but they mentioned that the design was not intuitive for pain and had incorrect colours. Design B was associated with fireworks, stars, a starry sky, the cosmos, space, an explosion and a light show. Respondents were unclear about what this design should visualize and had no association with pain. They found the design too positive, too easy to look at, too pretty, vague, abstract, too difficult and soft to display something like pain. The respondents thought design C was good and clear. It reminded them of calm and alarm, and they associated this design most with pain. Design C also reminded them of an eye, the sun, traffic light, and fire, though the colours were good. It displayed intensity and turbulence, and clearly visualized an increasing change.

FIGURE 5.10. The answers to the open-ended questions from the online questionnaire were translated and transformed into word clouds for each design. The letters on the bottom left of each word cloud represents the design it relates to.

5.2.4. Phase three: Discussion of phase two results with an 3expert group top create a final design that encompasses all important aspects for the user group

Phase 3 Methods

Via videoconference, results from the online questionnaire from phase two were discussed by another focus group of six experts. All members of this group were aware of the design's function and the end-user. The goal of this focus group was to decide, based on questionnaire results, which design was most adequate and whether and how this design could be adjusted.

The focus group was organized as follows: One of the three designs was shown, via screen sharing. Participants were invited to say anything that came to mind when viewing the design. Hereafter the results from the questionnaire were presented, starting with the results from multiple choice and numeric questions (e.g., 'This design is the most difficult to understand compared to the other two designs' or 'Participants think that this design shows the best display of pain'). Then common statements given in the questionnaire were shared and focus group participants were asked whether they agreed with these participants. Hereafter, the focus group was asked to discuss the design changes offered by questionnaire participants. And, due to the COVID-19 pandemic at that time, focus group participants were specifically asked whether one of the designs made them think of some of the used images of COVID-19, which was a question that was omitted in the online questionnaire since this was distributed before COVID-19 reached pandemic proportions. The three designs were shown to the focus group in a random order, to minimize the influence of the preferred order of the researcher.

At the end of the focus group discussion, the experts were asked which design they preferred as the best display of pain and whether this design needed to be adjusted, based on statements from the questionnaire or their own opinion. Focus group participants could either say they thought the design was suitable as is, or that adjustments were necessary, based on the discussion. The focus group experts were asked to vote, and choices were made based on a two-third-majority agreement. The entire focus group discussion was audio-recorded.

Phase 3 Results

Focus group participants agreed with questionnaire participants that colours used in design A were off target. Grey was more associated with sadness and yellow and grey contrasted insufficiently: The grey warning signal could attract equal attention as the yellow sun, which is undesirable. The focus group found using emoticons very intuitive and easy to understand, though the negative face was associated more with sadness than pain. A grimacing face with contracting eyes and mouth was recommended, which derived from literature on pain observations (Van der Putten & Vlaskamp, 2011) and the revised Faces Pain Scale (Hicks et al., 2001).

The focus group agreed with the questionnaire participants on design B being unintuitive and difficult to understand. They found the design beautiful, and too ‘easy’ to look at. This design would not cause stress in the end-user, but a small amount of stress was deemed necessary to prompt caregivers into quick pain relief action.

The expert group agreed with the questionnaire participants that design C intuitively visualized pain better than the other designs. The colours and shape changes created a good contrast, and the negative side would attract more attention than the positive side. Possible stress the design might cause did not worry them, though they agreed that the negative side had a resemblance to the visualization of the COVID-19 virus.

After discussing all designs, expert group participants voted on two queries; which design should be continued and should it then be changed? There was a unanimous agreement to continue with design C and another unanimous agreement to change this design to increase clarity and lessen the resemblance to a virus. An addition of a face inside the ring was furthermore unanimously agreed upon, using a smiling and grimacing face (Figure 5.11).

FIGURE 5.11. This final design transforms dynamically from a green, happy face, via an orange, neutral face, to a red, painful face. All designs presented in this paper can be viewed here.

5.3. Discussion

A co-creative design process is described for a visualization of pain of clients who cannot self-report, to be used in daily caregiving. Three designs were created, evaluated in three phases, and finally adjusted to reach a design that encompasses the wishes and demands of the end-users. The process shown is particularly suited for emotion-related design tasks with the two simultaneous difficulties that the key stakeholder is unable to provide input and that the validation during later use is expected to be tedious. The goal of the process was to make ambiguous data on pain unambiguous and easy to understand. Under such circumstances, it is essential that as much available knowledge and experience from various sources is utilized. And of course, the existing knowledge on pain, notably from literature, should be used. Several design methods and user groups were combined to generate a creative as well as a systematic multi-disciplinary design process.

The subjective experience of pain resonates with other areas of design theory and practice where both the subjective first-person perspective and the second and third-person perspectives are needed. We argue, that creating visualizations or tangible experiences with such an elusive and ill-defined experiences as pain and consciousness (Price et al. 2002) might benefit from the visualization of both as proposed by Frederiks et al. 2015 as a tool that can facilitate understanding of the interplay between the different perspectives in designs that should be used by several stakeholders. The visualization for pain in the system attempt to represent the first-person perspective of the patient and should encompass all requirements to make it useful in daily care. The three-step design process described in this article aimed to address several design challenges and resulted in a visualization encompassing all requirements from the user groups. The process also utilized a multi-disciplinary approach, giving end-users, both parents and professional caregivers, the tools to provide invaluable input at each step.

All three phases of the design process provided results on thoughts, feelings, and needs of professional caregivers and parents and the challenges they face in the daily care of a person or persons unable to communicate about their own experience of pain. With respect to associations to pain, we found that this niche group of end-users did not differ much from pain patients in their associations, though the resulting z-scores did indicate that pain associations that were possibly deemed obvious by many, such as the colour red, sharp edges and hardness, were not unanimously selected to represent pain by this group. Regarding workplace necessities, it was discovered that in an environment with many sounds, movements and distractions, a visualization should have the potential to attract the attention of the caregiver when necessary and stay neutral when no pain is experienced. Results from the literature search indicated that a warm/cool contrast regarding colours and a sharp/rounded contrast regarding shape would be quite useful to indicate the continuity from pain to no pain.

The designs created in the first phase of the process, shown in Figures 5.5, 5.8 and 5.9, were then further evaluated by more than a hundred parents and professional caregivers in an online questionnaire. Among many unique opinions on the usability of these three designs, many commonalities were also found. End-users were most positive about the usefulness of design C (Figure 5.9) as a representation of a pain experience and found design B (Figure 5.8) to generate the least amount of stress in the end-user. The face used in design A (Figure 5.5) was deemed the most intuitive, though the suggestion was made that the negative side represented sadness more than pain. With these evaluations and opinions, partially displayed in the word clouds of Figure 5.10, it was shown that in the three design processes from the first phase unique information was gathered, which was then evaluated in a ninety-minute focus group discussion that resulted in a final design (Figure 5.11), that combined an adaptation of the intuitive face of design A and the colours and shape of design C, creating something that would attract attention and motivate caregivers to react quickly and was simple to comprehend.

The design process shows how valuable the collaboration of end-users can be, especially when these end-users are a niche group on which very few studies focus. The authors have found no earlier studies that looked at pain associations within this user group. The resulting design created in this study will be integrated in a mobile application to be used by caregivers and parents of those with severe or profound intellectual and multiple disabilities. Next steps will be to create this app, test it in the target group and evaluate its usability with the end-users.

5.3.1. Limitations and strengths

While care was taken to conduct an extensive and thorough design study, there are limitations. In the first phase of this design study, small groups were assembled to collaborate with the researchers. Also, many of the participants were recruited from the networks of the authors, which may limit the variation of their opinions. However, all participants were very involved in the study and determined to co-create something useful for daily caregiving, providing quality input on all aspects. Also, thanks to the online nature of some aspects of the study, participants hailed from all corners of the country and had varied expertise (see table 5.1). As a result, the participation in the first phase led to three designs encompassing desires, demands, and needs of end-users, confirmed by a large number of participants in the second phase.

While semi-structured interviews could have provided more comprehensive information and design evaluations, we doubt whether this would have given a better representation of the end-users than the eventual participant group of phase two. The six expert focus group of phase three of the process thoroughly ran through and endorsed results from the online questionnaire and came to a unanimous agreement. Of course, further tests in daily practice should show whether this design fully subscribes to the wishes and demands of caregivers.

In this design study a variety of design aspects was used, ranging from semantic differential comparisons to a brainstorming session, using both end-users and design experts, to join co-creative development with proven design methods. The end-users formed a varied group with various levels of domain knowledge and design experience, though undoubtedly included those that had trouble with the semantic differential method or who did not fully grasp for whom they were making decisions (themselves or their clients). Furthermore, the design experts involved in the brainstorm session might not fully have been able to imagine the needs of the end-user, but the way in which several design methods were combined while involving the end-user in several different manners should minimize the effect of this limitation.

5.3.2. Practical implications

This study describes a process for designing visualizations of subjective (first-person) experiences, such as the experience of pain, which may have far-reaching consequences for design practice. The phenomenological approach in design, which takes a first-person perspective contrast with empirical science and clinical observations, often referred to as a third-person perspective (Thacker & Moseley, 2012). Here we see a new field for the design theory and practice to help to bridge the gap between the two perspectives by visualizing or materializing these perspectives and converging them in a solution that in our case can improve the understanding of the wellbeing of a client unable to communicate and ease the emotional workload of a parent or professional caregiver.

In the current study end-users were extensively involved, in many different roles, which gave them the opportunity to evaluate each design phase but also enlarged their involvement in the eventual product. In its core, the design task is the mapping from pain levels, which are emotional and subjective in nature, to visualizations which should convey the right semantics and intuitive associations. This core task is not solvable by pure logic and functional reasoning alone. This means that the sensitivity and creativity of trained designers should be used, while it is essential to give a voice to the caregivers and family, being both stakeholders and expert-proxies to the people with severe or profound intellectual and communicative disabilities.

5.5 Conclusion

The described process was designed in an eclectic manner, choosing state-of-the-art sub-methods to optimally use resources and optimize quality by working in small steps, not losing valuable options, and by careful decision making, balancing functional and emotional aspects. Lessons from the study and results from its systematic process could be extended to design for other non-verbal groups, such as neonates and comatose patients, for which similar challenges exist. One could also think of involving end-users in design for biofeedback, which is currently used in graphs and games, but could be extended to health and care.

5.6 Acknowledgements

The authors acknowledge contributions from miss M.E. Faas MSc, in programming and design (A and C), as well as miss Z. Zhang MSc, in performing part of the study and design (B).

We are thankful to all parents, professional caregivers and others who have given up some of their time to give advice, participate in interviews and focus groups and fill out online questionnaires.

Chapter 6

Development of a pain signalling system using machine learning[1]

---

[1] Published as: Korving, H., Li, S., Zhou, D., Sterkenburg, P., Markopoulos, P., & Barakova, E. (2023). Development of a pain signaling system using machine learning, *2023 IEEE International Conference on Acoustics, Speech, and Signal Processing Workshops (ICASSPW)*, Rhodes Island, Greece, 1-5, Doi: 10.1109/ICASSPW59220.2023.10193643.

Abstract

A wearable pain signalling system is introduced, to be used in the daily care for people with severe and profound intellectual disabilities. Due to several medical disorders, this group of people can experience daily acute pain and chronic pain, which they have trouble expressing and communicating to caregivers. The system consists of a smart sock with fabric sensors, a sensor unit sending a 6A current through the smart sock receiving electrodermal response and a mobile application containing a machine learning algorithm translating the signal. The pain signalling algorithm uses data of one to five painful stimuli from 28 healthy participants. Random forest modelling was used to classify moments of pain and train a model to predict pain from new data. The algorithm's accuracy could be improved by an ensemble of five models and voting, so this groundbreaking system can become a much-wanted attribution to daily caregiving of people with disabilities.

6.1. Introduction

In the realm of healthcare, the use of wearables has become more and more common. As early as 1956, wearable biosensors could provide information on a patient's health status and risks of certain diseases (Kim et al., 2019). Development and enhancement have navigated the wearables from one-time in-lab assessment devices to on-the-body sensors that can continually measure the health status of the wearer.

Outside of clinical settings, wearables can also be useful for a myriad of other purposes, including assisting athletes in improving their performance (e.g., Sensoria Fitness), assisting parents in monitoring their infant during sleep (e.g., Owlet Care), and providing daily caregivers of non-verbal people a caregiving aid to attune to clients' needs (Frederiks et al., 2019). The use of wearables as a communication tool with non-verbal clients is interesting, since there is often a learning curve for new caregivers and trainees to sensitively respond to the signals clients give out. A wearable that picks up physiological signs of stress can prevent escalations.

A potential target group for a wearable continuously measuring physiological signals are people with severe or profound intellectual disability (SID). A combination of severe to profound intellectual, motor and/or sensory disabilities and accompanying medical problems make this group very dependent on the people around them (Doodeman, Schuengel & Sterkenburg, 2021; Nakken & Vlaskamp, 2007). They need caregivers to provide their basic hygienic and nutritional needs, as well as stress regulation and coping with life's challenges (Janssen, Schuengel & Stolk, 2002; Poppen, van der Putten & Vlaskamp, 2010). Additionally, adults with SID run a higher risk of experiencing pain in daily life, due to various factors, including but not limited to existing medical disorders, an increased risk of accidental injury (IASP, 2021; Van der Putten & Vlaskamp, 2011), physical deformities causing infections (Rodriguez, 2014) and a lower-than-average immune response to pathogens combined with a higher infection risk that comes with living together in close quarters (Dworkin et al., 2006; Van Schrojestein Lantman-de Valk & Noonan Walsh, 2012).

Considering that causes of pain and the pain itself cannot be treated if these are unknown, pain recognition is a crucial part of daily care for people with SID. Caregivers and parents often describe an intuitive feeling of ‘wrong’ long before a cause is discovered. This increases the risk of exacerbating medical disorders and long hospital visits or stays (Schieve et al., 2012; Walsh et al., 2001).

To provide daily caregivers with an additional way to assess their clients’ health and pain status, a wireless pain signalling system is developed, consisting of a wearable sensor in a sock, a Bluetooth® transmitter and a mobile application. This article describes the system in detail, the experiments and machine learning modelling to create a pain classification algorithm and quantitative user experiences of the eventual user group, professional caregivers.

6.1.1. Relation to prior work

The use of in vivo sensors to measure pain is not a new development. Especially concerning people unable to communicate about pain, like newborn infants and comatose patients, physiological pain measurements in hospital settings have been researched and tested extensively (e.g., Hatfield & Ely, 2015; Roulin & Ramelet, 2012). Many measurement methods have been used, some more invasive than others, and not all have been deemed effective to detect pain (Korving et al., 2020). The invasiveness of several of the methods, such as brin scanning techniques, measures of muscle tension and electrocardiograms make them unfeasible to be used in daily caregiving for people with SID (Bentley et al., 2016; Waxman et al., 2016). The current study expands on existing research by testing a non-invasive pain assessment method (electrodermal activity in socks) to be used on a daily setting of caregiving.

Since the development of the smart sock in 2014, this item has been used to measure arousal in children and adults with intellectual disability. Originally, the socks were paired with a mobile app or smart watch depicting a butterfly opening and closing its wings (Frederiks et al., 2015). After consulting parents and professional caregivers, this was adjusted to a flower growing and shrinking to show higher and lower arousal, with the addition of showing extra petals to show peaks in arousal, i.e., acute reactions to stimuli (Sterkenburg et al., 2017). It had been the parents who consulted on these studies that suggested a new study to use the smart sock and a mobile app to measure pain, since this is one of the biggest challenges in daily caregiving of children and adults with SID.

The use of AI-enabled algorithms in application of wearables for emotion detection is not new. On the contrary, it is a popular method for the automatic recognition of pain, arousal, and stress in healthy adults (Martinez Mozos et al., 2017; Sánchez-Reolid et al., 2020; Werner et al., 2020). And while many machine learning methods have been tested, the Random Forest Prediction method has been deemed the most accurate to handle medical data (Kaur et al., 2019). The study by Kaur and colleagues found their Random Forest Prediction technique more accurate, sensitive and specific than other existing techniques.

6.2. Pain system development

The development of the SID Pain App System started with the development of the smart sock (Bremmer, Croes & Sterkenburg, 2014; Figure 6.1). This regular cotton sock is complemented with two fabric sensors on the inside sole, one by the toes and one by the heel. The fabric sensors contain silver thread, making them antibacterial, antiviral, and highly conductive. On the outside of the sock, silver-coated thread leads from either sensor to one of two metal push buttons at the sock's ankle. To these metal buttons, a Shimmer™ sensor unit is attached (Frederiks et al., 2015).

The smart sock is developed with comfort and ease-of-use in mind. Considering a subject group that has a severe or profound intellectual disability, many aspects of life are not or not completely understood. This can lead to heightened arousal, for clients cannot ascertain another's goal in behaviour, and have trouble figuring out what is going on around them (Frederiks et al., 2019). Therefore, wearable sensors that use a robust measurement such as galvanic skin response, are used in a garment that is part of clients' general outfit (Bremmer, Croes & Sterkenburg, 2014).

FIGURE 6.1. The smart sock and inlay of a fabric sensor.

The Shimmer™ sensor is a GSR+ unit of the third iteration (Shimmer Sensing, Dublin, Ireland; Figure 6.2 left side). With two plastic-coated wires it is attached to the metal buttons on the smart sock. A six Ampere current is sent through the wires to travel along the outside of the sock to the fabric sensors on the inside sole. It then travels over the skin to the other fabric sensor and back to the Shimmer™ unit. The amount of moisture, or sweat, on the skin determines the speed of the current (Korving et al., 2022b).

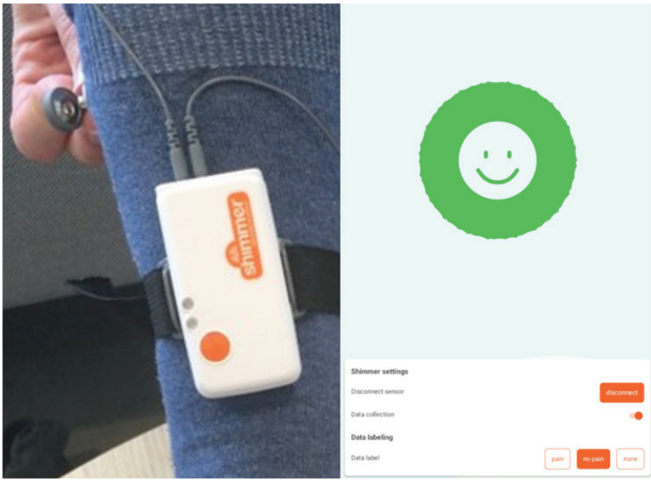
The Shimmer™ sends and receives sample currents up to 50 times a second (1–5 Hertz), measuring raw skin resistance in Kilo Ohms (kΩ) which is then converted to skin conductance in micro-Siemens (μS) by taking the inverse (1000/1 kΩ = 1 μS). The range of skin conductance measurement is between 0.2 and 125 μS. Via Bluetooth® the Shimmer™ sends the speed of every received current to a mobile application (Shimmer Sensing, Dublin, Ireland). first paragraph in each section should not be indented, but all following paragraphs within the section should be indented as these paragraphs demonstrate.

A mobile application was developed in 2021 to work in conjunction with the Pain System: the SID Pain App (Korving et al., 2022b; Figure 6.2 right side). This application receives the Bluetooth® signal of the Shimmer™ and runs it through a machine learning module to assess the wearer's pain state. This pain state is depicted visually, via two emoticons, depicting a happy, green face or a grimacing, red face. This visualisation was codesigned with a large and varied group of caregivers for people with SID (Korving et al., 2022a).

6.3. algorithm development

6.3.1. Pain experiment

A pain experiment was conducted on 30 physically and psychologically healthy adults between nineteen and 52 years old (M=32.17 SD=7.30), according to a standard procedure and COVID-protocol. Participants were invited to visit a lab room where 1.5 m distance could be maintained throughout the experiment to uphold social distancing rules relating to the COVID-19 pandemic. Participants were instructed to put on one smart sock and attach the Shimmer™ transmitter around their ankle. A stool was provided on which to rest their foot. The experiment started with a 6 min 45 sec relaxing video, to establish baseline electrodermal activity.



Shimmer settings

Disconnect sensor — disconnect

Data collection — ●

Data labeling

Data label — pain [✓ no pain] none

FIGURE 6.2. The Shimmer™ unit attached to a smart sock on the left and the SID Pain App on the right.

As the experiment started, participants were asked to submerge a hand up to the wrist in a tub of ice-cold water (M=6.15° Celsius SD=0.90° Celsius) and note their pain level out loud on a Self-Assessment Manikin Scale of one to seven. Participants were specifically instructed that level 7 did not equal the worst pain imaginable, but their pain tolerance threshold: The moment the feeling became so uncomfortable they would wish it to stop immediately. Due to a very slight risk of lasting pain or impairment to the hand because of a submersion in ice-water, the participants were asked to submerge their nondominant hand.

Participants alternated the submersion of their hand in an ice-cold water, as pain stimulus, and water of a moderate temperature, as a neutral yet similar stimulus, though they were unaware how cold or moderate the water temperature would be. Each submersion would last for a maximum of 4 min, since from 5 min onwards chances of damage, such as freezer burns, could emerge.

6.3.2. Model testing

An average of 1.378 seconds (SD = 367.4 s) of data was collected from each participant, for a total of approximately 68,900 points of raw skin resistance data. These data points were coded according to each participant's self-report (B1=pain, B2=no pain). Out of the 30 recruited participants, two showing errors in data were discarded. From the remaining 28 participants, three participants (P07, P15, and P21) were randomly selected as the testing set, while the remaining 25 were used for training.

For each participant, only the data with codes B1 (pain) and B2 (no pain) were extracted for use. Furthermore, to reduce the individual differences, these data were subtracted from each participant's average baseline (during nature video) before they were used for training and testing. As time series data, every 250 data points (nearly 5 seconds) with the same codes B1 or B2 were extracted as a sample. In this way, a total of 5332 samples labelled B1 and 31,238 samples labelled B2 were obtained, respectively, for the training set, while a total of 920 samples labelled B1 and 4,350 samples labelled B2 were obtained for the testing set. About 11-time domain features and 11 frequency domain features were used.

6.4. Pain system user experience

A group of eventual users, professional caregivers of adults with severe or profound intellectual disability, have used the Pain App System on themselves or a colleague and have filled out a survey. The User Experience Questionnaire (UEQ) was used (Laugwitz, Held & Schrepp, 2007). This questionnaire measures attractiveness, perspicuity, efficiency, dependability, stimulation and novelty of an experience of using a device or website. Available in 36 languages, the questionnaire consists of 26 items of opposing qualities, such as pleasant and unpleasant, with a seven-point Likert scale in between.

During two separate workshops, twenty professional caregivers were provided one or more Pain App Systems. They were invited to see what they could do with the smart sock, find out how far the Bluetooth® connection spanned and what information the SID Pain App could provide, and to discuss all these aspects among each other. Afterwards, they each filled out a UEQ individually.

The UEQ is provided with an analysis tool in Microsoft Excel. This provides numeric results and graphs, confidence intervals, answer distributions, benchmark and scale consistency and inconsistencies. Based on this tool, one questionnaire that showed critical inconsistency among answers (participant 10) was removed from the file and results are based on nineteen filled-out questionnaires.

6.5. Results

6.5.1. Model Testing

6.5.1.1. Data interpolation

This study used SMOTE and ClusterCentroids to create new data points between existing data points. This method involves calculating the slope between two adjacent data points and using that slope to estimate the value of a new data point at a specified location between those two points.

6.5.1.2. Training and testing data

The testing set was used to evaluate the performance of the classifier. In each experiment, K% data (K = 0, 10, 20, 30, 40, 50, 60, 70) were randomly selected from the testing set and added to the training set after interpolation. The same percentage of similar data as those K% were added to the training set.

6.5.1.3. Model settings

The Random Forest (RF) used in this study was optimized by applying a grid search strategy to identify optimal hyperparameters. The five-folded cross-validation was applied to determine the optimal tree number by grid searching in the range of {50, 100, 150, 200, 250, 300}. The optimized random forest classifier was found with 200 trees, Gini-Index, log2 for the number of features considered for splitting a given node.

6.5.1.4. Experimental results

In our previous work (Korving et al., 2022b), the RF-based classification model was trained from 25 randomly chosen participants and validated with the other three datasets. The resulting pain classification accuracy can range from 80–93%. We tried the LSTM-based neural network model. However, it achieved no improvements over the RF-based model.

We also discovered that data interpolation is effective. We applied SMOTE and ClusterCentroids-based data interpolation to solve the training data imbalance problem. As a result, the classification accuracy improved in F1 scores over the models trained from the original data. The higher the percentage of interpolated data, the better the classifier performed (detailed experimental results can be found in (Korving et al., 2022b).

In industrial applications, model ensemble strategies using voting on the results of more than three diverse models can improve classification performance, usually by 2-3% on average empirically. The diversity can be from either diverse data partitions or different model categories, such as LSTM and RF.

In the future, we will consider introducing more recent self-supervised learning models pretrained with large amounts of data. Recent ChatGPT plugins for time-series data processing can also assist our prediction.

6.5.2. Pain system user experience

The UEQ analysis tool provides calculations of reliability via Cronbach's alpha. The subscales attractiveness (α=0.91), efficiency (α=0.80), dependability (α=0.82) and novelty (α=0.86) all showed good reliability, while perspicuity (α=0.62) and stimulation (α=0.33) showed insufficient internal consistency. Considering the sample size of nineteen questionnaires is less than what is considered a sufficient sample (fifty or more; Cronbach, 1951) this may just be a result from sampling error (Schmitt, 1996).

Based on the experience of nineteen professional caregivers, the Pain App System was positively reviewed on all six aspects of the UEQ. With score range between -3 (the most negative value) and 3 (the most positive), the Pain app System was viewed as attractive (M=1.563 SD=0.76), perspicuous (M=1.063 SD=0.98), efficient (M=1.438 SD=1.05), dependable (M=1.188 SD=1.08), stimulating (M=1.406 SD=0.61) and novel (M=1.625 SD=1.95). Only on the aspect of perspicuity did the Pain App System score below average, with 25% of earlier results scoring lower and 50% scoring better. The system scored above average on attractiveness, efficiency, and dependability, good (10% scoring better and 75% worse) on stimulation and on the aspect of novelty it scored excellent (in the range of 10% of the best results).

Regarding answer distributions, two items in the questionnaire, both from the subscale perspicuity, showed the most variation in answers, with scores both on the lower end of the scale (-3/-2) and on the highest end (3). These items were 'complicated/easy' and 'difficult to learn/easy to understand'. The item 'dull/creative' (novelty) received the most negative answers, with over 35% of participants considering the system to at least be somewhat dull. On the other hand, the item 'bad/good' (attractiveness) received the most positive answers, with no scores on the neutral or negative side of the scale.

6.6. Discussion & Conclusion

This article introduces a system for pain detection in people with severe or profound intellectual disability (SID). The current algorithm created from Random Forest Modelling does not have the desired precision and accuracy, but a new idea is proposed to help us create a better predictive algorithm. As stated, future work will utilize voting of more than three diverse models to improve the classification of pain from new data.

Regarding the user experience of the future user group, the system's complexity was not regarded well. Results showed that a large part of the participants considered the system difficult to learn and complicated. Since the system consists of three separate parts and the user groups is very diverse in cognition and acceptance of technology, this result was not surprising. It is important that caregivers have no grievances about using the system. By providing a clear, visual and detailed user manual, hopefully the system's usefulness will outweigh its supposed complexity.

The goal of this study is the creation of a pain signalling system, able to detect a painful experience from a new client. Pain recognition in people with SID is an important but challenging part of each day. Because of their limited communicative skills, this group of people needs their environment for all manners of emotion regulation and stress relief. The proposed system will be a welcome aid.

6.7. Acknowledgements

Funding for this project was granted by the Netherlands Organisation for Health Research and Development, ZonMw, Den Haag, The Netherlands, under grant number 8084 5009 8345. This project and all its components were approved by the medical-ethical committee of the Vrije Universiteit Medical Centre (METc VUmc) in April 2020; NL69815.029.19.

Chapter 7

Testing a Pain Signalling App in Adults with Severe or Profound Intellectual Disability in a Residential Setting[1]

---

[1] Based on: Korving, H., Barakova, E. I., Markopoulos, P. & Sterkenburg, P. S. (2024) Testing a pain signaling app in adults with severe or profound intellectual disability in a residential setting, *Journal of Applied Research in Intellectual Disabilities*, in revision

Abstract

A challenge in caring for people unable to communicate is pain detection. Our golden standard is the self-report, which leaves those unable with lesser used and understood ways of pain detection. We have developed a pain signalling application (Pain App) designed specifically for adults with a severe or profound intellectual disability (SID). This article describes the testing of this application on adults with SID during scheduled physical therapy. Participants (N=14, 50% female) experienced pain moments, which were coded with two systematic pain observation lists for adults with intellectual disabilities. On average, pain was physiologically detected six to eight seconds before it was observed with either observation list. No difference was found between males and females and between mild, medium, and severe pain. This is the first study studying the difference between a physiological pain measurement and a pain observation in adults with SID. Implementations for research and practice are discussed.

7.1. Introduction

Adults with a severe or profound intellectual disability (SID) are often resident in a home care facility where they receive help and support from professionals (e.g., Esteban et al., 2021; Skoss et al., 2024). In the Netherlands, they may live in a group of up to seven cohabitants (Dutch Ministry of Health, Welfare and Sport, 2024a). The benefit of such an arrangement is that caregivers, who are available day and night, are educated and experienced in caring for adults with a severe or profound intellectual disability, the care work is divided among a larger team, as opposed to one or two parents, and various care aids are available, such as manual or mechanical hoists (e.g., Bigby, et al., 2014; Clement & Bigby, 2010; Dutch Ministry of Health, Welfare & Sport, 2024b). Care work is made lighter and less stressful by dividing it among several specialists, and there is still an atmosphere of homeliness in the group homes, as opposed to a hospital (Bigby et al., 2014).

Despite the advantages of people with a severe or profound intellectual disability living together in group homes, their lives are not without challenges. A severe or profound intellectual disability often coincides with a severe motor disability, one or more sensory disabilities, a lack of communicative skills and different medical disorders (Poppes, van der Putten & Vlaskamp, 2010; Van der Putten & Vlaskamp, 2011). A study in the Netherlands (Van Timmeren et al., 2016) has even determined that adults with a severe or profound intellectual disability, on average, suffer from 12 comorbid (medical) disorders, of which obstipation, a visual disability and epilepsy are the most prevalent. Obstipation, which was found to occur in 94% of persons with a severe or profound intellectual disability, is one of several of these comorbid disorders considered painful. Others include infections of facial cavities or urinary tract (Cuvertino et al., 2017; Rodriguez, 2014), gastro-oesophageal reflux (Böhmer et al., 1999), and skeletal deformities (Van Schrojestein Lantman-de Valk & Noonan Walsh, 2008). With living together in proximity, people with SID can also have a higher risk contracting and spreading infectious diseases (e.g., Dworkin et al., 2006).

While pain will most likely always cause a disruption of life, wellbeing and development (e.g., Attridge et al., 2015; Crombez et al., 1996), it is also a sign of illness, such as those mentioned, or injury (IASP, 2020). When pain is present in people who are unable to communicate about their pain, there exists an increased challenge for caregivers to recognize and treat that pain acutely and accordingly (e.g., Evenhuis, 2002). Unrecognized pain which is not timely treated can cause a reliably treatable infection, for example of the urinary tract, develop into something severe which may need an operation and a hospital stay to cure (World Health Organisation, 2024).

Unfortunately, the prevalence of pain in people with SID is insufficiently studied. Caregiver reports have stated that certain daily pain in individuals with an intellectual disability was present in 13% of clients, and suspected pain was thought to be much higher (Walsh, Morisson & McGuire, 2011). The problem is the uncertainty about the existence of pain in people with a severe or profound intellectual disability. A lack of communicative skills makes expression of pain difficult and recognizing signals from someone with SID is challenging for caregivers (Defrin, Lotan & Pick, 2006; IASP, 2021; Van der Putten & Vlaskamp, 2011).

Considering the challenge and the importance of recognizing pain in adults with a severe or profound intellectual disability, a pain signalling application is introduced, named the SID Pain App. This app estimates experienced pain through skin conductance measured with wearable sensors in a sock (Korving et al., 2022b). Skin conductance (galvanic skin response or GSR) is the conductivity of the skin, aided by sweat. Fabric silver sensors are placed on the inside sole of a sock, between which a 6 Ampère current is run. The variations in GSR-response may portray variations in arousal the wearer is experiencing. Pain is a highly arousing experience, so therefore, this system could theoretically measure pain.

Earlier research (Korving et al., 2020; 2022b) has focused on testing possibilities of galvanic skin response, gathering pain response data, and using that data to create an AI-enabled algorithm to classify pain. Originally, the system has been developed, tested, and found accurate with pain data from healthy adults without intellectual disability. Acknowledging the importance of validating the system with the target group (e.g., Calis et al., 2023; Korving et al., 2022a), this study was carried out to test (1) whether the mobile pain application can be used on adults with severe or profound intellectual disability, (2) whether a physiological pain classification coincides with a systematic behavioural observation of pain for the target group, and (3) whether the SID Pain App will classify a painful moment quicker than a systematic behavioural observation can classify it.

7.2. Methods

The current study was conducted to test a physiological pain signalling application on adults with a severe or profound intellectual disability, answering the questions: Will this SID Pain App signal a pain moment at the same time pain is observed in the behaviour of the participant? And will the SID Pain App classify a physiological response as pain faster than a systematic observation will code behaviours as pain?

Participants (N=14, 50% female) were recruited from several Dutch organizations who provide care for children and adults with SID. They were adults with a severe or profound intellectual disability, which was determined by either results of an IQ assessment or as reported in their general file. Participants' biological age ranged from twenty to fifty-five years (Mean = 33.14 years, SD = 11.90 years).

Table 7.1 shows the descriptives of the participants: demographics, the participants' capabilities of self-care, the participants' motoric capabilities, and the length of their physical therapy session. Motor disability varied from being able to walk with support (Gross Motor Function Classification System level II) to being quadriplegic (Gross Motor Function Classification System level V; Palisano et al., 1997). Some participants had a visual disability (N=6, 35.7%), ranging from severe near- or far-sightedness to (functional) blindness, and only few (N=2, 14.28%) had a known mild auditory disability. The average length of measurement was 22 min, 57 sec (SD=3 min, 37 sec).

TABLE 7.1. Demographics for participants with a severe or profound ID.

gender	age	IQ/DEV	self-care	motor function level	length of session
F	36	IQ<25	no	V	23:46
F	50	12m	limited	III	20:10
M	30	IQ<25	no	V	26:09
M	40	9m	some	V	22:47
M	44	10m	some	II	20:33
M	28	7m	no	V	27:23
F	44	6m	some	II	23:55
F	55	36m	some	III	28:00
M	20	5m	some	IV	19:47
F	24	IQ<25	no	IV	21:03
F	21	IQ<25	no	V	24:51
F	20	IQ<25	limited	II	20:55
M	32	IQ<25	limited	II	15:06
M	20	IQ<25	no	V	26:57

Note. IQ=intelligence quotient, DEV=developmental age in months (m), capable: capability of participant to perform self-care, motor function level according to the Gross Motor Function Classification System: level II (walking with balance and endurance limitations), III (walking with a hand-held mobility device and additional support), IV (limited self-mobility/powered mobility), and V (transported in wheelchair).

Intellectual disability was the result of complications during pregnancy (N=1, 7.14%), during delivery (N=3, 21.43%), or due to a congenital genetic disorder (N=8, 57.14%). For two participants, one male and one female, the reason for the intellectual and motor disability was unknown at the time of measurement.

All participants were residents of an organization for the care of people with intellectual, motor and/or visual disability, which means they received up to 24-hour care by professional caregivers in a home-care facility. The care facilities were situated in both urban (Amsterdam, Amstelveen) and more rural areas (Doorn, Ermelo, Purmerend). Three of the participants were born to parents who had immigrated to the Netherlands (21.4%), which is somewhat higher than the percentage of inhabitants with parents with a migratory background in the entire Dutch population (11.6%; Statistics Netherlands, 2023). All the participants were under the care of specialized physicians and developmental psychologists, though for most no specific problem behaviour was reported. They were visited in either their group home or the place they received day-care.

Inclusion criteria for participation are presented in Table 7.2. Attrition was moderately high (10.5%), due to the low number of participants. One possible participant underwent a pain-relieving procedure, and another passed away shortly before the scheduled measurement. Furthermore, eight participants were excluded because they did not meet all inclusion criteria (e.g., too young, higher developmental age).

TABLE 7.2. Inclusion criteria for adults with SID.

Inclusion	Explanation
Biological age ≥ 18 years.	
Developmental age ≤ 36 months.	Severe or profound intellectual disability.
Under regular treatment by physical therapist.	Participant needs to know their physical therapist and be comfortable with them.
Living in care organization.	Similar access to medical and behavioural help.
No MS or comparable disorder.	Physiological responses cannot be measured.
Not allergic to cotton, elastane, polyester or silver.	Smart socks contain these materials and must be worn.
Not currently participating in another pain study.	

7.2.1. Instruments

The smart sock is a regular sock adorned with two fabric sensors on the inside of the sole, one close to the toes and one by the heel (Figure 7.1). This sock was developed by the Eindhoven University of Technology, the Vrije Universiteit Amsterdam and care organization Bartiméus, Doorn (Bremmer, Croes & Sterkenburg, 2014). The fabric sensors contain silver for optimal conductance, with the added benefit that silver is both antiviral and antibacterial. The inside sensors are connected to metal push buttons on the part covering the ankle or calf, with a silver conductive wire that only covers the outside of the material. The push buttons also do not touch the wearer’s skin.

A Shimmer™3 GSR+ unit (Shimmer, Dublin, Ireland) is worn around the ankle, clipped into a plastic holder on an ankle band. The ankle band is made of stretching material and can be adjusted for comfort with a plastic clasp. The Shimmer™ is connected to the push buttons on the smart sock with two plastic-coated wires. Through these wires a 6A current is brought, travelling along the outside of the smart sock until it reaches the skin at one of the fabric sensors. Then it travels over the skin to the other fabric sensor and returns to the Shimmer™3 GSR+ unit. The amount of moisture, or sweat, on the skin determines the current. The Shimmer™ sends and receives sample currents at a frequency of up to 50 times a second (50 Hertz), measuring raw skin resistance in Kilo Ohms (kΩ) which is then converted to skin conductance in micro-Siemens (μS) by taking the inverse (1/1000 kΩ = 1μS). The range of skin conductance measurement is between 0.2 and 125μS. Via Bluetooth® the Shimmer™ sends every received measurement of the current to a mobile application. The measurements are conformed into a CSV-format displaying skin resistance, skin conductance, date & time, and whether and which button on the display was used.

FIGURE 7.1. The smart sock: On the left is a fabric sensor and the right shows the sock with the Shimmer™3 GSR+ unit.

The SID Pain App is a mobile application, including a user interface with several levels, starting with the Bluetooth® connection to a Shimmer™ unit in the vicinity and including a pain classification algorithm and the possibility for the user to input data (Korving et al., 2022b). The pain classification algorithm in the Pain App was developed with pain response data from 28 healthy adults with no intellectual disability, who received one to five painful experiences and self-reported their pain tolerance threshold on a Self-Assessment Manikin scale [30]. This resulted in approximately 69,000 data points of both pain and no pain. A Random Forest algorithm was used to create a model capable of distinguishing physiological pain data from no pain. The model obtained >80% reliability, though precision and sensitivity were only adequate when 50% of data were interpolated from the same participant (Korving et al., 2022b).

The user interface (Figure 7.2) and design used in the Pain App have been co-designed with professional caregivers and family members of people with intellectual disability (Korving et al., 2022a). As per the eventual users’ wish, the Pain App has an option to look back five minutes in the graph of the electrodermal activity measurement. Buttons on the user interface allow the user to input whether they think the wearer is or is not in pain. A warning signal will be given visually, audibly, and haptically, and the user can choose to disable either the auditory or the haptic warning.

Shimmer settings

Disconnect sensor

Data collection

Data labeling

Data label

FIGURE 7.2. The user interface and visualization design of the SID Pain App when it is in use and gathering data. The green face is shown in case of no pain, the red face in case of pain.

None of the participants observed were undergoing physical therapy for rehabilitation needs; they received physical therapy to keep mobility in their muscles, joints, and tendons, or to retain a skill, such as sitting unsupported, crawling or walking with support. There was insufficient information from physical therapists’ reports to ascertain whether the Pain App detected pain when the participant was also expected to experience pain. Therefore, physiological pain signals detected by the Pain App are compared to observations of pain behaviour based on two systematic pain observation scales, and the results from both observation lists are compared to improve the validity of the physiological pain detection.

The Non-Communicating Adults Pain Checklist (NCAPC; Defrin, Lotan & Pick, 2006; Lotan et al., 2009a) was developed to systematically observe pain in adults with an intellectual or developmental disability, ranging from mild to profound. Researchers found that existing systematic pain observation lists were not sensitive enough to pick up pain behaviour from adults with a severe or profound intellectual disability. The existing Non-communicating Children's Pain Checklist-Revised was adjusted and tested fully, both on internal consistency (alpha = .773) and sensitivity to pain (SRM, 1.20 – 2.07) (Lotan et al., 2009b). In total the observation list has 17 items within six themes: vocal reaction, emotional reaction, facial expression, body language, protective reaction, and physiological reaction. The first seven items of the NCAPC are shown in Table 7.3.

In the NCAPC, an observer scores a pain behaviour in two ways: whether it occurs and how often it occurs. No cut-off score was given, just that a greater score meant greater pain. A score of zero meant that the behaviour was not seen or shown, scoring one meant that the behaviour is present but rarely seen or heard, a two meant that the behaviour was shown a few times but not continuous, and scoring three meant that the behaviour was seen often and (almost) continuous; anyone would easily notice this if they saw the participant for only a few moments during the observation time. All observations were made with video material of at least 15 minutes up to the full length of the physical therapy session.

TABLE 7.3. The first seven items of the non-communicating adults pain checklist and its scoring scale.

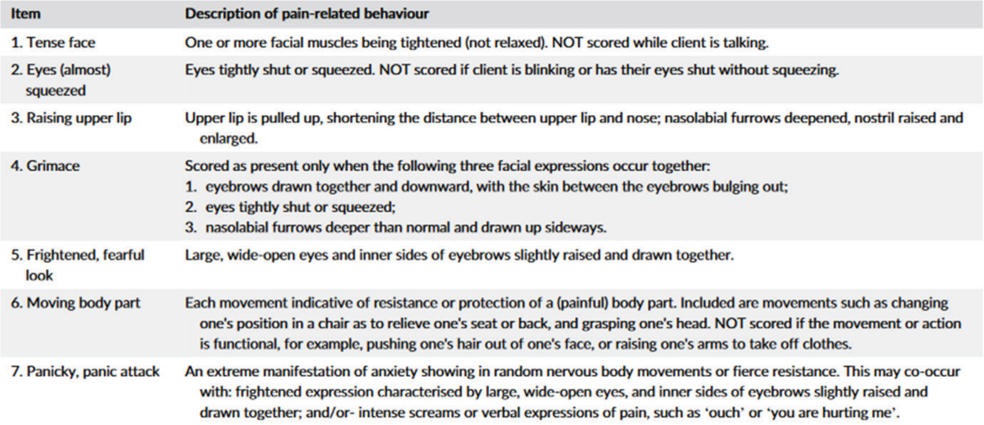
Item	Score			
	Not at all	Just a little	Fairly often	Very often
Vocal reaction				
Moaning, whining, whimpering (fairly soft)	0	1	2	3
Crying (moderately loud)	0	1	2	3
Screaming or yelling (very loud)	0	1	2	3
Emotional reaction				
Not cooperating, cranky, irritable, unhappy	0	1	2	3
Agitated, being difficult to distract, not able to satisfy or pacify	0	1	2	3
Facial expression				
Furrowed eyebrows, raising eyebrows	0	1	2	3
A change in eyes including (squinting of eyes, eyes opened wide, eye frowning)	0	1	2	3

The Non-Communicating Children's Pain Checklist-Revised has a cut-off score of seven based on a video observation of two hours. This cut-off was adjusted based on the length of video material per participant and knowledge of the target group. If the participant showed three different pain-related behaviours within 10 seconds of each other, as per the NCAPC, this was scored as a pain moment, no matter how often each behaviour occurred. The exact time index of a third pain behaviour (within 10 sec of the first pain behaviour) was compared to the time index the Pain App detected a physiological pain signal. The observations with the NCAPC were independently coded by two trained and instructed observers (master students). The first observer coded all 28 videos from all 14 participants (face and body), while the second observer coded 13 randomly chosen videos of 13 different participants (43.46%). Interrater reliability was measured by checking agreement during 100 seconds from four randomly chosen videos. Cohen's Kappa was moderate, κ=.410. Intra-rater reliability was measured for the first NCAPC-observer (κ=.556).

The Pain Observation Scale for Adults with Intellectual Disabilities (POSAID; Figure 7.3) has been in development since 2020 and is being validated specifically for adults with a profound intellectual disability (Enninga et al., 2023; Kreukniet, Bruns & Van der Putten, 2016). The scale consists of 12 items, drawn from other observation scales and literature, to assess pain in a residential setting. For assessment with the POSAID, first author and a master student received a five-hour training from the developer, followed by a short evaluation session to determine interrater reliability between developer and trainee.

The two observers finished the training and evaluation session and independently coded the videos with 12 items from the POSAID. The first observer coded all 28 videos from the 14 participants and the second observer coded six randomly chosen videos of six different participants (21.43%). Interrater reliability between both observers was measured during 100 seconds from four randomly chosen videos and deemed accurate (κ=.725). Intra-rater reliability was measured for the first POSAID-observer (κ=.809).

When using the POSAID, an observer watches two minutes of a video of a participant experiencing caregiving, physical therapy, or a comparable situation. The videos of the face are watched twice and the body once. Observations are made based on what is seen, interpretations are not allowed. Background noise is to be ignored and only sounds clearly made by the participant being filmed are taken into consideration. Cut-off score (for pain) was three behaviours, based on the provisional results of the POSAID's validation research Enninga et al., 2023).



Item	Description of pain-related behaviour
1. Tense face	One or more facial muscles being tightened (not relaxed). NOT scored while client is talking.
2. Eyes (almost) squeezed	Eyes tightly shut or squeezed. NOT scored if client is blinking or has their eyes shut without squeezing.
3. Raising upper lip	Upper lip is pulled up, shortening the distance between upper lip and nose; nasolabial furrows deepened, nostril raised and enlarged.
4. Grimace	Scored as present only when the following three facial expressions occur together: 1. eyebrows drawn together and downward, with the skin between the eyebrows bulging out; 2. eyes tightly shut or squeezed; 3. nasolabial furrows deeper than normal and drawn up sideways.
5. Frightened, fearful look	Large, wide-open eyes and inner sides of eyebrows slightly raised and drawn together.
6. Moving body part	Each movement indicative of resistance or protection of a (painful) body part. Included are movements such as changing one's position in a chair as to relieve one's seat or back, and grasping one's head. NOT scored if the movement or action is functional, for example, pushing one's hair out of one's face, or raising one's arms to take off clothes.
7. Panicky, panic attack	An extreme manifestation of anxiety showing in random nervous body movements or fierce resistance. This may co-occur with: frightened expression characterised by large, wide-open eyes, and inner sides of eyebrows slightly raised and drawn together; and/or- intense screams or verbal expressions of pain, such as 'ouch' or 'you are hurting me'.

FIGURE 7.3. The first seven items of the POSAID with explanation (Kreukniet, Bruns & Van der Putten, 2016).

Both the NCAPC and the POSAID were coded with Noldus The Observer XT software (Noldus, 2024). This software enables researchers to code video data (event coding) and aligns this to data from another type, such as physiological data in CSV-format. This way both measurements could be synchronized in the same program, and it could be made clear whether the observed event happened congruently or close to a physiological response.

7.2.2. Procedure

This project and all its components were approved by the medical-ethical committee of the Vrije Universiteit Medical Centre (METc VUmc; NL69815.029.19). Informed consent was provided by legal representatives of the participants with a severe or profound intellectual disability. Participants were informed of the presence of a researcher and equipment by their primary caregiver, if necessary, by use of graphic material. Signs of distress in participants were discussed with each participant's professional caregiver, and the behavioural code for recognizing resistance in people with an intellectual disability was followed (Centrale Commissie Mensgebonden Onderzoek, 1999).

Team managers of participating care organizations for persons with intellectual disability were asked to assess clients on inclusion criteria given in Table 7.2. Participant information, for legal representatives and physical therapists, was provided via email or post. This package included: an information folder, an informed consent form, (an envelope with) a postage-free return address, a research planning, and a general information folder about rights and considerations for participating in medical research in the Netherlands, provided by the Dutch government.

Once the legal representative's informed consent form was returned, an appointment was made for a measurement. These would take place on the day, time, and location the client would have scheduled physical therapy. The researcher or an assistant would arrive beforehand to go over the measurement procedure. After the physical therapist consented to be visible in the video, they would start the physical therapy session. The session would be proceeded or followed by a few minutes of no activity around the participant, so that an electrodermal activity baseline could be established.

Two cameras were set up, one to videotape the participant's face and one for the entire body. They would be either placed on a nearby surface, for example a counter facing the treatment table, or fixed on one tripod. The camera that was focused on the body was a Sony Zeiss, while a Galaxy S5 mini with Android 5 was used to film the participant's face. The set-up of both cameras on the tripod is shown in Figure 7.4.

Participants would wear a smart sock in their shoe size, or, when they wore braces or knee socks, a smart knee sock. The connection to the Pain App would be made before both video cameras would be turned on. In view of each camera, the researcher or research assistant would press a button on the Pain App's interface. This button press would appear in the data and would later be used to synchronize the video-material with the physiological data. Both video and physiological data would be gathered as long as the physical therapy session lasted. At the end of the session, the participant and the physical therapist received small presents.

FIGURE 7.4. The camera set-up videotaping the participant’s face and body simultaneously.

7.2.3. Data Analyses

The data consisted of demographics, electrodermal activity, in a format of micro-Siemens per one-fiftieth of a second, and coded video data. Physiological pain data was also coded as mild (1), moderate (2) or severe (3), based on the length and deviation from baseline of the electrodermal response. Observational data was coded as a pain experience at the time index of the third observed pain behaviour within 10 seconds of the first observed behaviour. The time index was the time since the start of the physiological measurement with the Pain App.

A difference score was calculated between the moment of a physiological pain response and the moment of a third observed pain behaviour. This difference score was used to compare pain experiences of male and female participants and between the three different levels of physiological response, to exclude differences in variation or result between these groups. To exclude variety in results between the NCAPC and the POSAID, the difference score of both observation lists were compared to each other.

IBM SPSS 26 was used for data analysis. Initially, a paired t-test was done to analyse the difference in speed between the physiological response and an observed response of pain. In case no significant results were found with the paired t-tests, an equivalence test was used (Lakens, 2017). Hereafter, differences between men and women, between the different levels of pain, and between the observation lists were analysed with several analyses of variance. A Cohen's d test would give information about the relevance of the t-test's results and post-hoc Tukey's tests would clarify the result of the ANOVA's.

7.3. Results

As measured by the Pain App, each participant experienced one to four painful moments during their physical therapy session, leading to a total of 40 pain instances over the entire group (mean = 2.86, median = 2). When only one or two different pain behaviours were coded within 10 seconds of a physiological pain response, the observational pain moment was coded as missing data. There was missing observational data from the NCAPC for 17 of the physiological pain moments, and five of the physiological pain moments had missing observational data from the POSAID, so analyses were done with the remaining 23 and 35 pain moments, respectively.

Out of 35 physiological pain moments, nine were mild, lasting to up to one second and showing a moderate change from the baseline. Another 17 pain moments were moderate, lasting one to two seconds and showing a moderate to high response. A severe pain response was seen in nine instances, lasting longer than two seconds and showing a large change from each participant's baseline. An example of physiological responses on these three pain levels is shown in Figure 7.5.

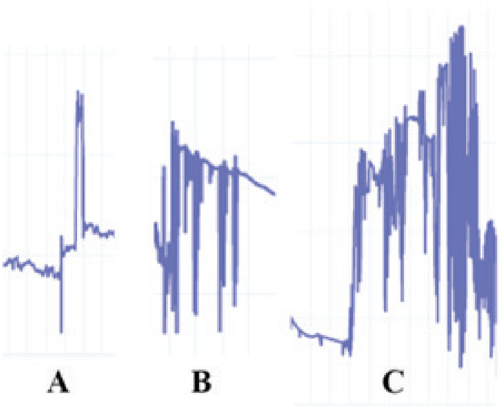


FIGURE 7.5. An example of a mild physiological pain response (A), a moderate physiological pain response (B) and a severe physiological pain response (C) taken from the data of two participants.

On average, the SID Pain App signalled a pain moment 9min 12.09sec after the start of the measurement (SD=6min 15.18sec), and a pain event was coded via systematic observation with the Non-Communicating Adults Pain Checklist after 9min 18.57sec (SD=6min 14.10sec). The difference between these measurements was 6.48sec (SD=5.99sec). A two-tailed paired t-test showed a significant result, t(22)= -5.340, p<.001. Cohen's d was calculated to assess effect size, which was small, d=.021.

To assess possible differences between the pain moments of participating male participants (N=10) and the pain moments of participating female participants (N=13), a one-way ANOVA was administered, with the difference score between Pain App and NCAPC pain events as outcome measure. The average difference between the physiological and NCAPC pain moments for men was 8.51sec (SD=8.36sec) and for women 4.93sec (SD=2.72sec). The Levene's test of homogeneity of variance was significant, therefore a Kruskal-Wallis test was administered, which was not significant: H(1)=1.574, p=.210.

On average, the SID Pain App signalled a pain moment 9min 44.56sec (SD=6min 01.07sec) after the start of the measurement and a pain event was coded via systematic observation with the POSAID after 9min 50.81sec (SD=6min, 01.63sec), a difference of 6.25sec (SD=6.55sec). Results of the two-tailed paired samples t-test were significant: t(34)=-5.646, p<.001. Cohen's d was calculated to assess effect size, which was small, d=.017.

To assess possible differences between pain moments of participating male participants (N=17) and pain moments of participating female participants (N=18), a one-way ANOVA was administered, with the difference score between Pain App and observational pain events as outcome measure. The average difference between the physiological and observational pain moments for men was 7.88sec (SD=6.89sec) and for women 4.71sec (SD=5.99sec). The Levene's test of homogeneity of variance was non-significant and neither was the result of the ANOVA, F(1,33)=2.124, p=.154.

The different levels of physiological pain responses showed various difference scores between physiological and observational pain moments, with pain events coded via a systematic observation made 4.39sec (SD=2.24sec) after a mild physiological response, 7.21sec (SD=6.20sec) after a moderate physiological response, and 6.29sec (SD=9.72sec) after a severe response. The Levene's test of homogeneity of variance showed equal variances between the three pain-level groups. The one-way ANOVA gave a non-significant result, F(2,32)=.532, p=.593.

There was no difference between the difference score of the physiological measurement of pain with the Pain App and NCAPC pain event, and the difference score of physiological measurement with the Pain App and POSAID pain event: t(21)=-.803, p=.431. The difference between the moment the Pain App detected a pain experience, and a third behaviour was shown according to either of the systematic observation lists was the same. The situations where a physiological response was measured, but no behavioural response was coded (missing observational data) were equally divided between men (NCAPC 47%; POSAID 40%) and women, and between mild (40%), moderate (40%) and severe pain levels.

7.4. Discussion

The current study uses observations of adults with severe or profound intellectual disability (SID) during a regular physical therapy session with possible painful moments to test a physiological pain measurement system, the 'SID Pain App'. Seven males and seven females with a severe or profound intellectual disability wore a smart sock connected to the SID Pain App while they were videotaped during a fifteen-to-twenty-five-minute physical therapy session. The videos were coded with two systematic pain observation lists and pain moments were compared to the time instances the physiological data signalled pain to test (1) whether the SID Pain App can be used on adults with severe or profound intellectual disability, (2) whether a physiological pain classification coincides with a systematic behavioural observation of pain for the target group, and (3) whether the Pain App will classify a painful moment quicker than a systematic behavioural observation can classify it.

Results of the study indicate physiological measurements of pain are possible by measuring electrodermal activity, but the measurements may not yet be as valid as they should be. In 17 cases, when observed with the NCAPC, and in five cases, when observed with the POSAID, the participants showed no or too few behavioural pain responses. This could either mean the systematic observational lists were insufficiently sensitive to behavioural pain responses in those specific cases, or the SID Pain App detected false positives for pain.

When conducting a pain study with adults who can self-report about their pain experience, it is possible to make a physiological distinction between signals that indicate stress and those that indicate pain. In cases of participants with severe or profound intellectual disability, with an inability to self-report, distinguishing pain and stress becomes more challenging. It is therefore impossible to completely rule out that the SID Pain App would signal a stress response as a pain response if the physiological deviation from baseline is similar. Nevertheless, considering the vulnerability of the subject group and their increased risk of painful medical disorders, any signal from the SID Pain App can be an indicator that something is amiss, and should certainly result in getting a caregivers attention.

As far as the first question from this study, whether the Pain App can be used to measure electrodermal activity in adults with a severe or profound intellectual disability, this can be answered positively. In all 14 participants, at least one moment of pain was classified by the Pain App, and in 35 of the 40 physiologically detected pain moments, a systematic observation registered three pain behaviours within 10 seconds of this physiological response. Furthermore, none of the participants showed any signs of distress, according to their professional caregivers, or resistance, according to the behavioural code for recognizing resistance in people with an intellectual disability, from wearing the smart sock, having a 6A current run over their foot sole, or being videotaped by a researcher.

Considering the second question, whether a physiological pain classification coincides with a systematic behavioural observation of pain for the target group, the data shows some variation between the two behavioural observation lists used. In over three times as many moments that the Pain App detected an instance of pain, a pain event could not be coded with the Non-Communicating Adults Pain Checklist (N=17), compared to the Pain Observation Scale for Adults with Intellectual Disabilities (N=5). Considering that all participants of this study had a severe or profound intellectual disability, a group for which the POSAID was specifically developed and validated, while the NCAPC was found to be reliable for non-communicating adults with intellectual disability of all levels, this result may indicate that the POSAID is more sensitive to pain behaviours shown by adults with more severe intellectual disabilities.

Results indicate that no differences were found between SID Pain App measurements and observed pain in male and female participants, and between mild, moderate or severe pain responses. Missing observational data was equally divided in all groups. Furthermore, the difference scores between the two systematic observation scales and the SID Pain App were similar, which indicates the observation scales have a similar sensitivity to recognize pain in adults with a severe or profound intellectual disability. The difference in missing observational data may have more to do with observer differences.

The two independent coders that observed using the NCAPC showed lower inter-rater and intra-rater reliabilities, compared to the two independent coders that observed pain behaviours with the POSAID. The training for using the POSAID was also more involved than that for using the NCAPC, therefore the variation in the results of these observation scales could be due to difference in coder training, and not due to sensitivity to cose pain. Future research using either or both of these pain observation scales will have to make sure the trainings for coders on each of the scales are equally comprehensive.

Overall, it seems that the SID Pain App does coincide with a moment that a pain event can be coded using a systematic pain observation scale, and therefore can be used by caregivers to help recognise pain experiences in adults with a severe or profound intellectual disability.

A third behavioural response of pain coded with the Non-Communicating Adults Pain Checklist would on average be observed nearly 8 seconds after a physiological pain response measured with the SID Pain App. When coded with the Pain Observations Scale for Adults with Intellectual Disabilities, the third pain behaviour was observed almost 6.5 seconds after the physiological pain response. This gives a strong indication that the Pain App does indeed classify a painful moment earlier than a systematic observation can detect it. This result is an important step towards providing caregiving with a tool to detect pain or pain-related distress in clients who are unable to communicate about their pain.

Considering that most clients with a severe or profound intellectual disability are not constantly observed by their caregivers during most of the day, the fact that the Pain App detects pain signals can help caregivers to timely evaluate their client's distress, provide care and support, and create a safer environment for clients unable to communicate about pain. Theoretically, this will improve the wellbeing of clients with a severe or profound intellectual disability, by minimizing the disruptive influence of pain on their quality of life and development. And furthermore, the earlier pain is detected, the earlier pain relief and medical treatment can be provided, avoiding an escalation of illness or injury that caused the pain.

This study offers a unique contribution to disability research and care for people with severe and profound intellectual disability. Not only does it show that physiological responses to pain in adults with SID are similar to those without an intellectual disability, but also that a physiological pain signal can indicate a pain moment before systematic observations can. This can be a tremendous help in caregiving, not only to detect pain faster, but also to recognize and understand an individual client's unique pain-related behaviour. Especially when clients with a severe or profound intellectual disability are cared for by several professional caregivers, who regularly change jobs or locations, introducing new caregivers to the clients, an automated system that detects pain or pain-related distress can become invaluable for the training of the new caregivers.

Within the field of disability research, this study is the first that looks at a way to measure physiological pain in adults with a severe or profound intellectual disability in a residential setting. Other studies have looked at behavioural pain detection in the target group (e.g., De

Knegt et al., 2013), or pain detection in clinical settings, for example during a hospital stay (Arbour & Gélinas, 2014; Roulin & Ramelet, 2012), or vaccinations (slifer et al., 2011). And despite the increased risks of necessary medical procedures and hospital stays for people with a severe or profound intellectual disability, most of their time is spent at their group home or their day care, and it is important for health and wellbeing that the possibility of pain can be evaluated at their home.

Unfortunately, this study did not look at what a caregiver will do once they become aware of a signal from the SID Pain App. Even after a pain signal from the SID Pain App, a caregiver has many choices concerning the possible pain. It would be interesting to find out what difference the SID Pain App can make in daily caregiving, both for the caregiver and the client. We recommend future research to investigate this question to bring the state of pain recognition and treatment for adults with severe or profound intellectual disability a step further.

7.5. Conclusion

Results of this study show that galvanic skin response is a physiological measure that can effectively be used to detect pain moments in adults with a severe or profound intellectual disability. The SID Pain App gave pain signals during physical therapy, and behavioural responses observed with the Pain Observation Scale for Adults with profound Intellectual Disability were seen after almost every physiological pain response. This indicates that a physiological measuring system could be a promising additional tool to detect and assess pain in people unable to communicate about their pain.

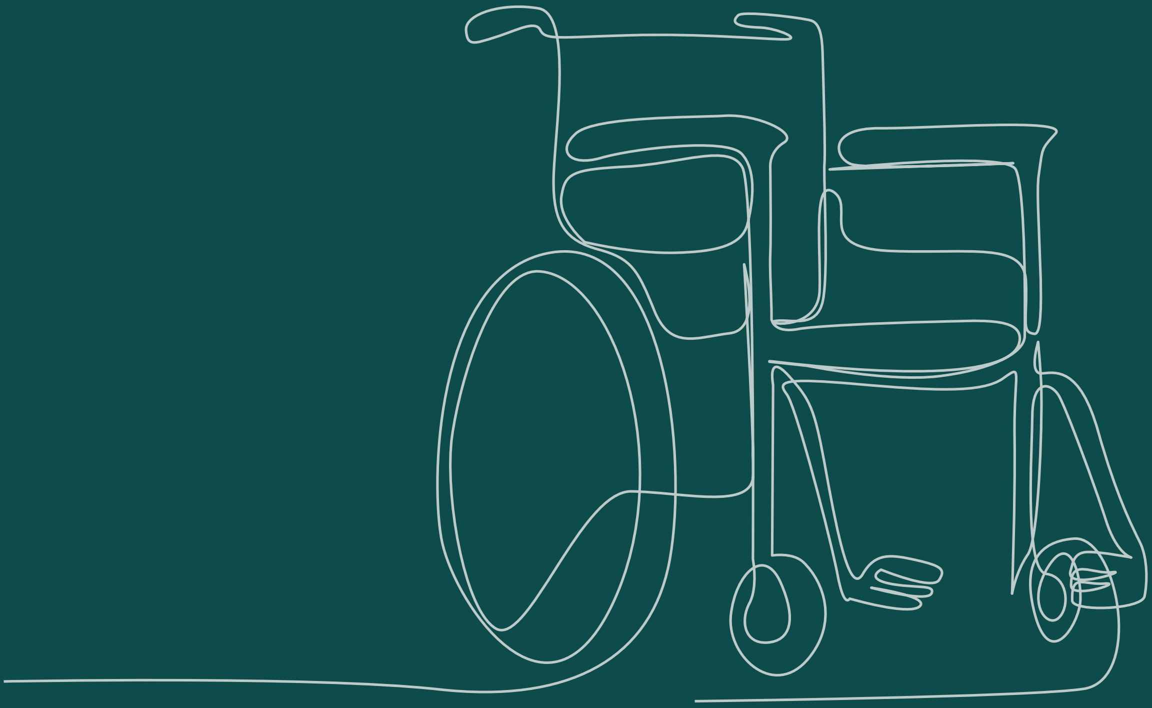
The physiological pain response signalled by the SID Pain App would come more than 6 sec before three different behavioural pain responses were seen, based on either the Non-Communicating Adults Pain Checklist, or the Pain Observation Scale for Adults with profound Intellectual Disability. This is an important result, since recognizing pain in persons with a severe or profound intellectual disability is a challenge for caregivers. The proposed automated system for measuring indications of pain can assist caregivers in closely monitoring their clients, recognising their unique pain-related behaviour, and identifying the underlying causes of pain before it escalates to a potentially life-threatening condition.

7.6. Acknowledgements

The authors would like to acknowledge this study’s fourteen participants with SID, and their legal representatives, professional caregivers, and physical therapists, for the trust they had in the researchers. Their participation made it possible to take further steps in the study of pain in people with a severe or profound intellectual disability. We also would

like to thank the independent coders Iris Hartog, MSc., Rebecca van Veldhuizen, MSc. and Adinda Blokker, MSc., as well as a special thanks to Tanja Doodeman, MSc. for her invaluable assistance in the use of Noldus The Observer.

7



Chapter 8

Discussion

This project was started to find ways to offer support in the lives of adults with a severe or profound intellectual disability and their caregivers for better detection and assessment of pain. Timely assessment of pain makes clients' daily life safer, improves their wellbeing, and prevents more severe illness or death (e.g., van Timmeren et al., 2016; York, Wechuli & Karbach, 2022). Since systematic pain observations are difficult in this target group, cost time and manpower, and may not reveal unique, subtle, and idiosyncratic pain behaviours (e.g., Defrin, Lotan & Pick, 2006; Millard & de Knegt, 2019; Zwakhalen et al., 2014), an automatic system to physiologically measure pain was developed and tested. The aims of the project were as follows: (1) To evaluate several physiological pain detection methods on usability, invasiveness and technological readiness; (2) To develop a reliable, valid and specific physiological pain detection algorithm to be programmed into a mobile application; (3) To test this mobile pain detection application on adults with a severe or profound intellectual disability and to assess the user experience of the caregivers using the mobile application.

The communication difficulties of adults with a severe or profound intellectual disability make it difficult to discover how many of them are in pain (IASP, 2021). What is known, is that with an increased risk of painful medical disorders (e.g., Evenhuis, 2002) and physical and medical comorbidities (e.g., Van der Putten & Vlaskamp, 2011), the chance of experiencing pain also increases (IASP, 2021). An experience of pain not only comes with a disruption in life, wellbeing, and development (e.g., Attridge, et al., 2015), it signals an injury or illness that should be treated. The speed and accuracy of the detection of pain in adults with a severe or profound intellectual disability will increase their quality of life (e.g., van der Putten & Vlaskamp, 2011) and will prevent an exacerbation of the cause of the pain (e.g., World Health Organisation, 2024).

Main findings of this project were positive: While not many studies have focused on pain measurement in adults with a severe or profound intellectual disability, many studies have looked at the effectiveness of physiological ways to measure acute or chronic pain in healthy adults or patients. For clients with a severe or profound intellectual disability, only the most non-invasive ways can be used. Therefore, a system that measures electrodermal activity with a sock was developed. With pain data of thirty healthy adults without intellectual disability a pain classification model was created, which, when using 50% interpolated data in the testing set, has an accuracy and sensitivity of over 80%. When tested on adults with a severe or profound intellectual disability, the mobile physiological pain detection application shows a pain warning on average seven seconds before a systematic observation will. User experience questionnaire research showed the pain detection system to score positive on attractiveness, perspicuity, effectiveness, dependability, stimulation, and novelty.

8.1. Main findings

To evaluate physiological pain detection measures on usability, invasiveness and technological readiness, a search for the physiological pain measurement methods used in research was done with a systematic review of meta-analyses and review papers. The usefulness of every method for pain measurement, their invasiveness for a patient, and their technology readiness as measuring systems varied substantially, therefore it was difficult to compare the physiological pain measurement methods with each other. The diversity in the quality of the reviews and their risks of bias created another impediment for a thorough comparison of the included research articles.

In the case of patient care in hospitals or care organisations, the assessment of both acute and chronic pain is a challenge. Unfortunately, an automatic measurement of both forms of pain in a low invasive way, is still unavailable. Some of the measurement methods reviewed, such as genetic testing, were only applicable to determine chronic pain, while most other systems, such as heart and respiratory measures and muscle tension, could only assess the direct physical changes to acute pain. Many of the physiological pain measurement methods showed inconsistent results, such as reliability in one subject group and not in another, or there were too few studies or participants for a thorough evaluation. Technological readiness of the used methods was generally high, except for electrodermal measures and automatic facial recognition.

When the invasiveness of the physiological pain measurement methods was correlated to the vulnerability of participants on which the methods were used, the trend showed that the less vulnerable the participants, the more invasive the measures that were tested, and vice versa. As a general agreement, researchers only test the invasive pain measures on the participants who can give informed consent. While the more vulnerable participants are protected from having to endure more invasive ways to physiologically measure pain, the result of this review also shows that participants with an intellectual disability are underrepresented in physiological pain research. Therefore, the result from this systematic review did not answer the question what physiological pain measurement measure would be best to use on very vulnerable participants.

As the increase of stress is related to an increase in skin conductance (Biedeman & Scheff, 1994; Flora, Wilkernon & Flora, 2003), a pilot study was set up to examine the electrodermal response to pain. Four healthy and well-informed participants between 28 and 52 years old underwent a painful stimulus once or twice while wearing the smart sock (Bremmer, Croes & Sterkenburg, 2014; Frederiks et al., 2015).

The results showed that skin conductance showed a clear response to pain, which deviated significantly from a relaxed disposition. Responses varied between and within individuals, with the second pain stimulus clearly showing less of a physiological reaction. This is not surprising, since expectation plays a role in pain response (Atlas & Wager, 2012). Participants knew what to expect and their physiological response to a repeated pain stimulus was less intense. Something similar occurs when acute or subacute pain becomes chronic, and the body's response becomes inadequate (Buchel, 2023). It was therefore important to manage future participants' expectations of the pain stimulus so that their physiological response would be as close to realistic as possible.

After establishing that measuring the galvanic skin response to pain is possible when using the smart sock, thirty healthy adult participants were recruited to contribute to a larger pain dataset for algorithm development. In the experiments, submersion of the non-dominant hand in ice-water was alternated with a submersion in water of room temperature or slightly warmer, without participants knowing the water's temperature beforehand. Expectations of pain were therefore managed. Participants submerged their hand in ice-water up to five times, leading to a dataset of approximately 69,000 data points of pain and no pain moments. On the created dataset a Random Forest algorithm performed better than Support Vector Machine.

At first glance, the results seemed promising, with 95% accuracy and 99% area under curve. Unfortunately, due to the imbalance of the data, specificity, precision, and F1-scores were around 50%. The unique physiological reaction to pain between participants is likely to have hindered the prediction of pain based on new physiological data. As a solution, data was artificially generated based on the testing set. With 50% generated data, the specificity, sensitivity, and f1-score of the algorithm increased to around 80%, while reliability remained high. This meant that the algorithm's specificity and sensitivity for classifying pain within a participant was only high enough when the data it used for testing was derived from pain moments from that same participant. Classifying pain from completely 'new' test samples was no better than chance.

Another group of participants, the eventual users of the mobile pain classification application, were asked to convey their wishes about the eventual mobile application in an online questionnaire. Five possible additions on the aspect of User Input, Pain Signals and App Interface could be arranged according to desirability. The answers of 32 end-users showed that on the aspect of User Input they would prefer to provide information on what is happening around the client and the client's medical disorders. On the aspect of Pain Signals, a signal when the client's arousal level had risen and a combined signal for pain that was visual, auditory, and haptic were preferred. In the App Interface, the end-users preferred to see changes in pain experience for the previous

15 minutes and changes for the previous twelve hours.

As the mobile pain classification application was intended to be used by caregivers in daily practice, it was important to design the app's interface and visualisation together with the end-users. To develop the actual mobile application, a comprehensive co-creation study was administered. With three different approaches and three different groups of eventual users, three initial visualisation designs were created, based on the specific necessities of the user group. The commonality between designs was that they had three positions: 'no pain', 'intermediate' and 'pain', and had to be at least subtly moving to convey that data was being gathered, as opposed to the mobile pain classification app having lost its connection to the smart sock. The evaluation of each of these three visualisations happened in two consecutive phases: comparison by end-users via online questionnaire and comparison by experts via online focus group.

Approximately 150 probable end-users participated in this design study, giving their opinion on their needs and possibilities, and assessing how each design would or could not meet those. At the start of the study, the COVID-19 pandemic had not yet reached global proportions, but when it did, one of the designs was deemed to resemble commonly used images of the virus. That same design did score the best in all phases; therefore, it was adjusted to minimise its resemblance. The eventual design encompassed all needs of the eventual user group, from workplace criteria to keeping the balance between attention grabbing and being a visual burden to already overworked professional caregivers. This design was then integrated into the mobile application that would also house the pain classification algorithm.

To conclude the development of the SID Pain App System, a study was conducted on the user friendliness of the system. This was done with the use of the User Experience Questionnaire (UEQ; Laugwitz, Held & Schrepp, 2008). This questionnaire contains 26 semantic differential scales with a seven-point Likert in between. For the study, 20 participants used the Mobile Pain Classification Application and filled out a questionnaire in their native language. The results were analysed with use of the UEQ analysis tool, a Microsoft Excel file with several tabs of options for checking the average scores, benchmarks, confidence intervals, scale consistency and answer inconsistencies (Laugwitz, Held & Schrepp, 2008).

"The Mobile Pain Classification App scored above average on all six subscales of the UEQ, though the benchmark comparison showed that the score on perspicuity, the quality of being discerning and comprehensible for future use, was below benchmark. Apparently, participants were not as confident the SID Pain App could stand the test of time in daily caregiving compared to other participants regarding similar products. Considering the fact that the two items with the most negative scores were ‘complicated/easy’ and ‘difficult/easy to learn’, it seemed that the complexity of the system was thought to influence long-term use in daily practice, which is something that was considered when co-designing the system and the visualisation with representatives of the targeted end-users. The results from this study make it clear that the complexity of the mobile application still needs to be taken into consideration when implementing the SID Pain App in practice.”

To examine whether the SID Pain App could be used for the intended target group, adults with a severe or profound intellectual disability, an observational study was conducted. During a scheduled physical therapy appointment, 14 participants with SID wore a smart sock which was connected to the SID Pain App. For each participant, videos were made of their face and their entire body, to be used to code their pain-related behaviour with two systematic pain observation scales: the Non-Communicating Adults Pain Checklist (NCAPC; Defrin, Lotan & Pick, 2006) and the Pain Observation Scale for Adults with Intellectual Disabilities (POSAID; Enninga et al., 2023).

When comparing the moment the SID Pain App signalled pain to a third pain behaviour from either of the pain observation scales, results showed that a signal from the Mobile App came six to eight seconds before a pain observation could be made. There were no differences between severity levels of experienced pain, according to the mobile app, between male and female participants, or between results from the pain observation scales. When looking at missing data, moments where the SID Pain App signalled pain, but no pain observation could be made, were equally divided among male and female participants and among pain severity levels.

This study showed that the SID Pain App can be used to measure physiological signals of pain in adults with a severe or profound intellectual disability, that a physiological signal from the Mobile App coincides with a pain observation in more than 80% of signals, and that the classification from the Mobile App based on physiological signals was significantly faster than a pain observation. This shows that a mobile app that classifies pain from the bodily responses of an adult with a severe or profound intellectual disability could be a helpful additional tool in daily caregiving. Since recognising pain is a challenge when caring for adults with a severe or profound intellectual disability, this study takes a step closer to timely identifying pain so that the underlying cause can be treated adequately.

8.2. Limitations and strengths

This project was started to develop a caregiving aid for classifying pain based on physiological signals of persons with a severe or profound intellectual disability with the following aims:

1) To evaluate several physiological pain detection methods on usability, invasiveness, and technological readiness;
2) To develop a reliable, valid, and specific physiological pain detection algorithm to be programmed into a mobile application;
3) To test this mobile pain detection application on adults with a severe or profound intellectual disability and to assess the user experience of the caregivers using the mobile application.

Several limitations and strengths can be put forward. Due to the limitations of the COVID-19 pandemic and consequent lockdown protocol, both the participants groups and the study procedures were altered. Participants who participated in the pain experiments consisted of a convenience sample of colleagues and their partners, family members and friends, instead of a random group of participants recruited via posters. The pain experiments were conducted keeping 1.5 meters distance, meaning that the researcher had less possibilities of helping participants and checking whether each participant wore their smart sock correctly. During the design study, questionnaires and focus groups were conducted online, which limited the full extent of information the researcher could gather. Possibilities for visiting caregivers and clients with a severe or profound intellectual disability at a group home were limited due to the danger of the COVID infection for clients, therefore just one workplace walk-through was conducted. Despite the alterations of plans in this project, none of these limitations led to any impossibility in reaching each of the research aims.

For this project, three national care organisations (Bartiméus, Cordaan, Ons Tweede Thuis) were partnered with the research group since its grant application. The constant involvement of these care organisations not only made sure that caregivers and parents of adults with a severe or profound intellectual disability were informed of the study and its process, but also created opportunities for the researchers to find enough representatives of end-users of the SID Pain App for each part of the project. Parents and caregivers not only welcomed participating in this project to help develop the SID Pain App, but also to make sure the app would be usable in daily caregiving. Since a lot of possible end-users had a personal or professional benefit from the results of this study, their participation was both serious and very committed.

Thanks to news releases on a national website for the cumulation and circulation of knowledge about people with disabilities (Kennisplein Gehandicaptensector), many more organisations not initially involved in the study showed their interest in being part in codesigning and/or testing the system. As soon as the SID Pain App was ready to be tested in the target group, adults with a severe or profound intellectual disability, the researchers could connect with these contacts to find enough clients who fit the inclusion criteria. And despite certain stringent criteria, such as low developmental age and regular physical therapy appointments, fourteen participants were found on which the SID Pain App was tested during their physical therapy session.

For the creation of the pain classification algorithm, we used data from 28 healthy adults who underwent one to five painful moments, while they self-reported their pain. Unfortunately, the model that came out as the best based on these data eventually was not as accurate, sensitive, and specific as desired. The model could reliably classify pain signals based on similar data, but not when new data were introduced. As this is not a useful result for persons with a severe or profound intellectual disability, since they cannot self-report their pain, some alternative modelling ideas are offered in chapter six.

Another possibility to improve the pain predicting algorithm is to not to look at the individual pain points, of which there were approximately 50 per second, but to look at the entire pain experience. These moments could last several seconds. If we would not consider each data point to be a pain datapoint, but instead consider 0.5 seconds or even 1 second of pain data one datapoint, this may improve the predictability of the algorithm. As we can see in the graphs provided of the pilot study in chapter 2, the physiological response to a pain stimulus is not just a deviation of skin conductance from baseline. The graph line jumps up and down in short intervals, making the response unique over a longer time span, but not necessarily per 1/50th of a second.

On the aspect of data analysis, the decision on what form of data to use for creating an AI-model was based on the machine learning program. This may not have been the best grounds to make that decision. Manual assessment of the data may have pointed to a different way to bundle data for machine learning. Since a painful moment does not give a clear-cut physiological response, but rather a quick succession of peaks and valleys, looking at averages could be the wrong approach, and the standard deviation should be considered as a primary data source for machine learning.

Additionally, this study makes use of quasi-experimental designs, and not the golden standard of social research: the randomised controlled trial. Participants were not randomised, researchers were not blinded, and the project’s goal made it necessary for researchers and therapists to know for which participant with a severe or profound intellectual disability pain was expected at which moments. When gathering data that could establish the ground truth, (i.e. when healthy adults without intellectual disability were included), the design was somewhat randomised. Though, since there were only four buckets of water, the submersion design varied between ABAB, BABA, ABBA, BAAB, AABB and BBAA. As the pain experiment progressed, participants could somewhat predict the order of submersions, thereby making it feasible that they were more prepared for the ice-cold water a second time, and their pain response may have been either less significant, or their anticipation of possible pain may have influenced their pain reaction.

Even though, the current SID Pain App does not yet work as intended, the results of this study show that a functional and user-friendly system to physiologically measure pain is feasible. The system makes use of fabric sensors in socks, to make the measurement as non-invasive as possible, and the Bluetooth connection to an application on a mobile device makes it wireless. If the mobile device is in the same space and within ten meters of the sensor unit, caregivers of adults with a severe or profound intellectual disability can use this system to assess their client's wellbeing.

8.3. Implications for research, practice, and design

This study does not stand alone. It has been built upon the work of many researchers that came before, those focusing on wearables, pain measurements, disability research and much more. Knowledge and theories brought out by peer-reviewed research have been vital to establish the foundation this project was built on. And just as the research described in this publication flows from established works, it has been carried out with the utmost care to be able to provide future researchers with a foundation to build upon.

As far as practical research is concerned, no other study has yet focused on developing and testing a physiological pain measurement system specifically validated for adults with severe or profound intellectual disability in daily situations. On that aspect, this project has tried to pave the way to provide a caregiving aid for physiological pain detection in the care for adults with a severe or profound intellectual disability, both improving their quality of life and lessening the uncertainty regarding the existence of pain for caregivers. Theoretically, this will improve caregiving, giving professional and family caregivers an early warning system for their client/charge's wellbeing, as well as some relief from worries accompanying caring for someone unable to clearly communicate.

This study builds further on research on wearables for medical purposes by introducing a group of wearers that is mostly unaware of the wearable. Since the wearer with a severe or profound intellectual disability cannot give informed consent, nor decide for themselves to wear or not wear a wearable, decisions were made by (professional) caregivers and medical personnel. Both for ethical purposes and just to make sure the wearable measures the right signals, a wearable for someone unable to communicate needs to be as non-invasive as possible. If a wearable device causes stress by itself, either due to its invasiveness or by being something different and new, using it to gather information about a client's wellbeing is nonsensical. The smart sock and mobile app introduced in this project serve the clients by being part of a regular occurrence – putting on socks – as well as being wireless and as non-invasive as possible.

For design, this project gives examples of user involvement in design phases that are based on necessity and opportunity. When is it necessary for the research to involve a vulnerable user group such as adults with a severe or profound intellectual disability and their caregivers, and when will just the caregiver's opinion be enough to get the input needed? Especially, considering a system that contains a wearable worn by the client with a severe or profound intellectual disability and a mobile app that will be used by their caregivers, involving vulnerable clients only during the project phases where the wearable is tested, and not when the mobile app and pain classification algorithm are being developed, protects them from overload. Furthermore, creating designs to be used in the workplace of caregivers will only be of practical use when designers are aware of the constraints a workplace can put on a caregiver's ability to work with a mobile app, such as background noise and attention span. Both end-user involvement and knowledge of workplace constraints will improve a product's practical and long-term use.

8.3.1. Lessons learned

The design, development and testing processes for this mobile pain application encountered substantial challenges, that are not addressed by current methodology. Most notably, designing for individuals with a severe or profound intellectual disability poses practical and ethical aspects that need to be conformed to fit the subject group's specific vulnerabilities. Furthermore, the interactive design methods used are unspecific for the inclusion of AI-technologies, specifically ensuring the integration of the AI system into existing workflows.

The ethical challenges of doing any type of collaborative research among participants that are vulnerable due to a severe or profound intellectual disability are summarised by Raskoff and colleagues (2023). They are divided into the following subjects: (A) collaborative partnership, (B) social or scientific value, (C) scientific validity, (D) fair participant selection, (E) favourable risk-benefit ratio, (F) independent review, and (G) informed consent. Each comes with ethical challenges and imperatives which will be separately discussed hereafter.

Forming a collaborative partnership with participants with a severe or profound intellectual disability (A) is challenging. Their restricted ability to speak and understand limits the possibilities to communicate with them. Though since they are going to be using, wearing, or becoming a recipient of a measurement system or a form of care, adjusting the eventual product to the specific needs of the target group increases its usability and perspicuity in health care. Therefore, adults with a severe or profound intellectual disability and their caregivers were involved in as many phases of the design, development, and testing of the SID Pain App, while also considering the confines of their time and attention level to invest in the project.

Hodson, Svandi, and Dadashi (2023) developed a map of engagement to show in which phase of a project the vulnerable target group was involved, and when and where proxies and secondary users were used. This map, filled out for the project of developing the SID Pain App, is shown in Table 8.1. When we consider adults with a severe or profound intellectual disability, the wearers of the smart sock, the primary users, this group was only involved in the final two phases of the project: the evaluation of prototypes (6) and the presentation of project deliveries (7). Secondary users and proxies, which are the professional caregivers, parents, behavioural therapists and physical therapists, the eventual users of the SID Pain App, were included in every project phase, from its problem and user definition (1) to the development (5), user testing (6) and final outcome (7) of the project.

TABLE 8.1. The Map of Engagement Template (Hodson, Svanda & Dadashi, 2023).

		Project phases						
		1. Problem and user definition	2. Pre-engagement	3. Problem redefinition	4. Design	5. Develop-ment	6. User testing	7. Final outcome
Stakeholder involvement	Design team and primary users						X	X
	Design team, proxies, and secondary users	X	X	X	X	X	X	X
	Design team only							

Note. The map of engagement covers seven design phases: (1) Conceptualisation of the project and user groups, background research, funding and ethnic proposals, (2) First contact and recruitment of users, (3) User engagement to focus project aims based on user needs and contexts, (4) Ideation with users to develop design concepts in response to needs identified in previous step, (5) Design development based on concepts generated in previous step, (6) Evaluation of prototypes by users leading to further refinement, (7) Presentation of project deliverables to service providers.

Once more returning to the ethical challenges described by Raskoff and colleagues, any study involving people with a severe or profound intellectual disability should have a high social and scientific value (B), such as research on interventions aimed at improving health, wellbeing, and quality of life. Considering the health inequities that are experienced by people with a severe or profound intellectual disability, leading to longer illness and greater risk of hospital stays, research on new diagnostic methods or treatments will have a great impact on the lives of this target group. This project fits that description, as the desired result is the creation of a physiological pain measurement system for a group unable to communicate about their pain. Reliable and timely pain signalling will lead to speedier recognition, treatment and conclusion of the illness of injury causing the pain, bringing about a safer environment, greater wellbeing and better quality of life for adults with a severe or profound intellectual disability.

The aspect of scientific validity (C) is important in any study, but more profoundly when involvement of a vulnerable group of people is a necessity for a project. When asking for considerations of caregivers with limited time and attention, and people with a severe or profound intellectual disability with limited understanding, scientific principles and methods should be solid to provide data that stands up to thorough scientific review. In the current project, every effort was made to adjust the research methods, so that the target group was protected, for example providing online design contributions during the COVID-19 lockdown and gathering pain data on the adults with severe or profound intellectual disabilities during a scheduled physical therapy appointment expecting pain moments that were not induced. Simultaneously, research methods and analyses were held to the highest standards and were reviewed by expert researchers as well as a medical-ethical review committee.

The involvement of an independent medical-ethical review committee covers another aspect of ethical challenges: the independent review (F). The research design, participant group and risk-benefit ratio should be assessed by those independent of the project. On the other hand, considering the specialised knowledge necessary to evaluate risk-benefit ratios of research on people with a severe or profound intellectual disability, the independent review committee would be advised to involve an expert on the target group. To the researchers of this project, the composition of the committee is not known at the time of review, but the organisation overseeing the independent review committees, the Central Committee on Research Involving Human Subjects, present guidelines on this aspect. Each application is examined by at least a legal expert, a medical expert and someone who represents the participant group. This would mean that an expert on people with a severe or profound intellectual disability was involved in the assessment of the design, participant group involvement, and risk-benefit ratio (E).

As in any study, fair participant selection (D) is an important aspect to consider, so that costs and benefits of research are not carried by one particular group or by two different groups. Preferable, research costs are carried by the participants that are the least vulnerable, for example experiments with induced pain are only carried out on participants able to give informed consent, while results and benefits of those pain experiments are enjoyed by all groups unable to communicate about their pain experience. For this project, the medical-ethical review committee thoroughly reviewed the study process and minimised the amount of vulnerable and other participants who could be involved in the pain research.

One of the most important aspects of conducting research on vulnerable subjects is getting informed consent (G). Adults with a severe or profound intellectual disability are considered incapable of making decisions about their own lives. Therefore, informed consent is gathered from a proxy, such as a parent or legal representative, and the participant with a severe or profound intellectual disability is informed as much as possible. For the legal representative asking to give consent, a comprehensive participant information packet was provided, containing information on the study design, study planning, data gathering, data storage, and manner to withdraw from the study. A flyer, provided by the government, on rights and responsibilities during medical research was also provided (Ministry of Health, Welfare and Sport, 2020). This way, the inability of getting informed consent of part of the participants included is ethically resolved.

Regarding the interaction design method, the double diamond process which was used in the design research for the SID Pain App provides a very generic framework. The integration of artificial intelligence (AI) in a health-related measurement comes with its own challenges, which can be tackled in the design and implementation phase, as described by Van Berkel and colleagues (2023). Their MAP-model covers an overview of the three stages of a system, the Measurement, Algorithm and Presentation, and the challenges for each of these stages. Table 8.2 covers all 13 challenges and whether they were sufficiently covered in this project.

While some of the described challenges have been met in this project, such as identifying valid measures to represent real-world (pain) data and communicating proxy variables to end-users in the measurement design, more attention should have been given to integrate a wider set of data sources on which to train the pain classification algorithm. The pain data that was used to train and test the Random Forest models came from one group of participants, who, in their mental and physical health, were quite dissimilar to the eventual wearers of the pain measurement sock. When we assess the validity and completeness of the data, we can conclude that a combination of pain data from both healthy participants with no intellectual disability and those with an intellectual disability and health problems would make for a more valid pain measurement system.

On the aspect of the AI-enabled algorithm, ensuring representative training data is difficult when the eventual system's users are vulnerable and cannot give informed consent. Representation could have been provided by gathering pain data from well-informed pain patients, who suffer from similar medical disorders as the adults with a severe or profound intellectual disability. On the other hand, the algorithm models provided were inspectable and adaptable, and computation used was relevant to the task at hand, for the computation was a necessity to get a working SID Pain App wanted by caregivers of adults with a severe and profound intellectual disability. Ensuring replicability and generalisability is crucial for the support and continued use of any product. Though replicability is somewhat ensured by the algorithm's reliability results, generalisability is not ensured as long as the algorithm needs similar data from one person to correctly classify new data from that one person.

The way pain data is presented in the SID Pain App is thoroughly research among end-users of the app, which means several challenges have been covered. The presentation has been adjusted to task context of the professional caregivers, by the workplace walkthroughs and the involvement of these end-user representatives in all the phases of design. The timeliness of the presentation is ensured by the speed of the skin conductance measurement and the simplicity of a classification algorithm. The computations that must be made are not very complex and can be done by a mobile device from up to ten years old. To ensure the interpretability of the results, the system does need a clear guideline, in which it will be stressed that team members need to collaborate to ensure they agree on whether the wearer of the smart sock is in actual pain, or perhaps highly stressed. Hopefully, this addition will then make sure that confirmation bias and automation complacency will be kept to a minimum during the use of the SID Pain App. While the SID Pain App will provide information on the wellbeing of an adult with a severe or profound intellectual disability, caregivers still need to base their subsequent actions on more than just a physiological measurement.

TABLE 8.2. The 13 challenges of the MAP model (Van Berkel et al., 2023) and whether these were sufficiently covered in this project.

Measurement challenges		Algorithm challenges		Presentation challenges	
MAP model	SID Pain App	MAP model	SID Pain App	MAP model	SID Pain App
Identifying valid measures to represent real-world phenomena.	✓	Ensuring representative training data.	/	Ensuring the interpretability of the results.	/
Integrating a wider set of data sources.	/	Providing inspectable and adaptable algorithms.	✓	Adjusting to task context.	✓
Assessing validity and completeness of the data.	/	Ensuring computation is relevant to the task at hand.	✓	Supporting collaboration between team members.	/
Communicating proxy variables to end-users.	✓	Ensuring replicability and generalisability.	/	Ensuring timeliness of presentation.	✓
				Minimising confirmation bias and automation complacency.	✗

Note: ✓ means this challenge is sufficiently met in this project, / means this challenge was partly covered, and ✗ means this challenge was not (yet) covered in this project.

8.4. Future plans

This dissertation describes a thorough process of design, development, and testing of a mobile physiological pain measurement system. Nevertheless, both improvements and expansions can be made to the existing system. This final part of the dissertation describes possible further steps to take to execute these adjustments to the SID Pain App and the smart sock system.

First, any system that provides real-time information of the health or wellbeing status of someone unable to communicate needs clear and simple guidelines for use. Especially if the interpretation of the physiological data is done by artificial intelligence, without the supervision of a medical expert, the guidelines should make sure that caregivers know to keep using their own knowledge and expertise on their clients or patients. In this project, these guidelines have not been established, and it will be necessary to create them in collaboration with the end-users, so guidelines and the way these are presented are adapted to the end-users needs and caregiving tasks.

Furthermore, on the side of application software, improvements need to be made to make the pain signalling system more sensitive and valid. The current pain classification algorithm is only sensitive and specific enough to be used in daily practice, if it can be trained on pain data from the person that is wearing the smart sock. It cannot classify a pain signal from 'new' data, which is preferred. Therefore, either the algorithm needs to be re-trained with more data, among which pain data from the participants in this study with a severe or profound intellectual disability and perhaps chronic pain patients, or perhaps new machine learning methods could be used to attempt to improve the validity of each pain classification. Chapter 6 of this dissertation provides some ideas for this next step.

FIGURE 8.1. The intermediate visualisation, to indicate GSR signs of heightened arousal.

Moreover, this system for pain detection is further developed from a similar system for detecting physiological signals of arousal in clients with a severe or profound intellectual disability. At the moment, two separate mobile applications receive input from a smart sock and Shimmer™ unit and display their results in separate ways. For many adults with a severe or profound intellectual disability in any caregiving situation, it would be desirable to combine these pain and arousal presentations in one mobile application, to provide their caregivers with more information about their wellbeing. It seems that a combination of the two apps could increase the system's usefulness in caregiving.

During the visualisation design process for the SID Pain App, the possibility of combining the codes of the two mobile apps has already been foreseen by creating an intermittent visualisation, between 'no pain' and 'pain, as shown in Figure 8.1, but since the pain measurement has been proven to be more complex than an arousal measurement, a simple combination may not be possible. Although parents and professional caregivers will undoubtedly welcome a mobile app that will provide them with information on both pain and arousal, the mobile app will need to keep the speed of measurement and clarity of presentation it has now. If that can be ensured, then such a mobile app will surely be a benefit to the lives and safety of adults with a severe or profound intellectual disability.

8.5. Conclusion

Within this project, researchers have (1) evaluated several physiological pain detection methods on usability, invasiveness, and technological readiness; (2) developed a physiological pain detection algorithm to be programmed into a mobile application, the SID Pain App; and (3) tested the SID Pain App on adults with a severe or profound intellectual disability and assessed the user experience of the caregivers using the SID Pain App. For Andy, who is described at the start of this dissertation, and his parents, this pain classification app has unfortunately come too late, but considering the many other children and adults unable to communicate about pain, who also suffer from painful medical disorders or run a higher risk of contracting infections, anything that will help them communicate pain to their caregivers will be welcomed.

What this project has contributed, is a collaborative design and development approach for a much-wanted caregiving aid, that is specifically adjusted to the needs and constraints of professional caregivers of adults with a severe or profound intellectual disability. Nevertheless, the SID Pain App can be embedded in the caregiving for any person unable to communicate about their pain, such as comatose patients, people with severe dementia, or pre-term neonates. The benefit of such a mobile app to the wellbeing and safety of those, who run a higher risk of medical disorders and are unable to clearly communicate about their pain, will be great. As for caregivers, for whom timely recognition of pain in their patients or clients is a challenge, providing them with an aid that will give them physiological information on top of their observations, the SID Pain App will hopefully alleviate some of their stress.

With any automatic measurement, especially when artificial intelligence is involved, it is important to have clear guidelines on how it should be used. Caregivers are and will always be the experts on the wellbeing of their client with a severe or profound intellectual disability. A pain classification algorithm will not change that, but it may enhance their observation skills and how caregivers will regard the behaviours they observe. If the SID Pain App provides caregivers of people with a severe or profound intellectual disability an aid for collaboration on observing pain behaviour, discussion of, and, hopefully, timely detection of pain, it will serve a great purpose.

Appendix A

References

Abu-Saad, H. H. (2000). Challenge of pain in the cognitively impaired, *The Lancet, 365*(9245), 1867-1868.

Aguilar Cordero, M. J., Mur Villar, N., & García García, I. (2015). Evaluation of pain in healthy newborns and in newborns with developmental problems (Down Syndrome), *Pain Management Nursing, 16*(3), 267-272. Doi: 10.1016/j.pmn.2014.08.001.

Altan, H., Çevik, H., Doğru, S., Coşgun, A., Süren, M., & Okan, I. (2019). The pain colour of children with toothache in Turkish population, *BMC Oral Health*, 19, 59-67. Doi: 10.1186/s12903-019-0756-y.

American Psychiatric Association. (2013). *Diagnostic and Statistical Manual of mental disorders (5th edition)*. Washington, DC: Author.

Arbour, C., & Gélinas, C. (2014). Behavioral and physiologic indicators of pain in nonverbal patients with a traumatic brain injury: an integrative review, *Pain Management Nursing, 15*(2), 506-518. Doi: 10.1016/j.pmm.2012.03.004.

Arts, W. F. M. (1999). Epilepsie. In H. Evenhuis & L. Nagtzaam (Eds.), *Wetenschap en geneeskunde voor mensen met een verstandelijke handicap: Een nieuw ontgonnen gebied in de nederlandse gezondheidszorg*. Den Haag. The Netherlands: NWO.

Atlas, L. Y., & Wager, T. D. (2012). How expectations shape pain. *Neuroscience Letters, 520*(2), 140-148. Doi: 10.1016/j.neulet.2012.03.039

Attridge, N., Noonan, D., Eccleston, C., & Keogh, E. (2015). The disruptive effects of pain on n-back task performance in a large general population sample, *Pain, 156*(10), 1865-1891. Doi: 10.1097/j.pain.0000000000000245.

Aslanidis, T., Grosomanidis, V., Karakoulas, K., & Chatzisotiriou, A. (2018). Electrodermal activity monitoring during painful stimulation in sedated adult intensive care unit patients: A pilot study, *Acta Medica, 61*(2), 47-52, Doi: 10.14712/18059694.2018.50.

Avila, Francisco R., et al., Wearable Electronic Devices for Chronic Pain Intensity Assessment: A Systematic Review. *Pain Practice* (2021).

Baeyer, C. L. von (2013). Self-report: the primary source in assessment after infancy. *Oxford Textbook of Pediatric Pain*, 1-21.

Baeyer, C. L. von, & Hicks, C. L. (2000). Support for a common metric for pediatric pain intensity scales, *Pain Research and Management, 5*, 157-160.

Baeyer, C. L. von, Piira, T., Chambers, C. T., Trapanotto, M., & Zeltzer, L. K. (2005). Guidelines for the cold pressor task as an experimental pain stimulus for use with children, *The Journal of Pain, 6*(4), 218-227. Doi: 10.1016/j.pain.2005.01.349.

Baldridge, K. H., & Andrasik, F. (2010). Pain assessment in people with intellectual or developmental disabilities. *American Journal of*

Nursing, 110, 28-35. Doi: 10.1097/01 NAJ.0000391236.68263.90.

Banathy, B. H. (1996). *Designing Social Systems in a Changing World.* Springer US. p. XV, 372. ISBN: 978-0-306-45251-2.

Banke, J. (2010). *Technology readiness levels demystified.* Retrieved on June 20th, 2019, from https://www.nasa.gov/topics/aeronautics/features/trl_demystified.html

Baranyi P., & Csapo A. (2012). Definition and Synergies of Cognitive Info-communications. *Acta Polytechnica Hungarica, 9*(1), pp. 67-83.

Basbaum, A. I., Bautista, D. M., Scherrer, G., & Julius, D. (2009). Cellular and molecular mechanisms of pain, *Cell, 139*(2), 267-284. Doi: 10.1016/j.cell. 2009.09.028.

Benoit, B., Martin-Misener, R., Newman, A., Latimer, M., & Campbell-Yeo, M. (2017). Neurophysiological assessment of acute pain in infants: A scoping review of research methods. *Acta Paediatrica, 106*, 1053-1066. Doi: 10.1111/apa.13839.

Benromano, T, Pick, C. G., Granovsky, Y., & Defrin, R. (2017). Increased invoked potentials and behavioural indices in response to pain among individuals with intellectual disability. *Pain Medicine, 18*(9), 1715-1730. Doi: 10.1093/pm/pnw349.

Bentley, L. D., Duarte, R. V., Furlong, P. L., Ashford, R. L., & Raphael, J. H. (2016). Brain activity modifications following spinal cord stimulation for chronic neuropathic pain: A systematic review, *European Journal of Pain, 20*, 499-511. Doi: 10.1002/ejp.782.

Berg, R. van den, Awh, E., & Ma, W. J. (2014). *Factorial comparison of working memory models, I*, 121(1), 124-149. Doi: 10.1037/a0035234.

Berkel, N. van, Bellio, M., Skov, M. B., & Blandford, A. (2023). Measurements, Algorithm, and presentations of reality: Framing interactions with AI-enabled decision support, *ACM Trans. Comput.-Hum. Interact. 30(2)*, Article 32 (March 2023), 33 pages. Doi: 10.1145/3571815.

Bessom, J. M. (1999). The neurobiology of pain, *The Lancet, May 08*; 353(9164), 1610-1615. Doi: 10.1016/s0140-6736(99)01313-6.

Biederman, J. J., & Schefft, B. K. (1994). Behavioral, physiological, and self-evaluative effects of anxiety on the self-control of pain, *Behav Modif, 18*, 89-105.

Bigby, C., Knox, M., Beadle-Brown, J., & Bould, E. (2014). Identifying good group homes: Qualitative indicators using a quality of life framework, *Intellectual and Developmental Disabilities, 52*(5), pp. 248-266, Doi: 10.1352/1934-9556-52.5.348.

Birx, H. J. (2006). *Encyclopedia of Anthropology*, Thousand Oaks, California, USA: Sage Publications Inc. Doi: 10.4135/9781412952453.

Böhmer, C. J., Niezen-de Boer, M. C., Klinkenberg-Knol, E., Devillé, W. L., Nadorp, J. H., & Meuwissen, S. G. (1999). The prevalence of gastroesophageal reflux disease in institutionalized intellectually disabled individuals. *The American Journal of Gastroenterology, 94*(3), 804–810. Doi: 10.1016/S0002-9270(98)00735-7.

Bonan, K. C. S. C., Pimentel Filho, J. C., Tristão, R. M., Lacerda de Jesus, J. A., & Campos Junior, D. (2014). Sleep deprivation, pain and prematurity: *A review study, Arquivos de Neuro-Psiquiatria, 73*(2), 147-154. Doi: 10.1590/0004-282x20140214.

Bonica, J. J. (1953). *The management of pain*. Philadelphia: Lea & Febiger.

Bowlby, J. (1973). *Attachment and loss*. Vol 2: *Separation*. London: Hogarth press

Bradley, M. M., & Lang, P. J. (1994). Measuring emotion: The self-assessment manikin and the semantic differential, *Journal of Behavioural Therapy and Experimental Psychiatry, 25*(1), 49-59.

Brand, A. E., Allen, L., Altman, M., Hlava, M. M. K., & Scott, J. (2015). Beyond authorship: Attribution, contribution, collaboration, and credit, *Learned Publishing, 28*(2), 151-155, Doi: 10.1087/20150211.

Breau, L. M., McGrath, P. J., & Zabalia, M. (2006). *Assessing pediatric pain and developmental disabilities*. In: Oberlander, T. F., & Symons, F. J. (Eds.), "Pain in children & adults with developmental disabilities" (pp. 49-72). Baltimore, MD: Paul H brooks publishing.

Bremmer, M., Croes, M., & Sterkenburg, P. (2014). *An arousal communication system for parents and their child with Prader-Willi syndrome: The development of a new system*. Leiden, The Netherlands: Prader-Willi Fonds.

Brodal, P. (2004). *The Central Nervous System: Structure and Function (3 ed.)*. Oxford University Press US. pp. 369–396. ISBN 0-19-516560-8.

Buchel, C. (2023). The role of expectations, control and reward in the development of pain persistence based on a unified model. *ELife, 12*, e81795, Doi: 10.7554/elife.81795.

Bughin, J. (2016). Big data, big bang?, *Journal of Big Data, 3*(2), 1-14. Doi: 10.1186/s40537-015-0014-3.

Burns, A., & Adeli, H., Wearable Technology for Patients with Brain and Spinal Cord Injuries, *Reviews in the Neurosciences, 28*(8), 2017, 913–920.

Cagnie, B., Coppetiers, I., Denecker, S., Six, J., Danneels, L., & Meeus, M. (2014). Central sensitization in fibromyalgia? *A systematic review on structural and functional brain MRI, Seminars in Arthritis and Rheumatism, 44*, 68-75. Doi: 10.1016/j.semarthrit.2014.01.001.

Calis, J. F. E. van, Bevelander, K. E., Cruijsen, A. W. C. van der, Leusink, G. L., & Naaldenberg, J. (2023). Toward inclusive approaches i n the design, development, and implementation of eHealth in the intellectual disability sector: Scoping review, *J Med Internet Res, 25*, p. e45819, Doi: 10.2196/45819.

Cardinali, D. P. (2018). *Autonomic Nervous System: basic and clinical aspects*. Cham: Springer.

Catani, M., Dell'Acqua, F., & Thiebaut De Schotten, M. (2013). A revised limbic system model for memory, emotion and behaviour. *Neuroscience and Biobehavioral Reviews, 37*(8), 1724–37. Doi: 10.1016/j.neurobiorev.2013.07.001.

Cello, 2022, *Wat is EMB?* Visited on July 4, 2022, via https://zorgprogrammas.cello-zorg.nl/emb/wat-is-emb/

Centraal Bureau voor de Statistiek (2019). *Werknemers met een Baan in de Zorg en Welzijn; persoonskenmerken, regio.* [Dataset]. Consulted on June 1st, 2020, via https://azwstatline.cbs.nl/#/AZW/nl/dataset/24016NED/table?ts=1589191622259.

Centrale Commissie Mensgebonden Onderzoek (1999, Jan 1), *Gedragscode verzet bij mensen met een verstandelijke handicap in het kader van de Wet Medisch-Wetenschappelijk Onderzoek met Mensen*, [online document], Available: https://www.ccmo.nl/binaries/ccmo/documenten/publicaties/1999/01/01/gedragscode-verzetbij-mensen-met-een-verstandelijke-handicap-Gedragscode+verzet+bij+mensen+met+een+verstandelijke+handicap.pdf

Chiarotto, A., Maxwell, L. J., Ostelo, R. W., Boers, M., Tugwell, P., & Terwee, C.B. (2019). Measurement properties of visual analogue scale, numeric rating scale, and pain severity subscale of the brief pain inventory in patients with low back pain: a systematic review, *The Journal of Pain, 20*(3), 245-263. Doi: 10.1016/j.jpain.2018.07.009

Chen, J., Abbod, M., & Shieh, J-S., (2021). Pain and stress detection using wearable sensors and devices—A review, *Sensors 21*(4), p. 1030.

Chen, J., Kandle, P. F., Murray, I. V., Fitzgerald, L. A. & Sehdev, J. S. (2023). Physiology, pain, *Statpearls*, last updated on July 24, 2023, Visited on March 23, 2024, via https://www.ncbi.nlm.nih.gov/books/NBK539789/

Chen, M., & Floridi, L. (2013). An analysis of information visualization, *Synthese, 190*, 3421-3438, Doi: 10.1007/s11229-012-0183-y.

Choon Wyn Lim, E., Steling, M., Stone, A., & Vincenzino, B. (2011). Central hyperexcitability as measured with nociceptive flexor reflex threshold in chronic musculoskeletal pain: A systematic review, *Pain, 152*, 1811-1820. Doi: 10.1016/j.pain.2011.03.033.

Clement, T., & Bigby, C. (2010). *Group Homes for People with Intellectual Disabilities: Encouraging Inclusion and Participation*, 1st Ed., London, Jessica Kingsley Publisher.

Coppetiers, I., Meeus, M., Kregel, J., Craeyenberghs, K., De Pauw, R., Goubert, D., & Cagnie, B. (2016). Relations between brain alterations and clinical pain measures in chronic musculoskeletal pain: a systematic review, *The Journal of Pain, 17*(9), 949-962. Doi: 10.1016/j.jpain.2016.04.005.

Cordier, L., & Diers, M. (2018). Learning and unlearning pain. *Biomedicins, 6*(2), 67. Doi: 10.3390/biomedicines6020067

Critical Appraisal Skills Programme (2018). *CASP Systematic Review Checklist*. [online] Accessed: July 1st, 2019 via https://casp-uk.net/casp-tools-checklists/.

Crombez, G., Eccleston, C., Baeyens, F., & Eelen, P. (1996). The disruptive nature of pain: An experimental investigation, *Behaviour Research and Therapy, 34*(11-12), 911-918. Doi: 10.1016/S0005-7967(96)00058-7.

Cronbach, L. J. (1951). Coefficient alpha and the internal structure of tests. *Psychometrika, 16*, 297-334.

Cuvertino, S., Stuart, H. M., Chandler, K. E., Roberts, N. A., Armstrong, R., Bernardini, L., Bhaskar, S., Callewaert, B., Clayton-Smith, J., Hernando Davalillo, C., Deshpande, C., Devriendt, K., Digilio, M. C., Dixit, A., Edwards, M., Friedman, J. M., Gonzalez-Meneses, A., Joss, S., Kerr, B., Lampe, A. K., Langlois, S., Lennon, R., Loget, P., Ma, D. Y. T., McGowan, R., Des Medt, M., O’Sullivan, J., Odent, S., Parker, M. J., Pebrel-Richard, C., Petit, F., Stark, Z., Stockler-Ipsiroglu, S., Tinschert, S., Vasudevan, P., Villa, O., Whitte, S. M., Zahir, F. R., The DDD Study, Woolf, A. S., & Banka, S. (2017). ACTB loss-of-function mutations: Result in a pleiotropic developmental disorder, *The American Journal of Human Genetics, 101*, 1021-1033. Doi: 10.1016/j.ajhg.2017.11.006

De Jonckheere, J., Bonhomme, V., Jeanne, M., Boselli, E., Gruenewald, M., Logier, R., & Richebé, P. (2015). Physiological signal processing for individualized anti-nociception management during general anaesthesia: A review, *IMIA Yearbook of Medical Informatics, 10*, 95-101. Doi: 10.15265/IY-2015-004.

De Knegt, N. C., Pieper, M. J. C., Lobbezoo, F., Schuengel, C., Evenhuis, H. M., Passchier, J., & Scherder, E. J. A. (2013). Behavioral pain indicators in people with intellectual disabilities: a systematic review, *The Journal of Pain, 14*(9), 885-896. Doi: 10.1016/j.jpain.2013.04.016.

De Knegt, N. C., Schuengel, C., Evenhuis, H. M., Lobbezoo, F., & Scherder, E. J. A. (2016). Apolipoprotein E ε4, cognitive function, and pain experience in Down Syndrome: A pilot study. *Archives of Clinical Neuropsychology, 31*, 389-400, Doi: 10.1093/arclin/acw022.

Defrin, R., Lotan, M., & Pick, C. G. (2006). The evaluation of acute pain in individuals with cognitive impairment: A differential effect of the level of impairment, *Pain, 124*(3), pp 312-320. Doi: 10.1016/j.pain.2006.04.031.

Defrin, R., Pick, C. G., Peretz, C., & Carmelli, E. (2004). A quantitative somatosensory testing of pain threshold in individuals with mental retardation, *Pain, 58*, 58-66. Doi: 10.1016/j.pain.2003.12.003.

Demiris G. (2006). *e-Health: current status and future trends*. In: Studies in health technology and informatics. Amsterdam: IOS Press.

Design Kit (2020). Design Kit by Ideo.org. San Francisco, USA, New York City, USA, Nairobi, Kenia. https://www.designkit.org/

Dewan, P. (2015). Words versus pictures: leveraging the research on visual communication. *Partnership: The Canadian Journal of Library and Information Practice and Research, 10*(1), 1-10, Doi: 10.21083/partnership.v10i1.3137.

Djajadiningrat, J. P., Gaver, W. W., & Frens, J. W. (2000). Interaction relabeling and extreme characters: Methods for exploring aesthetic interactions, *Proceedings of the 3rd Conference on Designing Interactive Systems: processes, practices, methods, and techniques*, Brooklyn, New York, p 66-71.

Doodeman, T. W. M., Schuengel, C., & Sterkenburg, P. S. (2021). Expressions of stress of people with severe intellectual disabilities and sensitive caregiving to regulate stress: A qualitative study. *Journal of Intellectual and Developmental Disability, 47*(4), 308 – 317. Doi: 10.3109/13668250.2021.2011171.

Doodeman, T. W. M., Schuengel, C., & Sterkenburg, P. S. (2023). Effects of the attune & stimulate-checklist for caregivers of people with severe and profound intellectual disabilities: A randomised controlled trial, *Journal of Applied Research in Intellectual Disabilities, 36*(5), 1136-1149. Doi: 10.1111/jar.13135.

Doody, O., & Bailey, M. E. (2006). Pain and pain assessment in people with intellectual disability: issues and challenges in practice, *British Journal of Learning Disabilities, 45*, 157-165. Doi: 10.1111/bld.12189.

Dorfman, T. L., Sumamo Schellenberg, E., Rempel, G. R., Scott, S. D., & Hartling, L. (2014). An evaluation of instruments for scoring physiological and behavioural cues of pain, non-pain related distress, and adequacy of analgesia and sedation in pediatric mechanical ventilated patients: A systematic review, *International Journal of Nursing Studies, 51*, 654-676. Doi: 10.1016/j.ijnurstu.2013.07.009.

Dubois, A., Capdevila, X., Bringuier, S., & Pry, R. (2010). Pain expression in children with an intellectual disability. *European Journal of Pain, 14*, 654-660. Doi: 10.1016/j.ejpain.2009.10.013.

Dutch Ministry of Health, Welfare and Sport, (2020). Medical Research. [Flyer]. Available via https://english.ccmo.nl/human-subjects.

Dutch Ministry of Health, Welfare and Sport, (2024a). *Regelhulp Verstandelijke Beperking*, [website]. Available: https://www.regelhulp.nl/onderwerpen/verstandelijke-beperking.

Dutch Ministry of Health, Welfare and Sport, (2024b). *Regelhulp Wet Langdurige Zorg: Hulpmiddelen*, [website]. Available: https://www.regelhulp.nl/onderwerpen/wlz/hulpmiddelen.

Dworkin, M. S., Park, L., Barringer, J., & Curtis, R. (2006). An outbreak of non-invasive group A streptococcal disease in a facility for developmentally disabled. *American Journal Infect Control, 34*, 296-300. Doi: 10.1016/j.ajic.2005.10.006.

Elliot, A. J. (2015) Colour and psychological functioning: a review of theoretical and empirical work, *Frontiers in Psychology, 6*, 1-8. Doi: 10.3389/fpsyg.2015.00368.

Enninga, A., Waninge, A., Post, W. J., & Putten, A. A. J. van der, (2023). Reliable assessment of pain behaviour in adults with profound intellectual and multiple disabilities: The development of an instruction protocol. *Journal of Applied Research in Intellectual Disability, 2023*, 1-11. DOI: 10.1111/jar.13089

Esteban, L., Navas, P., Verdugo, M. Á., & Arias, V. B. (2021). Community living, intellectual disability and extensive support needs: A r ights-based approach to assessment and intervention, *Int J Environ Res Public Health, 18*(6), p. 3175, Doi: 10.3390/ijerp18063175.

European Association of Research and Technology Organisations (2014). *The TRL scale as a research & innovation policy tool, EARTO recommendations*. Retrieved on April 24th 2019 from https://www.earto.eu/wp-content/uploads/The_TRL_Scale_as_a_R_I_Policy_Tool_-_EARTO_Recommendations_-_Final.pdf

European Pain Federation EFIC (2022). *EFIC Pain Research*, visited on 01 March 2023 via https://europeanpainfederation.eu/efic-pain-research/

Evenhuis, H. M. (2002). Want ik wil nog lang leven. *Moderne gezondheidszorg voor mensen met een verstandelijke beperking. [Because I want to live longer. Modern health care for people with a mental handicap]*.

Flora, S. R., Wilkerson, L. R., & Flora, D. B. (2003). Effects of cold pressor pain on human self-control for positive reinforcement, *Psychol Rec, 53*, 243-252, Doi: 10.1007/BF03395443.

Frederiks, K., Croes, M., Chen, W., Bambang Oetomo, S., & Sterkenburg, P. (2015). Sense — A biofeedback system to support the interaction between parents and their child with the Prader–Willi syndrome: A pilot study, *J. Ambient Intell. Smart Environ., 7*, 449–459. Doi: 10.3233/AIS-150327.

Frederiks, K., Sterkenburg, P., Barakova, E., & Feijs, L. (2019). The effects of a bioresponse system on the joint attention behavior of adults with visual and severe or profound intellectual disabilities and their affective mutuality with their caregivers, *J. Appl. Res. Intellect. Disabil. 32*(4), 890–900.

Garland, E. L. (2012) Pain processing in the human nervous system: a selective review of nociceptive and biobehavioral pathways. *Prim Care, 39*(3), 561-71. Doi: 10.1016/j.pop.2012.06.013

Gazdi, L., Pomazi, K. D., Radostyan, B., Forstner, B., & Szegletes, L. (2016). Experimenting with classifiers in biofeedback-based mental effort measurement, *7th IEEE International Conference on Cognitive Info-communications (CogInfoCom)*, Wroclaw, Poland. October 16-18, 2016.

Greenhalgh, T., Jackson, C., Shaw, S., & Janamian, T. (2016). Achieving research impact through co-creation in community-based health services: literature review and case study, *The Milbank Quarterly, Vol. 94*(2), 392-429. Doi: 10.1111/1468-0009.12197.

Godden, J. O., Roth, G. M., & Hines, E. A. (1955). The changes in the intra-arterial pressure during immersion of the hand in ice-cold water, *Circulation, Volume XII*, p. 963-973.

Gonzalez-Polledo, E., Cornish, F., & Tarr, J. (2015). Making chronic pain matter – How can qualitative research shape the conversation, *BMJ open, 5*(4), A4. Doi: 10.1136/bmjopen-2015-UCLSymposiumAbstracts.10

Gooberman-Hill, R., Woolhead, G., MacKichan, F., Ayis, S., Williams, S., & Dieppe, P. (2007). Assessing chronic joint pain: Lessons from a focus group study, *Arthritis & Rheumatism (Arthritis Care & Research), 57*(4), 666-671. Doi: 10.1002/art.22681.

Griffiths, C., & Smith, M. (2016). Attuning: A communication process between people with severe and profound intellectual disability and their interaction partners, *Journal of Applied Research in Intellectual Disabilities, 29*, 124-138. Doi: 10.1111/jar.12162.

Grossi, E., Borghi, E. L., Cerchiari, T., Della Puppa, T., & Francucci, B. (1983). Analogue chromatic continuous scale (ACCS): a new method for pain assessment, *Clinical and Experimental Rheumatology, 1*, 337-340.

Günther, A. (2016). *Skin conductance variability and stressful exposures in critical care*. Stockholm, Sweden: Karolinska Institutet, 2016.

HandicapNL, 2022, *Wat is een ernstig meervoudige beperking?* Visited on July 4, 2022, via https://handicap.nl/wat-is-een-ernstig-meervoudige-beperking-emb/

Hassanpour, A., Moradikia, M., Adeli, H., Khayami, S. R., & Shamsinejad, P. (2019), A Novel End-to-End Deep Learning Scheme For Classifying Multiclass Motor Imagery EEG Signals, *Expert Systems, 2019 36*(6), Doi: 10.1111/exsy.12494.

Hatfield, L. A., & Ely, E. A. (2015). Measurement of acute pain in infants: A review of behavioural and physiological variables, *Biological Research for Nursing, 17*(1), 100-111. Doi: 10.1177/1099800414531448.

Heales, L. J., Bergin, M. J. G., Vicenzino, B., & Hodges, P. W. (2016). Forearm muscle activity in lateral epicondylalgia: A systematic review with quantitative analysis, *Sports Medicine, 46*, 1833-

1845. Doi: 10.1007/s40179-016-0539-4.

Hecke, O. van, Kamerman, P. R., Attal, N., Baron, R., Bjornsdottir, G., Bennett, D. L. H., Bennett, M. I., Bouhassira, D., Diatchenko, L., Freeman, R., Freynhagen, R., Haanpää, M., Jensen, T. S., Raja, S. N., Rice, A. S. C., Seltzer, Z., Thorgeirsson, T. E., Yarnitsky, D., & Smith, B. H. (2015). Neuropathic pain phenotyping by international consensus (NeuroPPIC) for genetic studies: A NeuroPSIG systematic review, Delphi study and expert panel recommendations, *Pain, 156*, 2337-2353. Doi: 10.1097/j.pain.0000000000000335.

‘s Heerenloo, 2022, *Ernstig Meervoudig Beperkt*, visited on July 4, 2022, via https://www.sheerenloo.nl/kennis-en-onderzoek/voor-wie-zijn-we-er/emb-ernstig-meervoudig-beperkt

Henry, D. E., Chiodo, A. E., & Yang, W. (2011). Central nervous system reorganization in a variety of chronic pain states: *A review. Journal of Physical Medicine and Rehabilitation, 3*, 1116-1125. Doi: 10.1016/j.pmrj.2011.05.018.

Herr, K., Coyne, P. J., Manworren, R., McCaffery, M., Merkel, S., Pelosi-Kelly, J., & Wild, L. (2006). Pain assessment in the nonverbal patient: position statement with clinical practice recommendations. *Pain Management Nursing, 7*, 44-51. Doi: 10.1016/j.pmn.2006.02.003.

Heslop, P., & Houghton, M. (2019). *Mortality in people with intellectual disability*. In: Seminars in the Psychiatry of Intellectual Disability. Mark Scheepers, Mike Kerr, Eds. Cambridge, England: Cambridge University Press, 31 January 2019.

Hicks, C. L., Baeyer, C. L. von, Spafford, P. A., Korlaar, I. van, & Goodenough, B. (2001). The Faces Pain Scale-Revised: toward a common metric in pediatric pain measurement, *Pain, 2001 Aug; 93*(2), 173-183. Doi: 10.1016/S0304-3959(01)00314-1.

Ho, T. K. (1995). Random decision forests. *Proceedings of the 3rd International Conference on Document Analysis and Recognition*, Montréal, QC, 14 – 16 August. Pp. 278-282.

Hodson, E., Svanda, A., & Dadashi, N. (2023). Whom do we include and when? Participatory design with vulnerable groups, *CoDesign, 19*(4), 269-286, Doi: 10.1080/15710882.2022.2160464.

Houghton, A. R., & Gray, D. (2012). *Making sense of the ECG, Third edition*, Glasgow, UK: Hodder Education. ISBN: 978-1-4441-6654-5.

Huang, M.-H., & Rust, R. T. (2017). Technology-driven service strategy, *Journal of the Academy of Marketing Science, 45*(6), 906-924. Doi: 10.1007/s11747-017-0545-6.

Interagency Pain Research Coordinating Committee IPRCC, (2019). Pain Research Advances, visited on 01 March 2023 via https://www.iprcc.nih.gov/node/2/2019- pain-research-advances

International Association for the Study of Pain, 2020, *IASP Announces*

Revised Definition of Pain, [news]. Published online on 16 July 2020, last visited on 25 March 2024. Available: https://www.iasp-pain.org/publications/iasp-news/iasp-announces-revised-definition-of-pain/ (IASP) (iasp-pain.org)

International Association for the Study of Pain, 2021, *Pain in individuals with an intellectual disability: Scope of the problem and assessment challenges*, [factsheet]. Published online 9 July 2021, last visited on 25 March 2024 via https://www.iasp-pain.org/resources/fact-sheets/pain-in-individuals-with-an-intellectual-disability-scope-of-the-problem-and-assessment-challenges/

International Association for the Study of Pain, 2021, *Learn more about acute pain*, published online in 2021, last visited on 25 March 2024 via https://www.iasp-pain.org/resources/topics/acute-pain/

ISO 9241-11: 2018. “ISO 9241-11:2018(En), *Ergonomics of Human-System Interaction — Part 11: Usability: Definitions and Concepts*. Accessed February 21, 2023 via https://www.iso.org/obp/ui/#iso:std:iso:9241:-11:ed-2:v1:en.

Izsó, L. (2015). The significance of cognitive infocommunication in developing assistive technologies for people with non-standard cognitive characteristics: CogInfoCom for people with non-standard cognitive characteristics, *6th IEEE International Conference for Cognitive Info-communciations (CogInfoCom), Györ,* Hungary, 19-21 October, 2015.

Jackson, D., Horn, S., Kersten, P., & Turner-Stokes, L. (2007). Development of a pictorial scale of pain intensity for patients with communication impairments: initial validation in a general population, *Clinical Medicine, 6*(6), 580-585. DOI: 10.7861/clinmedicine.6-6-580

Jansen, S. L. G., Putten, A. A. J. van der, & Vlaskamp, C. (2013). What parents find important in the support of a child with profound intellectual and multiple disabilities. *Child: care, health and development, 39*(3), 432-441.

Janssen, C. G. C., Schuengel, C., & Stolk, J. (2002). Understanding challenging behaviour in people with severe and profound intellectual disability: A stress-attachment model. *Journal of Intellectual Disability Research, 46*(6), 445–453. Doi: 10.1046/j.1365-2788.2002.00430.x.

Jensen M. P., Karoly P., & Braver S. (1986). The measurement of clinical pain intensity: a comparison of six methods. *Pain, 27*(1), 117–126. Doi: 10.1016/0304-3959(86)90228-9.

Katona, J., & Kovari, A. (2018). The evaluation of BCI and PEBL-based attention tests, *Acta Polytechnica Hungaria, 15*(3), 225 – 249.

Kennisplein Gehandicaptensector, 2021, Gehandicaptenzorg ZEVMB, visited on July 4, 2022, via https://www.kennispleingehandicaptensector.nl/ernstige-meervoudige-beperkingen-gehandicaptenzorg-zevmb

Kaur, M., Gianey, H. K., Singh, D., & Sabharwal, M. (2019). Multi-objective differential evolution based random forest for e-health applications, *Mod. Phys. Lett. 33*(05), Doi: 10.1142/S02179849500222.

Kim, J., Campbell, A. S., Esteban-Fernández de Ávila, B., & Wang, J. (2019). Wearable biosensors for healthcare monitoring, *Nature Biotechnology, 37*, 389-406. Doi: 10.1038/s41587-019-0045-y.

Knudsen, L. F., Terkelsen, A. J., Drummond, P. D., & Birklein, F. (2019). Complex regional pain syndrome: A focus on the autonomic nervous system, *Clin. Auton. Res. 29*(4), 457–467, Doi:10.1007/s10286-019-00612-0.

Kochanowska, M., & Weronika R. G. The Double Diamond Model: In Pursuit of Simplicity and Flexibility. *Perspectives on Design II*. Springer, Cham, 2022. 19-32.

Koenig, J., Falvay, D., Clamor, A., Wagner, J., Jarczok, M. N., Ellis, R. J., Weber, C., & Thayer, J. F. (2016). Pneumogastric (vagus) nerve activity indexed by heart rate variability in chronic pain patients compared to healthy controls: A systematic review and meta-analysis. *Pain Physician, 19*, E55-E78. PMID: 26752494.

Koenig, J., Jarczok, M. N., Ellis, R. J., Hillecke, T. K., & Thayer, J. F. (2014). Heart rate variability and experimentally induced pain in healthy adults: A systematic review. *European Journal of Pain, 18*, 301-314. Doi: 10.1002/j.1532-2149.2013.00379.x.

Korving, H., Enninga, A., Huisman, S., Waninge, A., Van der Putten, A. & Sterkenburg, P. (2021). Signaleren van pijn bij mensen met een (zeer) ernstige verstandelijke beperking, *Tijdschrift voor Artsen van Verstandelijk Gehandicapten, jaargang 93, September, nummer 3*, 168-175.

Kotler, P., Kartajaya, H., & Setiawan, I. (2010). *Marketing 3.0: From products to customers to the human spirit*. John Wiley and Sons, 2010.

Kreukniet, E., Bruns, A., & Putten, A. van der, (2016). *Pain observation scale for adults with intellectual disabilities Instructiekaart*, 's Heerenloo Zorggroep.

Kruithof, K., Willems, D., Etten-Jamaludin, F. van, & Olsman, E. (2020). Parent's knowledge of their child with profound intellectual and multiple disabilities: An interpretative synthesis. *Journal of Applied Research on Intellectual Disabilities, 1-10*, Doi:110.1111/jar.12740.

Kyle, B. N., & McNeil, D. W. (2014). Autonomic arousal and experimentally induced pain: a critical review of the literature, *Pain Research and Management, 19*(3), 159-167. Doi: 10.1155/2014/536859.

Lakens, D. (2017). Equivalence tests: A practical primer for t tests, correlations, and meta-analyses, *Soc Psychol Personal Sci, 8*(4), pp. 355-362, Doi: 10.1177/1948550617697177.

Lalloo, C., Stinson, J. N., Brown, S. C., Campbell, F., Isaac, L., & Henry, J. L. (2014). Pain-QuILT Assessing clinical feasibility of a web-based tool for the visual self-report of pain in an interdisciplinary pediatric chronic pain clinic, *Clinical Journal of Pain, 30*(11), 934-943. Doi: 10.1097/AJP.0000000000000049.

Laugwitz, B., Held, T., & Schrepp, M. (2008). *Construction and evaluation of a user experience questionnaire*. In: Holzinger, A. (Ed.): USAB 2008, LNCS 5298, pp. 63-76. Doi: 10.1007/978-3-89350-9_6.

Lemaître, G., Nogueira, F., & Aridas, C. K. (2017). Imbalanced-learn: A python toolbox to tackle the curse of imbalanced datasets in machine learning. *The Journal of Machine Learning Research, 18*(1), 559-563.

Linton, S. J., & Shaw, W. S. (2011). Impact of psychological factors in the experience of pain, *Physical Therapy, 91*(5), 700-711. Doi: 10.2522/ptj.20100330

Loeser, J. D. (1980). Perspectives on Pain, *Proceedings of First World Conference in Clinical Pharmacology and Therapeutics London*: MacMillan Publishers Ltd. 1980.

Loeser, J. D., & Melzack, R. (1999). Pain: an overview. *Lancet, 1999 May 08*, 353(9164), 1607-1609. Doi: 10.1016/S0140-6736(99)01311-2.

Lootens, C. C., & Rapoff, M. A. (2011). Measures of pediatric pain, *Arthritis Care & Research, 63* (11), S253-S262. Doi: 10.1002/acr.20634.

Lor, M., Vang, X., Ragabo, D., Brown, R., & Backonja, M. (2019). It hurts as if: Pain language, visual characterization and story-telling in Hmong older adults, *Pain Medicine, 0*(0), 1-13. Doi: 10.1093/pm/pnz268.

Lotan, M., Ljunggren, E. A., Johnsen, T. B., Defrin, R., Pick, C. G., & Strand, L. I., (2009a). A modified version of the Non-Communicating Children Pain Checklist-Revised, adapted to adults with intellectual and developmental disabilities: Sensitivity to pain and internal consistency, *The Journal of Pain, 10*(4), pp. 398-407. Doi: 10.1016/j.jpain.2008.09.006.

Lotan, M., Moe-Nilssen, R., Ljunggren A. E., & Strand, L. I., (2009b). Reliability of the Non-Communicating Adult Pain Checklist (NCAPC), assessed by different groups of health workers, *Research in Developmental Disabilities, 30*, pp. 735-745. Doi: 10.1016/j.ridd.2008.10.005.

Machata, A. M., Kabon, B., Willschke, H., Fäßler, K., Gustorff, B., Marhofer, P., & Curatolo, M. (2009). A new instrument for pain assessment in de immediate postoperative period, *Anaesthesia, 64*, 392-398. Doi: 10.1111/j.1365-2044.2008.05798.x.

Maehara, Y., & Saito, S. (2007). The relationship between processing and storage in working memory span: Not two sides of the same coin, *Journal of Memory and Language, 56*(2), 212-228. Doi: 10.1016j.jml.2006.07.009.

Manocha, S., & Taneja, N. (2016). Assessment of pediatric pain: a critical review, *Journal of Basic Clinical Physiological Pharmacology, 27*(4), 323-331. Doi: 10.1515/jbcpp-2015-0041.

Martinez Mozos, O., Sandulescu, V., Andrews, S., Ellis, D., Bellotto, N., Dobrescu, R., & Ferrandez J. M. (2016). Stress detection using wearable physiological and sociometric sensors. *International Journal of Neural Systems, 27*(02), Doi: 10.1142/S0129065716500416.

McCaffery M. (1968). *Nursing practice theories related to cognition, bodily pain, and man-environment interactions*. Los Angeles: UCLA Students Store.

McCaffery, M., Herr, K., & Pasero, C. (2011). Assessment tools. *Pain assessment and pharmacologic management. 1st ed*. St. Louis: Mosby Elsevier, 55.

McGrath, P. A., Seifert, C. E., Speechley, K. N., Booth, J. C., Stitt, L., & Gibson, M. C. (1996). A new analogue scale for assessing children’s pain. An initial validation study, *Pain, 64*, 435-443. SSDI: 0304-3959(95)00171-9.

McGuire, B. E., Daly, P., & Smyth, F. (2010). Chronic pain among people with an intellectual disability: Under-recognized and under-treated, *Journal of Intellectual Disability Research, 54*(3), 240-245. Doi: 10.1111/j.1365-2788.2010.01254.x.

MedlinePlus [Internet]. Bethesda (MD): National Library of Medicine (US); [updated 2020 Jun 24]. *Mucopolysaccharidosis type III*; [updated 2020 Nov 7; reviewed 2024 March 25; cited 2024 March 25]; [about 3 p.]. Available from: https://medlineplus.gov/genetics/condition/mucopolysaccharidosis-type-iii/

Meeus, M., Goubert, D., De Backer, F., Struyf, F., Hermans, L., Coppetiers, I., De Wandele, I., Da Silva, H., & Calders, P. (2013). Heart rate variability in patients with fibromyalgia and patients with chronic fatigue syndrome: A systematic review, *Seminars in Arthritis and Rheumatism, 43*, 279-287. Doi: 10.1016/j.semarthrit.2013.03.004.

Melzak, R. (1961). The perception of pain. *Scientific American, 204*(2), 41-49.

Mencap. (2013). *Death by indifference*. London: Mencap.

Merkel, S., Voepel-Lewis, T., Shayevitz, J. R., & Malviya, S. The FLACC: A behavioral scale for scoring postoperative pain in young children, 1997, *Pediatr Nurse 23*(3), 293-297.

Merskey, H., & Bogduk, N. (Eds.). (1994). *Classification of chronic pain. Descriptions of chronic pain syndromes and definitions of pain terms* (2nd ed., p. xi). Seattle: IASP Press.

Mihaly, H. (2017). From NASA to EU: the evolution of the TRL scale in public sector innovation. *The Innovation Journal, 22*, 1-23.

Millard, S. K., & De Knegt, N. C. (2019). Cancer pain in people with intellectual disabilities: systematic review and survey of health care professionals. *Journal of Pain and Symptom Management, 58*(6), 1081-1099.e3. Doi: 10.1016/j.jpainsymman.2019.07.013.

Mills, P., (2011). "Efficient statistical classification of satellite measurements". *International Journal of Remote Sensing. 32*(21), 6109–6132. Doi: 10.1080/01431161.2010.507795.

Mitchell, L. A., MacDonald, R. A. R., & Brodie, E. E. (2004). Temperature and the cold pressor test, *The Journal of Pain, 5*(4), 233-238. Doi: 10.1016/j.pain.2004.03.004.

Moher, D., Liberati, A., Tetzlaff, J., Altman, D.G., & The PRISMA Group (2009). Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement, *PLoS Med 6(7)*, e1000097. DOI: 10.1371/journal.pmed.1000097.

Morris, J. D. (1995). Observations: SAM: The self-assessment Manikin. An efficient cross-cultural measurement of emotional response. *Journal of advertising Research, 35*(6), 63-68.

Morrison, I., Perini, I., & Dunham, J. (2013). Facets and mechanisms of adaptive pain behavior: predictive regulation and action, *Front Hum Neurosci, 7*, 755. Doi: 10.3389/fnhum.2013.00755

Moulster, G. (2020). Identifying pain in people who have complex communication needs. *Clin. Pract. Rev. Learn. Disabil, 116*, 19-22.

Nakken, H., & Vlaskamp, C. (2007). A need for a taxonomy for profound intellectual and multiple disabilities. *Journal of Policy and Practice in Intellectual Disabilities, 4*(2), 83–87. Doi: 10.1111/j.1741-1130.2007.00104.x.

Naresh, V., & Lee, N. (2021, Feb). A review on biosensors and recent development of nanostructured materials-enabled biosensors, *Sensors (Basel), 21*(4), 1109. Doi: 10.3390/s21041109.

National Institutes of Health, 2023. *Pain: considering complementary approaches*, National Centre for Complementary and Integrative Health. US Department of Health & Human Services.

National Institute for Public Health and the Environment, 2022, visited on July 4, 2022, via https://vzinfo.nl/verstandelijke-beperking/verantwoording/definities

Nay, R., & Fetherstonhaugh, D. (2012). What is pain/ A phenomenological approach to understanding, *International Journal of Older People Nursing, 7*(3), 233-239. Doi: 10.1111/j.1748-3743.2012.00329.x.

Noldus, (2024), *Ideal integration platform The Observer XT*, [website] Available: https://www.noldus.com/observer-xt/

Novak P. (2019). Electrochemical skin conductance: a systematic review. *Clinical Autonomic Research. Feb, 29*(1), 17-29.

O'Flynn, B., & Tedesco, S. (2021). Wearable Textile-Based Device for Human Lower-Limbs Kinematics and Muscle Activity Sensing In *Wearables in Healthcare: Second EAI International*

Conference, HealthWear 2020, Virtual Event, December 10–11, 2020, Proceedings (p. 70). Springer Nature.

O’Leary, H. M., Marschik, P. B., Khwaja, O. S., Ho, E., Barnes, K. V., Clarkson, T. W., Bruck, N. M., & Kaufmann, W. E. (2015). Detecting autonomic response to pain in Rett syndrome, *Developmental Neuro-rehabilitation, 20*(2), 108-114. Doi: 10.3109/17518423.2015.1087437.

Osgood, C. E., Suci, C. J., & Tannenbaum, P. H. (1957). *The Measurement of Meaning*. University of Illinois Press: Urbana, Illinois, USA.

Owlet Care: http://dream.owletcare.com, visited on 14-12-2021.

Palisano, R., Rosenbaum, P., Walter, S., Russell, D., Wood E., & Galuppi, B. (1997). Development and reliability of a system to classify gross motor function in children with cerebral palsy, *Developmental Medicine and Child Neurology, 39*(4), pp. 214-223, Doi: 10.1111/j.1469-8749.1997.tb07414.x.

Palmer, S. E., & Schloss, K. B. (2010). An ecological valence theory of human colour –preference, *Proceedings of the National Academy of Sciences, 107*(19), 8877-8882. Doi: 10.1073/pnas.0906172107.

Parker, R.S., Lewis, G.N., Rice, D.A., & McNair, P.J. (2016). Is motor cortical excitability altered in people with chronic pain? A systematic review and meta-analysis, *Brain Stimulation, 9*, 488-500. Doi: 10.1016/j.brs.2016.03.020.

Pi Sunyer F. X., Becker D. M., Bouchard C., et al., (1998). Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults: executive summary. *American Journal of Clinical Nutrition, 68*, 899-917.

Podzemny, V., Pescatori, L. C., & Pescatori, M. (2015). Management of obstructed defecation, *World Journal of Gastroenterology, 21*(4), 1053-1060. Doi: 10.3748/wjg.v21.i4.1053.

Poppes, P., Putten, A. J. J. van der, & Vlaskamp, C. (2010). Frequency and severity of challenging behaviour in people with profound intellectual and multiple disabilities. *Research in developmental disabilities, 31*(6), 1269-1275. Doi: 10.1016/j.ridd.2010.07.017.

Prahalad, C. K., & Ramaswamy, V. (2000). Co-opting customers competence. *Harvard Business Review, 78*(1), 79-90.

Price, D. D., Barrell, J. J., & Rainville, P. (2002). Integrating experiential–phenomenological methods and neuroscience to study neural mechanisms of pain and consciousness. *Consciousness and Cognition, 11*(4), 593-608.

Pudas-Täkhä, S-M., Axelin, A., Aantaa, R., Lund, V., & Salanterä, S. (2008). Pain assessment tools for unconscious or sedated intensive care patients: A systematic review. Journal of Advanced Nursing, 65(5), 946-956, Doi: 10.1111/j.1365-2648.2008.04947.x.

Putten, A. van der, & Vlaskamp, C. (2010. Pain assessment in people with profound intellectual and multiple disabilities: a pilot study into the use of the Pain Behaviour Checklist in everyday practice, *Research in Developmental Disabilities, 32*, 1677 – 1684, DOI: 10.1016/j.ridd.2011.02.020.

Qualtrics (company name and development company). First release: 2005. Copyright Year: 2020. Location: Provo, Utah, USA, Version: XM, January 2020, available at https://www.qualtrics.com/

Racine, M., Tousignant-LaFlamme, Y., Kloda, L.A.Dion, D., Dupuis, G., & Choinière, M. (2011). A systematic literature review of ten years of research of sex/gender and experimental pain perception – Part 1: Are there really differences between women and men, *Pain, 153*, p. 602-618. Doi: 10.1016/j.pain.2011.11.025.

Raeside, L. (2011). Physiological measures of assessing infant pain: a literature review, *British Journal of Nursing, 20*(21), 1370-1376. Doi: 10.12968/bjon.2011.20.21.1370.

Raghavendra, U., Acharya, U. R., & Adeli, H. (2020), Artificial intelligence techniques for automated diagnosis of neurological disorders, *European Neurology, 82*, 1-3.

Rao Veeranki, Y., Ganapathy, N., & Swaminathan, R. (2021). *Fluctuation and Noise Letters*, Doi: 10.1142/S0219477522500134.

Raskoff, S. Z., Thurm, A., Miguel, H. O., Kim, S. Y. H., & Querzado, Z. M. N. (2022). Pain research in children and adolescents with severe intellectual disability: ethical challenges and imperatives, *Lancet Child Adolesc Health, 7*(4), 288-296, Doi: 10.1016/S2352-4642(22)00346-7.

Relland, L.M., Gehred, A., & Maitre, N.L. (2019). Physiological signs for pain assessment in preterm neonates during a nociception-specific response: A systematic review, *Pediatric Neurology, 90*, 13-23. DOI: 10.1016/j.pediatrneurol.2018.10.001.

Road2Results, Agile Value Proposition Tower, accessed on March 12, 2020 via https://road2results.nl/agile-customer-value-proposition-development (link has since been updated: https://road2results.nl/value-proposition).

Rodriguez, M. M. (2014). Congenital anomalies of the kidney and the urinary tract (CAKUT). *Fetal and Pediatric Pathology, 33*(5-6), 293-320. Doi: 10.3109/15513815.2014.959678.

Roulin, M-J., & Ramelet, A-S. (2012). Pain indicators in brain-injured critical care adults: an integrative review, *Australian Critical Care, 25*, 110-118. Doi: 10.1016/j.aucc.2011.10.002.

Roy, A., & Simon, G. B. (1987). Intestinal obstruction as a cause of death in the mentally handicapped, *Journal of Intellectual Disability, 31*(2), 193-197. Doi: 10.1111/j.1365-2788.1987.tb01355.x.

Sánchez-Reolid, R., Martínez-Rodrigo, A., López, M. T., & Fernández-Caballero, A. (2020). Deep support vector machines for the identification of stress condition from electrodermal activity, Int.

J. Neural Syst. 30(7). Doi:10.1142/S0129065720500318.

Schieve L. A., Gonzalez V., Boulet S. L., et al. (2012). Concurrent medical conditions and health care use and needs among children with learning and behavioral developmental disabilities, National Health Interview Survey, 2006–2010. *Res Dev Disabil, 33*, 467–76.

Schmidt, J., & Martin, A. (2017). Hertzratenvariabilitäts-Biofeedback in der klinischen Praxis. Grundlagen, Anwendung und Evidenz auf Basis eines systematischen Reviews, *Psychotherapeut, 62*, 498-506. Doi: 10.1007/s00278-017-0236-2.

Schneider, W. L., & Severn, M. (2018). Prevention of plantar ulcers in people with diabetic peripheral neuropathy using pressure-sensing shoe insoles. www.imedicalapps.com

Schrojestein Lantman-de Valk, H. M. J. van, & Noonan Walsh, P. (2008). Managing health problems in people with intellectual disabilities, *BMJ, 337*, a2507. Doi: 10.1136/bmj.a2507.

Skoss, R., Chivers, P., Arendts, G., Bulsara, C., Vithiatharan, R., & Codde, J. (2024). What supports are people with intellectual disability living in group homes provided to access health care? A case study, *British Journal of Learning Disabilities*, pp. 1-13, Doi: 10.1111/bld.12601.

Slifer, K. J., Hankinson, J. C., Zettler, M. A., Frutchey, R. A., Hendricks, M. C., Ward, C. M., & Reesman, J. (2011). Distraction, exposure therapy, counterconditioning and topical anesthetic for acute pain management during needle sticks in children with intellectual and developmental disabilities, *Clinical Pediatrics, 50*(8), pp. 688-697, Doi: 10.1177/0009922811398959.

Stappers, P. J. (2007). *Doing research as part of doing research*. In: Michel, R. (Ed.), *Design research now: essays and selected projects.* Basel: Birkhäuser, 81-91.

Stappers, P. J., & Giaccardi, E. (2012). Research through design. In: Bowman, D. A. (Ed.) *The encyclopedia of human-computer interaction, 2nd Edition*. Online: Interaction Design Foundation.

Statistics Netherlands, (2023, March 1). *Hoeveel inwoners hebben een herkomst buiten Nederland?*, [website]. Available: https://www.cbs.nl/nl-nl/dossier/dossier-asiel-migratie-en-integratie/hoeveel-inwoners-hebben-een-herkomst-buiten-nederland

Sterkenburg, P., Frederiks, K., Barakova, E., Chen, W., Peters, P., & Feijs, L (2017). A Bioresponse System for Caregivers of Adults with Severe or Profound Intellectual Disabilities, *Journal of Mental Health Research in Intellectual Disabilities. 10*(1), 121.

Subramaniam, S. D., Doss, B., Chanderasekar, L. D., Madhavan, A., & Rosary, A. M. (2018). Scope of physiological and behavioural pain assessment techniques in children – a review, *Healthcare Technology Letters, 5*(4), 124-129. Doi: 10.1049/htl.2017.0108.

Symons, F. J., ElGhazi, I., Reilly, B. G., Barney, C. C., Hanson, L., Panoskaltsis-Mortari, A., Armitage, I. M., & Wilcox, G. L. (2015). Can biomarkers differentiate pain and no pain subgroups of nonverbal children with cerebral palsy? A preliminary investigation based on noninvasive saliva sampling. *Pain Medicine, 16*, 249-256. Doi: 10.1111/pme.12545.

Taelman, J., Vandeput, S., Spaepen, A., & Van Huffel, S. (2009). Influence of mental stress on heart rate and heart rate variability. *In the 4th European conference of the international federation for medical and biological engineering* (pp. 1366-1369). Springer, Berlin, Heidelberg.

Tamizi, E. B., Mohd Anwar Z., & Roszitaida A. (2021). Wearable optical sensor for low back pain monitoring. *2021 International Conference on Electrical Engineering and Informatics (ICEEI)*. IEEE.

Tennant, F. (2013). The physiologic effects of pain on the endocrine system, *Pain Therapy, 2*(2), 75-86. Doi: 10.1007/s40122-013-0015-x.

The Netherlands Institute for Social Research, 2013, visited on July 4, 2022, via https://www.vzinfo.nl/verstandelijke-beperking#node-prevalentie-van-verstandelijke-beperking.

Thacker, M. A., & Moseley, G. L. (2012). First-person neuroscience and the understanding of pain. *Med J Aust, 196*(6), 410-1.

Timmeren, E. A. van, Putten, A. A. J. van der, Schrojestein Lantman-de Valk, H. M. J. van, Schans, C. P. van der, & Waninge, A. (2016). Prevalence of reported physical health problems in people with severe or profound intellectual and motor disabilities: a cross-sectional study of medical records and care plans, *Journal of Intellectual Disability Research, 60*(11), 1109-1118. Doi: 10.1111/jir.12298.

Timmeren, E. A. van, Schans, C. P. van der, Putten, A. A. J. van der, Krijnen, W. P., Steenbergen, H. A., Schrojenstein Lantman-de Valk, H. M. J. van, & Waninge, A. (2017a). Physical health issues in adults with severe or profound intellectual and motor disabilities: a systematic review of cross-sectional studies. *Journal of Intellectual Disability Research, 6*(1), 30-49.

Timmeren, E. A. van, Waninge, A., Schrojenstein Lantman-de Valk, H. M. J. van, Putten, A. A. J. van der, & Schans, C. P. van der, (2017b). Patterns of multimorbidity in people with severe or profound intellectual and motor disabilities. *Research in Developmental Disabilities. 67*, 28–33.

Tran, T., Lowry, A. M., & El-Serag, H. B. (2007). Meta-analysis the efficacy of over-the-counter gastro-oesophageal reflux disease drugs, *Alimentary Pharmacology and Therapeutics, 25(*2), 143-153. Doi: 10.1111/j.1365.2006.03135.x.

Tulder, M. W. van, Koes, B. W., & Bouter, L. M. (1997). Conservative treatment of acute and chronic nonspecific low back pain.

A systematic review of randomized controlled trials of the most common interventions. Spine, 22, 2128–2156.

Tuyll van Serooskerken, J. M. van, Willemen, A. M., Croix, A. de la, Embregts, P. J. C. M. & Schuengel, C. (2022). Satisfying basic psychological needs among people with complex support needs: a self-determination theory-guided analysis of primary relatives' perspectives, *Disabilities, 2*, 330-347. Doi: 10.3390/ disabilities2020024.

United States of America Department of Defense (2010). *Technology Readiness Levels in the Department of Defense (DoD)*. Defense Acquisition Guidebook. Accessed and downloaded on December 12th, 2019, from https://api.army.mil/e2/c/downloads/404585.pdf

Valkenburg, A. J., Tibboel, D., & Dijk, M. van (2015). Pain sensitivity of children with Down syndrome and their siblings: quantitative sensory testing versus parental reports, *Developmental Medicine & Child Neurology, 57*(11), 1049-1055. Doi: 10.1111 dmcn.12823.

Walsh, M., Morrison, T. G., & McGuire, B. E. (2011). Chronic pain in adults with an intellectual disability: Prevalence, impact, and health service use based on caregiver report, *Pain, 152*, 1951-1957. Doi: 10.1016/j.pain.2011.03.014.

Walsh, P. N., Heller, T., Schupf, N., & Schrojenstein Lantman-de Valk, H. van, (2001). Healthy ageing – adults with intellectual disabilities: Women's health and related issues. *Journal of Applied Research in Intellectual Disabilities, 14*, 195–217. Doi: 10.1046/j.1468-3148.2001.00070.x.

Waxman, J. A., Pillai Riddell, R. R., Tablon, P., Schmidt, L. A., & Pinhasov, A. (2016). Development of cardiovascular indices of acute pain responding in infants: A systematic review. *Pain Research and Management, 2016*, 1-15. Doi: 10.1155/2016/8458696.

Werner, P., Lopez-Martinez, D., Walter, S., Al-Hamadi, A., Gruss, S., & Picard, R., Automatic Recognition Methods Supporting Pain Assessment: A Survey, *in IEEE Transactions on Affective Computing*, Doi: 10.1109/TAFFC.2019.2946774.

World Health Organisation, (2024). *Health Inequity Disability*, [website]. Available: https://www.who.int/health-topics/disability#tab=tab_2.

World Health Organisation, 2024. Health Topics: Disability: Health Inequity. Viewed online via https://www.who.int/health-topics/ disability#tab=tab_2 on 25 March 2024.

World Health Organisation (2019). *Patients' rights*. Retrieved on September 30th 2019 from https://www.who.int/genomics/ public/patientrights/en/

Wylde, V. Jeffery, A., Dieppe, P., & Gooberman-Hill, R. (2012). The assessment of persistent pain after joint replacement, *Osteoarthritis Cartilage, 20*(2), 102-105. Doi: 10.1016/j. joca.2011.11.011.

Wylde, V., Wells, V., Dixon, S., & Gooberman-Hill, R. (2013). The colour of pain: Can patients use colour to describe osteoarthritis pain?, *Muscoskeletal Care, 12*, 34-46. Doi: 10.1002/msc.1048.

York, J., Wechuli, Y., & Karbach, U. (2022). Emergency medical care of people with intellectual disabilities: A scoping review, *Open Access Emergency Medicine, 14*, 441-456. Doi: 10.2147/OAEM.S361676.

Zahavi, Da. (2003). *Husserl's Phenomenology, Stanford, USA: Stanford University Press*.

Zamzmi, G., Kasturi, R., Goldgof, D., Zhi, R., Ashmeade, T., & Sun, Y. (2018). A review of automated pain assessment in infants: Features, classification tasks, and databases, *IEEE Reviews in Biomedical Engineering, 11*, 77-96. Doi: 10.1109/
RBME.2017.2777907.

Zhang, Z., Korving, H., Sterkenburg, P., Feijs, L., & Barakova, E. (2021). Peripheral display for conveying real-time pain condition of persons with severe intellectual disabilities to their caregivers, *The Ninth International Symposium of Chinese CHI (Chinese CHI 2021)*, Oct 2021, Hong Kong, pp. 63-71, Doi: 10.1145/3490355.3490362.

Zwakhalen, S. M. G., Dongen, K. A. J. van, Hamers, J. P. H., & Abu-Saad, H. H. (2004). Pain assessment in intellectually disabled people: non-verbal indicators, *Journal of Advanced Nursing, 45*(3), 236-245. Doi: 10.1046/j.1365-2648.2003.

Appendix B

Summary
Samenvatting

SID
pain app

Pain is a common occurrence in the life of a person with a severe or profound intellectual disability (SID). They often have comorbid illnesses and run a higher risk of contracting infections or getting injured. Due to the severity of their intellectual disability, people with SID have trouble expressing and communicating their pain, leading caregivers to find pain assessment one of the most challenging parts of caring for someone with SID. Pain can be missed, or detected too late, which can lead to a worsening of an illness, hospital stays or premature death.

Since self-report of pain is impossible and systematic pain observations can miss subtle and idiosyncratic ways of pain expression, a system was developed to measure pain physiologically. This system consists of a smart sock measuring skin conductance, a transmitter that sends the physiological data via Bluetooth®, and the SID Pain App on a mobile device. This dissertation describes the design, development and testing of the SID Pain App, with the aims to (1) evaluate several physiological pain detection methods on usability, invasiveness and technological readiness; (2) develop a reliable physiological pain detection algorithm to be programmed into a mobile application, the SID Pain App; and (3) test the SID Pain App on adults with a severe or profound intellectual disability and assess the user experience of the caregivers using the app.

To evaluate several physiological pain detection methods on usability, invasiveness and technological readiness a systematic review was conducted. From 29 review articles, describing results from 540 unique articles, 1,054 combinations were found of a physiological pain detection method and a target group. Examples of physiological pain detection methods were heart rate variability, magnetic resonance imaging (MRI), and automatic facial recognition and examples of target group were comatose patients, people with a moderate intellectual disability, and children. The invasiveness of each physiological method was measured on two scales with four levels (score from 0 to 6) and the vulnerability of each target group on two scales with three levels and one scale with two levels (score from 0-7). When vulnerability of target group and invasiveness of measurement method was graphically displayed, the trend showed that more invasive methods were mostly used on the least vulnerable target groups, and vice versa.

The quality of each review, assessed with the Critical Appraisal Skills Programme checklist, was generally high, and the technological readiness of the most-used apparatus for nearly all physiological pain detection methods was in the highest or second highest level. Usability of the physiological pain detection methods varied, based on contradictory results, small sample sizes and confounding variables. Reliable physiological pain detection methods for acute pain are respiratory measures, muscle tension, and pupillometry, while brain scans and genetic testing showed a clear difference between healthy adults and those with chronic pain.

The physiological pain detection algorithm to be placed in the SID Pain App was developed with pain data from thirty healthy adult participants without intellectual disability, medical disorders, or psychological concerns. Each participant had to put a hand in a tub of ice-water, up to five times in a row, until the pain threshold was reached Participants self-reported that they felt no pain, felt discomfort, or had reached their pain tolerance threshold. This resulted in 68,900 data points of pain and no pain, which were used to train and test models using Random Forest Prediction, a form of machine learning.

In the Random Forest Prediction technique, independent decision trees are made with a subset of the data, and these trees then classify features and variables to vote for the final tree class. The tree with the most votes was the one which made the best classifications based on the pain data. While the reliability of the final tree model was high, disbalance in the data cause the precision and accuracy to be around 0.50. When 50% of pain data was interpolated, which means that similar data was generated based on the test data, precision and accuracy rose to 80%.

In order to make sure that this algorithm was the most accurate based on the pain data that was gathered, other artificial intelligence techniques were tried, such as Support Vector Machines and a Long Short-Term Memory neural network model. Neither of these were an improvement on the Random Forest Prediction model with 50% interpolated data. The possibility of other ideas, that may improve the algorithm, such as model assembling strategies and ChatGPT are discussed on their merit in chapter 6.

To ascertain what a pain detection application would need to be functional and useful in daily practice, the SID Pain App was designed in collaboration with the end-users; caregivers and parents of adults with a severe or profound intellectual disability. Via workplace walk-throughs, interviews, questionnaires, and focus groups, wishes, needs, constraints and opinions were gathered among caregivers, which led to three distinct designs. In an online questionnaire, 115 caregivers and parents judged each of the three designs on clarity, fitting, understanding, ability to bring to action and visual stress. The design that was deemed the best by caregivers was evaluated by a focus group of experts and adjusted to be placed in the SID Pain App.

The usability of the SID Pain App was examined among twenty end-users, who were asked to use the app with a client or colleague. Answers on the user experience questionnaire demonstrated that the SID Pain App had positive scores on the six aspects: attractiveness, dependability, efficiency, novelty, perspicuity, and stimulation. On every aspect, besides perspicuity, the SID Pain App scored above average compared to a benchmark of similar products. Since the participants found the SID Pain App difficult to use and complex, the SID Pain App had a lower-than-average score on perspicuity.

As a final step in this project, the SID Pain App and its pain classification algorithm was tested on 14 adults with a severe or profound intellectual disability during a scheduled physical therapy appointment. The participants all experienced two to four painful moments during their physical therapy session. Of the 40 physiological pain moments measured by the SID Pain App, 35 were accompanied by a systematic observation of pain made with a pain observation list for adults with intellectual disabilities. The SID Pain app would detect the painful moment at least 6 seconds before a pain observation was made. There were no differences found between male and female participants, and between mild, moderate, and severe pain.

This study is the first study to design, develop and test a physiological pain detection method on adults with a severe or profound intellectual disability. The results are promising, because timely pain detection is very important in people who are unable to communicate about their pain. Not only will accurate and quick pain treatment lead to pain relief, better wellbeing, and a greater quality of life, but it will also decrease the risk of exacerbated illness or injury, unnecessary hospital stays and, possibly, avoidable death.

In de zorg voor mensen met een ernstige of zeer ernstige verstandelijke beperking (mensen met EMB) hebben begeleiders veel uitdagingen. Mensen met EMB kunnen vaak niet praten en daardoor niet doorgeven hoe zij zich voelen. Dit betekent dat begeleiders goed op moeten letten als zij wat willen weten over de gezondheid of over de emoties van mensen met EMB.

Een hele belangrijke taak van begeleiders is om te ontdekken of iemand met EMB pijn heeft. Want deze mensen hebben niet alleen een ernstige verstandelijke beperking, vaak hebben zij ook verschillende ziektes, aan hun hart, hun darmen, hun botten, enzovoort. Een aantal van deze ziektes zorgen voor pijn. Ook raken mensen met EMB makkelijk gewond. Als begeleiders de pijn niet ontdekken, dan kan de ziekte of de wond erger worden. Mensen met EMB moeten dan naar een dokter, of het ziekenhuis.

Het is belangrijk om pijn bij mensen met EMB op tijd te ontdekken, zodat de oorzaak opgelost kan worden, ze een pijnstiller kunnen krijgen, of geholpen kunnen worden om de pijn op een andere manier te verminderen.

Omdat het moeilijk is om te zien of iemand met een ernstige of zeer ernstige verstandelijke beperking pijn heeft, willen we kijken of we de pijn lichamelijk kunnen meten. Als iemand pijn heeft, dan gebeurt er namelijk heel veel in het lichaam, en dat kunnen we meten op de huid. Zo hoeft de persoon zelf niet te vertellen of te laten zien dat hij of zij pijn heeft.

Als eerste stap hebben we gekeken op welke manieren de pijn allemaal lichamelijk gemeten kan worden. Dat hebben we uitgezocht door 29 artikelen te lezen van onderzoekers die hierover hebben geschreven. Wat blijkt? Pijn werd op wel 18 verschillende manieren op het lichaam gemeten. Het kan bijvoorbeeld door de hartslag te meten, de snelheid waarmee het bloed stroomt, of in de hersenen. Sommige van deze manieren meten pijn die net is gebeurd, en sommige manieren meten pijn die al langer duurt. De beste manieren om snelle pijn te meten zijn de ademhaling, spanning in de spieren, de grootte van de pupil en hersenfoto’s.

We hebben ook gekeken bij wie pijn op welke manier lichamelijk werd gemeten in andere onderzoeken. Was dat bijvoorbeeld bij gezonde, volwassen mensen, of bij kinderen? Hadden de mensen een verstandelijke beperking, of waren zij ziek? We hebben zeven verschillende groepen ontdekt: gezonde volwassenen, zieke mensen die kunnen praten, zieke mensen die niet kunnen praten, mensen met een lichte verstandelijke beperking, mensen met een ernstige verstandelijke beperking, kinderen en baby’s.

Als we keken naar de kwetsbaarheid van de mensen en hoe makkelijk of moeilijk de pijn lichamelijk gemeten kon worden, dan was te zien dat de makkelijkere metingen vooral gebruikt werden bij de kwetsbare mensen en de moeilijkere metingen bij mensen die minder kwetsbaar zijn. En als we keken naar de meetapparaten, dan zagen we dat er bijna geen nieuwe apparaten werden gebruikt. Onderzoekers waren goed bekend met de meetapparaten die werden gebruikt om pijn lichamelijk te meten.

Een makkelijke en bekende manier om pijn te meten op het lichaam is om te kijken hoeveel iemand zweet. Als er iets spannends gebeurt, zoals pijn, dan zweet je meer. Als je tot rust komt, dan zweet je minder. Meten hoeveel iemand zweet kan op de handen of op de voeten. Daarom is de slimme sok gemaakt. De slimme sok meet hoeveel iemand zweet op de onderkant van de voet en stuurt dat dan draadloos naar een app op een mobiele telefoon, de EMB Pijn App.

Nadat we hebben gekozen om pijn te meten met de slimme sok, wilden we kijken wat er gebeurt als iemand pijn heeft. Dertig gezonde volwassenen zonder verstandelijke beperking hebben meegedaan aan een test. Zij deden een hand in een bak met ijswater totdat het pijn deed. En ze vertelden aan de onderzoeker wanneer het wel en wanneer het geen pijn deed. Ook droegen zijn allemaal een slimme sok die verbonden was aan de EMB Pijn App. Zo zagen wij hoe het zweten bij dertig mensen veranderde bij pijn en bij geen pijn.

Hierna hebben we een computerprogramma gebruikt om te zorgen dat de EMB Pijn App pijn automatisch kan herkennen. Het resultaat dat uit dat computerprogramma kwam, een algoritme, moet van alle informatie over het zweten kunnen zeggen of het pijn is of geen pijn. Dat blijkt moeilijk te zijn. Het algoritme kon wel goed zeggen dat iemand pijn had, als er al eerder pijn bij die persoon was gemeten, maar kon het niet goed zeggen van een nieuw persoon. Als het algoritme al wist wat er verandert in het zweet als iemand pijn heeft, dan werd dat daarna van 8 op de 10 keer goed voorspeld.

Om te kijken of het mogelijk was om de voorspelling van pijn beter te maken, hebben we nog gekeken of we andere computerprogramma’s konden gebruiken, of meer computerprogramma’s samen. We hebben naar twee andere programma’s gekeken en één combinatie. Die waren geen van allen beter in het voorspellen van pijn dan het eerste programma. Er zijn nog meer manieren en programma’s die we nog niet hebben geprobeerd, dus wie weet kan er een beter algoritme worden gemaakt.

Het is belangrijk dat ouders en verzorgers, de mensen die later de EMB Pijn App gaan gebruiken, meedenken over hoe de app werkt. Dat deden ze in twee verschillende onderzoeken:

Eerst konden ouders en begeleiders van mensen met EMB aangeven hoe de EMB Pijn App eruit moest zien. We hebben hen vragen gesteld, vragenlijsten gemaakt voor iedereen, meegelopen op het werk van begeleiders, over andere onderzoeken gelezen en het aan experts gevraagd. Zo kwamen we uit met een lijst wensen, benodigdheden, meningen en onmogelijkheden. Daarmee hebben we drie verschillende ontwerpen gemaakt, die we weer aan begeleiders en ouders hebben laten zien. Meer dan honderd mensen hebben meegedaan. We vroegen ze om de ontwerpen te beoordelen op heel veel verschillende manieren, en of ze de ontwerpen zouden willen veranderen. Uiteindelijk hebben ouders, begeleiders en experts één ontwerp gekozen die in de EMB Pijn App is gekomen.

Hierna konden begeleiders van mensen met EMB de EMB Pijn App testen met een cliënt of collega. Twintig mensen hebben hieraan meegedaan. Ze hebben een vragenlijst ingevuld over hoe makkelijk ze de EMB Pijn App in gebruik vonden. De deelnemers vonden de EMB Pijn App aantrekkelijk om te gebruiken, betrouwbaar en nieuw, maar ook moeilijk te leren. Vergeleken met andere apps, vonden deelnemers de EMB Pijn App goed, maar ook lastig.

Als laatste stap hebben we de EMB Pijn App getest op mensen met EMB. Dit gebeurde tijdens een geplande fysiotherapie behandeling. Tijdens deze behandeling droegen 14 mensen met EMB een slimme sok verbonden aan de EMB Pijn App. Ze hadden gemiddeld twee keer pijn tijdens hun behandeling, en dat konden we terugzien in de EMB Pijn App.

We hebben de fysiotherapie behandelingen ook gefilmd. Zo konden we zien of de mensen met EMB ook in hun gezicht of lichaam lieten zien of zij pijn hadden. Dat was meestal wel te zien. De EMB Pijn App kon de pijn aangeven meer dan zes seconden voordat het te zien was in het gezicht of lichaam. De EMB Pijn App ontdekt de pijn dus sneller dan dat wij het kunnen zien aan iemand met EMB.

Er was geen verschil tussen de mannen en de vrouwen met EMB die meededen, of tussen pijn die licht is, gemiddeld, of erg.

Dit onderzoek is heel belangrijk voor mensen met een ernstige of zeer ernstige verstandelijke beperking, omdat naar een manier wordt gekeken om pijn lichamelijk te meten. Het is belangrijk om pijn te ontdekken bij mensen met EMB, omdat zij meer risico lopen op een ziekte of een wond, en omdat een snelle behandeling van pijn zal zorgen dat zij zich beter en veiliger voelen. Zo kunnen wij misschien wel vermijden dat iemand met EMB pijn blijft houden, in het ziekenhuis terechtkomt, of overlijdt.

---

[1] According to Contributor Roles Taxonomy (Brand et al., 2015).

Appendix C

Contribution of authors[1]

Chapter 1

H. Korving: Writing – original draft
E. Barakova: Writing – review and editing
P Markopoulos: Writing – review and editing
P. Sterkenburg: Writing – review and editing

Chapter 2

H. Korving: Project administration, conceptualisation, methodology, validation, formal analysis, writing – original draft, writing – editing, visualisation

E. Barakova: Funding acquisition, conceptualisation, methodology, writing – review and editing, visualisation, supervision
L. Feijs: Funding acquisition, conceptualisation, methodology, writing – review and editing, supervision
P. Sterkenburg: Funding acquisition, conceptualisation, methodology, validation, formal analysis, writing – review and editing, supervision

Chapter 3

H. Korving: Project administration, conceptualisation, methodology, validation, formal analysis, writing – original draft, writing – editing. visualisation

E. Barakova: Conceptualisation, methodology, writing – review and editing, supervision
L. Feijs: Conceptualisation, methodology, writing – review and editing, supervision
P. Peters: Methodology and software, validation
P. Sterkenburg: Conceptualisation, methodology, writing – review and editing, supervision

Chapter 4

H. Korving: Project administration, conceptualisation, methodology, validation, formal analysis, writing – original draft, writing – editing. visualisation

E. Barakova: Conceptualisation, methodology, writing – review and editing, supervision
P. Markopoulos: Conceptualisation, methodology, writing – review

and editing, supervision
P. Sterkenburg: Conceptualisation, methodology, writing – review and editing, supervision
H. Xiang: Methodology and software
D. Zhou: Methodology and software, validation, writing – original draft

Chapter 5

H. Korving: Project administration, conceptualisation, methodology, validation, formal analysis, writing – original draft, writing – editing. visualisation

E. Barakova: Conceptualisation, methodology, writing – review and editing, supervision
L. Feijs: Conceptualisation, methodology, writing – review and editing, supervision
P. Sterkenburg: Conceptualisation, methodology, validation, formal analysis, writing – review and editing, supervision

Chapter 6

H. Korving: Project administration, conceptualisation, methodology, validation, formal analysis, writing – original draft, writing – editing. visualisation

E. Barakova: Conceptualisation, methodology, writing – review and editing, supervision
S. Li Methodology and software, writing – original draft
P. Markopoulos: Conceptualisation, methodology, writing – review and editing, supervision
P. Sterkenburg: Conceptualisation, methodology, writing – review and editing, supervision
D. Zhou: Methodology and software, validation, writing – review and editing

Chapter 7

H. Korving: Project administration, conceptualisation, methodology, validation, formal analysis, writing – original draft, writing – editing. visualisationE.

Barakova: Conceptualisation, methodology, writing – review and editing, supervision
P. Markopoulos: Conceptualisation, methodology, writing – review and editing, supervision

P. Sterkenburg: Conceptualisation, methodology, writing – review and editing, supervision

Chapter 8

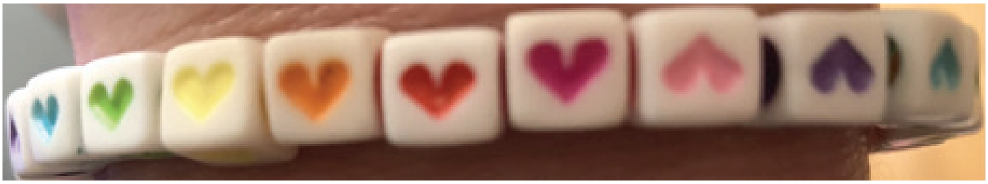
H. Korving: Writing – original draft

E. Barakova: Writing – review and editing
P Markopoulos: Writing – review and editing
P. Sterkenburg: Writing – review and editing

Appendix D

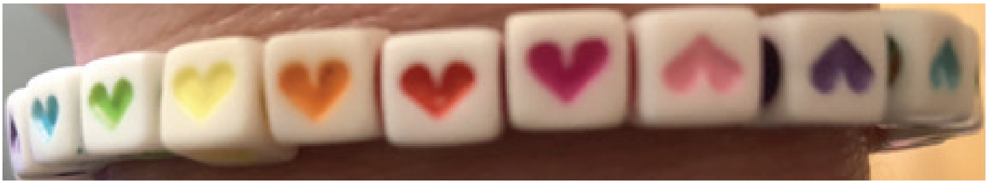
Word of thanks

During the process of conducting my research and writing my dissertation, I owe thanks to many people, both in a personal and a professional capacity. None of us stand alone when we partake on a long journey, and the people we meet along the way can help us in unexpected ways. Though I will try to be thorough, I may not be able to remember everyone that had a part in my success. For those I missed, I thank you!
This new title is mine, but for all that I mention below: you deserve a title of your own!



First, I would like to acknowledge all the **participants with a severe or profound intellectual disability**, their parents and legal representatives, professional caregivers, and physical therapists, for the trust they had in the researchers and this project. Their participation made it possible to take further steps in the study of pain in people with a severe or profound intellectual disability.
The participating organisations were **Bartiméus, Cordaan, Odion** en **Ons Tweede Thuis**, and their help and input has been invaluable.

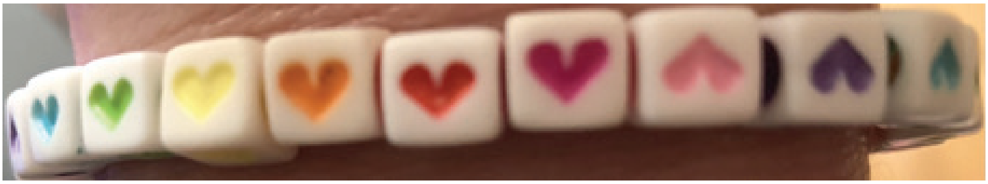
Also, a special thanks to the 30 **healthy participants** without intellectual disability who were willing to endure painful moments for the pursuit of science. Thank you for taking the time out of your day to participate in my experiments. You have been instrumental in creating a physiological way to measure pain in those unable to communicate.



During this project, I received regular advice from two important groups: **The panel of parents and caregivers of people with SID**, who gave their thoughts and insights, based on their experience and life expertise, and the **panel of experts** in research and care for people with SID, who helped me solidify the theoretical background and practical application of the SID Pain App. You have been invaluable.

Aan de **familie Plasmeijer**: Jullie waren betrokken bij dit project sinds het prille begin. Jullie waren niet alleen waardevolle adviseurs, jullie waren het voorbeeld voor wie dit project is uitgevoerd. Bedankt voor alle tijd die jullie hebben gegeven, het meedenken, en het delen van (levens)ervaringen.

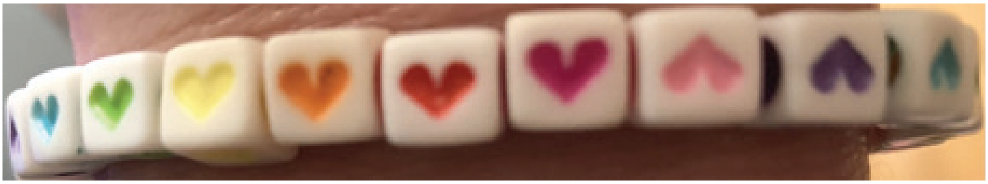
Aan **Anne de la Croix**: Jouw bijdrages, jouw ervaringen en jouw verhalen hebben me zoveel geleerd gaandeweg dit project. Bedankt voor je enthousiasme elke keer als ik je om hulp vroeg en de tijd en het advies dat je hebt gegeven.



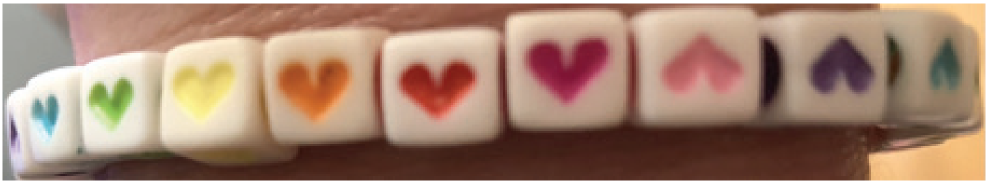
To my **family**, I was happy sharing this journey with you and I appreciate you standing by me as I bring it to a conclusion. Especially, to my two wonderful brothers **René** and **Edwin**, thank you for literally standing by me as my paranymphs. The position may be ceremonial, your support is not. To my dad, thank you for all your hard work on the lay-out of this beautiful manuscript!

Aan mijn nichtjes **Fabiënne**, **Freya**, **Phileine** en mijn neefje **Frenkie**: het zien van jullie foto's op mijn bureau hebben me vaak geholpen om door te zetten. Als ik het moeilijk vond om mezelf te motiveren, vond ik het makkelijk om het voor jullie te doen.
Freya (5) created and gifted me the hearts, which illustrate my feelings with my words.

To my bestest friend in the whole world, **Marlous**: you were my constant support, a support everyone should have. You are kind and loyal, and firm and honest. You were the one telling me to be kind to myself when I had a hard week, and a no-nonsense driving force when I needed to finish something. I stand taller for knowing you.



To my wonderful partner, **Marali**, you have been my cheerleader during the final steps of the project, during the chaos of combining a new career with finishing my PhD, and while I navigated the maze of defence planning. I could and can always count on you to give me structure when my head is filled with chaos. Ek is baie lief vir jou!



To my former partner, **Micky**. Thank you for your help in designing a logo, programming two of the pain visualisations, and creating a website on which to display and manipulate them. Thank you for standing by me at the beginning of my PhD. And most of all, thank you for believing in me when I had trouble believing in myself.

To **Franny**: Ik ben blij met alles wat wij kunnen delen. Weet dat ik altijd voor je klaar sta, zoals ik weet dat jij er voor mij zal zijn met een luisterend oor.

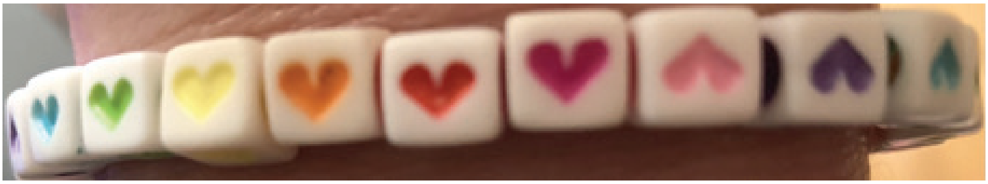
To **Ariane & Chad**, my critical friends: Keep on asking critical questions <3

To **Sam**, my port in the storm: You were always there when I needed time to unwind, with a listening ear, a plate full of good food and a tarot card or two. I hope to spend many more enjoyable evenings together in the most creuvex of ways.

To **Frank-Jan**: Sharing professional and personal triumphs with you has been amazing all these years. Even though neither of us use our law degree, I am happy and grateful that it gave us the opportunity to meet each other. To many more experiences!

To **Kaat**: Onze kaartjes over en weer betekenen heel veel voor mij.

To **Koen,** mijn broer van een andere moe'r: Jij houdt me nuchter. Ironisch, maar waar.

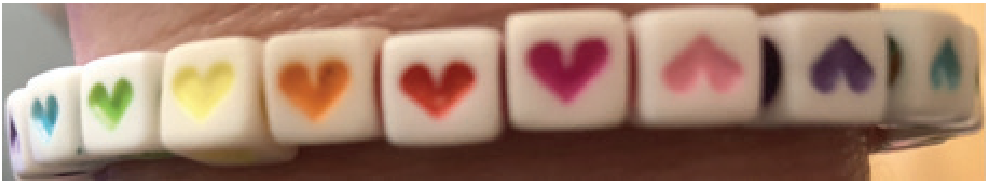


I owe a lot of thanks to my wonderful **colleagues**, both those who have had an active hand in getting this project to the finish line and those that were always there for me when I needed a listening ear:

Jessica Braakman, Annelies Christiani, Sara Colijn, Paula Dekkers, Vernandi Dyzel, Debora van Elst, Hannelies Hokke, Aline Honingh, Gloria Kempelmann, Dieuwke Kluvers, Astrid Kok, Yvonne Kruithof, Beanka Meddeler-Polman, Linda Messemaker-Veerman, Ilona Olofsen, Martine Rikken-Evers, Altine de Reus, Joyce Schroor, Lucia Willems & Mirjam Wouda.

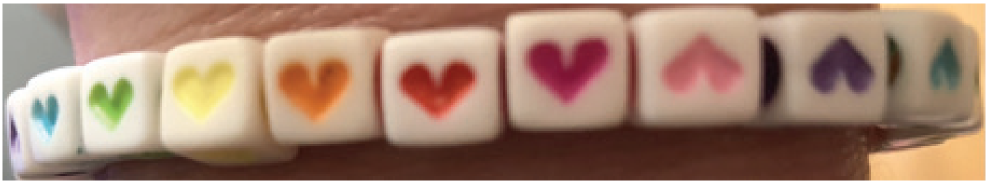
To my writing group: without you on my screen, I would have been struggling much more to get things done. **Veerle** Andries and **Jacqueline** van Tuyll van Serooskerken; you showed up to be a quiet, or sometimes not so quiet, motivation, a wonderful and necessary distraction, and a cheer in my ear. Do not change your ways.

To my current team: **Hanna, Maurice, Naomi en Sharon**. Thank you for helping and understanding, giving me time to work on my dissertation, and advising me on what to expect in this journey.



To my amazing former colleagues, **Kyra** Frederiks and **Evelien** van Wingerden, I hope you realise how your friendship, calm presence and professional knowledge helped me on my way. I have had the luck to have you as my colleague and friend, and I had the hardship of missing you as a colleague, but I will never have to go without the things you have shown me, brought me, shared with me, and taught me. I carry that with me.

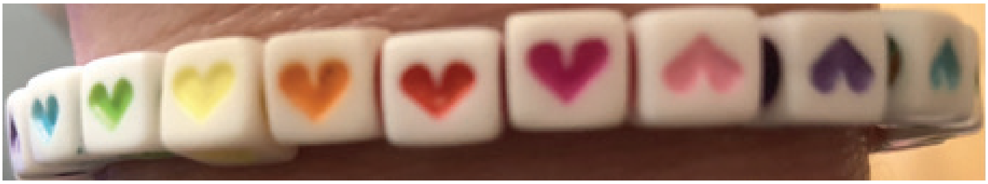
And then there are the two colleagues with whom I started this path to a PhD, **Suzanne** Derks and **Tanja** Doodeman. Both of you were there from the beginning, when we were finding our footing in the world of academia and figuring out the specific goals we had to meet to get our PhD’s. I look back fondly at our brainstorms for each other’s projects, the joy when one of us had puzzled something out, and our celebrations when a difficult part of our projects was over. Your edits of my articles have made me a better writer, your keen eyes at my presentations a better presenter, and your loyal trust have made me a better colleague and friend.



To my **opposition committee** Bea Maes, Dederieke Maes-Festen, Ignacio Malagon-Calle, Rong-Hao Liang and PJ Beek: A warm thanks for taking the time and effort to read through my manuscript and evaluate it on its scientific contribution.

To my incredible team; **Emilia Barakova, Loe Feijs and Panos Markopoulos**. Your expertise and support have improved the quality of this project and my work. The difference in our expertises, from psychology to industrial design and artificial intelligence, have made this project the perfect combination of technology and practice. It has been great to share this work and all publications with you.

And lastly, to my promotor **Paula Sterkenburg**: Vreeslik dankie vir jou tyd, jou geduld en advies hierdie afgelope 6 jaar. Having you as a supervisor has improved my scientific knowledge, my writing, my analytic skills, my confidence, my discipline, and my self-efficacy. I would not have made it this far, producing this great dissertation.



Appendix E

About the author
Over de auteur

Helen Korving was born in Leidschendam, the Netherlands, in 1984. After finishing secondary school (Atheneum, Dalton college, Voorburg), she started studying Law at the University of Utrecht. After a short career in law research at the youth law department of the municipal court of Amsterdam, she realized that psychology was where her interests were. Another stint at Utrecht University (2010-2014) led to a Bachelor's in Developmental Psychology and a Master's (Cum Laude) in Applied Cognitive Psychology.

Together with her thesis supervisors, Helen decided to adapt her master thesis on the effect of the visibility of a teacher in web lectures on the attention of the student to a scientific article, which was published in Computers & Education in 2016. She also collaborated on another research study for the validation of an evidence-based knowledge questionnaire for medical students, which was published in 2017 in the Journal of Clinical Epidemiology.

Helen started her ten year career in social science at the Institute for Road Safety Research in Den Haag, where she gained experience in writing reports, factsheets and subsidy proposals. Later on, she moved to Goudappel-Coffeng in Deventer, a commercial company for traffic research. The realization dawned that commercial research was not her forte and she preferred to work on longer research studies.

At the end of 2018, Helen started her PhD in a collaboration project between the department of Child and Family Studies of the Vrije Universiteit and the department of Industrial Design, Future Everyday group, of the Eindhoven University of Technology. The research study aimed to see whether a physiological measurement using a smart sock for skin conductance could be adapted to be used for pain signaling in adults with a severe or profound intellectual disability. This research combined the use of technology and IT in caregiving with a very interesting and vulnerable target group. Making the world understandable, accessible and safe for people with a severe or profound intellectual disability was the aim of the project.

A pandemic, many publications, presentations and visits to (inter) national conferences, and a long breath later, Helen moved on from disability research to create opportunities of inclusion and diversity in tertiary education. At the University Teacher Education department of the Vrije Universiteit Amsterdam, she conducted research to create a digital inclusion framework to be used by teachers and educational specialists on all three levels of tertiary education. Results of this project can be viewed at the Dutch website www.kijkkaderinclusiviteit.nl (the framework is provided in English).

Helen Korving is geboren in Leidschendam in 1984. Na het behalen van haar middelbare school diploma (Atheneum, Dalton college, Voorburg), startte zij een studie rechten aan de Universiteit van Utrecht. Na een korte carrière als onderzoeker in het jeugdrecht bij het arrondissementsparket in Amsterdam, bleek dat psychologie haar passie was. Aan de Universiteit van Utrecht (2010-2014) behaalde Helen een Bachelor in ontwikkelingspsychologie en een Master (Cum Laude) in Toegepaste Cognitieve Psychologie.

Samen met haar begeleiders besloot Helen haar masterthese naar het effect van de zichtbaarheid van een docent op de aandacht van een student in een online college (weblecture) om te vormen naar een wetenschappelijk artikel. Deze is in 2016 gepubliceerd in het tijdschrift Computers & Education. Ook werkte zij mee aan de validatie van een evidence-based kennisvragelijst voor huisartsen in opleiding, welke in 2017 gepubliceerd werd in het Journal of Clinical Epidemiology.

Haar tienjarige carrière in onderzoek in sociale wetenschappen startte Helen bij het SWOV Instituut voor Verkeersveiligheidsonderzoek in Den Haag, waar ze ervaring opdeed met het schrijven van rapportages, factsheets en subsidieaanvragen. Hierna werkte ze bij het commerciële verkeersonderzoekbedrijf Goudappel Coffeng in Deventer. Het bleek echter dat commercieel onderzoek haar niet lag en dat Helen de voorkeur had voor langer durende onderzoeksprojecten.

Eind 2018 startte zij haar PhD project in een samenwerking tussen de afdeling Orthopedagogiek van de Vrije Universiteit Amsterdam en de afdeling Industrieel Ontwerp, Future Everyday Group, van de Technische Universiteit Eindhoven. Het onderzoeksproject was opgezet om te kijken of een slimme sok die gebruikt werd om huidgeleiding te meten kon worden aangepast om pijn te meten bij volwassenen met een ernstige of zeer ernstige verstandelijke beperking. Het onderzoek was een combinatie van de inzet van technologie en IT bij een interessante en zeer kwetsbare groep. Het doel van het project was om de wereld begrijpelijker, toegankelijker en veiliger te maken voor mensen met een (zeer) ernstige verstandelijke beperking.

Na een pandemie, vele publicaties, presentaties en bezoeken aan (inter) nationale congressen, en een lange adem, heeft Helen haar carrière voortgezet aan de Universitaire Lerarenopleiding. Hier werkte ze met docenten en onderwijskundigen van MBO, HBO en WO aan een kijkkader voor het verbeteren van diversiteit en inclusie in het beroepsonderwijs. De resultaten en producten van dit onderzoek zijn te zien en te downloaden via www.kijkkaderinclusiviteit.nl.

Publications / publicaties

Korving, H., Calor, S., Schols, M., Bredeweg, B., Marcellis, M., Boxtel, C. van, Goei, S., Laan, H. van der & Westbroek, H. (2025). Inclusivity in Tertiary Education: Cocreation of a Digital Inclusivity Framework, in progress.

Korving, H., Barakova, E., Markopoulos, P. & Sterkenburg, P. (2025). Testing a Pain Signalling App in Adults with Severe or Profound Intellectual Disability in a Residential Setting, Journal of Applied Research in Intellectual Disability, in revision.

Korving, H., Zhou, D., Sheng, L., Sterkenburg, P., Markopoulos, P. & Barakova, E. (2023). Development of a pain signaling system using machine learning, IEEE International Conference of Acoustics, Speech and Signal Processing (ICASSP), 4-10 June, Rhodes Island, Greece.

Korving, H., Zhou, D., Xiang, H., Sterkenburg, P. Markopoulos, P. & Barakova, E. “Development of an AI-enabled system for pain monitoring using skin conductance sensoring in socks.” International Journal of Neural Systems, 32(10), 2250047 (11 pages). 2022. DOI: 10.1142/S0129065722500427.

Korving, H., Sterkenburg, P., Barakova, E. & Feijs, L. “Designing pain visualisation for caregivers of people with special needs: A cocreation approach.” Heliyon, 8(12), December 2022, e11975, DOI: 10.1016/j.heliyon.2022.e11975.

Zhang, Z., Korving, H., Sterkenburg, P., Feijs, L. & Barakova, E. (2021). Peripheral display for conveying real-time pain condition of persons with severe intellectual disabilities to their caregivers, in Chinese CHI 2021, October 6, 7 2021, Online, Hong Kong. DOI: 10.1145/3490355.3490362

Korving, H., Enninga, A., Huisman, S., Waninge, A., Van der Putten, A. & Sterkenburg, P. (2021). Signaleren van pijn bij mensen met een (zeer) ernstige verstandelijke beperking. Tijdschrift voor Artsen voor Verstandelijk Gehandicapten, jaargang 29 nummer 3, september 2021, p. 168-175.

Korving, H., Peters, P., Barakova, E., Feijs, L. & Sterkenburg, P., Pain signalling with physiological data for persons with communication difficulties: A pilot study of the pain app, in 11th IEEE Int. Conf. Cognitive Infocommunications (CogInfoCom) (Mariehamn, Finland, 2020).

Korving, H., Sterkenburg, P.S., Barakova, E.I. & Feijs, L.M.G. “Physiological measurements of acute and chronic pain within different subject groups: A systematic review.” Pain Research and Management, 2020, Article ID 9249465, 10 pages. DOI: 10.1155/2020/9249465

Aarts, L., Loenis, B., Korving, H., Guiking, C. (2017). Risicofactoren op 50km/uur-kruispunten met verkeerslichten. Rapport R-2017-21. Instituut voor Wetenschappelijk Onderzoek Verkeersveiligheid SWOV, Den Haag.

Kortekaas, M. F., Bartelink, M. L. E., de Groot, E., Korving, H., de Wit, N. J., Grobbee, D. E., & Hoes, A. W. (2017). The Utrecht questionnaire (U-CEP) measuring knowledge on clinical epidemiology proved to be valid. Journal of Clinical Epidemiology, 82, 119-127.

Korving, H., Hernández, M., & De Groot, E. (2016). Look at me and pay attention! A study on the relation between visibility and attention in weblectures. Computers & Education, 94, 151-161.

Korving, H. et al. (2016). Monitor Verkeersveiligheid – achtergrondinformatie en onderzoeksverantwoording. Rapport R-2016-14A. Instituut voor Wetenschappelijk Onderzoek Verkeersveiligheid SWOV, Den Haag.

Weijermans, W., Korving, H., Schagen, I., van Goldenbeld, Ch., Bos, N., Stipdonk, H. (2016). Monitor Verkeersveiligheid 2016. Rapport R-2016-14. Instituut voor Wetenschappelijk Onderzoek Verkeersveiligheid SWOV, Den Haag.

Weijermans, W.A.M., Stipdonk, H.L., Wijnen, W., Goldenbeld, Ch. van, Bijleveld, F.D., Korving, H., Bruin, J. de, Bos, N.M. (2016). Toename aantal verkeersdoden in 2015. Rapport R-2016-14B. Instituut voor Wetenschappelijk Onderzoek Verkeersveiligheid SWOV, Den Haag.

De Craen, S., Korving, H., Schagen, I. (2015). Het effect van begeleid rijden (2todrive) op zelfgerapporteerde ongevallen en overtredingen. Rapport R-2015-11A. Instituut voor Wetenschappelijk Onderzoek Verkeersveiligheid SWOV, Den Haag.

Korving, H., Boele, M.J., De Craen, S. (2014). Zichtbaarheid van motorrijders onderzocht met ‘eye tracking’. Rapport R-2014-30. Instituut voor Wetenschappelijk Onderzoek Verkeersveiligheid SWOV, Den Haag.

Presentations / presentaties

Poster presentation “Visibility and perspicuity of motorcyclists with eye tracking” at the Scandinavian Workshop for Advanced Eye-Tracking. June 2016, Turku, Finland. H. Korving (presentation), S. de Craen & M. Boele.

Presentation “One project --> Three studies on how ICT can contribute to making the world safe, understandable and accessible for persons with a severe intellectual disability” during a Research Meeting for employees of the department of Child and Family Studies of the Vrije Universiteit (January, 2019: Amsterdam). H. Korving, T. Doodeman. & E. van Wingerden

Network meeting Academische Werkplaats, Doorn, 14 May 2019. Knowledge market products ‘Sociale relaties en ICT’ en ‘EMB & ICT’. H. Korving and others.

Round table discussion “Pain in persons with severe intellectual and motor disability.” EAMHID 23 – 25 May 2019. Barcelona. Korving, H., Colijn, S. & Sterkenburg, P.

Network meeting Academische Werkplaats, Amsterdam, 14 November 2019. Workshop smart sock and design questionnaire. H. Korving.

Presentation “EMB&ICT: Bevorderen van welzijn met behulp van technologie.” Platform EMG behavioural expertise day. 18 December 2019. H. Korving.

Presentation “Op welke manieren kan pijn gemeten worden?” At FORTIOR: ‘Omgaan met pijn bij kinderen en volwassenen met ernstig en zeer ernstige verstandelijke en meervoudige beperkingen (EMB en ZEVMB): signalering en begeleiding’. Utrecht. 24 January 2020. Korving, H. (plenary presentation).

Presentation “Pain signaling with physiological data for persons with communication difficulties: A pilot study of the pain app” at the 11th IEEE International Conference for Cognitive Infocommunications (CogInfoCom), 23 September 2020, online. Korving, H. (presentation), Peters, P., Barakova, E., Feijs, L. & Sterkenburg, P.

Network meeting Academische Werkplaats, online, 20 May 2021. “De EMB pijn app en de slimme sok: een korte update”. H. Korving

Presentation “Het signaleren van pijn bij volwassenen met ZEVMB.” Kennisdag Next Level - Visio/Bartiméus/RC, 7 June 2021, online. Enninga, A. & Korving, H.

IASSIDD. 2021. 6-8 July 2021. Amsterdam, The Netherlands. “The SID Pain App”. Korving, H. (presentation), Sterkenburg, P., Barakova, E. & Feijs, L.

Presentation “Pain recognition and treatment in rare genetic disorders and intellectual disability” during a Research Meeting for employees of the department of Child and Family Studies of the Vrije Universiteit (September, 2021: online). H. Korving.

EAMHID. 2021. 23-25 September 2021. Berlin, Germany. “Pain recognition and treatment in rare genetic disorders and intellectual disability”. Korving, H. (presentation), Huisman, S., Menke, L. & Sterkenburg, P.

Presentation “The development of the smart sock and its uses in research” during a Research Meeting for employees of the department of Child and Family Studies of the Vrije Universiteit (November, 2021: online). T. Doodeman, K. Frederiks & H. Korving.

Presentation “Het signaleren van pijn met fysiologische maten bij mensen met EMB en ZEVMB: Wat we nu weten en waar we naartoe gaan” At FORTIOR: ‘Omgaan met pijn bij mensen met EMB en ZEMVB’. Utrecht. 26 November 2021. A. De la Croix & H. Korving (plenary presentation).

Presentation: “Het signaleren van pijn met fysiologische maten bij mensen met EMB en ZEVMB: Wat we nu weten en waar we naartoe gaan.” At the Alzheimercafé in Amsterdam Zuidoost. 10 February 2022. H. Korving.

Presentation: “Pain signaling with physiological measures for persons with severe intellectual disability” at the PhD colloquium of the Eindhoven University for Technology, Industrial Design Department. 16 March 2022: Eindhoven. H. Korving.

Presentation “Pain signaling with physiological measures for persons with severe intellectual disability” during a Research Meeting for employees of the department of Child and Family Studies of the Vrije Universiteit (April, 2022: online). H. Korving.

Presentation: “Onderzoek naar de EMB pijn app”. During a Focus group meeting NL/BE. 25 April 2022: online. H. Korving.

Workshop “Use of the smart sock and SID Pain App”. Vilans Conference: Zoek Het Uit! 7 September 2022: Nieuwegein. H. Korving.

Guest Lecture “Pijn App, Slimme Sok en andere onderzoeken van de Academische Werkplaats” during the course ‘Opvoeding en Onderwijs in de 21e eeuw’ at the Vrije Universiteit Amsterdam. 21 October 2022. H. Korving.

Poster presentation: “The SID Pain App System: Introducing a system to physiologically measure pain in people with severe intellectual disability”. Amsterdam Public Health (APH) annual meeting. November 1, 2022: Amsterdam. H. Korving.

Network meeting Academische Werkplaats, Amsterdam, 22 november 2022. “De EMB Pijn App voor het lichamelijk meten van pijn bij volwassenen met EMB”. K. Frederiks (presentation) & H. Korving.

Guest lecture on Attachment Theory at the Vrije Universiteit Parents Day. Amsterdam. 15 April 2023. H. Korving.

Presentation “Het signaleren en monitoren van pijn via observatie of fysiologische maten bij mensen met EMB of ZEVMB.” At FORTIOR: ‘Omgaan met pijn bij kinderen en volwassenen met ernstige en zeer ernstige verstandelijke en meervoudige beperkingen’. Utrecht. 2 June 2023. Enninga, A. & Korving, H. (plenary presentation).

EAMHID. 2023. 21-23 September 2023. Helsinki, Finland. Pre-conference workshop. “Assessing and treating pain experienced by people with severe or profound intellectual disabilities”. Enninga, A. & Korving, H.

EAMHID. 2023. 21-23 September 2023. Helsinki, Finland. “Introducing a mobile pain signaling system for people with severe/profound intellectual disability”. Korving, H. (presentation), Sterkenburg, P, Barakova, E. & Markopoulos, P.

Guest lecture “Inclusieve Digitale Didactiek in het Beroepsonderwijs” at the blended learning course of the University Teacher Education of the Vrije Universiteit Amsterdam. 25 May 2024. Amsterdam, the Netherlands.

Guest lecture “Inclusieve Digitale Didactiek in het Beroepsonderwijs” at the AI and blended learning course of the University Teacher Education of the Vrije Universiteit Amsterdam. 23 September 2024. Amsterdam, the Netherlands.

Presentation “Inclusieve Digitale Didactiek in het Beroepsonderwijs” at the NRO Kennisfestival. 9 October 2024. Amersfoort, the Netherlands.

Symposium “Inclusieve Digitale Didactiek in het Beroepsonderwijs” at the Vrije Universiteit Amsterdam. 25 October 2024. Amsterdam, the Netherlands.

Workshop “Een dobbelspel voor inclusieve digitale didactiek” at the SURF Onderwijsdagen. 12 & 13 November 2024. Almare, Den Haag, The Netherlands.

Other / overige media

Korving, H., Sterkenburg, P.S., Barakova, E.I., Feijs, L.M.G. & Markopoulos, P. (2021). De EMB Pijn Applicatie (The SID Pain Application). Voor het lichamelijk meten van pijn bij volwassenen met EMB of ZEMB (Unpublished mobile app). Amsterdam, Eindhoven. Vrije Universiteit Amsterdam, Eindhoven University of Technology.

Korving, H., Calor, S., Schols, M. & Westbroek, H. (2024). Kijkkader Inclusieve Digitale Didactiek (Framework for inclusive digital education). Vrije Universiteit Amsterdam.

Expert panel EMB&ICT; A group of 8-15 parents of a person with a severe or profound intellectual disability and professionals working with clients with a severe or profound intellectual disability, to give advice on the research and the planning of activities. From March 2019 until April 2023, three times a year, physically (Amsterdam, Amstelveen, Doorn) or online. H. Korving, T. Doodeman & E. van Wingerden.

Newsletters: Nieuwsbrief van de Academische Werkplaats ‘sociale relaties en gehechtheid’ (previous to 2021: nieuwsbrief ‘sociale relaties en ICT’ en ‘EMB&ICT’), online edition four times a year. Currently on https://affect-us.nl/actueel/

Website: https://www.embenict.nl
Website: www.kijkkaderinclusiviteit.nl

Vlog: Het onderzoek naar de EMB pijn app, 2020: De EMB pijn app
Vlog: De EMB pijn app testen in de praktijk, 2022: EMB Pijn App - Experimenten
Vlog: Gesprek over pijn, 2022: https://youtu.be/BMFAN7CcI2s

Aanwezig met stand op de VEINEdagen (29-30 oktober 2021); een beurs voor ouders en professionals in de zorg rondom kinderen met een beperking. (6 afgevaardigden van de academische werkplaats).

Aanwezig met stand op de Kangoeroebeurs (11-12 maart 2022); een beurs in België voor ouders en professionals in de zorg rondom kinderen met een beperking. (3 afgevaardigden van de academische werkplaats).

Aanwezig met stand op de VEINEdagen (11-12 november 2022); een beurs voor ouders en professionals in de zorg rondom kinderen met een beperking. (5 afgevaardigden van de academische werkplaats).

Aanwezig met stand op de VEINEdagen (6-7 oktober 2023); een beurs voor ouders en professionals in de zorg rondom kinderen met een beperking. (6 afgevaardigden van de academische werkplaats).

Projectenwaaier Bartiméus (intern document).