# THE INFLUENCE OF PSYCHOLOGICAL, SOCIAL, AND NEUROBIOLOGICAL FACTORS ON 'EVERYDAY' CHILDHOOD PAIN EXPERIENCES

Thesis submitted in fulfilment of the requirements for the

*Degree of Doctor of Philosophy (Psychology and Health)*

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## TABLE OF CONTENTS

## LIST OF APPENDICES

## ABSTRACT

**Introduction:** The Early Years period (0-5 years) is a critical time of physical, social, and emotional development. During this period, acute 'everyday' pain incidents, such as those leading to bumps, scrapes, and cuts, are some of the most frequent pain experiences for pre-school-aged children (2-5 years of age), and parents typically guide their children through these experiences by offering comfort and support. The biopsychosocial model of pain posits that pain experiences are constructed from the interaction of biological, psychological, and social influences, and this model has previously been used to explore parental influences during child pain experiences in clinical contexts. However, similar research exploring parental influences on their child's experiences with *everyday* pains is lacking, and more specifically, research describing everyday pain experiences during the preschool period is sparse, despite the frequency of everyday pains for pre-school-aged children and the opportunities these provide for investigating mutual biopsychosocial influences between parent and child. This thesis explored the association between parental social support and the experience of their pre-school-aged children during 'everyday' pain incidents. Studies 1 and 2 explored psychosocial influences during everyday pain in parent-child pairs using novel observational and diary methodologies, while Study 3 employed preclinical laboratory methods to explore the biological mechanisms associated with pain experienced in juvenile rats across different social contexts.

**Methods:** In Study 1, 12 families were video recorded within their own home either with or without a researcher present, to capture the natural context for everyday pains. These methods were evaluated against an existing method for capturing everyday pain behaviour, a behavioural checklist used in day-care centres. In Study 2, the use of diary-keeping to report on their child's everyday pains was explored in a sample of 21 parents, and a novel EMA (ecological momentary assessment) was trialled in 9 parent-child pairs to capture real-time

insights into their child's everyday pain events. In Study 3, two cohorts of juvenile female rats (10 in each group) underwent a series of pain and nociceptive tests, either in the presence or absence of the mother ("dam"). Behavioural data was analysed, and brain tissue samples were compared against a behaviourally-naïve control group (N = 10).

**Results:** Findings from Study 1 established that children respond differently to everyday pain experiences when alone with their parent versus when a researcher was also present. The presence of researchers and video-recording equipment proved disruptive to the family's natural environment, affecting the frequency of pain events, the distress that children demonstrated, and the parent's ability to act naturally. In Study 2, the diary proved an acceptable method of capturing everyday pain events, without disrupting the natural environment. Contextual factors such as parental levels of distress and catastrophizing were a strong influence on parental responses to their child's everyday pain experience. Parental expectations of their behaviours and thoughts during their child's pain experiences were not strongly associated with their actual behaviours and thoughts. The EMA revealed that parent and child ratings of pain diverge significantly, with children giving substantially higher ratings than their parents. Study 3 revealed that juvenile female rats isolated from the dam demonstrated blunted responding to thermal and mechanical testing but demonstrated hyper-sensitivity to cold and inflammatory pain testing, compared to rats experiencing pain in the presence of the dam. Social support from the dam was associated with reduced levels of anandamide in the prefrontal cortex, while the experience of pain itself resulted in decreased expression of CB2 receptors, compared to the control group. This suggests that pain may be expressed within the brain through alterations to the endocannabinoid system within the prefrontal cortex.

**Conclusions:** These findings confirm that a child's everyday pain experiences are heavily influenced by psychosocial factors present in their environment during the pain

incident. Parental behaviours are a particularly strong indicator of their child's response to pain, with adaptive behaviours and responses being generally regarded to improve the experience of pain for their child and the psychological wellbeing of both parent and child. Finally, social support during pain experiences is associated with biological changes within the brain. These findings are consistent with previous literature indicating that parents can influence their child's behaviour during painful experiences in clinical settings. Further investigation is needed to confirm whether parent-child interactions are consistent between different types of pain and between pain experiences in different contexts (e.g., everyday versus clinical experiences; longitudinal observations; cultural values). The continued integration and translation of knowledge between preclinical and clinical research is vital to enriching the study of pain in pre-schoolers.

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*"Let us step out into the night, and pursue that flighty temptress: Adventure"*

- Albus Percival Wulfric Brian Dumbledore (1996)

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## STATEMENT OF CONTRIBUTION

The author of this thesis was responsible for leading all aspects of this research, including the study design, data collection, analysis and interpretation, the write-up of each of the three studies that comprise this thesis, and the dissemination of the study findings. The supervisory team, and Graduate Research Committee advised and provided support in conducting this research.

## LIST OF WORKS

Below is a list of dissemination outputs, which have been derived (directly and indirectly) from this thesis:

### Publications

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### *Upcoming*

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O'Sullivan, G., McGuire, B., Roche, M., & Caes, L. (2017, March). *Trialling two methodologies for conducting home-based observations of parent-child mutual interactions during everyday pain experiences: A pilot study*. Poster presented at the Centre for Pain Research Annual Research Day; NUI Galway, Ireland.

O'Sullivan, G., McGuire, B., Roche, M., & Caes, L. (2016, September). *Conducting home-based observations of parent-child mutual interactions during everyday pain experiences.* Poster presented at Annual Scientific Meeting of the Irish Pain Society; Dublin, Ireland.

# LIST OF TABLES

## LIST OF FIGURES

## LIST OF ACRONYMS

| | |
|---|---|
| AEA | Anandamide |
| ACC | Anterior cingulate cortex |
| ADT | Acetone drop test |
| $CB_1$ | Cannabinoid receptor 1 |
| $CB_2$ | Cannabinoid receptor 2 |
| CNS | Central nervous system |
| CPS | Composite Pain Score |
| DEPS | Dalhousie Everyday Pain Scale |
| FAAH | Fatty acid amide hydrolase |
| FPS-R | Faces Pain Scale - Revised |
| HPT | Hot plate test |
| IRPEDNA | Inventory of Parent/Caregiver Responses to the Children's Pain Experience |
| MAGL | Monoacylglycerol lipase |
| MPFC | Medial prefrontal cortex |
| PAG | Periaqueductal grey |
| PCS-P | Pain Catastrophizing Scale – Parent Edition |
| PDSQ | Parental Distress and Sympathising Questionnaire |
| PFC | Prefrontal cortex |
| RVM | Rostral ventromedial medulla |
| S-FPS | Simplified Faces Pain Scale |
| VMPFC | Ventromedial prefrontal cortex |
| VFT | Von Frey test |
| 2-AG | 2-Arachidonoylglycerol |

# CHAPTER I

# INTRODUCTION

## Chapter overview

Chapter I introduces the evidence base for this research project and outlines the key areas of interest to this thesis. This is presented in four sections: Section 1 defines pain and highlights why "everyday" pain experiences are different from clinical pain experiences, partly due to the unique influences that exist between parent and child during such experiences. Section 2 explores the relevant theoretical models to the childhood experience of pain and outlines relevant evidence from observational and imitative learning and social reinforcement by parents during pain experiences. Section 3 presents an overview of the current literature which has documented parent and child influences during painful encounters within natural contexts, to provide a rationale for this research. Section 4 explores the benefits of utilising pre-clinical models to gain a clearer picture of the biological processes associated with pain and illustrates the significant overlap between human and rodent experiences of pain. The chapter concludes with a brief outline of the format of this doctoral thesis, containing the objectives of each study supporting this research.

## Section 1: What is pain?

Pain is described as an "*unpleasant sensory and emotional experience that is associated with, or resembling that associated with, actual or potential tissue damage*" (IASP; Raja, Carr et al., 2020). Pain is not solely provoked by a noxious stimulus, nor is potential damage the defining element of pain. Rather, pain is a complex and subjective *experience* which varies amongst individuals. This is particularly relevant for children, whose experiences with pain have historically been overlooked as they were unable to "describe" their pain adequately. The

field of paediatric pain emerged in the mid-1970s, seeking to provide evidence to confirm the (at that time, controversial) concept that children had pain experiences distinct from those of adults. Early paediatric studies confirmed that under-medication and poorer pain management were common, and often anaesthesia was considered too "risky" for use in children (Caes, Boerner et al., 2016). As recently as 1986, physicians were operating on infants without anaesthesia, under the impression that "*the smallest babies are such primitive organisms that they are oblivious to pain*" (Boffey, 1987, p. 3). Pain management was also "*widely withheld from babies and small children*", preventing adequate postoperative pain relief or analgesia for burns, cancer and similarly painful conditions (Harrison, 1987, p. 34). Thus, the physical experience of pain for children was a mostly negative experience. Since the 1980's paediatric pain research has grown exponentially, with research being largely devoted to improving pain experiences such as needle-pain procedures, surgery-related pains, and chronic pain as these can cause the greatest distress to children.

The toddler and preschool period of development (0-5 years) is a stage of emotional and social learning for young children, and also the period in which the earliest experiences with pain are encountered: "*Each individual learns the application of the word [pain] through experiences related to injury in early life*" (IASP, 1994, p. 209). Pain experiences are common during childhood, including minor medical procedures such as immunisations, blood tests, dental care, and "everyday" incidents which lead to minor injuries such as bumps, scrapes, and cuts (Fearon, McGrath et al., 1996; Noel, Chambers et al., 2018; Young, 2005). Regardless of the severity or duration of the pain, these experiences are shaped by a range of cognitive and affective factors, such as attention, perceptions, beliefs, and current mood (Che, Cash et al., 2018). For example, children reported higher pain tolerance if distracted while undergoing procedures (Weiss, Dahlquist et al., 2011), while children who did not believe in their ability to control their pain reported higher pain intensity (Miró, Huguet et al., 2014). In particular, it

has been suggested that pain experiences are substantially shaped by social factors (Craig, 2009), and that definitions of pain should be updated to emphasise this (Williams & Craig, 2016). Notably, IASP has recently revised its definition of pain for the first time since 1979, alongside accompanying notes which emphasise that "*pain is always a personal experience that is influenced to varying degrees by biological, psychological and social factors*" (Raja et al., 2020).

A particularly well-studied social component is the role of social support, which is the experience of being loved and cared for by others, or the perception of the availability of these resources (Che et al., 2018). An increasing number of studies have demonstrated that social support from a loved one during pain can decrease pain severity (Brown, Sheffield et al., 2003; López-Martínez, Esteve-Zarazaga et al., 2008; McClelland & McCubbin, 2008), increase tolerance to pain (Master, Eisenberger et al., 2009; Roberts, Klatzkin et al., 2015), and promote reduced stress and improved coping strategies and health outcomes (Che et al., 2018; Krahé, Springer et al., 2013; Uchino, Carlisle et al., 2011). More specifically, social support is particularly influential during a child's experiences of pain. Young children can identify when they experience pain, but they may not yet fully understand it, and their strategies for coping with pain typically rely on their parents (Harbeck & Peterson, 1992; Liossi, Noble et al., 2012; Power, Liossi et al., 2007). The influence of parental support in helping children to navigate painful experiences is well-established within clinical pain experiences such as immunisations and post-procedural pain (Brown, De Young et al., 2018; Campbell, DiLorenzo et al., 2017; Eccleston, Fisher et al., 2015; Harrison, Timmers et al., 2020; Krahé et al., 2013; Piira, Sugiura et al., 2005; Taddio, Ilersich et al., 2009; Taddio, Shah et al., 2013). For example, distress scores were lower in parents and children when parents attended needle-pain procedures, and parental presence did not impact clinician performance (Wolfram & Turner, 1996). Accordingly, parental involvement is recommended as best practice for clinicians conducting

such procedures (Blount, Bachanas et al., 1992; Manimala, Blount et al., 2000; WHO & HELPinKids, 2015). Next, Section 2 will describe the key theoretical models of relevance to our understanding of social support mechanisms during painful experiences in childhood.

## Section 2: Theoretical considerations

### Social learning theory and the Biopsychosocial Model of Pain

Social learning theory encompasses the notion that acquiring knowledge about one's environment is a "reciprocal determinist" cycle, wherein internal behaviour and environmental conditions each influence the other, and highlights the role of vicarious and imitative processes in cognitive development (Bandura & Walters, 1977). Building on this, Vygotsky's theory of Sociocultural Development emphasised that a child's cognitive development is particularly dependent on social interaction, and posited that parent socialisation methods are instrumental learning tools for the child's socio-emotional development during the preschool (2-5 years) period of development (Langford, 2005). Social learning and imitation play a key role in how children experience and interpret pain; for example, a child watching their parent respond to their own pain acquires knowledge on pain management (Goubert, Craig et al., 2005; Goubert, Vlaeyen et al., 2011).

The biopsychosocial model of pain was derived from these social learning theories, proposing that pain responses arise from a three-way interaction of biological, psychological, and social influences (Engel, 1977). Its predecessor, the biomedical model, had assumed that pain was merely a symptom of underlying disease or tissue damage and that treating the physical damage would eliminate pain entirely, dismissing the potential contribution of social, psychological or behavioural dimensions towards illness (Keefe, Abernethy et al., 2005). Comparatively, the biopsychosocial model allowed practitioners to account for the individual

experience of the patient and the social context in which they live, for "*the boundaries between health and disease are…diffused by cultural, social, and psychological considerations*" (Engel, 1977, p. 132). Where the biomedical model had prioritised intrapersonal (biological) factors, the biopsychosocial model places a distinct emphasis on interpersonal (psychosocial) factors in pain (Craig, 2009; Engel, 1977). Pain experiences are both intra- and interpersonal, as pain can be shared by those around us, with empathy allowing us to 'feel' another's pain; thus, pain experiences should be examined within the social context in which they occur (Engel, 1977; Karos, 2017). The biopsychosocial model of pain is of particular relevance to paediatric pain, as children rely on caregivers to interpret their distress and their pain responses can be influenced by who is present (Engel, 1977; Hadjistavropoulos, Craig et al., 2011; Harrison et al., 2020). In this regard, parents are uniquely positioned to "*sense a child's pain and distress, acknowledge the child's feelings and calmly kiss the hurt knee*" without betraying their own (potentially distressed) feelings (Goubert et al., 2005, p. 287), and shape how their child will respond to pain through observational learning (Goubert et al., 2011).

**Communications model**

Children learn pain management behaviours from observing how their parents manage their own pain, and from observing how their parents respond to them when they experience pain (Goubert et al., 2011). This fits within the theoretical outline of the communications model of pain (Hadjistavropoulos et al., 2011). The communications model maps onto the biopsychosocial framework, emphasising that while biological mechanisms are the foundations of the psychological processes engaged during pain experiences, social processes are a key determinant in the causes and outcomes of pain experiences and in how pain behaviours are expressed (Engel, 1977). It proposes that the communication of one's pain experience is a multi-step process: first, the person's internal experience of pain is encoded through the input of behavioural, affective, and cognitive processes, which are influenced by interpersonal and

social determinants. As pain is a subjective experience, the person then communicates their experience as an action to observers, who must decode the action successfully if they are to support the person through pain. In this regard, pain communication is a social "transaction" between the person experiencing pain and those observing (Hadjistavropoulos et al., 2011).

Thus, the ability of parents to decode and understand their child's pain experience is an essential element of the social transaction of pain communication, dependent on the parent's own emotional response during their child's pain experiences (Dahlquist & Shroff Pendley, 2005; Goubert et al., 2005). Empathy – or recognising the experience of another person – involves both "top-down" processes (e.g., a parent's knowledge and prior experience of pain situations) and "bottom-up" processes (e.g., their child's facial cues while in pain). From these processes, the parent gains a sense of understanding for their child's pain experience and this evokes affective responses such as parental distress or anxiety. Finally, their understanding and the resulting affective responses combine to reciprocally-influence the behavioural responses they provide to their child (Goubert et al., 2005). These responses cannot necessarily be taught: parents naturally engage in soothing methods if their child is in pain, offering both physical comfort and verbal reassurance without prompting (Lisi, Campbell et al., 2013).

Parental responses to their child's pain experiences are influenced by a complex amalgamation of factors. In particular, pain-related catastrophizing is an "*exaggerated and negative cognitive-affective schema during actual or anticipated painful stimulation*" (Quartana, Campbell et al., 2009, p. 746). Catastrophizing is a multidimensional construct, falling into three distinct categories: Rumination, Magnification, and Helplessness, which are strongly associated with affective and sensory dimensions of pain (Sullivan, Bishop et al., 1995; Sullivan, Lynch et al., 2005). In parents, catastrophizing about their child's pain is associated with increased parental distress and anxiety, resulting in higher estimates of their child's pain (Caes, Goubert et al., 2016; Goubert, Eccleston et al., 2006; Goubert, Vervoort et

al., 2009) and attempts to restrict their child's activities to prevent additional pain (Caes, Vervoort, Eccleston et al., 2012; Caes, Vervoort et al., 2011). In children, catastrophizing is associated with depression, poorer functioning and increased disability (Goubert et al., 2006; Guite, McCue et al., 2011), resulting in increased displays of pain when parents were present (Vervoort, Caes et al., 2011; Vervoort, Goubert et al., 2008) and lower pain tolerance and increased avoidance of pain faces among children reporting high magnification (Vervoort, Trost et al., 2013). Consequently, parent responses towards their child can differ depending on the level of catastrophizing they display (Caes, Vervoort, Eccleston, et al., 2012), the perceived severity of different pain events (e.g., during immunisations versus "everyday" pains) (Walsh, McGrath et al., 2008), and the 'certainty' they feel when interpreting their child's distress (Franck, Noble et al., 2010b). For instance, parents identified more child pain behaviours and responded more confidently when their child experienced a minor illness than when they experienced a minor injury (Franck et al., 2010b). In short, parental behaviours such as catastrophizing may represent key indicators of how they respond to their child's pain, and in turn, may indicate how their child responds to pain in front of their parent.

## Observational learning

### Vicarious learning

The central concept in social learning theory, "observational learning", is the vicarious process of imitating and modelling behaviours by observing the behaviour of other people and its consequences (Bandura, 1969; Bandura & Walters, 1977). Infants have the innate ability to communicate pain and distress to parents, initially through cries or facial cues (Hadjistavropoulos et al., 2011), and eventually, language (Franck, Noble et al., 2010a). Children learn that their parents will comfort and relieve their pain and as their communication skills improve, they can request specific forms of comfort, such as "kiss it better", or "pick me up" (Franck et al., 2010a; Noel, Chambers, et al., 2018). Thus, parents are well-placed to model

appropriate pain management behaviours for their child. For example, teaching the child to take deep breaths, or use their imagination to lessen the pain; e.g., using water to "wash the pain away" (Power et al., 2007). Throughout the preschool stage of development, children continue to learn from the examples offered by their parents and others before learning to act independently (Craig, Stanford et al., 2006; Shneidman, Buresh et al., 2009; Stanford, Chambers et al., 2005).

The capacity to learn through observation entails that children do not necessarily need to *experience* pain to learn from it, if they have *observed* pain in others, such as parents, siblings, peers, or strangers (Shimpi, Akhtar et al., 2013). Observational learning is robust enough that any 'teacher' will suffice, but young children may benefit most from models they feel closest to (Bandura, 1969; Palermo, Valrie et al., 2014; Shimpi et al., 2013). Parents often experience minor everyday pains around the home (e.g., stubbing their toe, occasional headaches, etc.) and such observations offer children a multitude of valuable information. By observing their parent managing those painful moments, children recognise the minor pains they experience themselves, and learn which actions can reduce pain (e.g., rubbing the sore toe) (Goubert et al., 2005; Goubert et al., 2011). Children also learn to anticipate situations which could potentially cause pain; e.g., watching their parent grimace when lifting a heavy object will teach the child that such actions may cause pain and they should react similarly to avoid hurting themselves (Goubert et al., 2011). Thus, it is reasonable to conclude that children acquire pain behaviours through the vicarious observation of role models.

Within paediatric research, the majority of observational learning studies within families have involved children observing parents during experimental pain tests (Boerner, Chambers et al., 2017; Chambers, Craig et al., 2002), or exploring functioning in children of a parent living with chronic pain (Evans & Keenan, 2007; Palermo et al., 2014; Walker, Williams et al., 2006). Such studies have demonstrated that parents and children influence each other's

approaches to pain: for example, children reported higher anxiety when watching their parent exaggerate their response to pain (Boerner et al., 2017), and girls – but not boys – reported increased pain if their mother engaged in distress-promoting behaviours (such as criticising or apologising to the child) instead of pain-reducing behaviours (such as distraction or humour) (Chambers et al., 2002). Children of parents with chronic pain were more likely to report increased pain symptoms, compared to children of healthy parents (Evans & Keenan, 2007), and parental chronic pain behaviours were strongly associated with child pain and functioning (Cordts, Stone et al., 2019). Given that children have been shown to respond vicariously to parent behaviours during pain experiences in clinical and experimental settings, it is equally likely that children also learn through observational (or vicarious) learning during pain experiences within *other* settings, such as at home. It is worth exploring parent-child interactions during everyday pain experiences, to observe how children learn about pain at home in a familiar setting. In addition to providing evidence of the specific nature and role of vicarious learning within the home, it is worth noting that vicarious learning may not be the only approach that parents utilise when modelling appropriate behaviours for their child, and home-based studies may capture *other forms* of learning in action.

**Social reinforcement**

Observational or vicarious learning about pain is a relatively passive activity, where the child observes pain management techniques being used by their parent or other suitable role models. Conversely, operant learning about pain management is a more 'active' form of engagement. Operant learning (or reinforcement) is the concept that pain behaviours are positively or negatively-reinforced by others, to strengthen or weaken those respective behaviours (Fordyce, Fowler et al., 1973). Current literature indicates that parents are equally likely to use positive and negative reinforcement during their child's pain experiences, suggesting that parents are unaware of the potential for *negative* reinforcement in their

responses to their child's pain (Buenaver, Edwards et al., 2007; Vervoort et al., 2011). Protective (or perhaps more accurately, *over*-protective) parental behaviours such as reassurance or over-explaining can, counter-intuitively, be detrimental to the child's experience of pain (Lisi et al., 2013). For instance, solicitousness, in which *"parents or caregivers attend to the child's pain behaviours by giving positive or negative reinforcement"* (Huguet, Miró et al., 2008, p. 136) can encourage the over-expression of pain, while discouragement can deter expression of pain; both of which can lead to negative child pain outcomes (Birnie, Boerner et al., 2013). In general, it has been shown that parents who engage in protective behaviours, also referred to as distress-promoting behaviours magnify the child's negative responses (e.g., explaining impending procedures, offering reassurance, or apologising) (Cohen, Rodrigues et al., 2015; Jacobsen, Manne et al., 1990), while parents who use coping-promoting behaviours buffer pain experiences, producing more positive child outcomes (e.g., distraction, deep breathing, and problem-solving) (Cohen, 2008; Cohen et al., 2015; Young, 2005). Even the act of putting a sticky plaster over the wound promotes positive reinforcement, by encouraging the child to forget about the injury ("*out of sight, out of mind*") (Power et al., 2007).

Reinforcement behaviours have been widely explored in both chronic and experimental pain literature. Parents of children with chronic abdominal pain rated both attention to the child and distraction as being equally beneficial for relieving their child's discomfort, but while parents perceived that distraction had greater potential to negatively-impact their child, they did not feel that giving attention to their child had any potentially-negative impact. Yet, the study findings revealed that symptom complaints doubled when parents gave their child attention, and halved when distracting them (Walker et al., 2006). Elsewhere, parents instructed to reassure their child during a procedure reported more personal distress afterwards than parents instructed to distract their child, despite feeling less upset and more confident than other parents prior to the procedure (Manimala et al., 2000). Finally, following an educational

intervention, parents had better knowledge of the potential negative impacts of certain behaviours (i.e., reassurance or explaining procedures) and positive impacts of other behaviours (i.e, distraction and breathing techniques), their children used more breathing techniques than children in the no-intervention group, and this increased parent knowledge was retained three months post-intervention (Cohen et al., 2015). There is also ample evidence that the beliefs and actions of parents can actively modulate and reinforce desirable actions in their child *after the event itself* (Whalley & Hyland, 2013). Reminiscing with children about past events enhances socioemotional and cognitive development, by imparting empathy and improving attention, memory, and language (Salmon & Reese, 2016). For instance, following minor surgeries, parents had the ability to reshape their child's memory of the pain, using emotion-centric prompts to positively influence recall, or pain-centric prompts to negatively influence recall (Noel, Pavlova et al., 2019; Noel, Pavlova et al., 2018). Additionally, parents utilised different elaboration strategies when prompting their child about *painful* versus *sad* events, socialising their children to regard pain as distinct from other forms of distress (Pavlova, Graham et al., 2019). In short, parents play a key role in reinforcing how children reflect on past and current pain experiences and potentially how they will cope with future pain (Franck et al., 2010b; Noel, McMurtry et al., 2017; Noel, Pavlova et al., 2017).

Though the majority of this literature has centred on clinical or experimental environments, it is also likely that parents respond instinctively during their child's painful moments within the home environment, and that parental responses at home could unknowingly reinforce maladaptive behaviours to the same extent if they do not understand the influences they exert over (or receive from) their child, or the impact of engaging in certain behaviours over others when their child experiences pain. Educating parents about learning and reinforcement could be helpful in preventing parents from falling prey to instinctive or societal biases where parents feel they *should* attend to their child's symptoms and reassure them,

thereby reducing the potential for negative child pain outcomes. Both vicarious and operant learning have been shown to play a role in parental modelling of *pain behaviours* in clinical and experimental settings, and in parental modelling of *other behaviours* for their child at home (e.g., learning to share, good table manners, etc.). As there is already evidence for the role of vicarious and operant learning in the home environment for non-pain behaviours, it is reasonable to conclude that both play a role how parents model behaviours for "everyday" childhood pains. However, the precise nature of these techniques may be modality-specific, and depend on the desired outcome by the parent. For instance, parents may demonstrate soothing techniques such as rubbing the sore spot (i.e., vicarious learning) for the child to use following a painful incident, but may switch to preventative techniques such as admonishing the child, or instructing them to be more careful (i.e., operant learning and reinforcement) to reduce the likelihood of subsequent incidents. As little is currently known about how parents teach their child to manage everyday pain experiences, it is prudent to investigate and observe the use of behavioural reinforcement at home. The studies outlined in Sections 1 and 2 support the notion that parental social reinforcement – even unintended – plays a key role in their child's experience of pain, and confirm that clinical and experimental child pain experiences are bidirectional. In Section 3, I will review the literature that has demonstrated bidirectional influences during "everyday" child pain experiences in naturalistic environments.

## Section 3: Literature review of "everyday" pains

### What is the relevance of studying "everyday" pains?

"Everyday" pains are generally classified as minor incidents that lead to injuries such as bumps, scrapes, and cuts. Children cite such incidents as causes of pain more often than any other type of pain (Harbeck & Peterson, 1992). It is estimated that pre-school-aged children

experience an "everyday" pain approximately every 3 waking hours (Fearon et al., 1996), during which children typically rely on parents or caregivers for comfort (Hadjistavropoulos et al., 2011). These experiences are influenced by environmental factors including who is present (Fearon et al., 1996; Gonzalez, Routh et al., 1989; Noel, Chambers, et al., 2018; von Baeyer, Baskerville et al., 1998), and the responses given by those present (Blount et al., 1992; Manimala et al., 2000; Penner, Cline et al., 2008). The predominant evidence for parental support during their child's painful experiences has been drawn from clinical (e.g., needle-pain procedures) and experimental literature (e.g., cold-pressor tests or hypothetical pain scenarios). It is important to acknowledge that clinical and experimental pain experiences differ from those experienced within natural settings: in the former, a level of pain is often expected (e.g., immunisations), which can be anticipated in advance, creating the potential for fear or anxiety to develop (McMurtry, Riddell et al., 2015; Racine, Riddell et al., 2016). Furthermore, these pains typically occur in unfamiliar environments, with unfamiliar medical staff or researchers present (Pritchett, Minnis et al., 2013). Conversely, everyday pains are often spontaneous, cause varying degrees of actual injury, and neither parent nor child can typically anticipate them. In this regard, everyday pains are closely related to unintentional injuries (e.g., burns, shocks, accidental ingestion). However, unintentional injuries are often narrowly defined as "*tissue damage lasting longer than 30 minutes, including evidence suggesting internal (non-visible) tissue damage… e.g., vomiting*" (Morrongiello, Ondejko et al., 2004a). While the two undoubtedly overlap in several respects (location, spontaneity, etc.), everyday pains are generally more fleeting than injuries, which often excludes them from injury studies given their lack of "*lasting tissue damage*". Indeed, everyday pain incidents are so commonplace that they are considered the "*foundations of all pain management behaviour*" (Eccleston, 2012, p. 47), and represent key opportunities to study social modulation of pain and the reciprocal influences

between parent and child (Fearon et al., 1996; Gilbert-MacLeod, Craig et al., 2000; Goubert et al., 2011; Noel, Chambers, et al., 2018; von Baeyer et al., 1998).

**Summary of current research examining "everyday" pain experiences**

Though the evidence of caregiver influences over clinical pain is well-established, their role in everyday pain is less clear. We reviewed literature that observed caregiver responses to children's everyday pains in naturalistic settings. Despite their potential insight into the social modulation of pain, studies of parent-child interactions during "everyday" pain events are scarce. To-date, only a small number of studies have directly observed everyday pain in children aged 2-7 years old (Fearon et al., 1996; Gilbert-MacLeod et al., 2000; Noel, Chambers, et al., 2018; von Baeyer et al., 1998). Of these studies, most utilised online (in-person) behavioural observations of children in day-care environments, and logged staff, child, and/or peer responses during minor pain events (Fearon et al., 1996; Gilbert-MacLeod et al., 2000; von Baeyer et al., 1998), while one study observed child and parental responses during pain events within a play activity centre (Noel, Chambers, et al., 2018) (Table 1.1).

The studies were well-powered, ranging from 50 to 60 children, with the total number of observed pain events ranged from 51-300 pain events. The age range across these studies mapped the full preschool period (1-6 years old), with several studies reporting age differences (see Table 1.1). Children engaged in fewer help-seeking behaviours as they got older (Fearon et al., 1996), the study with the youngest cohort reported that parents were more likely to pick up older toddlers (Noel, Chambers, et al., 2018), and a correlation was reported between child age and display of anger, in developmentally-delayed children (Gilbert-MacLeod et al., 2000). As the developmental capabilities of one or two-year-olds differ from six or seven-year-olds, it is difficult to draw overarching findings.

**Table 1.1: Overview of the currently published literature on "everyday" pain events (from 1996 to 2019)**

| Authors | Setting | Observation type | Measures | N (Male; Female) | Age range (Months) | # pain events | Outcomes |
|---|---|---|---|---|---|---|---|
| Noel et al., 2018 | Indoor play centre | In-person coding *(Audio-video coding used but not reported)* | DEPS-R TTS | **52** 28 M 24 F | 12 - 32 | 101 | Pain events were more common with parents present, compared to previous studies involving pre-schoolers and day-care staff (1.02 events per hour). Parents most often used verbal (reassurance) and non-verbal (hugging, kissing, etc.) behaviours to soothe their child. Boys were less likely to exhibit protective behaviours (e.g., rubbing the injured area) than girls. Older toddlers were more likely to be picked up and soothed by parents |
| Gilbert-McLeod et al., 2000 | Day care | In-person coding | DEPS IBES | **60** 36 M 24 F | 24 - 60 | *Not stated* | Pain events occurred at a mean rate of 0.22 per hour for non-delayed children, and 0.25 for delayed children (*no difference*). Developmentally-delayed children were less likely to display reactions to pain, and less likely to engage in help-seeking or to display social responses than children without developmental delays. Sex difference (only in developmentally-delayed group): boys more likely to use self-protective behaviours than girls. Age difference (only in developmentally-delayed group): correlational relationship between age and use of anger following pain incident |
| von Baeyer et al., 1998 | Day care | In-person coding | DEPS FPS | **50** 28 M 22 F | 37 - 68 | 51 | Pain events occurred at a mean rate of 0.41 per child per hour. Children receiving attention from day-care staff exhibited more visible distress (based on facial coding). Physical comfort and first aid were offered most frequently by adult caregivers. Significant sex difference only for expression of anger (more common in boys); sex differences did not affect the type of response to their pain, nor influence the |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | | | | cause/source of the pain incident; non-significant trend for girls to display more distress than boys. No significant age differences on any observed variables |
| Fearon et al., 1996 | Day care | In-person coding | DEPS | **56**<br>31 M<br>25 F | 28 - 81 | 300 | Pain events occurred approximately every 3 hours (0.33 per child per hour). Children experiencing more pain events showed longer lasting and more intense distress. Day-care staff did not respond to majority of incidents. If responding, behaviours included verbal and physical comfort. Sex differences in both child and adult response: girls showed higher distress than boys; received more physical comforting from day-care staff. Girls were more vocal about distress than boys. Age difference in social response only: children were less likely to exhibit help-seeking behaviours as they got older (3yrs vs 4, 5, and 6yrs). No significant relationship between age and other observed variables. |

*Abbreviations: N=number in sample; M=Male; F=Female; DEPS=Dalhousie Everyday Pain Scale; DEPS-R=Revised Dalhousie Everyday Pain Scale; FPS- Faces Pain Scale; IBES=Illness Behaviour Encouragement Scale; TTS= Toddler Temperament Scale*

All studies reported sex differences in reactions from children and their caregivers. Boys and girls were equally likely to experience pain events, but girls exhibited more visible distress than boys and were more likely to receive physical comfort from caregivers (Fearon et al., 1996). Boys expressed more anger following pain events (von Baeyer et al., 1998) and exhibited fewer protective behaviours (i.e., holding the injured area) than girls (Noel, Chambers, et al., 2018), with one exception: developmentally-delayed boys exhibited more self-protective behaviours than developmentally-delayed girls (Gilbert-MacLeod et al., 2000).

Caregiver responses depended on their relationship with the child. Day-care staff typically dealt with minor pain incidents in a neutral, less emotive manner and often gave no response to the child (Fearon et al., 1996), while parents were less neutral and often responded to their child's pain with protective behaviours (physical comfort or verbal reassurance) rather than coping-promoting behaviours (distraction or offering toys) (Noel, Chambers, et al., 2018). Parental behaviours may be of particular importance during early life, when their influence on the child is strongest (Noel, Chambers, et al., 2018).

All studies utilised the same few suitable measures for online observation of child pain: the *Dalhousie Everyday Pain Scale* (DEPS; Fearon et al., 1996) and the *Faces Pain Scale-Revised* (FPS-R; Hicks, von Baeyer et al., 2001). One study attempted to use audio-visual recording of scheduled "play parties" at a play activity centre, featuring 17-18 parent-child dyads per recording; however, the footage was deemed too poor quality for coding purposes, and the data were not reported (Noel, Chambers, et al., 2018).

Everyday pain events were associated with a range of contextual factors. Environment influenced the frequency of pain events, occurring frequently in day-care centres, but even more frequently in the play centre (Noel, Chambers, et al., 2018). Children who experienced a high number of pain events responded to subsequent incidents with longer, more intense distress (Fearon et al., 1996). To an extent, children could influence the attention they received

following a pain event: stronger facial cues and visible distress attracted caregiver intervention more often (von Baeyer et al., 1998), and individual child characteristics, such as temperament, predicted the emotional and behavioural responses they received from caregivers (Noel, Chambers, et al., 2018).

These studies, though limited in number, have highlighted that children may act differently to minor pains in different environments, and in the presence of different people. There is extensive evidence from clinical experiences that child responses are impacted by social influences and are malleable by the reactions of their parent. Yet, similar, consistent, and strong evidence of social learning within the context of everyday pain experiences is lacking. As these constitute the most common types of pain for young children, it is prudent to explore everyday pain experiences and expand our understanding of how children learn to cope with pain, and how different factors play a role in their experience of pain and development of pain coping strategies.

**Questions still to be answered**

The preschool period is characterised by the development of socioemotional regulation through interactions with caregivers (Failo, Giannotti et al., 2019). Child pain is not merely a miniature version of adult pain, as unique challenges in this developmental period provide a very different context for minor pains and injuries. Young children have less refined motor skills and are at higher risk for accidents and injuries, making the likelihood of pain higher than for adults (Morrongiello, Corbett et al., 2009; Morrongiello et al., 2004a; Morrongiello, Ondejko et al., 2004b). Additionally, the near-permanent presence of caregivers in the nearby environment – to prevent injuries – provides a unique opportunity to employ methods which observe interactions between caregiver and child and can identify potential social influences on pain behaviours. From the small number of previous studies in natural settings, parents and

caregivers can influence a child's general behaviour and responses during painful experiences (Campos, Graesch et al., 2009), and the response of the child can influence caregiver responses in return (Noel, Chambers, et al., 2018). While these studies have greatly enhanced our understanding of naturalistic pain events, much remains unclear: *Why are parental responses different during certain pain experiences? Can we apply evidence from clinical pain experiences to other environments, such as at home or at day-care?* We cannot say whether the experiences are interchangeable, nor whether certain types of pain experience impact more on a child's development: *Do children recall 'everyday' pain events when defining their coping strategies, as they occur frequently, in familiar territory? Or are clinical interactions more memorable, due to their rarity, the presence of unfamiliar people in unfamiliar surroundings, and potential anxiety or apprehension associated with the visit?*

It is possible that limitations with existing research measures prevent us from answering these questions. Changes in methodology when investigating child pains are necessitated by the still-developing cognitive abilities of young children: for example, an inability to use numerical reasoning or to fully interpret their pain may render pain rating scales or diagnostic interviews unsuitable (Stanford, Chambers et al., 2006). This has also constrained previous assessments of child pain, which often rely on parental responses only (Palermo & Chambers, 2005). To combat this, methodologies employed in some areas of paediatric research could be utilised to expand our understanding of everyday pain experiences; for example, audio-visual recording is already used in certain clinical settings (e.g., venepuncture studies). If utilised within everyday pain situations, recordings could enable the objective and reliable observation of both parent and child responses, and capture pain management strategies unfolding in real-time. Additionally, if audio-visual observations were conducted longitudinally they could explore how child pain responses are shaped *throughout* this developmental period, as motor and cognitive improvements advance their understanding and interpretation of pain (Noel,

Chambers, et al., 2018; Schinkel, Chambers et al., 2017). Integrating recordings with innovative, multi-method approaches (e.g., diaries, electronic momentary assessment, and qualitative reflective interviews) presents an exciting opportunity to advance our knowledge of parent-child interactions during everyday pain experiences.

Finally, it must be acknowledged that precise methodologies already exist which can explore the impacts of parental social support on pain outcomes, but which are simply not available within *clinical* paediatric research. For instance, *preclinical* (animal) models possess a distinct advantage as they can investigate the *neurobiological underpinnings* of pain, an avenue of research that is not possible in human studies. Paediatric pain research could benefit tremendously from adopting a multidisciplinary, "translational" approach which integrates both clinical and pre-clinical methods to examine key questions related to the study of child pain (Krahé et al., 2013; Mogil, 2015). Section 4 will discuss the valuable contribution made by preclinical models to our understanding of pain and outline their potential contribution in answering unresolved questions about the role of social support in pain.

## Section 4: Understanding the neurobiology of pain: a key role for animal studies

Earlier, we defined pain as an "*unpleasant sensory and emotional experience…*" (IASP, 1994; Raja et al., 2020). Psychology has focused primarily on the human *experience* of pain while other disciplines have focused on the basic *physiological mechanisms* and underlying properties of pain perception, transmission, and expression. Collectively, these can inform our understanding of pain in different social contexts. The social complexities of appealing to others when in pain are particularly well-defined in humans (Craig, 2009), with empathy resulting from the cooperation of high-level cognitive abilities including language, theory of mind, and executive functioning, in addition to basic reward processes "associated with

attachment, parental care and motivation to care for others" (Decety & Norman, 2015; Goubert et al., 2005). These basic reward processes are also experienced amongst other mammals, where social support is tied to the phylogenetic practice of caring for their offspring. In having fewer offspring than other animals, mammals develop a strong emotional attachment to their young, which predisposes them to be sensitive to signs of suffering in order to ensure the survival of their offspring (Decety & Norman, 2015; Hadjistavropoulos et al., 2011). The influence of parental support on pain sensitivity, responding, and distress during painful events has been well-reviewed in both human (Boerner et al., 2017; Chambers et al., 2002; Goubert, Vervoort et al., 2012; Schinkel et al., 2017; Vervoort et al., 2008) and rodent studies (Burke, Finn et al., 2017; Burke, Geoghegan et al., 2013; Burke, Llorente et al., 2013; de Medeiros, Fleming et al., 2009; Mogil, 2015; Walker, Xu et al., 2008; Weaver, Diorio et al., 2007).

The "social brain" paradigm suggests that mammals are particularly motivated by social encounters, and that similar brain regions are implicated in these rewarding experiences in both humans and rodents (Eisenberger, 2013; Ko, 2017). Verbal communication of pain and distress is common in both species and influenced by others in much the same way (Craig, 2009; Hadjistavropoulos et al., 2011; Mogil, 2015). Infant cries can communicate distress to their caregivers, though the precise nature of the distress (e.g., hunger, discomfort, or shock) may be difficult to interpret (Craig, Gilbert et al., 2000; Grunau & Craig, 1987). Similarly, rats use ultrasonic vocalisations to alert cage-mates or other animals to their pain and distress (Bartal, Decety et al., 2011; Brudzynski, 2013), modulate their reactions to pain based on their neighbour's pain reactions (Langford, 2006; Langford, Tuttleb et al., 2010; Mogil, 2015), and demonstrate prosocial behaviour to reduce distress in cage-mates (Bartal et al., 2011; Meyza, Bartal et al., 2017). Non-verbal pain behaviours are also exhibited in both species: humans and rodents demonstrate behaviours such as guarding, holding, or rubbing the afflicted area (Mogil, 2015). Furthermore, the facial expressions which indicate discomfort in human neonates (e.g.,

brow lowering, eyelid tightening, and nose wrinkling) (Ekman & Friesen, 1978; Grunau & Craig, 1987) have analogous pain identifiers for discomfort in mice, rats, rabbits, and horses (Dalla Costa, Minero et al., 2014; Dolensek, Gehrlach et al., 2020; Langford, Bailey et al., 2010; Mogil, Pang et al., 2020; Sotocina, Sorge et al., 2011). Thus, the study of pain and the effects of social support during painful events do not necessarily have to be restricted to humans: animals are equally capable of displaying pain behaviours both alone and in company.

The strongest advantage of preclinical models, over clinical models, is that they can examine the *neurobiological* properties of pain. Previously, these have confirmed that similar pathways are involved in pain processing in both humans and rodents (Ong, Stohler et al., 2019). The ascending pain pathway carries pain signals via afferent nerve fibres (Figure 1.1, from Yam, Loh et al., 2018). Aδ fibres are myelinated and conduct signals encoding sharp, localised pains, while C fibres are unmyelinated and conduct signals for slow, dull pains. Pain signals are conducted through the dorsal root ganglion of the spinal cord where they travel to the thalamus. The signals are then processed and relayed to the somatosensory cortex and related cortical regions, including the anterior cingulate cortex (ACC), which decode the emotional and cognitive aspects of pain. The descending pain pathway coordinates pain modulation for acute pain in a "top-down" manner (Figure 1.1). Activation of the prefrontal cortex, ACC and amygdala are associated with increased activity in the periaqueductal grey (PAG) which modulates transmissions indirectly through the rostral ventromedial medulla (RVM) in the brainstem to the dorsal horn of the spinal cord, to inhibit pain (Ong et al., 2019).

The prefrontal cortex (PFC) is a key structure of the descending pain pathway, as it is involved in both social responding through high-level cognitive abilities within the medial (MPFC) and ventromedial (VMPFC) areas of the prefrontal cortex (Craig, 2009; Decety & Norman, 2015; Eisenberger, 2013), and in the modulation of affective components of pain processing through connections to the ACC and infra-limbic cortices (Corcoran, Roche et al.,

2015; Ong et al., 2019). Previous work has revealed an association between early-life stress (such as maternal separation), neuroimmune alterations, and pain responding in the PFC (Burke, Llorente, et al., 2013), and demonstrated that increased pain sensitivity may result from pronounced activation of key structures in the descending pain pathway, including the PFC (Jennings, Okine et al., 2014). Given the role of the PFC in the experience of acute pain, it is of relevance to the study of "everyday" pain incidents at a biological level.

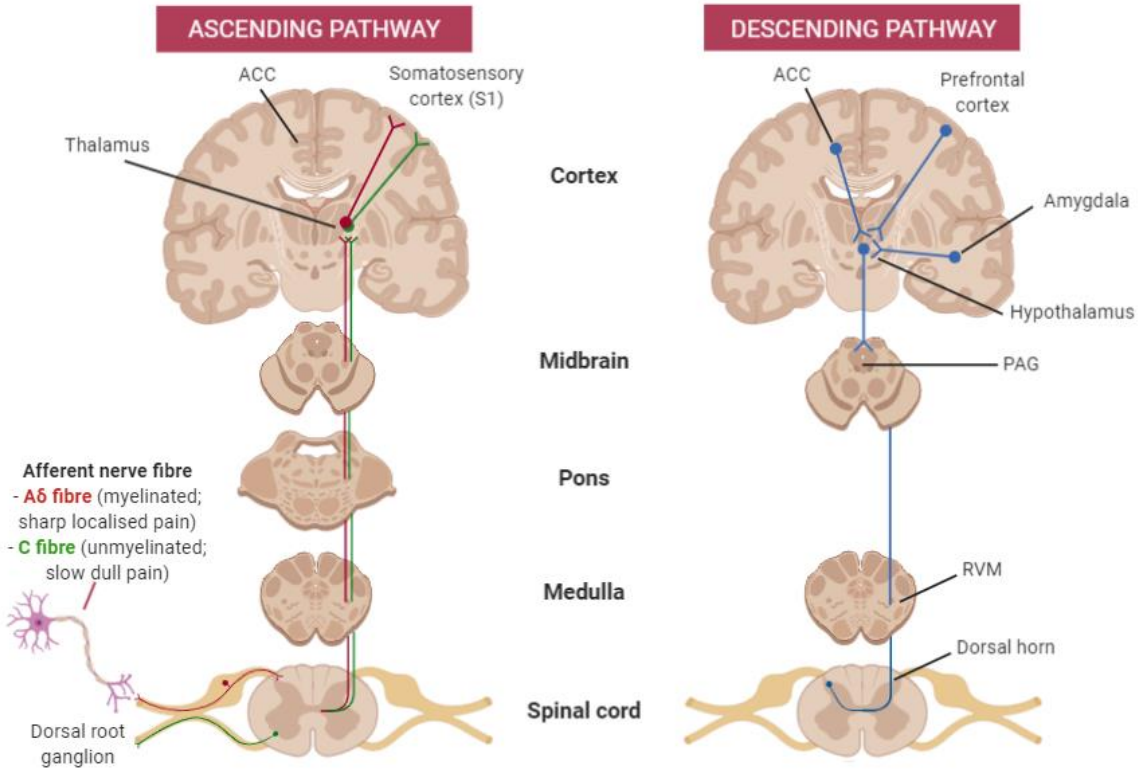


**Figure 1.1: The ascending and descending pain pathways**

Preclinical models have further suggested that painful experiences may result in alterations within the endocannabinoid system (ECS) (Burke et al., 2017; Corcoran et al., 2015; Jennings et al., 2014). For instance, exposure to pain increases levels of the endocannabinoid anandamide within the PAG, while inhibition of FAAH (*fatty acid amide hydrolase*; the enzyme which breaks down anandamide) in the RVM attenuates increased or excessive responses to pain (i.e., hyperalgesia) suggesting that endocannabinoid release can suppress pain

via the descending pathway (Jennings et al., 2014). The ECS has been implicated in several physiological functions including social responding and pain (Corcoran et al., 2015; Marco, Rapino et al., 2011; Schneider, Bindila et al., 2016), with numerous studies reporting ECS signalling during social behaviour and nociceptive responding (Marco, Echeverry-Alzate et al., 2014; Schneider, Hannusch et al., 2014; Schneider, Pätz et al., 2016; Trezza, Baarendse et al., 2010; Vangopoulou, Bourmpoula et al., 2018).

Given the similarities between human and rodent pain behaviours, it is plausible that utilising animal models can answer key questions in relation to the biological underpinnings of pain in the presence or absence of social support, which are currently unresolved by using clinical methods alone. By adopting a "translational" approach, we hope to gain a richer understanding of the role of social context during pain events.

**Thesis format**

In line with the core tenets of social learning theory and the biopsychosocial model, this thesis intends to assess "everyday" pains within the social context in which they naturally occur, and to appraise the influences of social, psychological, and biological factors during childhood everyday pain experiences.

Given the highlighted lack of research within naturalistic environments, Study 1 develops and compares two video-recording methodologies for capturing the mutual social influences between parent and child during pain events within the family home. These methods are critically appraised against the established method of online (in-person) observation (*Chapter II*).

Building on these findings, Study 2 explores the impact of parental psychological factors when observing their child in pain, using a novel electronic diary methodology to gather daily parental reports of their child's "everyday" pains (*Chapter III)*.

Lastly, questions remain as the precise biological underpinnings of pain, which are unanswerable using clinical methods alone. The focus of Study 3 is a pre-clinical laboratory experiment to examine behavioural differences during acute pain conditions when the parent is either present or absent and determine whether social support during pain is associated with alterations in key neurobiological substrates *(Chapter IV)*.

The final chapter of this thesis presents a general overview of the findings. The strengths and limitations of the research are outlined and compared against similar research in the field. Finally, the theoretical and methodological implications of the thesis work are discussed, and suggestions for further research are highlighted (*Chapter V*).

# CHAPTER II

## AM I BEING WATCHED? THE ROLE OF RESEARCHER PRESENCE ON TODDLERS' BEHAVIOUR DURING 'EVERYDAY' PAIN EXPERIENCES: A PILOT STUDY

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### Introduction

Pain is an unavoidable experience in childhood, with frequent experiences of falling or scraped knees (Perquin, Hazebroek-Kampschreur et al., 2000). This is a necessary learning experience, and children mainly depend upon their parents for help and care in such situations (Hadjistavropoulos et al., 2011; Noel, Chambers, et al., 2018; Palermo et al., 2014). Common support strategies are to provide physical and verbal comfort to soothe their pain (e.g., Blount, Devine et al., 2008; Brown et al., 2018; Claar, Simons et al., 2008), or to distract the child with toys or other novelties (e.g., Kleiber & Harper, 1999; MacLaren & Cohen, 2005; Manimala et al., 2000; Noel, Chambers, et al., 2018; Weiss et al., 2011). Debate is ongoing regarding the most appropriate caregiver response to children experiencing acute pain, with current evidence favouring the use of distraction (Birnie, Chambers et al., 2015; Chambers, Taddio et al., 2009). However, a limitation of the existing evidence is the disproportionate focus on pain experienced within medical settings (e.g., vaccinations) or pains which may indicate an

underlying medical problem (e.g., headaches or abdominal pains). Spontaneous pain experiences are a common part of childhood: abdominal pains have an estimated prevalence of 10-20% in school-aged children worldwide (Chitkara, Rawat et al., 2005; Perquin et al., 2000). Vaccinations are more common: infants in the UK and Ireland receive over a dozen scheduled vaccinations within the first twelve months, with further inoculations at pre-school and school ages, providing a wealth of data on pain interactions during vaccinations (Blount et al., 1992; Blount et al., 2008; HSE, 2016; Lisi et al., 2013; Manimala et al., 2000; NHS, 2016; Pillai Riddell, Taddio et al., 2015). Yet, 'everyday' pains (bumps, scrapes, etc.) are the most frequent of all, especially in toddlers who may experience minor pains multiple times per day (Fearon et al., 1996). These typically produce mild, brief distress but usually do not require intervention beyond reassurance (von Baeyer et al., 1998). Despite potentially being a lesser cause for concern, 'everyday' pain experiences represent a model for children to learn pain management skills from those in their social environment, including parents (Blount et al., 1992; Boerner, 2017; Boerner et al., 2017; Brown et al., 2018), day-care staff (Fearon et al., 1996; Gilbert-MacLeod et al., 2000; von Baeyer et al., 1998), and other children (Goubert et al., 2011; Zeman & Garber, 1996). In turn, as pain skills develop, the child's response to minor pain events may influence those around them; i.e., if the child is managing adequately, caregivers may be less likely to intervene or attempt to control the situation (Caes, Vervoort, Eccleston, et al., 2012; Fearon et al., 1996; Goubert, Vervoort et al., 2008; von Baeyer et al., 1998). As minor everyday pain experiences may impact on how a child develops pain responses, it is crucial to gain a better understanding of child-caregiver reciprocal influences during these painful situations (Blount et al., 2008; Kochanska & Aksan, 2004), and the development of pain management skills in early years (Gilbert-MacLeod et al., 2000).

There is a paucity of paediatric research on everyday pains: Noel and colleagues found that just three studies in the previous two decades had examined everyday pain in children aged

2-7 years old (Noel, Chambers, et al., 2018). The limited coverage of everyday pain within the literature could stem from the spontaneity of such events, the inability to control extraneous factors, and a lack of rigorous methodologies (or difficulties with adapting existing methodologies) to capture such experiences adequately (Christensen, 2007; Fearon et al., 1996; von Baeyer et al., 1998). Existing studies have relied on self-reports from parents, which feature subjective elements such as incomplete recall of events or bias to increase social desirability; i.e., only reporting use of 'good' parenting methods (Morsbach & Prinz, 2006). Other studies have gathered self-reports from children; however, many pain assessment tools are unsuitable for younger children (3-4 years), who cannot distinguish between items reliably (Emmott, West et al., 2017; Tomlinson, von Baeyer et al., 2010; von Baeyer, Jaaniste et al., 2017; von Baeyer & Spagrud, 2007). Observational studies within day-care centres can objectively capture large quantities of pain events, but at a cost: logistical barriers to video-recording events, including data protection and child anonymity considerations; and practical difficulties with moving equipment and ensuring that every child is clearly visible on recordings, to gather adequate data from pain events; hence, 'in-the-moment' coding is common, though potentially less reliable. Furthermore, as parents are usually not present in day-care settings, key interactions and learning opportunities may be missed (Hadjistavropoulos et al., 2011; Kochanska & Aksan, 2004; Noel, Chambers, et al., 2018). Given these methodological challenges to gaining insight into children's everyday pain experiences, it is imperative to develop and implement a systematic approach to the study of everyday experiences to facilitate the expansion of our understanding in this domain.

The aim of this pilot study was to explore the feasibility of conducting naturalistic observations of pre-schoolers' everyday pain experiences within their home; as such, no hypotheses were defined *a priori*. Based on previous observational procedures (Campos et al., 2009; Fearon et al., 1996; Gilbert-MacLeod et al., 2000), this pilot study firstly intended to

determine the feasibility of two methods for home-based observation of everyday pain experiences in pre-schoolers by video-recording parent-child interactions during a typical morning or afternoon at home. To establish the viability of these home-based methods, they were compared with an established method of observation, within a day-care setting (Fearon et al., 1996). Specifically, the goals were to explore:

1. whether researcher surveillance during home-based observations is necessary, and/or creates feelings of intrusion in parents and children
2. whether a 3-hour timeframe is sufficient to capture at least one painful event
3. whether observation in the home environment captures different pain experiences to a day-care environment

**Methods**

Quantitative research places strong emphasis on the ability to rigorously observe and measure social or psychological phenomena, and elicit a standardised, objective and accurate representation of that phenomenon (Golafshani, 2003). Thus, confidence in the ability to capture unique elements of a specific phenomenon, and to develop instruments or tools to measure it, is paramount. Observational studies of 'everyday' pains are particularly challenging in this regard: as spontaneous occurrences, there is no guarantee of capturing them within laboratory settings, but the ability to study 'everyday' pains in more natural settings is hindered by a lack of suitable methodologies (Christensen, 2007; Fearon et al., 1996). Such studies face difficulties in finding adequate tools, in terms of reliability and validity, to capture the behaviours. Reliability refers to the *"extent to which results are consistent over time and an accurate representation of the total population under study"* (Joppe, 2006). Previous observational studies have encountered issues related to reliability of existing scales, leading some to develop new measures to capture the events more accurately, such as more detailed

scales or the use of video-recording (Noel, Chambers, et al., 2018). Validity is generally described as "*whether the research truly measures that which it was intended to measure*" (Joppe, 2006). Previous observational studies have questioned how to maintain validity across different contexts, as pain experiences in one setting may not translate elsewhere (Gilbert-MacLeod et al., 2000). These considerations are particularly relevant to the current study: while the chosen measures have been established as reliable in age groups which overlapped with the current sample (e.g., DEPS: 3-7 year olds; FPS-R: 4-12 year olds), not all measures have not all been tested with younger cohorts before (e.g., PDSQ: tested widely in parents of 6-15 year olds, but not in 3-5 year olds) nor has the validity of these measures been explored in a new context (e.g., the family home). Thus, care must be taken when interpreting the results of these measures when used in contexts other than which they were intended.

These challenges informed the design of the current study, to combine objective (recordings) and subjective data (face scales and pain rating scales), given the lack of suitable measurements for the chosen age group. Steps were also taken to preserve natural behaviours through minor restrictions on activities (e.g., no TV watching), based on previous observational studies (Campos et al., 2009; Gilbert-MacLeod et al., 2000). A small sample (N = 12) was chosen, to identify challenges with recruitment for home-based research, and potential logistical or equipment difficulties, while still meeting sample guidelines for pilot studies (Hertzog, 2008). Furthermore, to reduce novelty and preserve the natural environment, researchers in each setting were introduced to the children with the explanation that they would be doing homework during the session and should not be disturbed. In the event that children initiated contact, the researcher would politely explain that they were not allowed to play as they had to do their homework (Fearon et al., 1996); this procedure did not need to be implemented ultimately, as children generally went about playing and did not appear interested in interacting with the researcher beyond initial introductions.

***Procedures for home-based observations***

For home-recordings, families with a child between 3 and 5 years old were recruited at local child-care centres and play groups, through posters and flyers circulated at each location. Interested parents contacted the research team via phone-call or email, and a member of the research team would complete eligibility screening. Eligibility criteria included: at least one child aged 3-5 years; parent and child both generally pain-free and healthy; parent able to read and write in English. Once eligibility was confirmed, the family could choose a time-slot for their recording.

Participating families were recorded within their own home over a 3-hour observation period (usually in the morning or afternoon). This duration was chosen in line with previous studies in day-care settings (Fearon et al., 1996; Gilbert-MacLeod et al., 2000; von Baeyer et al., 1998). Families were randomly assigned to one of two methodologies: half of the families completed the observation period while a member of the research team remained within their home for additional note-taking on the interactions between parent and child ('*Researcher Present Home*'). For the other families, the researcher did not remain present during the observation period; after setting up the camera equipment and collecting consent sheets, they returned only at the end of the session ('*Researcher Not Present Home*'). Independent of the assigned methodology, two cameras were set up to capture two rooms and all events during recording. To capture natural parent-child interactions some minor restrictions were placed on the families, following previous observational research: parents should remain nearby in case a pain event occurred; no visitors or outgoing phone calls were allowed during the recording; and TV watching should be kept to a minimum to encourage active play (Campos et al., 2009; Gilbert-MacLeod et al., 2000).

Before the recording started, consent and assent were gathered from parent and child, and special care was taken to ensure that the child understood the assent process, using verbal

exercises to emphasise their right to say no (e.g., '*If I asked you to eat a bug, do you have to do it?*' or '*Will your mum or dad be upset if you don't want to take part?*') (Weiss et al., 2011) (Appendix D). Following this, the three-hour recording began. Pain events were operationalised as being any event in which (1) the child appeared to be in minor discomfort, or (2) expressed pain or exhibited pain-related behaviours (such as crying, anger, or protective motions, such as rubbing the affected area). Each time a pain event occurred, the child was asked by the parent (or the researcher, if present) to rate their experienced level of pain using the Faces Pain Scale-Revised (FPS-R; Hicks et al., 2001) (Appendix F). Parents then provided a proxy rating for their child's pain using the FPS-R, and rated their own distress on a numeric rating scale (Caes et al., 2011) (Appendix H). Researchers completed the Dalhousie Everyday Pain scale (DEPS) for each pain event, detailing the context of the event and the responses of the child and caregiver(s) involved (Fearon et al., 1996). In the 'Researcher Present Home' condition, DEPS was completed either during or immediately after each pain event; in the 'Researcher Not Present Home' condition, DEPS was completed afterwards by one member of the research team while watching the video-recordings. At the end of the recording, all parents were asked to complete an anonymous survey detailing feedback on their experience of participation in the study.

***Procedures for day-care observations***

The 'Researcher Present Day-care' observations took place at the *University of Stirling, Division of Psychology Kindergarten*. During enrolment in this day-care, parents sign a general consent form for their child to participate in research. Before the start of this study, parents received informed consent sheets and had two weeks to opt out. Five 3-hour observation periods were conducted over a three-week period. Each observation consisted of covert observation via one-way screens during morning drop-off (30 minutes); overt recording during the morning (2 hours); and covert observation at pick-up time (30 minutes). During

observations, children carried out standard activities such as creating art, free play, reading, etc. As in the home, the researcher was careful to not initiate contact directly with the children and would politely decline if children attempted to initiate contact. For each pain event that occurred, the researcher would ask the child to rate their pain using the Faces Pain Scale-Revised (FPS-R) (Hicks et al., 2001) before completing the Dalhousie pain scale themselves (Fearon et al., 1996). Caregivers were not asked to complete either pain scale.

## Materials

### *During observation*

#### 1. Faces Pain Scale-Revised (FPS-R)

The child completed the FPS-R immediately after each pain event that occurred. The FPS-R comprised six faces, showing increasing amounts of pain, scored from 0-10 in 2-pt intervals. Children were asked to indicate which face represented the level of pain they were experiencing at that moment (Hicks et al., 2001) (Appendix F.1). As one of the leading scales for paediatric self-report, the FPS-R has been validated extensively in preschool populations and can be administered without extensive training, making it suitable for teachers or parents (Hicks et al., 2001; von Baeyer et al., 2017). As outlined above, the validity of the FPS-R had not yet been explored in this age group, nor in the context of the family home. In the home observations, parents also used the FPS-R to give a proxy rating of the level of pain they thought their child was experiencing (Appendix F.2).

#### 2. Dalhousie Everyday Pain Scale

The Dalhousie scale (DEPS; Fearon et al., 1996) was completed by the researcher for each pain event that occurred (Appendix I). This scale contained 15 items relating to the context of a pain situation: 1) location of the incident (one item); 2) description of the incident (three

items: *bodily location of pain, who/what caused the pain, researcher perception of pain severity*); 3) physical and behavioural context (four items: *activity level, emotional tone, level of personal control (defined as "the amount of personal control the child was exercising immediately prior to the incident"* (Fearon et al., 1996)), *and number of people involved*); 4) child's response to the incident (six items: *intensity of anger, direction of anger (e.g., to self or another), intensity of distress, duration of distress, nature of any protective behaviours (e.g., holding or favouring the injured area), and social response ('withdrawn', 'neutral', or 'help-seeking' from others*) and 5) adult's response (one item). Body location, cause of pain, protective behaviour, social response, and adult response were recorded using nominal scales, and answers were mutually-exclusive (researchers are instructed to list the most prominent answer, should multiple answers be applicable; e.g., location of injury) (Fearon et al., 1996). Activity level, number of participants, perceived severity, intensity of distress, and intensity of anger were recorded using ordinal scales (e.g., 0='Low/no'; 4 (or 5)='High/a lot'), and level of personal control was rated inversely (1=high control; 5=low control) (Fearon et al., 1996). Duration of distress was measured with a stopwatch. The DEPS is the current standard for assessing everyday pain experiences in preschool children, having been used in multiple studies, and exhibits good validity and inter-rater reliability for young ages (3-7 years) (Fearon et al., 1996; von Baeyer et al., 1998). As previously highlighted, the DEPS-R had not previously been tested with younger age groups (3-4 years) and it had not yet been validated within the home context.

For use within the day-care, minor modifications were made to the Dalhousie scale: first, within the item *Adult Response*, the measure '*first aid'* was replaced by '*conflict negotiation'*, as staff had indicated that the newer item would be more relevant, as pain events within the day-care often result from fighting between 2 or more children (and this was not always relevant within the home-based recordings where there was often only one child).

Finally, the original item *Protective Behaviours* and its measures *(0-4: none, holding, favouring, reduction of activity)* was eliminated. Within the day-care, our primary interest lay in social responses to pain events, rather than protective behaviours, which were not central to this research question.

### *Post-observation*

#### Research participation evaluation survey

As this study aimed to assess the feasibility of video recording to capture natural interactions, it was crucial to gather feedback from those participating in the home-recording sessions. All participating parents completed an anonymous survey to give feedback on the study, detailing (a) their overall experience during participation, e.g., level of comfort, feelings of intrusion, and level of satisfaction with the duration of recording; (b) whether their behaviour or that of their child had changed due to the presence of recording equipment; (c) any negative experiences during their participation; and (d) any other issues that arose during the session, along with any additional comments they wished to make (Appendix J).

#### Data analysis

Demographic data and quantitative survey responses were analysed using descriptive tests in SPSS 24.0 (IBM Corp, Armonk, NY). As one of the primary aims was to determine whether home-based recording methodologies were feasible, and comparable to an existing methodology, one key characterisation was whether pain experiences were similar across the three conditions: several Dalhousie variables were compared using one-way ANOVA: *distress intensity, distress duration, social response, adult response, level of personal control,* and *observer pain estimates*; with Fisher's post-hoc tests when appropriate. To test association within categories (e.g., high versus low), Chi-Square analysis was conducted on two Dalhousie

variables: *adult response*, and *people involved in pain event*. Age effects (3 vs 4 vs 5-year-olds) were compared using one-way ANOVA; sex effects (Male vs Female) were compared using independent t-tests. Due to high levels of missing data within the day-care, the *FPS-R* and the Dalhousie *duration of social response* were compared only in the home-based conditions, using independent t-tests. Statistical significance for all tests was set at α level of $p < .05$. Open-ended survey responses were examined independently and agreed upon by two researchers (GOS; LC), to identify common themes including best or worst elements of participation, or suggestions for improving the study design.

## Results

### Participants

Twelve families participated in the home-based recordings. As one family had two participating children, the total number of children was 13, and 17 parents (12 mothers; 5 fathers). Families were divided equally between the two recording methodologies: Researcher-Present-Home (N = 6); Researcher-Not-Present-Home (N = 6) (Table 2.1). These figures were suitable for a pilot study, based on previous recommendations (Hertzog, 2008). Average parental age was 38 years (SD = 3.97). Most parents were married (94.4%) and 10 families (83%) had more than one child (M = 2.1 children; range: 1-4 children). There were 14 pain events observed from 12 recordings (M = 1.16 per home). Pain events occurred approximately twice as often in the researcher-not-present condition (N = 9) compared to the researcher-present condition (N = 5); $t(11) = 1.82$, $p = .049$.

Within the day-care, 33 children attended the day-care on at least one test date; one parent of a child attending on a test date opted out of the study, leaving a sample of 32 children. 44 pain events were observed, involving 17 of the 32 children (53%) (Table 2.1). This echoes

previously-reported figures (58%; von Baeyer et al., 1998), though lower than the 81% reported in an observation of pain events within play activity centres (Noel, Chambers, et al., 2018).

**Table 2.1: Demographic information for each condition**

| Condition | # participating children | Age (mths) (SD) | Age range (mths) | # pain events | Sex | Location | Pain events /hour |
|---|---|---|---|---|---|---|---|
| **Home** | 13<br><br>6 M<br>7 F | 45.37<br>(8.59) | 37-68 | 14 | 4/14<br>Male<br><br>(29%) | 0/14<br>Outside<br><br>(0%) | **0.39** |
| ***Researcher present*** | *6* | *44.6*<br>*(4.98)* | | *5* | *1M*<br>*4F* | - | |
| ***Not present*** | *7* | *45.11*<br>*(10.06)* | | *9* | *3M*<br>*6F* | - | |
| **Day-care** | 32<br><br>17 M<br>15 F | 48.4<br>(6.46) | 38-63 | 44<br><br>25 M<br>19 F | 25/44<br>Male<br><br>(57%) | 25/44<br>Outside<br><br>(57%) | **2.93** |

*Legend: SD = standard deviation; M = male; F = female; mths = months*

## Researchers

As recruitment difficulties had been reported by similar studies, four researchers were enlisted to complete observations, to ensure availability for participants. All were trained to code the Dalhousie scale by the PI, until a satisfactory level of agreement was reached. The four researchers did not overlap between locations: within the home, two researchers attended observations individually to avoid unnecessary intrusion. Within the day-care, two other researchers initially coded events together, and once a satisfactory level of agreement was reached, only one researcher coded events at any given time. The PI and researchers independently scored the home-recording videos, to provide validity and inter-rater reliability checks. Agreement was generally high, aside from items relying on personal interpretation

(e.g., distress intensity), as reported previously (Noel, Chambers, et al., 2018; von Baeyer et al., 1998).

**Settings**

Some logistical differences between the home and the day-care required adjustments: parents were not present in the day-care, so parental reactions could not be observed; instead, reactions from day-care staff were observed. The use of video-recording within the day-care was not possible: while parents consented to allow their child to be observed, not all consented to video-recording; thus, data collection in the day-care relied on the completion of the Dalhousie pain scale (Fearon et al., 1996) and the FPS-R (Hicks et al., 2001), to allow as many children as possible from the Kindergarten to participate. These changes ensured that study procedures were similar enough between the home and day-care settings to allow feasibility testing of the video-recording methodologies against traditional data collection methods in the day-care observations (Fearon et al., 1996).

As the Dalhousie scale was used in all three methodologies, it offers insight into how pain experience might vary with each observation type. The analyses presented contain the core items which were assessed in all locations and were relevant to the focus of this study (to determine feasibility of home versus day-care observation); thus, some items which are not likely to be affected by the use of different methodologies have not been reported; e.g., 'Bodily location of injury', 'Cause of injury', etc.

**Does observation type influence child behaviours during pain events?**

Following a pain event, children across all three conditions appeared to favour 'help-seeking' (36/58) or 'neutral' behaviours (19/58); thus, observation type did not influence type of response: $F(2,55) = .227$, $p > .05$, $\eta^2 = .008$. Within the home, mean duration of child responses was significantly increased for Researcher Present Home (M = 8.3 secs) compared

to Researcher Not Present (M = 1.67 secs), t(12) = -.2.24, $p$ = .04, d = 1.21 (Duration of social responses was not assessed in the day-care).

Intensity of child distress (e.g., screaming, crying) was significantly influenced by observation type: Researcher Present Home (M = 4.4; SD = .89), Researcher Not Present Home (M = 2.78; SD = .97), and Researcher Day-care (M = 1.46; SD = 1.32), $F(2,55) = 15.06$, $p$ = .001, $\eta^2$ = .35. Post-hoc (Fisher's LSD) tests confirmed that child distress was significantly lower in Researcher-Day-care observations than Researcher-Present-Home ($p$ = .00) or Researcher-Not-Present-Home ($p$ = .005). Both home-recording conditions differed significantly from each other ($p$ = .023), with more distress observed when researchers were present. Distress lasted, on average, 9.2 seconds (SD = 5.07; range: 1-15 secs) in the Researcher-Present-Home condition, 8.44 seconds (SD = 8.49; range: 3-30 secs) in the Researcher-Not-Present-Home condition, and 25.45 seconds in the Researcher-Day-care condition (SD = 44.38; range: 5-80 seconds). Despite duration of distress varying greatly, differences were not significant, $F(2,55) = .96$, $p > .05$, $\eta^2 = .034$.

Observation type significantly affected the child's level of personal control (e.g., how much control they had over their own behaviour); $F(2,55) = 30.82$, $p < .0001$, $\eta^2 = .53$. Post-hoc (Fisher's LSD) tests revealed that children in Researcher-Day-care observations had lower control (M = 4.16, SD = 1.08) than children in Researcher-Present-Home (M = 1.80, SD = .84), and Researcher-Not-Present-Home observations (M = 1.67, SD = .71); $p < .0001$. Furthermore, within the home, children demonstrated lower control when experiencing pain events with their parent present, regardless of how many other observers were present (i.e., siblings and/or a researcher); t(12) = 2.27, $p$ = .043, d = 1.35.

**Does observation type influence adult responses to pain?**

Observation type did not alter adult responses to pain events: Adults in all three conditions favoured comforting behaviours (physical or verbal comfort) over other behaviours, $\chi^2$ (10,58) = 26.32, $p$ = .003, V = .48. In all settings, adults responded similarly: adults in the home favoured physical comfort (9/14), verbal comfort (2/14), distraction (1/14), first aid (1/14), regardless of researcher presence or absence; $p$ > .05, d = .98. Adults in the day-care favoured physical comfort (27/44) regardless of whether the child was seeking help, followed by distraction (8/44), conflict resolution (8/44), and verbal comfort (1/44). As almost all adults favoured physical comfort, this category was further assessed using Chi Square analysis, to explore whether adult responses corresponded to child distress: Adults favoured physical comfort more often if the child's distress was particularly intense and prolonged; $\chi^2$ (50,58) = 68.23, $p$ = .044, V = .61 ("High" distress represented the child being rated as "Sobbing"/option 3 or above on *Distress Intensity*; or if *Distress Duration* lasted 8 seconds or longer, based on Fearon et al., 1996). Though adults appeared to respond more frequently if a child actively sought their help than if a child was withdrawn or neutral, this was not significant: $p$ > .05, $\eta^2$ = .054.

**Does observation type influence pain estimates?**

Observation type significantly affected pain estimates. Child estimates on the FPS-R were lower in Researcher-Present-Home observations (M = 4.00, SD = .00) than in Researcher-Not-Present-Home observations (M = 7.80, SD = 2.68); t(14) = 3.17, $p$ =.03, d = 1.87. Though parents tended to give lower FPS-R estimates for their child's pain (M = 3.83, SD = 2.57), compared to the child's own estimates (M = 6.71, SD = 2.87), their ratings did not significantly differ; $p$ = .057, d = 1.05. In Researcher-Day-care observations, researchers encountered difficulties administering the FPS-R following pain events, as the children were not interested

in completing it, or said they "did not know" which face applied best. As the FPS-R was used successfully in only 3 of 44 events, these results were not analysed, due to missing data.

Finally, observation type influenced researcher estimates of pain severity: Researcher-Present-Home (M = 1.40, SD = .55; N = 5); Researcher-Not-Present-Home (M = .33, SD = .50, N = 9); day-care (M = .89, SD = .62, N = 44); $F(2,55) = 5.56$, $p = .006$, $\eta^2 = .17$. Post-hoc (Fisher's LSD) tests revealed that pain estimates in the Researcher-Not-Present-Home observations were significantly lower than either Researcher-Present-Home ($p = .002$) or Researcher-Day-care estimates ($p = .014$); these did not differ from each other; $p > .05$.

**Influence of other factors on behavioural responses**

***Location***

The *Location of event* Dalhousie item was cross-checked with the video-recordings. As parents in both home conditions had been instructed to move the cameras when the child moved to a new space, both indoor and outdoor spaces were recorded. The observation type strongly influenced the location of pain events, $F(2,55) = 16.22$, $p = .001$, $\eta^2 = .37$: Significantly more outdoor pain events occurred in Researcher-Day-care observations than either Researcher-Present-Home ($p = .001$) or Researcher-Not-Present-Home ($p = .001$) observations. In all observation conditions, children were more likely to favour 'help-seeking', $t(56) = 2.15$, $p = .036$, $d = .57$, or 'neutral' behaviours while outdoors, $t(56) = -2.01$, $p = .049$, $d = .54$; and children playing outdoors demonstrated lower control than children indoors; $t(56) = 3.07$, $p = .005$, $d = .79$. However, being outdoors did not have influence the child's distress, nor were there any differences in responses from caregivers while outdoors; all $p > .05$.

***People involved in pain event***

Within both home-observation conditions, the presence of additional people increased the likelihood of further pain events occurring later in the session; $\chi^2$ (4, N = 13) = 9.75, $p =$

.045, V = .61. The increased number of people also contributed to more intense displays of distress; $\chi^2$ (12, N = 13) = 24.81, $p$ = .016, V = .77. These effects were not seen in the day-care.

***Age and sex effects***

There were limited sex effects: in all conditions, girls displayed higher personal control prior to pain events than boys; t(56) = 2.14, $p$ = .036, d = .57; and girls were more likely to be playing alone at the time of pain events (23/38), while boys were more likely to get hurt while playing with others (14/20); $\chi^2$ (1, N = 58) = 4.88, $p$ = .027, V = .29.

There were no age or sex effects for *distress; social response; adult response; location of pain events;* or *researcher pain ratings*.

**Research participation evaluation survey**

As this study intended to determine the feasibility of home-recording methodologies, all participating parents were invited to complete an anonymous survey to evaluate whether the methodologies used in the current study were acceptable or could be improved for future use (Appendix J). If both parents participated, only one survey was completed, representing the views of the whole family. The Researcher-Present-Home and Researcher-Not-Present-Home methodologies were both considered acceptable to parents and produced similar outcomes (Table 2.2). Some differences emerged based on researcher presence: Parents rated their participation as 'Very positive' more often in the Researcher-Present-Home condition; t(10) = 3.30, $p$ = .008, V = .78 (Q1). Parents also gave higher ratings of the researcher's influence on their experience in the Researcher-Present-Home condition; t(8) = 3.80, $p$ = .005, V = .76 (Q8). While parents tended to rate participation as 'intrusive' in the Researcher-Not-Present-Home condition (Q5), this was not significant, $p$ = .054, V = .81. It was confirmed that researcher presence impacted parent behaviour; $r$ = .677, $p$ = .022, V = .82.

**Table 2.2: Home research participation evaluation responses, by condition**

| Question | Range | Researcher (M; SD; N) | No researcher (M; SD; N) | Sig. |
|---|---|---|---|---|
| 1) Participation experience | 0-10 | 9.57 (.79; N=7) | 7.00 (1.87; N=5) | t(10)= 3.30, p = .008 |
| 4) Child acting the same as usual | 0-4 | .50 (.85; N=6) | .50 (1.00; N=4) | t(9)= -1.11, p > .05 |
| 5) Did the observation and/or recording feel intrusive? | 0-10 | 2.00 (1.92; N=7) | 5.80 (4.09; N=5) | t(10)= 2.18, p = .054 |
| 6) Were things different because you were being videotaped? | 0-10 | 3.71 (2.14; N=7) | 5.80 (1.92; N=5) | t(10)= 1.73, p > .05 |
| 7) Did you feel comfortable with the duration of the observation (i.e. 3 hours)? | 0-10 | 7.86 (2.19; N=7) | 6.80 (1.10; N=5) | t(10)= .98, p > .05 |
| 8) What influence did the researchers have on your experience in this study? | 0-10 | 9.29 (1.89; N=7) | 5.00 (.00; N=3) | t(8)= 3.80, p = .005 |

*Note: Q2, 3, 9-12 were open-ended, and are not represented in this table

Regarding the video recording, the open-ended responses revealed that parents in both conditions felt uncomfortable at being filmed, stating it disrupted their own routine; e.g., *'I didn't do [household tasks] as I felt I needed to be ready to record things or intervene if he got hurt'*; however, parents felt their child's behaviour did not change with the presence of cameras. Parent opinions about the length of recording varied: *'Even though it was long, it wasn't intrusive'; 'The observation was just right. 3 hours was perfect'; 'Length of filming should be longer to increase possibility of experiencing pain'.* Others noted difficulties with keeping their child within range of the cameras: *'Keeping the kids within two rooms was difficult'; 'Wearable cameras would have been better'.* If pain events did not occur, parents suggested methods that might increase the frequency of pain events: *'I wonder [if] this work better in a play centre/playground, where there would be greater likelihood of a fall/bang'.*

**Discussion**

Childhood pain experiences, and especially 'everyday' pains, allow children to learn pain management skills from those in their social environment. However, pain research in 'everyday' settings is still lacking (Noel, Chambers, et al., 2018). This exploratory study intended to assess whether the video recording of observations during 'everyday' painful experiences presents a viable methodology for conducting naturalistic paediatric pain research, and whether familial behaviour is altered when being observed by recording equipment and/or a researcher. Importantly, while parents felt that video-cameras within the family home influenced their own behaviour, they reported no such influences on their child's behaviour.

The survey findings confirmed that the recording methodologies were both acceptable to parents and provided valuable insight into the impact of slight differences in study set-up (e.g., researcher presence or absence). The behaviour of an observer can impact on the actor and be impacted in return (Cook & Kenny, 2005); this potentially reduced the viability of recording the natural routine of families. While parents reported their study experiences as being more positive in the Researcher-Present-Home condition, researcher presence unduly influenced typical behaviour within the home: influencing the number of pain incidents that children experienced, the pain estimates given by children, the intensity of child distress, and the duration of social behaviours, compared to when families were video-recorded without a researcher present. It is possible that children behaved more cautiously than usual around the researcher, and that in their absence, children may have felt more relaxed, engaging in more boisterous play, and more opportunities for pain events. This was reflected in the Researcher-Present-Day-care observations, where the children were surrounded by peers, and were used to having strangers present as the Kindergarten was affiliated with University research centres. As video recording within the day-care centre was not possible, we cannot confirm if child behaviour would differ had there been cameras present instead of researchers.

Notably, the Researcher-Present-Home condition affected the researcher's own ability to objectively estimate child pain: 'perceived hurt' scores were significantly lower in the Researcher-Not-Present-Home (i.e., completed the scale during video playback), and Researcher-Present-Day-Care conditions. It may be that researchers present within the home – who had just presented the Revised Faces Pain Scale (FPS-R) to the child – were aware of the child's ratings of the pain, and this influenced their own pain estimations, while researchers in the other two conditions were not influenced by this. Alternatively, researchers within the home were able to see the child's facial expressions more closely which may have influenced their pain estimations compared to researchers scoring the video tapes or observing in the day-care. As researchers in the day-care typically observed from a greater distance than researchers in the home-based observations, they might not have seen the child's facial expressions clearly. Facial expressions provide a considerable influence on pain estimation; hence different levels of access to facial expressions could explain the variation of pain estimates across settings (Hadjistavropoulos et al., 2011; von Baeyer et al., 1998).

In comparing the innovative home-based observations to the established day-care observations, several differences must be considered: pain events were far more frequent in the day-care (2.93 events per hour) than within the home (0.39 events per hour), although the home-based pain events occurred at similar rates from previous day-care studies (i.e., one event per 3 hours) (Fearon et al., 1996; von Baeyer et al., 1998). Noel et al reported a similar rate of pain events to our day-care observations (approximately three per hour) in their observations of everyday pain events in a play activity centre (Noel, Chambers, et al., 2018). Furthermore, while the Dalhousie scale was used by all observers to assess the pain event immediately after it had happened, the context of the settings was different: parents were present in the home to provide support to their child after pain events, but not present in the day-care, leaving staff-child interactions as the primary source of communication during pain events. This made for

an interesting comparison with how children managed pain in different settings and in the presence of different caregivers, but it does limit our ability to compare this outcome equally. Given the small sample, the use of inferential statistics to further sub-divide the group may seem at odds with the stated desire to present an overview of the *feasibility* of the methods, rather than our statistical confidence in them. Specifically, conclusions drawn from the inferential statistics were limited in power due to the small sample size and need to be interpreted cautiously. The presentation of the statistics was to inform our discussion of the feasibility of these methods, by identifying differences within the group that were related to the condition in which they were being observed. All things being equal, there should have been no significant differences between the conditions (i.e., each should have been equally suitable for observing children and their parents). In that light, the findings that child distress was less intense, and their pain ratings were lower when in the presence of a researcher informed our assessment of (and ultimately, our preference for) the "Researcher-not-present" condition, as researcher presence having an impact on the natural behaviour of the child was detrimental to our exploration of parent-child responses to everyday pains.

In general, child behaviour within the home was consistent with behaviours within the day-care suggesting that the presence of video-cameras was not a notable distractor from the child's "everyday" experience of pain. However, certain pain-related behaviours were different between the home and the day-care centre, e.g., intensity of distress, and the child's personal control over their behaviour were both lower in the day-care than in the home. Previous day-care studies on everyday pain in older children similarly reported that the majority of pain incidents were of low severity and caused low levels of distress (Fearon et al., 1996; von Baeyer et al., 1998). Even young children might be more reluctant to express pain in front of peers than parents (Craig, 2009; Deyo, Prkachin et al., 2004; Larochette, Chambers et al., 2006; Zeman & Garber, 1996), as a result of social strictures such as avoiding embarrassment in front

of peers, worrying their friends, or disrupting playtime. As other behaviours were consistent within the conditions, the presence of peers in the day-care may have inhibited the children from displaying distress, contributing to the notable difference from children within the home. The different observation types in this study were useful for demonstrating subtle differences in the child's response to pain in a group setting, compared to when the child experienced the pain event at home.

While the Researcher-Day-care environment was more efficient in capturing larger numbers of everyday pain events, it had drawbacks: video recording was impossible to use, given data protection considerations, and the logistical issues of moving the equipment to keep the children within a close-enough distance to code effectively. Use of the FPS-R within the day-care was challenging and only administered sporadically: researchers found it difficult to approach the child once they had relaxed, as children were often uninterested in responding or said they didn't know which pain rating applied to them. As one of the stalwart scales for paediatric self-report, the FPS-R was chosen to fit within the existing body of work; however, newer instruments considered more appropriate for younger children have since been identified (von Baeyer et al., 2017), and this may resolve some of the challenges faced in this study. Only one previous observational study attempted video-recording, but the recordings were of too-low quality to code (Noel, Chambers, et al., 2018). The increased burden directly observing multiple children in the day-care centre, and the associated increase in activity level, prevented us from asking day-care staff for deeper insight into individual pain events. In contrast, the home-based video observations allowed for rich interpretation of each pain event, as the video-recordings captured contextual details to supplement the pain scales completed by the parents and children. The continued development of methodologies specifically for use in naturalistic observations (or refinement of existing procedures) may resolve these issues. The Dalhousie Everyday Pain Scale, used within the current study, has recently been adapted to include

objective parental responses to pain, and can be used in the home (Noel, Chambers, et al., 2018); future studies could benefit from similar efforts to improve existing observation tools.

Naturalistic observation of children is not without some practical issues, as reported previously (Campos et al., 2009; Fearon et al., 1996; Gilbert-MacLeod et al., 2000; Noel, Chambers, et al., 2018). The post-participation survey revealed that the home-observation conditions suffered from equipment limitations: parents were loaned two cameras, which meant restricting the child to only two rooms during recording or moving and re-setting the cameras each time the child entered a new room. The parents felt that these restrictions impacted their behaviour, affecting interactions with their child and the estimates they gave for pain events. Parents still regarded their participation as positive, so the intrusion imposed by the cameras was not a detrimental factor; however, such restrictions should be considered when designing studies involving video recording. Additional equipment, or less cumbersome equipment (e.g., wearable cameras) could allow families to move freely within the house and contribute to the naturalistic representation of their normal routine. Another commonly reported issue from the post-participation survey concerned the time-commitment for participation: The lengthy sessions proved to be a detractor when recruiting families and posed logistical issues for researchers attending the recordings. In each session, considerable time was given to parents for completing various psychometric measures, along with consent and assent forms and the evaluation survey. While participating families mostly found this experience (and the time commitment) to be acceptable, these families were already enrolled in the study and thus, more likely to report positive outcomes. Considering the difficulties associated with recruitment, the acceptability of the methodologies by the general public may be lower than that reported here, and recruitment for similar studies may also face similar challenges. To reduce the time commitment and make participation more attractive, it might be less burdensome if measures were completed prior to the session (by mailing the forms in

advance), and for any evaluation surveys to be returned afterwards. While the researchers within the home reported no difficulties sustaining attention during the observations, there were periods with little activity during which fatigue or distraction could set in; we attempted to counteract this by alternating which researcher attended each session, and by scoring the videos afterwards, to ensure the scores remained consistent with the in-person coding. The day-care centre sessions were attended by pairs of researchers, so such issues were avoided; however, this was not practical in the home without disrupting the environment.

Within paediatric pain literature, there is a disproportionate representation of pain within clinical contexts or of clinical relevance: they are often easier to report, and their controllable context and specified time of onset make them 'methodologically cleaner' than everyday pains (Fearon et al., 1996). Everyday pains are spontaneous and occur randomly, if at all (von Baeyer et al., 1998), which often requires a trade-off in external validity (Gilbert-MacLeod et al., 2000). We found several instances where pain events did not occur at all within the home, reducing the efficiency of a three-hour recording period. In such situations, it may be possible to supplement observational data by asking parent and child to discuss a recent pain experience; a similar approach was recently established for clinical pains, such as experimental, procedural, and post-surgical pains (Noel, Pavlova, et al., 2017). This technique could be adapted for use with everyday pain experiences; for example, a brief discussion of how the child felt about a pain such as a tummy-ache or falling over. Such approaches could facilitate recording everyday pains and increase study in this area.

In summary, all three methods of observation captured broadly similar behaviours by the children. Minor influences resulted from the presence of researchers but not from the presence of cameras, which indicates the feasibility of using video recording to conduct naturalistic observational research within family home environments, at least equivalent to currently established direct observation techniques. These methodologies provided a

complementary outlook on how children experience "everyday" pain events: the video-recorded home observations provided clearer insight into the unique relationship between parent and child, and the shared interactions during a painful event; while the day-care observations allowed insight into how children utilise pain-management skills while with peers, and the potential influence of peers over their experience of pain. Subsequent paediatric research efforts should continue examining everyday pain experiences, to supplement the wealth of research on clinically presented pains and strengthen our understanding of the social context of pain in childhood. This exploratory study has confirmed that paediatric research is feasible beyond clinical or experimental settings, and the continued development of new methodologies, or the novel combination of methodologies suitable for this research focus, are crucial endeavours to significantly improve the quality of studies being conducted and the options available for future research.

**Limitations**

The participants of the home-study were recruited from day-care centres and playgroups located within Galway, Ireland. The sample was quite small (N = 13 children) and may have been overly homogenous, reducing the ability to draw firm conclusions regarding behaviours within each setting. The children in the day-care study were enrolled in one university nursery in Stirling, Scotland. As a university research facility, the families lived locally, which may have affected the diversity of the sample, and findings may not translate to areas with a more culturally diverse population. The sample size was within recommended limits for pilot studies (Hertzog, 2008), and allowed us to explore the feasibility of recruiting for and conducting at-home video-recording, and to identify logistical issues which might impact its effectiveness. For instance, having access to only two video-cameras may have impacted the quality of the data, as parents had to either restrict their child within the rooms with cameras, or move the cameras whenever the child left the designated rooms. Despite this,

the technique proved effective: all pain events within the home were either captured on video or through audio (i.e., the child was just out of frame but could clearly be heard), and no pain data was lost. Future studies may benefit from additional equipment, to allow the children to move freely about their home and capture more natural experiences. A significant limitation of the current study was the lack of validated measures specifically designed for the chosen age group (3-5 years). The FPS-R was chosen as it was the 'gold standard' scale at the time of designing the study and had been used widely by previous studies, allowing us to more easily relate our findings to previous literature within the field. However, questions have been raised about the reliability of the FPS-R (and indeed, other facial rating scales) in the 4-5-year age range, and doubts remain about its suitability for 3-year-olds. Newer scales (such as the S-FPS; Emmott et al., 2017) have since been developed and validated in 3-5-year olds and represent a more reliable measure for future studies.

**Overall conclusions**

This research corroborated previous findings that children react differently to pain depending on who is present, and that caregiver responses are influenced in turn by the child's pain response. Although this study has contributed to a still-emerging body of literature focusing on acute "everyday" pains, the reported methods were disruptive to the natural home environment and were, at times, a little burdensome. While great strides have been made to develop methods to assess and treat paediatric pain, these have largely examined the experience of chronic pain or post-surgical pain, which both have a significant impact on child health and wellbeing. Comparatively, research assessing the experience of everyday pains is still relatively scarce, and the development of methodologies to capture the unique context of everyday pains is lacking. Further research investigating the experience of everyday pains for parent and child, using innovative and feasible methodologies, will be examined in Chapter 3.

# CHAPTER III

## EXPLORING PARENTAL RESPONSES TO PRE-SCHOOLERS' 'EVERYDAY' PAIN EXPERIENCES THROUGH DIARY AND ECOLOGICAL MOMENTARY ASSESSMENT METHODOLOGIES

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### Introduction

"Everyday" pain events are common experiences for young children, occurring approximately every three waking hours (Fearon et al., 1996). Such pain events can lead to minor injuries such as bumps, scrapes, or cuts, which often require no treatment. On most occasions, parents will ask their child about the pain and offer a solution to "make it all better" (Franck et al., 2010a), such as instructing their child to take deep breaths, or using water to "wash the pain away" (Power et al., 2007). Pain communication is limited in the early years, and during this time, parents acquire extended experience of interpreting their child's needs from the distressed cries (Hadjistavropoulos et al., 2011; Liossi et al., 2012; Power et al., 2007). Pain communication serves multiple functions, such as expressing distress; seeking comfort from parents; or regulating pain reactions to continue playtime activities or avoid embarrassment or reprimands from parents (Franck et al., 2010a; Liossi et al., 2012; Noel,

Chambers, et al., 2018). As such, a significant portion of a child's pain experience is governed by their parent's interpretation of and response to the situation.

Given their frequency, it is reasonable to assume that everyday pain events present significant opportunities for understanding how parents and children learn how to manage child pain experiences. However, research on everyday pain experiences is scarce, which might in part result from the difficulties in capturing such pains, as everyday pains events are spontaneous and impossible to replicate faithfully in a laboratory setting (Fearon et al., 1996). Equally, child self-reports of pain are often unreliable (Chambers et al., 2002; Emmott et al., 2017), and heavily dependent on the still-developing cognitive capabilities of the child (von Baeyer et al., 2017) and the social context in which the pain occurs (von Baeyer, 2009). As such, observational methods present the best means to capture the *context* surrounding everyday pain events, having been previously employed in day care centres (Fearon et al., 1996; Gilbert-MacLeod et al., 2000; von Baeyer et al., 1998), play activity centres (Noel, Chambers, et al., 2018), and family homes (O'Sullivan, McGuire et al., 2019). Each of these studies utilised behavioural checklists, and two studies also attempted to use audio-visual recordings, though not without difficulties. Within an activity centre setting, large numbers of parent-child pairs were hard to observe reliably, resulting in poor quality video-camera footage (Noel, Chambers, et al., 2018). On the other hand, the presence of cameras and researchers in the family home impacted child and parent behaviour during everyday pain events, resulting in increased child distress, increased parental discomfort, and reduced child pain estimates (O'Sullivan et al., 2019). Thus, alternative measures are still needed to reliably capture the context surrounding pain events without impacting the natural behaviour of families.

Electronic diaries allow parents to capture their insights into pain events in real-time, without intrusion from researchers and/or recording equipment. The data is recorded instantaneously, reducing the likelihood of biased recall or insufficient detail associated with

retrospective accounts (Gil, Porter et al., 2000; Palermo, Valenzuela et al., 2004; Stinson, Petroz et al., 2006). End-of-day pain diaries are widely used and accepted in clinical practice, as an effective means for children and parents to record daily fluctuations in pain intensity (Gaertner, Elsner et al., 2004), and monitor recurrent pains such as persistent headaches or juvenile chronic pain (Palermo et al., 2004; Stinson et al., 2006). Furthermore, a specific diary methodology, ecological momentary assessment (EMA), can instantly capture "in-the-moment" reflections from parent and child, which further increases rating accuracy and reduces recall bias (May, Junghaenel et al., 2018). Within clinical settings, both end-of-day reporting and EMA allow patients and practitioners to chart peaks in pain intensity, emotional changes, or sleep disturbances (May et al., 2018). However, neither method has previously been utilised to gather data on minor pains. If used in conjunction, parents and children could immediately report pain events and accurately capture the context surrounding everyday pains without disrupting the environment. This could provide valuable insight into bidirectional influences between caregiver and child in the early years.

Furthermore, diary methods may allow us to explore variations between parent anticipated and actual thoughts and behaviours in response to their child's pain experiences. For instance, across various pain events, parental responses such as catastrophizing have been found to strongly influence their emotional and behavioral responses to their child's pain, with parents who reported high levels of catastrophizing experiencing more distress and attempting to curtail their child's activities to prevent further pain (Caes et al., 2011; Caes, Vervoort, Trost et al., 2012; Goubert et al., 2008). However, while strongly correlated, variations have been found between parents' anticipated or general (trait) levels and actual (state) levels of catastrophic thinking about their child's pain, which in turn impacts their emotional and behavioral responses differently. In particular, state levels of catastrophic thinking were more strongly associated with pain-related outcomes such as parent distress than trait levels of

catastrophic thinking (Durand, Birnie et al., 2017). Even the most vivid description of a pain scenario may not match the parent's real-life responses when their child actually experiences pain (Caes, Vervoort, Eccleston, et al., 2012). Thus, repeated measurements of parent behaviours in everyday situations is critical to furthering our understanding of the differences in how parents expect they will respond versus how they respond "in the moment" (Goubert et al., 2012).

As the potential array of "everyday" pains is so vast, it is unclear how parents devise their personal taxonomy of pain events or decide how to respond. Parents often have to make snap judgements on pain intensity or severity, and their responses are likely to be moderated by a variety of factors (von Baeyer, 2009), including their child's age or sex, or their own level of supervision of the child. For example, drawing from childhood injury literature, active parental supervision of pre-schoolers is the most effective means to prevent injuries and avoid hazards (Dowswell, Towner et al., 1996; Morrongiello et al., 2004b). Passive/absent supervision is associated with increased frequency and increased severity of injuries (Morrongiello et al., 2009; Schnitzer, Dowd et al., 2015). Different supervision strategies affect the capacity to intervene and prevent injuries in a timely manner; thus, parents who actively supervise their child may respond differently to parents who do not, when incidents occur (Peterson, DiLillo et al., 2002). Parental supervision strategies differ with child sex, with parents of boys employing more effort-intensive strategies to prevent injuries, compared to parents of girls (Morrongiello et al., 2004b). Similarly, child age influences supervision strategies: parents monitor younger children more than older children, and direct supervision time decreases as children age (Morrongiello et al., 2004a; Pollack-Nelson & Drago, 2002). Parental monitoring may be particularly relevant if they have multiple children to safeguard: mothers and fathers both spend more quality time with first-born children, even after siblings are born (Price, 2008). This may place later-born children at increased risk of pain events if

they are monitored less by their parents. Thus, it is possible that contextual factors influence parental responses towards their child during everyday pain events.

Consequently, the aims of this study were to (1) assess the capability of a novel self-report diary measure for parents to describe "everyday" pain events occurring within the family home, and gain detailed insight into the characteristics of everyday pain experiences; (2) explore the use of EMA to determine whether parent and child estimates of everyday pain differ from each other; (3) examine the association between parents expected and actual responses during their child's pain experiences; and (4) explore whether parental behaviours are influenced by additional contextual factors.

## Methods

All study procedures and materials were granted ethical approval by the University Research Ethics Committee at NUI Galway (Galway, Ireland).

### *Participants*

Families with a child between 2.5 and 6 years old were recruited through national and local media outlets (including radio, newspaper releases, and social media adverts), posters and flyers circulated to local child-care centres, playgroups, and activity centres, and through a study-specific website. Interested parents contacted the research team via email or social media messaging, and a member of the research team completed eligibility screening. Eligibility criteria included: 1) at least one child aged 2.5-6 years; 2) parent and child are both generally pain-free and healthy; and 3) parent can read and write in English.

A total of 40 parents completed the demographics and pre-diary questionnaires. Of these, 21 parents participated in the diary part of the study (52.5%). Most of the parents listed themselves as the child's biological mother (N = 20; 95.2%) with one parent listed as the

biological father (N = 1; 4.8%) (Table 3.1). The average parental age was 39.24 years (SD = 4.77). The child sample contained 8 girls and 13 boys, and the average age was just under 4 years (44.24 months; SD = 11.74 months). Most parents were married (81%), and 11 families (52.4%) had more than one child (M = 1.95 children; range= 1-5 children). Parents with more than one child in the target age range could participate with each child separately if they wished, or if preferred, these parents could instead choose one eligible child to participate with.

**Table 3.1: Demographic information for participating parents**

| **Parent** | **N** | **Percentage (%)** |
|---|---|---|
| Mother | 20 | 95.2 |
| Father | 1 | 4.8 |
| Mean age | 39.24 years (SD=4.77) | |
| **Child** | | |
| Female | 8 | 61.9 |
| Male | 13 | 38.1 |
| Mean age | 44.24 months (SD=11.74) | |
| Mean children per family | 1.95 (range: 1-5) | |
| **Country of residence** | | |
| Ireland | | 90.5 |
| UK | | 4.8 |
| Canada | | 4.8 |
| **Marital status** | | |
| Married | | 81 |
| Single/unmarried | | 14.3 |
| Other | | 4.8 |
| **Level of education** | | |
| Bachelor's degree | | 38.1 |
| Master's degree | | 19 |
| PhD | | 4.8 |
| Other (e.g., diploma, certificate) | | 33.3 |

***Procedure***

Once eligibility was confirmed, participants were directed to the study website to begin participation in the study. This site presented the full information brief, the informed consent

brief, a demographic survey, pre-participation questionnaire, and external links to both the diary and the EMA assessment. Participants were invited to bookmark the website links for easy access throughout the study period.

All questionnaires and assessments from this study were implemented in electronic format and hosted by LimeSurvey (LimeSurvey GmbH; Hamburg, Germany), a GDPR-compliant software package, per the University's ethics policies on data collection and retention. Paper copies of all surveys were also available upon request in case parents did not have access to a smartphone or computer to complete the surveys electronically. Consent and demographic information were requested and stored separately from other data. Participation was anonymised, though an email address was requested to link diary entries together, and to send automated reminder emails about diary completion during the study period. As a participation incentive, all parents were invited to enter a prize draw for a €50 gift voucher.

***Pre-diary questionnaires***

Parents completed two measures prior to participating in the diary study. First, parents completed the *Inventory of Parent/Caregiver Responses to the Children's Pain Experience* (IRPEDNA), measuring a parent's typical behaviours when their child is in pain (Huguet et al., 2008). Next, parents completed the *Parental Catastrophizing Scale-Parent Version* (PCS-P; Goubert et al., 2006). Once these were completed, the parent proceeded to completing their first diary entry.

***Diary***

One of the hallmark benefits of diary methodology is the ability to assess intra-person changes over time (Stinson et al., 2006). As everyday pain events occur frequently but spontaneously, a reporting period of fourteen consecutive days was considered sufficient. Parents completed one electronic diary entry at the end of each day, describing one pain event

that their child had experienced that day. Where multiple pain events occurred in a single day, parents were asked to report the most "memorable" event. When parents clicked the diary survey link, an information screen explained how to complete the survey, and parents were advised they could skip any question they did not wish to answer. This introduction screen also featured contact details of the lead researcher in case parents had queries or wanted to withdraw their participation. The second screen contained the diary questions, with a progress bar along the top of the screen. The third and final screen confirmed their submission, where parents were greeted with a "Thank you" message, and a reminder to complete another diary entry the following day. The page would automatically refresh back to the introduction screen, if not closed by the parent.

### *EMA*

As the diary was completed solely by parents, an EMA (ecological momentary assessment) was incorporated to explore the child's perspective of everyday pains. Parent-child pairs were invited to complete at least one EMA assessment together, during the same fourteen days that parents completed the end-of-day diaries. Parents were instructed that the EMA questions should be completed on their smartphone *immediately* after a chosen pain event took place, rather than at the end of the day. As the EMA was designed to capture instantaneous reactions, it took only 2-3 minutes to complete.

## Materials

### *IRPEDNA*

Parents completed the *IRPEDNA* (Huguet et al., 2008), a 37-item inventory of a parent's typical behaviours when their child experiences pain (Appendix N). The three subscales, Solicitousness, Discouragement, and Promotion of Well-behaviours and Coping present self-oriented statements *(e.g., 'I use humour to take his/her mind off the*

*discomfort'*), scored on a scale of 0-5 *(*0=*'Never'* to 5=*'Always'*). Scores are calculated by averaging the items for each subscale, with higher scores indicating higher levels of the respective behaviour. For this study, two items from the Solicitousness subscale were removed, as they were not relevant for pre-school children: (1) *"I accept that, in these circumstances, he/she need not do his/her homework"*, and (2) *"I tell his/her teachers how he/she is feeling so that they are aware of the problem during school hours"*. Two further items had their wording amended, to make them applicable to younger children: (1) "I help him/her to do certain things, *i.e., get dressed, do homework*" (words in italics were removed from the original item); and (2) "I try to get him/her to be optimistic about the pain, *i.e., I told them the pain will go away soon*" (words in italics were added to the original item). Scores were calculated as described, minus the two omitted subscale items. The IRPEDNA has been validated for parents of school-age children, but to our knowledge, has not been used in parents of younger children; thus, a reliability analysis was conducted on our sample. The Cronbach's alpha for all subscales was excellent (Solicitousness, $\alpha = 0.89$; Discouragement, $\alpha = 0.91$; Coping-Promoting, $\alpha = 0.88$).

***PCS-P***

Parents completed the *Parental Catastrophizing Scale-Parent Version* (PCS-P; Goubert et al., 2006) (Appendix O). The PCS-P contains 13 statements describing catastrophic thoughts and feelings that parents may have about their child's pain, divided into three subscales: *Rumination, Magnification,* and *Helplessness*. Each item was rated using a six-point scale *(*0=*'Not at all'* to 5=*'Extremely'*) and scores were calculated by averaging the item scores, with higher scores indicating higher levels of catastrophizing (Goubert et al., 2006). This scale demonstrates good validity in parents of children of different ages (Caes, Vervoort, Trost, et al., 2012; Goubert et al., 2006), but was originally validated in parents of school-aged children (9-16 years) and of children with chronic pain, and has not previously been tested in

younger cohorts nor those experiencing milder pains; thus, a reliability analysis was conducted. The Cronbach's alpha for the PCS-P scale (13 items) showed excellent reliability, $\alpha = 0.90$. All items appeared to be worthy of retention and would decrease the alpha if deleted.

***End-of-day diary***

The end-of-day pain diary contained twenty-three items (Appendix P). Parents were first asked to confirm if their child had experienced a pain event that day, and to state the number of pain events that had occurred, if any. If no pain events occurred, parents were not required to complete the remaining questions and could just submit that day's diary. All remaining questions in the diary asked the parent to answer in relation to whichever they felt had been the "*most memorable pain event"* of that day (if more than one event had occurred). The following questions were derived from validated reporting measures of child pain:

A **pain manikin** (modified from DEPS-R; Noel, Chambers, et al., 2018) visually indicated the bodily location of the pain. This modified version included numbered body parts, to allow parents to indicate the numeral associated with the affected body part (the paper version allowed participants to circle the affected location). If none of the numbered body parts matched the location of their child's pain, parents could manually type the affected area.

Next, parents rated the level of pain intensity they felt their child had experienced using the **Faces Pain Scale-Revised (FPS-R)** (Hicks et al., 2001). This scale comprised six faces showing increasing amounts of pain, scored from 0-10 in 2-point intervals, with higher scores indicating more pain. As one of the leading scales for paediatric self-report, the FPS-R has been validated extensively in preschool populations and can be administered without training, making it suitable for parents or teachers (Hicks et al., 2001; von Baeyer et al., 2017).

Two items were included from the **Dalhousie Everyday Pain Scale (DEPS)** (Fearon et al., 1996) to assess parents' estimation of their child's *"pain severity"* and "*intensity of child*

*distress"* during the chosen pain event. Both items were recorded on ordinal scales, with higher scores indicating higher pain severity (0=*'No hurt'* to 4=*'Severe hurt'*) and child distress (0=*'No distress'* to 5=*'Screaming'*), respectively. The DEPS exhibits strong validity and inter-rater reliability for 3–7 year olds, having been used in multiple previous studies which examined everyday pain experiences in preschool children (Fearon et al., 1996; Gilbert-MacLeod et al., 2000; Noel, Chambers, et al., 2018; O'Sullivan et al., 2019; von Baeyer et al., 1998).

To give daily insight into parent behaviours during the pain events, and to explore whether daily behaviours correlated with parental perceptions about their behaviours prior to participating, seven items from the **IRPEDNA** (Huguet et al., 2008) were included: three from the Solicitousness subscale, one from the Discouragement subscale, and three from the Coping-Promoting and Wellbeing subscale. The items chosen were those with the highest factor loading on each subscale. For the end-of-day diary, all items were rephrased into past tense (i.e., "When my child *was* in pain…") to reflect that parents were reporting on a past event, and each item was rated on a five-point scale (0=*'Not at all'* to 4=*'Extremely'*). Mean scores were calculated by averaging the items for each subscale. The Cronbach's alpha scores were acceptable: Solicitousness subscale, $\alpha = 0.79$; Coping-Promoting subscale, $\alpha = 0.71$. An alpha-score for Discouragement could not be computed, as only one item was included.

Three items from the **State Pain Catastrophizing Scale-Parent version** (Durand et al., 2017) were included: one item from each of the three subscales (Rumination, Magnification, and Helplessness), to assess state-level catastrophic thoughts specifically related to the pain event that occurred that day, and explore whether parental reported feelings correlated with perceptions about their feelings prior to participating (see *Pre-diary Questionnaires*, above). Each statement was rephrased into past tense (i.e., "I *stopped* what I was doing…") and each item was rated on a five-point scale (0=*'Not at all'* to 4=*'Extremely'*)

Mean scores were calculated by averaging the item scores. The Cronbach's alpha for the diary PCS-P was excellent; $\alpha = 0.70$.

The four-item distress subscale from the **Parental Distress and Sympathy Questionnaire (PDSQ)** was included (Caes et al., 2011). The diary version of the scale comprised four self-oriented statements of distress, 'I felt _____ (worried/upset/anxious/sad)'. All statements were rated on an 11-point scale (0=*'Not at all'* to 10=*'Extremely'*). Mean distress scores were calculated by averaging the item scores. The Cronbach's alpha for the PDSQ was excellent; $\alpha = 0.87$. The use of emotional adjectives to measure parental emotions has proven to be a reliable method and has previously been validated in parents of young children (Caes et al., 2011; Goubert et al., 2008).

The remaining three questions were designed specifically for this study: first, drawing from relevant work on childhood injuries (Morrongiello et al., 2004b), parents were asked "*At the time of the pain event, were you nearby?*" This measure contained five decreasing levels of supervision, with higher scores indicating lower levels of parental supervision (Q8, Appendix P). Next, two questions were open-ended, allowing parents to provide a description of the context surrounding the event (Q3, Appendix P), and include any additional details which they felt were relevant (Q10, Appendix P). This would offer insight into which details parents considered "memorable" from their child's pain events.

***EMA***

The EMA was completed by child and parent on the parent's smartphone, immediately after any pain event of their choosing (Appendix Q). Parents were instructed to ask their child to confirm ('*Yes/No*') whether they were currently experiencing pain. If 'Yes', the child answered the second question ('*How much pain?*') using the *Simplified Faces Pain Scale (S-FPS)* (Emmott et al., 2017). This three-point visual scale shows three faces of increasing pain

or discomfort (*0=No hurt; 1=Some hurt; 2=A lot of hurt*). If the child indicated "No" to the first question, they were not asked the second question. The S-FPS has been validated for use with 3-4 year olds, making it more reliable for this cohort than other pain scales (Emmott et al., 2017). Next, the parent gave a proxy estimate for their child's pain, also using the S-FPS, and completed the Parental Distress and Sympathy Questionnaire (Caes et al., 2011) *(see: Diary, above)*. The EMA contained the four-item distress subscale (worried, upset, anxious, sad), using a modified rating scale. While the original PDSQ scale is an 11-point scale, the EMA used a 6-point scale (0=*'Not at all'* to 5=*'Extremely'*) to improve usability, as a shorter scale was easier to complete on narrow smartphone screens. Mean scores were calculated for the distress subscale, with higher scores indicating higher levels of the respective emotion (Caes et al., 2011).

**Data analysis**

Demographic data and quantitative responses were analysed using descriptive tests in SPSS 24.0 (IBM Corp, Armonk, NY). Sex effects, parental supervision, and EMA ratings were compared using independent t-tests, while group effects (e.g., age, birth order) were compared using one-way ANOVA, followed by post-hoc (Fisher's LSD) tests where appropriate. Spearman's correlations were used to detect relationships between parental distress and their pain estimates in the EMA. Hierarchal Level Modelling (HLM) is the most accurate analysis for data collected by diary or EMA methods (Connelly, Bromberg et al., 2017).

A series of five hierarchical regression analyses were conducted on the diary entries using HLM 8.0 (Scientific Software International, Inc., Skokie, IL). Maximum likelihood estimation was used for all models, which consisted of data from daily diary entries (level 1; N = 151), nested within parental characteristics (level 2; N = 21). This is considered an adequate sample size for obtaining reliable parameter estimates (Snijders & Bosker, 2011).

Missing data was excluded prior to analysis. Level 1 and Level 2 predictors were each grand mean centred. For each model, analyses were conducted in three phases: unconstrained (null) model, random intercepts model, and means-as-outcomes model. Statistical significance for all tests was set at α level of $p < .05$. The five models explored the contribution of contextual factors on the parent's daily responses to their child's everyday pain experience: (1) Parental distress, (2) Parental solicitousness, (3) Parental discouraging, (4) Parental coping-promoting, and (5) Parental catastrophizing. At level one, parental supervision, mean state (daily) parental catastrophizing, and child pain intensity, severity and distress were entered. At level two, child sex, child age, birth order, parent age, and mean trait (pre-diary) parental catastrophizing were entered. Additionally, when analysing the contribution of trait-level responses from the IRPEDNA and PCS-P, the trait scores from these measures were also entered at level 2.

## Results

### Description of the typical daily pain events

The average number of completed diary entries per family was M = 8.52 entries (range: 1-19). A total of 197 end-of-day diary entries were completed: 157 entries (79.7%) described a pain event, while 40 diary entries (20.3%) reported no pain events for that day. The total number of pain events ranged from 0-6 incidents each day (M = 1.83; SD = 1.33).

Parents reported crying as the predominant child response to pain events (N = 71; 46.1%), while a large proportion of children also made verbal comments (e.g., "Ouch!") (N = 38; 24.7%). Other behaviours included sobbing (N = 23; 11.7%), screaming (N = 10; 6.5%), facial expression (N = 10; 6.5%), while in only two incidents, the child gave no sign of distress (1.3%). Parents generally estimated that pain events were of low pain severity (M = 1.65, SD = 0.89) and the majority of events were rated as mild (N = 64; 40.8%) or moderate severity (N = 56; 35.7%). Regarding estimates of their child's pain intensity, on average, parents reported

a moderate level of pain intensity (M = 4.20, SD = 1.5). Low intensity ratings (scored as mild or moderate) were reported in one-third of events (N = 54; 34.4%), while high intensity ratings (scored as severe or extreme) were reported in just over half of pain events (N = 81; 51.6%).

The sites of injury were varied. Over one-third of all reported incidents involved an injury to the child's head (N = 58; 36.9%), with the next most frequent sites of injury being hands (N = 24; 15.3%) and knees (N = 20; 12.7%) (Table 3.2). Parents gave additional detail on pain events in the open-ended diary comments. Most of the injuries were incidental and caused by the child themselves: *"[#10] He was eating a rice cake and bit his finger"; "[#19] He got an eyelash stuck in his eye"; "[#28] She trapped her finger in the car seat buckle"*. In several instances, parents were indirectly or directly responsible for several pain events: *"[#4] He had a scratch on his forehead that I bumped… I felt guilty"; "[#2] I poked a tissue into his eye when blowing his nose"; "[#14] I accidentally rolled over her socked feet with the buggy"*.

**Table 3.2: Breakdown of the reported sites of injury in "everyday" pain events**

| Site of injury | Number of incidents | Percentage (%) |
|---|---|---|
| Head | 58 | 36.9 |
| Hand | 24 | 15.3 |
| Knee | 20 | 12.7 |
| Foot | 14 | 8.9 |
| Back | 9 | 5.7 |
| Leg | 9 | 5.7 |
| Buttocks | 7 | 4.5 |
| Elbow | 5 | 3.2 |
| Shoulder | 4 | 2.5 |
| Multiple sites | 3 | 1.9 |
| Stomach | 2 | 1.3 |
| Other/Do not know | 2 | 1.2 |

**Parental emotional and behavioural responses during daily pain events**

Parents reported low levels of Solicitousness (M = 1.55, SD = 1.09), low levels of Discouragement (M = .38, SD = .81), and low levels of Coping-Promoting behaviours (M = 1.55, SD = 1.12) during their child's daily pain events. Parents also reported low daily levels of catastrophizing thoughts (M = .86, SD = .74) and gave low ratings for their own distress (M = 1.60; SD = 1.71): Out of 156 pain events, parents rated 140 events (89.7%) as causing a low level of distress (i.e., a score of 5 or below on the 11-point scale).

The responses to the open-ended questions highlighted how parents mostly used physical and verbal comfort, such as cuddling and rubbing the injury, to soothe their child after a pain event: *"[#1] We had a cuddle and a kiss of the elbow and she went off happily"; "[#4] I rubbed it 'til he felt better"; "[#21] He started crying, came to me, and I hugged him. He quickly calmed down and became distracted with cartoons on TV"*.

Several parents also used their child's pain event as an opportunity to prevent future injuries: *"[#4] I also talked to him about running on the pool deck as he's been told not to before"; "[#19] I cuddled him and said he has to be more careful next time"; "[#21] [Son] caught his finger in the closet door. I had warned him not to close the door!"*

**Influence of parental supervision**

In just over half of events (N = 87, 55.8%), parents indicated that they had directly observed or witnessed their child's pain event incident, while in a further 54 incidents (34.6%), parents indicated that they had been listening in either constantly or occasionally. Only a small proportion of events were not observed by the parent. As such, the original five categories were collapsed down into two levels for all remaining analysis: "Present" (*directly observed the*

*event*) or "Not present" (all other levels: *listening in constantly or occasionally, supervised by another adult, no supervision*) (Figure 3.1).

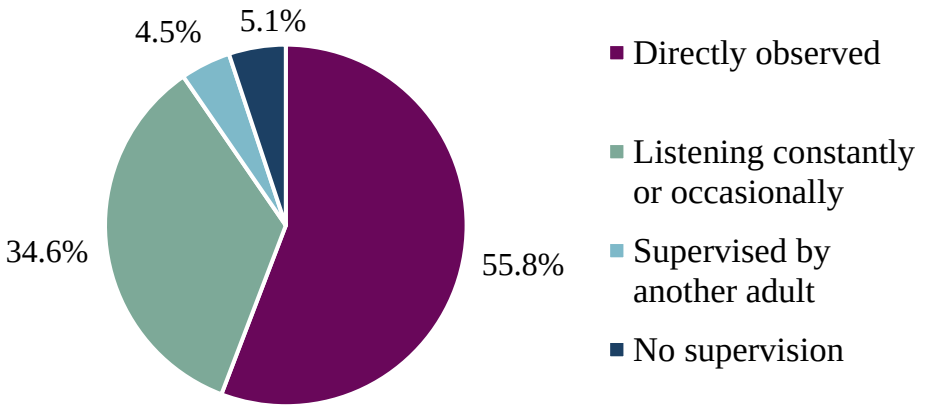


**Figure 3.1: Levels of parental supervision**

Pain events occurred less frequently when parents were present and supervising (M = 1.84, SD = 1.08) compared to when parents were not supervising (M = 2.26, SD = 1.45); t(154) = 2.11, $p$ = .037. Parents who were present for the pain event reported significantly lower levels of personal distress (M = 5.02, SD = 5.96) compared to parents who were not present (M = 8.39, SD = 7.62); t(153) = 3.09; $p$ = .002. Parental catastrophizing was significantly elevated if parents had not been present for the pain event (M = 3.11, SD = 2.44) compared to parents who had been present and supervised their child's pain event (M = 2.20, SD = 1.99); t(153) = -2.55, $p$ = .012. There was no significant association between parental supervision and estimates of child pain severity, pain intensity, or child distress; all $p > .05$.

**Influence of child sex, age, and birth order on parental pain estimates**

Child sex was an influential factor in how parents estimated their child's pain experiences. Parents gave significantly higher pain estimates of pain intensity for girls (M = 4.81, SD = 1.36) than for boys (M = 3.84, SD = 1.47); t(155) = 4.12, $p < .001$. Parents of boys

reported 109 pain events (M = 1.76, SD = 1.23), while parents of girls reported 62 pain events (M = 1.98, SD = 1.48); this difference was not significant, t(169) = 1.06; $p > .05$. Child sex did not influence parent judgements of child distress, pain severity, or parental supervision; all $p > .05$.

Child age was a significant factor in parent judgements of child pain intensity, $F_{(3,153)} = 4.01$, $p = .009$. Post-hoc (LSD) tests revealed that parents gave significantly lower estimates for 5-year olds (60+ months) (M = 3.46, SD = 1.44; N = 22) compared to 2-year olds (M = 4.88, SD = 1.33, N = 24; $p = .001$), and 3-year olds (M = 4.36, SD = 1.45, N = 50; $p = .016$), but not 4-year olds; $p > .05$. Child age also significantly influenced parent estimates of child distress, $F_{(3,150)} = 2.91$, $p = .036$. Post-hoc (LSD) tests revealed that parents gave significantly lower estimates for 5-year olds (M = 2.70, SD = 0.73, N = 20) compared to 3-year olds (M = 3.50, SD = 1.07, N = 50), $p = .008$, but not 2-year olds or 4-year olds; both $p > .05$. Child age did not influence number of pain events, parental supervision, or parent ratings of pain severity; all $p > .05$.

Pain experiences were significantly influenced by the child's birth order within the family (e.g., only/single child, youngest/middle/oldest child). There was a significant difference in the number of pain events, $F_{(3,167)} = 8.41$, $p < .001$: youngest children experienced fewer pain events (M = .91; N = 34) than only/single children (M = 2.10, N = 101), $p < .001$, or oldest children (M = 2.15, N = 26), $p < .001$, but not at a rate different from middle children, $p > .05$. Birth order significantly impacted parental estimates of child pain intensity; $F_{(3,153)} = 6.31$, $p < .001$. Parents reporting on their youngest child gave significantly higher estimates (M = 4.69, N = 26) than parents of only children (M = 3.92, N = 95), $p = .015$, or middle children (M = 3.40, N = 10), $p = .016$, but no different to parents of oldest children; $p > .05$. Finally, birth order influenced parental estimates of child distress; $F_{(3,150)}=3.19$, $p = .026$: parents reporting on their youngest child gave significantly higher estimates (M = 3.58, N = 26) than

parents of only children (M = 3.03, N = 92), $p = .031$, or middle children (M = 2.60, N = 10), $p = .021$, but no different from parents of oldest children; $p < .001$. There was no significant impact of birth order on pain severity estimates or parental supervision prior to pain events; both $p > .05$.

**Influence of contextual factors on parental responses**

A series of five hierarchal linear regression analyses were conducted on the influence of contextual factors in contributing to parental responses. The analysis with parental daily distress as an independent variable returned an ICC of .432 (43.2% of the variance was between parents, and 56.8% was within parents). Parent distress was significantly associated with pain severity ($\beta = .34$, $p = .013$, $r = .16$), and parent daily catastrophizing ($\beta = 1.28$, $p < .001$, $r = .45$). This reveals that parents distress levels are increased when they interpret their child's pain event as more severe, and when parents report higher levels of state-level catastrophic thinking. Parent daily distress was also closely, but not significantly, associated with the child's birth order ($\beta = .51$, $p = .056$) (Table 3.3).

Parental daily solicitousness returned an ICC of .415 (41.5% of the variance was between parents, and 58.5% was within parents). Parent solicitousness was significantly associated with child sex ($\beta = .58$, $p < .05$, $r = .26$), child distress ($\beta = .23$, $p = .01$, $r = .17$), and daily catastrophizing ($\beta = .67$, $p < .001$, $r = .34$). This reveals that parental solicitousness was increased in parents of girls, when parents interpret their child as being more distressed, and when parents report higher levels of state-level catastrophic thinking. Parent daily solicitousness was also closely, but not significantly, associated with child age ($\beta = -2.07$, $p = .057$) and pre-diary (trait) solicitousness ($\beta = .50$, $p = .08$).

Parental daily discouragement returned an ICC of .586 (58.6% of the variance was between parents, and 41.4% was within parents). Discouragement was significantly associated

with child age (β = -.29, $p < .05$, $r = .27$) and birth order (β = .32, $p = .05$, $r = .16$). This reveals that parental discouragement decreased with increasing child age and was more frequent in parents participating with their oldest child. Parent discouragement was closely, but not significantly, associated with pain severity (β = -.17, $p = .09$).

Parental daily coping-promotion returned an ICC of .590 (59% of the variance was between parents, and 41% was within parents). Parent daily (state) coping-promotion was significantly associated with daily catastrophizing (β = .55, $p < .001$, $r = .25$). This reveals that parental coping behaviours were increased when parents reported higher levels of state-level catastrophic thinking. Parent coping-promotion was closely, but not significantly, associated with pre-diary (trait) coping-promotion (β = .49, $p = .055$).

In the final model, parental daily catastrophizing returned an ICC of .287 (28.7% of the variance was between parents, and 71.3% was within parents). Catastrophizing was significantly associated with pain severity (β = .44, $p < .001$, $r = .43$) and parent age (β = -.05, $p < .05$, $r = .28$). This reveals that higher levels of catastrophic thinking are reported when parents interpret the event as more severe and by younger parents. Catastrophizing was closely, but not significantly, associated with parent estimates of child distress (β = .11, $p = .063$).

**Table 3.3: The contribution of contextual factors on daily parental responses to everyday pain experiences**

| | Parental distress | | | Parental solicitousness | | | Parental discouragement | | | Parental coping-promoting | | | Parental catastrophizing | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Variable | β coeff. | SE | T | β coeff. | SE | T | β coeff. | SE | T | β coeff. | SE | T | β coeff. | SE | T |
| Intercept (β0) | 1.64 | 0.19 | 8.49 | 1.60 | .11 | 14.87 *** | .47 | .11 | 4.33 *** | 1.70 | .14 | 12.40 *** | .81 | .08 | 10.42 *** |
| Child age (γ01) | -.03 | 0.22 | -.15 | -.26 | .13 | -2.07 # | -.29 | .13 | -2.31 * | -.25 | .16 | -1.59 | -.07 | .09 | -.79 |
| Parent age (γ02) | -.03 | .05 | -.67 | -.03 | .03 | -.90 | -.03 | .03 | -1.13 | -.03 | .04 | -.82 | -.05 | .02 | -2.43 * |
| Child sex (γ03) | -.40 | .42 | -96 | .58 | .24 | 2.41 * | .10 | .24 | .42 | -03 | .30 | .09 | -.19 | .17 | -1.16 |
| Birth order (γ04) | .51 | .24 | 2.07 # | -.05 | .13 | -.36 | .32 | .15 | 2.11 * | .27 | .17 | 1.55 | .12 | .10 | 1.18 |
| Mean (pre-diary) PCSP-State (γ05) | .24 | .26 | .94 | -.20 | .15 | -1.30 | .04 | .14 | .26 | -.04 | .18 | -.21 | -.04 | .10 | -.37 |
| Mean (pre-diary) IRPEDNA score (γ05) | - | - | - | .50 | .27 | 1.88 # | .05 | .11 | .51 | .50 | .24 | 2.09 # | - | - | - |
| Pain severity (γ10) | .34 | .14 | 2.51 * | .06 | .11 | .51 | -.17 | .10 | -1.69 # | -15 | .11 | -1.41 | .44 | .07 | 6.70 *** |
| Pain intensity (γ20) | -.02 | .10 | -.17 | -.05 | .08 | -.68 | -.04 | .07 | -.50 | .09 | .08 | 1.23 | -.04 | .05 | -.75 |
| Estimates of child distress (γ30) | .08 | .11 | .69 | .24 | .09 | 2.61 ** | .03 | .08 | .32 | .09 | .09 | 1.09 | .11 | .06 | 1.88 # |
| Parental supervision (γ40) | -.07 | .14 | -.52 | -.02 | .11 | -.16 | -.15 | .10 | -1.44 | -.01 | .11 | -.11 | -.09 | .08 | -1.16 |
| Mean (daily) PCSP-State (γ50) | 1.28 | .15 | 8.53 *** | .67 | .12 | 5.65 *** | -.13 | .11 | -1.16 | .55 | .12 | 4.73 *** | - | - | - |

Note: Coeff. = coefficient; PCS-P state = State version of Pain Catastrophizing Scale – Parent version; * p<.05; ** p<.01; *** p<.001. #p-value was borderline of significance (p=.051 - .09)

**Feasibility of EMA**

In total, 47 EMA entries were collected across 9 parents (42.9% of the parents completing the end-of-day diary entries during the same period), with parent-child pairs completing, on average, one EMA entry per day (range: 0-3 per day). There was a significant difference between parent and child ratings of the child's pain, with children reporting higher pain estimates (M = 2.43; SD = .77; N = 37) compared to their parents (M = 1.88; SD = .59; N = 42); t(77) = 3.83; $p < .001$. Parents who had indicated that their child experienced a high level of pain or hurt gave higher ratings for their own distress than parents whose child experienced a low level of pain or hurt: $r_s(46) = .46$, $p < .001$. The EMA was well-received by parents and children, with one parent mentioning that their child became more interested in reporting their pains each day as a result: *"[#9] He asked me if we could do the "feelings" on my phone, which meant record the pain"*

**Discussion**

This study investigated the context surrounding parental responses to minor everyday childhood pain experiences, through the diary records of parents as the primary "witnesses" to these experiences, and the novel use of electronic momentary assessment (EMA) to compare parent and child ratings of everyday pain events. The pain diary methodology allowed for a clearer appreciation of the context surrounding everyday pain events, as parents provided their own observations on these events and gave insights into their child's experience of pain. The EMA provided valuable insight into the child's own experience of pain in comparison to parental estimates; however, it is unclear whether the EMA was of interest to parents and a feasible method on a larger scale as uptake was low, and most parents typically only completed the EMA once per day. We are unable to explore this within the presented study, so additional studies are needed to explore this further. The diary incorporated items from existing scales, including the Dalhousie Everyday Pain Scale (DEPS). The DEPS has previously been utilised

by researchers in a range of natural environments, including day-care, play centres, and at home (Fearon et al., 1996; Noel, Chambers, et al., 2018; O'Sullivan et al., 2019). Within this study, the DEPS and DEPS-R were used solely by parents at home, yet the reporting is consistent with previous literature. For example, the most-reported sites of pain (e.g., head, hands and knees) were similar to those reported in a day-care environment (Fearon et al., 1996), and similar estimates of pain severity were given by the parents in this study and by parents observing their child's pain events in an activity centre (e.g., approximately 75% of incidents in both settings were considered low severity) (Noel, Chambers, et al., 2018). This suggests that minor pain events were similar across settings, and that the DEPS and DEPS-R can adequately capture pain events in the home, even when used by parents with no formal observational training.

In the present study, the DEPS revealed a notable disparity in parent estimations of pain situations: while parents rated most incidents as low severity, they simultaneously indicated that the child was demonstrating severe or extreme pain intensity. This might indicate that parents may feel more comfortable assessing an incident than assessing their child's *experience* of the incident, and supports recommendations that contextual observation by clinicians and caregivers should be complemented with self-report from the child (von Baeyer, 2009). This recommendation seems to be further confirmed by the data captured through EMA, which revealed that parental estimates of pain intensity were consistently lower than the child's own estimates. These findings echo those from clinical settings, wherein parent proxy ratings have continually been shown to underestimate pain compared to the child's self-report (Manne, Jacobsen et al., 1992), and highlights that incongruous pain ratings also extend beyond clinical settings. While pain intensity is not typically informative where pain is already anticipated to be strong (i.e., post-surgery), it is relevant to caregivers who manage acute pain events regularly. Gathering pain intensity ratings from the child, using validated but simple

assessments such as the S-FPS, may allow caregivers to assess pain quickly and determine whether further treatment is required (Cohen, Donati et al., 2019). Future studies could consider whether additional measures can provide a reliable means of drawing young children into conversations about their own pain. For example, a body outline tool was used by the parents in this study, and similar tools have been used previously by older children and adolescents (Savedra, Tesler et al., 1989) but have not yet been validated in younger children (Mesko & Clark, 2019). Equally, the use of colouring tools could allow preschool children to report differing levels of pain (Mahon, Holsti et al., 2015).

In exploring the role of influencing factors on parental responses towards their child's everyday pain experiences, our findings revealed that parental trait levels or expectations of their behaviours and catastrophizing thoughts during their child's pain experiences (taken from their pre-diary questionnaire responses) did not always correlate with their actual or state responses (reported in the daily diaries). Instead, contextual factors (e.g., estimated child pain severity or distress) and child characteristics (e.g., sex, age, and birth order) were typically stronger predictors of parental feelings, thoughts, and behaviours. For instance, parental estimates of their child's pain severity and distress increased with their own distress levels and influenced increased solicitousness, in line with previous literature (Langer, Romano et al., 2014; Sieberg, Williams et al., 2011). Child sex was a significant influence on parental solicitousness, and reaffirmed previous findings that parents respond more protectively towards girls than boys (Langer et al., 2014). Child age was a significant predictor of the increased use of discouragement by parents and was associated with increased parental solicitousness. This reaffirms findings that suggest parent (trait) expectations of their thoughts and behaviours do not necessarily match their (state-dependent) behaviours during their child's pain in real life (Durand et al., 2017). Previous studies tried to overcome this by exploring how parents respond to their child's pain using hypothetical scenarios (Caes, Vervoort, Eccleston,

et al., 2012; Goubert et al., 2012). The findings here suggest that such methods may however not faithfully capture parent responses to everyday pain situations, but additional exploration of the relationship between parental state behaviours and contextual factors during everyday child pains is needed to reaffirm these findings.

State (daily) levels of catastrophic thinking represented a significant influence on how parents responded during pain events, as parental levels of distress, solicitousness, and coping-promoting were all increased when parents reported increased catastrophizing thoughts for that particular pain event. This echoes previous findings from clinical and experimental pain situations (Caes et al., 2011; Goubert et al., 2009; Langer et al., 2014; Sieberg et al., 2011), and also extends our understanding of pain catastrophizing outside of these settings, by demonstrating that catastrophizing is also a potent influence on parental behaviours in everyday pain situations. We further found that parents who reported increased catastrophizing also engaged in more coping-promoting behaviours; this is a departure from existing literature which has generally demonstrated that parental catastrophizing is not associated with adaptive behaviours. It is plausible that everyday pain experiences represent an entirely different context to those previously reported, given that they occur in the family's natural environment without the added input of researchers or medical professionals. Thus, behaviours demonstrated by parents in everyday pain contexts, such as those reported here, may be a natural or instinctive response of parents to their child's pain, and these may, in fact, include efforts to encourage or otherwise engage their child in coping-promoting behaviours and teach them to manage pain effectively. However, additional research is still required before we can draw sharper insights into the potential differences in parental catastrophizing behaviours between everyday pain contexts and other pain contexts.

Beyond the influence of parental daily catastrophic thinking, parental level of supervision was key in understanding both the child's pain experience and parental responses:

pain events occurred more frequently, and parents reported higher catastrophizing and higher levels of personal distress if they had not been actively supervising their child during the pain event. This correlates with previous findings that active supervision is protective against in-home injuries (Morrongiello et al., 2009; Morrongiello et al., 2004b), while greater parental distress is associated with increased rates of child injury (Schwebel, Roth et al., 2011). However, level of supervision in the present study did not influence how parents responded to their child during a pain event: independent of the level of supervision, parents reported using equal amounts of solicitousness, discouragement, and coping-promoting behaviours. Equally, parental estimates of pain severity, intensity, and child distress did not differ whether they had been supervising or not. This echoes previous findings that parents did not often change their responses or strategies following an incident, if they felt they were already doing all they could to prevent it (Morrongiello et al., 2004b). The design of this study was drawn from longitudinal studies of childhood injuries, which explore supervision in relation to pain events occurring during short, defined periods (e.g., 12 weeks). Future studies could explore supervision within the home over similar periods, to determine whether parental responses to everyday pains change over time (for example, as their child grows older and in less need of supervision).

Our findings also revealed that parent's interpretations of everyday pain experiences were moderated by several child characteristics, such as sex, age, and birth order. Parents of girls gave much higher estimates of their child's pain intensity than parents of boys. These findings contrast against recent literature which indicated that adults often rate pain more highly in boys than in girls (Cohen, Cobb et al., 2014; Earp, Monrad et al., 2019). However, sex differences in parent ratings are widely inconsistent, with evidence that parents give higher intensity ratings to boys' pain (Moon, Chambers et al., 2008), over- and underestimate girls' pain (Schinkel, Boerner et al., 2018), or give equivalent ratings for boys' and girls' pain (Goodenough, Thomas et al., 1999). As there is extensive evidence that sex differences are

rarely found in *children's own estimates* of pain intensity, tolerance, or affect (Boerner, Birnie et al., 2014), this suggests that adult ratings may be biased by gender stereotypes regarding pain in boys versus girls (Earp et al., 2019). Given our own findings, we propose that sex differences in parental ratings may also vary depending on the *types of pain* being rated, as the listed studies examined medical or experimental procedures while the present study captured everyday pains. Previous studies of everyday pains have demonstrated that girls exhibited higher personal control and were often playing alone prior to pain events (O'Sullivan et al., 2019), but exhibited more visible and vocal distress during pain events (Fearon et al., 1996). Thus, while pain events may be of lower impact amongst girls due to a more reserved play style, their responses may induce adults to rate pain events as more intense for girls. Notably, child sex did not influence level of supervision or the number of pain events that boys versus girls experienced. This confirms previous findings, wherein both high and low levels of supervision resulted in similar rates of injury for both boys and girls (Morrongiello et al., 2004b).

With respect to child age, parents of older children gave consistently lower pain ratings, lower estimates of child distress, and used fewer discouraging behaviours than parents of younger children. Previous literature has confirmed that children exhibit less help-seeking from adults as they grow older (Fearon et al., 1996), and parents are more likely to pick up older toddlers (Noel, Chambers, et al., 2018). As that cohort (1-3 years) was at the lower age range of our sample, this matches our findings that parents were more likely to use comforting behaviours with younger children (2-3 years). Conversely, parents of older children (4-5 years) reported using pain events as "teachable moments" to instruct their child about hazard prevention or following safety rules, strategies which were not evident amongst parents of younger children. This reaffirms existing findings that parents only begin using "teaching strategies" in place of direct supervision once their child grows older and can more clearly

comprehend potential injury risks (Morrongiello et al., 2004b; Pollack-Nelson & Drago, 2002). It must be acknowledged that these examples were drawn from childhood injury literature, as studies exploring everyday pain strategies are scarce. To confirm the applicability of these examples for everyday pains, future studies could examine whether parents utilise unique strategies during everyday pain events (compared to injury events) or explore the effectiveness of "teachable moments" in everyday pain events among different age ranges of children.

Correlating with the findings on child age, the birth order of the focal child (e.g., only/single child, youngest/middle/oldest child) was a significant influence on the child's experience of pain. Parents participating with their *oldest* child reported significantly more pain events, echoing findings that first-borns are more likely to experience pain, despite parents spending more time monitoring their first-born child than later-born siblings (Defee Jr & Himelstein, 1969; Price, 2008). In our study, youngest children experienced the fewest pain events of any group, but their parents gave higher pain intensity ratings and higher estimates of child distress than other parents. Furthermore, birth order was associated with use of parental discouragement and exhibited an additional trend for association with parental distress. Notably, the parents of only/single children reported more catastrophizing and distress than parents of multiple children. Understandably, parents with no previous experience of managing a child's pain may become more stressed during minor pain incidents than parents with multiple children. Unfortunately, relating these findings to previous literature is difficult, as the available research on birth order and child pain responses has primarily been derived from clinical settings (Defee Jr & Himelstein, 1969; Ghaderi, Fijan et al., 2015). Given clinical evidence that first-born and only/single children are more anxious and less cooperative during clinical pains, and our evidence that parents rated everyday pains differently in youngest versus other children, future studies should continue to explore how birth order influences parent and child responses to pain.

**Limitations**

Attrition rates between recruitment and daily reporting were high: only 58% of recruited parents moved onto diary completion following the demographics stage, and only 43% of parents completing diaries also completed EMA. Similar attrition rates have previously been reported among electronic diary users (Gaertner et al., 2004). While the final sample was adequate for this study, a larger sample could increase the strength of some findings, and similar designs should account for this within their estimations. Furthermore, the sample was overly homogenous: 90% of participants were resident in Ireland, and 95% of diary entries were completed by mothers. These factors reduce the ability to extend our findings to other populations. Finally, selection bias cannot be ruled out as parents may have chosen events that they could more clearly recall, or events which would appear socially acceptable. For example, most incidents were reported when parents were actively supervising, as parents may not have wanted to divulge that they were not monitoring their child. While the diary and EMA prevented us from examining the pain events that were not reported, they give insight into the types of pain events that parents consider "memorable" enough to report. Future studies may benefit from asking parents to report multiple pain events within the same day, to ensure a better representation of pain events within the home.

**Overall conclusions**

This research reaffirmed the findings from Chapter 2, that caregiver responses are influenced by contextual factors, such as the severity of the incident or the child's distress. The parent pain diary provided a feasible method of capturing the context of "everyday" pain experiences around the family home and included the first-reported use of the DEPS-R within the family home. Formal assessments of pain are inappropriate outside of clinical settings, but as parents naturally engage in investigation about their child's pain events, the use of short assessments (such as those described in this chapter) may assist parents in gaining information

about everyday pain events and provide opportunities to model adaptive coping behaviours to their child. In summary, this study has made a modest contribution to paediatric pain literature by exploring the psychosocial context surrounding acute everyday pains. However, pain can best be described as a biopsychosocial experience, and while the two studies described thus far have demonstrated the role of psychological and social influences on pain experience, questions remained as to the precise nature of the relationship between these psychosocial influences and the biological mechanisms that govern the sensation of pain. Translational research, to share expertise between clinical and preclinical disciplines, was determined to be the most suitable method of exploring whether biological mechanisms of pain are altered by the presence or absence of social support. This research will be described in greater detail in Chapter 4.

# CHAPTER IV

## MATERNAL PRESENCE OR ABSENCE ALTERS NOCICEPTIVE RESPONDING AND CORTICAL ANANDAMIDE LEVELS IN JUVENILE FEMALE RATS

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### Introduction

Pain is a common experience for young children, and responses to these experiences are constructed through biopsychosocial influences, including the presence of other people, and the perceived severity of the incident (Fearon et al., 1996; Gatchel, Peng et al., 2007; Hadjistavropoulos et al., 2011; Vervoort et al., 2011). The presence of other people when we experience pain provokes similar comforting sensations in humans and in other mammals (Craig, 2009; Decety & Norman, 2015; Hadjistavropoulos et al., 2011). In particular, the influence of parental support on pain sensitivity, responding, and distress during painful events has been well-reviewed in both human (Boerner et al., 2017; Chambers et al., 2002; Goubert et al., 2012; Schinkel et al., 2017; Vervoort et al., 2008) and rodent studies (Burke et al., 2017; Burke, Geoghegan, et al., 2013; Burke, Llorente, et al., 2013; de Medeiros et al., 2009; Mogil,

2015; Walker et al., 2008; Weaver et al., 2007). Evidence on the benefit of parental presence during painful procedures is mixed and seems to largely depend on the parent's behaviour. Parental presence during painful experiences has been shown to modulate their child's responses to pain, including reducing pain sensitivity and distress. Recent evidence has shown that, when parents react calmly and distract their child from the pain, the child reports lower pain than if they were focused on the pain (Boerner et al., 2017; Caes, Vervoort, Trost, et al., 2012; Goubert et al., 2012; Piira et al., 2005; Schinkel et al., 2017; Vervoort et al., 2011). Elsewhere, parents and children both reported lower distress scores when parents were present during needle-pain procedures (Wolfram & Turner, 1996). Similarly, preclinical animal studies have manipulated dam-pup interactions during the first 2 weeks of life to model early-life stress (Ellenbroek, Derks et al., 2005; Viveros, Llorente et al., 2009), an effect which results in an array of physiological changes including altered nociceptive responding (for reviews, see: Burke et al., 2017; Vilela, Vieira et al., 2017). Several studies have demonstrated that short term (up to 30 minutes) isolation of neonatal rodent pups from the dam and siblings result in thermal hypoalgesia (Kehoe & Blass, 1986a; Kehoe & Blass, 1986b; Kozlov, Nizhnikov et al., 2013; Kozlov, Nizhnikov et al., 2012; Nizhnikov, Kozlov et al., 2014; Spear, Enters et al., 1985), while longer-term isolation (4-6hr) is associated with either no change (Kozlov et al., 2013) or thermal hyperalgesia (Blass, Shide et al., 1995). Furthermore, high levels of maternal care to pups following an early-life pain experience has been shown to result in reduced nociceptive responding (hypoalgesia) to thermal noxious stimuli in adulthood (Walker et al., 2008). Beyond parental presence, studies involving social support (or lack thereof) from *non-familial sources* also reinforce the general view that support reduces pain behaviours while isolation increases them: female rats experiencing social rejection during adolescence exhibit decreased thermal sensitivity in adulthood (Schneider, Bindila, et al., 2016; Schneider et al., 2014), and social reunion following separation at weaning between male - but not female -

adult sibling mice, results in an increased heat nociceptive threshold (D'Amato, 1994; D'Amato & Pavone, 1993, 1996). Parental presence presents a significant source of support, and for the most part, parental presence in both humans and rodents exerts a positive effect on their offspring's behaviour during pain; however, the precise effects depend on the nature, timing and stress status of the caregiving (Caes, Goubert, et al., 2016; Caes, Vervoort, Eccleston, et al., 2012; Filippa, Poisbeau et al., 2019; Grunau, Whitfield et al., 2009). While the effects of maternal support versus isolation on thermal nociceptive responding have been examined during the early neonatal and post-weaning periods in preclinical literature, there has been a lack of studies examining the effects on nociceptive responding to mechanical, cold, or inflammatory stimuli, and of studies examining effects during the juvenile pre-weaning period (i.e., the period which corresponds most closely to the preschool period of development in children).

The endocannabinoid system (ECS) is a retrograde neuromodulatory lipid signalling system known to play a key role in a host of physiological functions including stress, pain and social responding (Corcoran et al., 2015; Marco et al., 2011; Schneider, Bindila, et al., 2016; Starowicz & Finn, 2017). Comprised of the $CB_1$ and $CB_2$ receptors, the naturally-occurring endogenous ligands (endocannabinoids) – namely, anandamide and 2-arachadonyl glycerol (2-AG) - and the enzymes involved in the synthesis and degradation of the endocannabinoids, the ECS is uniquely positioned to modulate synaptic transmission and plasticity. Early-life stress has been shown to result in immediate and lasting alterations in the ECS (Hill, Eiland et al., 2019; Marco et al., 2014; Vangopoulou et al., 2018). Furthermore, several studies have revealed an important role for the ECS in mediating and modulating social behaviour during adolescence and its impact on nociceptive responding (Schneider et al., 2014; Schneider, Pätz, et al., 2016; Trezza et al., 2010). In addition to its role in executive and social functioning, the prefrontal cortex (PFC) is a key brain structure involved in sensory and affective pain

processing (for review, see: Fuchs, Peng et al., 2014; Ong et al., 2019). Furthermore, several studies have demonstrated an important modulator role for the ECS in the PFC in mediating and modulating nociceptive responding in preclinical pain models (Corcoran, Mattimoe et al., 2020; Hoot, Sim-Selley et al., 2010; Rea, McGowan et al., 2019). However, there have been no studies examining whether the ECS in the PFC is altered during acute social withdrawal and pain during the juvenile period.

The present study examined the effects of maternal presence versus absence on nociceptive responding to thermal heat, cold, mechanical, and inflammatory noxious stimuli in juvenile female rat pups. Despite calls to include females in preclinical research (Mogil, 2020; Mogil & Chanda, 2005), pain studies continue to be predominantly conducted in males. There has been a lack of studies examining pain responses to brief social isolation and to our knowledge no study investigating such responses in female rodents. Female rats have been demonstrated to exhibit pronounced changes in pain sensitivity and endocannabinoid function as a result of prolonged isolation and peer rejection (Schneider, Bindila, et al., 2016; Schneider et al., 2014; Schneider, Pätz, et al., 2016). Thus, a further aim of this study was to examine endocannabinoid levels and expression of receptors and enzymes of the ECS in the prefrontal cortex and determine if maternal presence/absence-induced changes in nociceptive responding in female rats are associated with alterations in the ECS.

## Materials and Methods

### *Animals and Experimental Design*

Male and female Sprague-Dawley (200–340 g; Charles River Laboratories, UK) rats were group-housed under controlled conditions (temperature 20-24ºC, 40-50% relative humidity, and 12/12h light cycle with lights on at 07:00) and allowed 7 days to acclimatise before mating. Food and water were available *ad libitum*. Ten pregnant females were singly

housed and allowed to raise their own pups. Litters ranged in size from 7-12 pups (3-7 females per litter; no litters were exclusively male or female) and weaning took place between PND21-24 (PND21: 4 litters; PND23: 5 litters; PND24: 1 litter). At the time of weaning, three female pups from each litter were assigned to one of three groups (1) *Dam-paired* nociceptive tested, (2) *Isolated* nociceptive tested, and (3) *Behaviourally-naïve/control* (N = 10 per group). Male and unselected female pups were rehoused in same-sex groups and used in other experiments. Pups assigned to the dam-paired nociceptive tested group were kept in the original home cage with the dam (siblings removed 1hr prior to testing), and the dam was present during nociceptive testing. The pups in the isolated group were taken from the dam and siblings and singly housed in a new cage for 1hr prior to and throughout nociceptive testing (total period of isolation approx. 4 hours). Nociceptive responding was carried out between 09:00-15:00 hr and each animal was tested in the same sequential order: responding to noxious heat was assessed with the hot plate (HPT), followed by mechanical responding with the Von Frey (VFT), cold hypersensitivity with the acetone drop test (ADT) and inflammatory nociception with the formalin test. In order to ensure that all testing occurred between 09:00-15:00, and animal were isolated/weaned between PND21-24, the experiment was conducted over a five-day period with pups from two litters tested in the three experimental groups per day (2 pups x 3 groups x 5 days = 30 animals). Animals were sacrificed immediately following nociceptive testing (*Dam-paired* and *Isolated* groups) or taken directly from the home cage (*Control* group) and sacrificed. The brain was removed and frozen at -80°C. Dissection of the prefrontal cortex (PFC) involved cutting a 1.5mm coronal tissue section containing the PFC (Bregma 4.7 to 3.2mm) from the frozen brain using a rat brain matrix (Paxinos & Watson, 2006): the olfactory bulbs were removed from this section and PFC was dissected from the right and left sides (see: Figure 4.2, *Results*), and randomly assigned for either the assessment of endocannabinoid levels or mRNA expression of enzymes and receptors. The experimental protocol was carried

out in accordance with the guidelines of the Animal Care and Research Ethics Committee, National University of Ireland Galway under licence from the Health Products Regulatory Authority, in compliance with the European Communities Council directive 2010/63/EU and the ARRIVE guidelines.

***Behavioural testing***

*The Hotplate Test (HPT)*

The HPT apparatus (Harvard Apparatus; Kent, United Kingdom) was set to a test temperature of 55 ± 1°C, in line with previous studies (Burke, Hayes et al., 2010; Kerr, Gilmartin et al., 2016). The latency to hind-paw lick was recorded with a maximum cut-off at 40 seconds, to prevent tissue damage. To accommodate the dam-paired pups, their home cage (open top cage containing the dam only) was placed at a maximum distance of 40cm from the HPT apparatus while the pup was tested. The animal was returned to its home-cage (containing the dam (*Dam-paired*), or singly (*Isolated*)) following testing and the test arena was cleaned and wiped down between uses, using 0.5% acetic acid solution.

*The Von Frey test (VFT) and Acetone Drop Test (ADT)*

The VFT and ADT were conducted sequentially in a six-compartment Perspex arena (11cm x 20cm x 15cm) with wire mesh flooring, as previously described (Burke, Kerr et al., 2014; Flannery, Kerr et al., 2018). To accommodate the dam-pup group, the divider walls were substituted for Perspex partitions punched with holes of 0.5 cm diameter at 2 cm intervals, to enable the dam and pup to see and smell each other without physical contact during both habituation and testing. Pups in the isolated group were tested in the same arena, with no animal in the second testing chamber. Five minutes following the HPT, pups (+/- dam) were habituated to the arena for 25 minutes, after which time von Frey filaments (Touch-Test®Sensory

Evaluators; North Coast Medical Inc., Gilroy, CA, USA) of increasing forces (0.16g – 180g) were applied perpendicular to the plantar surface of the hind paw, up to a maximum of 5 seconds or until flinching, licking or withdrawal of the paw occurred. Each filament was applied five times on each hind paw (alternating between right and left paws), for a total of ten withdrawals. Filament force was increased until a 100% positive response (5 responses to 5 applications) was observed for two consecutive filaments. Results were expressed as the lowest filament to elicit a response and the percentage response of paw withdrawals (number of withdrawals/10 x 100), and EC50 values were generated for each animal.

Immediately following VFT, the animals remained in the apparatus for ten minutes, before being assessed for cold allodynia with the ADT. In brief, a 0.2ml droplet of acetone (Sigma-Aldrich, Dublin, Ireland) was applied to the plantar surface of each hind paw in turn, ensuring to avoid foot pads. Behaviours were scored for latency to first response (flinch, lick, paw shake, or withdrawal of paw) within the cut-off time of 60 seconds. If the animal did not respond within 60s, the cut-off time was recorded as the latency. Three trials per paw were conducted, and the average of the 3 trials for each hind paw was calculated.

*Formalin test*

Immediately following the ADT, the pups were placed back into their home cage and transferred to a new procedure room where they were immediately placed into the formalin arena for a 10-minute habituation period. The arena consisted of a black Perspex observation chamber (30 x 30 x 30 cm), divided in 2 equal parts by a Perspex panel (holes of 0.5 cm diameter punched at 2 cm intervals); this enabled the dam-pup pairs to see and smell each other, but not interact, during both the habituation and the formalin trial (Appendix R). Light intensity was maintained at 35 lux and behaviour recorded by a video camera mounted beneath the

observation chamber. Testing was carried out as previously described (Burke et al., 2010; Fitzgibbon, Kerr et al., 2019).

Distance moved, rearing, and grooming during the 10-minute habituation trial was recorded. Immediately following habituation, the pup was removed, gently restrained and the right hind paw diameter was measured using Vernier callipers, before administering an intra-plantar injection of 20µl 1% formalin in sterile saline. The pup was then placed back into the arena for 60 minutes and behaviour was recorded onto video and analysed with the aid of EthoVision® XT11.5 video-tracking software (Noldus; Netherlands). Formalin-evoked nociceptive behaviour was scored over the entire 60 min trial and analysed in 5 minute time bins using the weighted composite pain scoring technique (CPS-$WST_{0,1,2}$) (Watson, Sufka et al., 1997): time spent elevating the injected paw (C1), and licking, shaking, biting, or holding the injected paw (C2) were combined to obtain a composite pain score (CPS = C1+2(C2)/(duration of analysis period)). There are 3 distinct phases to the formalin test (Fischer, Carli et al., 2014): Phase 1 (0-5 min time period: which represents direct activation of peripheral nociceptors), the interphase (5-10min period; hyperpolarization of nociceptors) and Phase 2 (>10 min period: which represents engagement of inflammatory and/or central nociceptive responses including sensitization). As such, CPS was also calculated for Phase 1 (0-5 min) and phase 2 (10-20min) of the formalin test. Distance moved, duration of rearing and grooming were also recorded. At the end of the test period, paw diameter was recorded again before sacrifice. Two pups from the isolated cohort received incorrect concentration of formalin into the hind paw and thus were excluded from formalin and post-mortem analysis (final group number for the formalin test are Dam-Pup group, N = 10; Isolated group, N = 8).

***Quantification of endocannabinoid levels in the PFC using LC-MS/MS***

Quantitation of endocannabinoids using mass spectrometry was carried out as described previously (Fitzgibbon et al., 2019; Flannery, Henry et al., 2018). In brief, PFC samples were

homogenized in 400 µl 100% acetonitrile containing deuterated internal standards (0.014 nmol AEA-d8, 0.48 nmol 2-AG-d8), centrifuged at 14,000g for 15 min at 4°C, and then the supernatant was evaporated to dryness. Lyophilized samples were re-suspended in 40 µl 65% acetonitrile and separated on a Zorbax C18 column by reversed-phase gradient elution (65% to 100% acetonitrile with 0.1% formic acid). Analyte detection was carried out in electrospray-positive ionization and multiple reaction monitoring mode on an Agilent 1100 HPLC system coupled to a triple quadrupole 6460 mass spectrometer (Agilent Technologies Ltd, Cork, Ireland). Quantification of each analyte was performed by ratiometric analysis using Masshunter Quantitative Analysis Software (Agilent Technologies, Cheshire, UK) and expressed as nmol or pmol per gram of tissue.

***Expression of endocannabinoid-related catabolic enzymes and receptors in the PFC***

PFC tissue was placed into RA1 buffer and mRNA was extracted using the NucleoSpin RNA II total RNA isolation kit, in accordance with manufacturer instructions (Macherey-Nagel, Germany). mRNA was reverse transcribed into cDNA using a High Capacity cDNA Archive kit (Applied Biosystems, UK) and Taqman gene expression assays (Applied Biosystems, UK) were used to quantify the gene of interest using real-time PCR performed using a StepOne Plus instrument (Applied Biosystems, UK), as previously described (Fitzgibbon et al., 2019; Flannery, Henry, et al., 2018). Assay IDs for the genes were $CB_1$ (Rn02758689), $CB_2$ (Rn03993699), FAAH (Rn00577086) and MAGL (Rn00593297), and VIC-labelled β-actin was used as an endogenous control to normalize gene expression data. PCR was performed using Taqman PCR Master Mix, and samples were run in duplicate. The cycling conditions were 90°C for 10 min and 40 cycles of 90°C for 15 min followed by 60°C for 1 min. Relative gene expression was calculated using the ΔΔCT method and expressed as % change from behaviourally-naïve control group.

**Data analysis**

The SPSS 24.0 (IBM Corp, Armonk, NY) statistical program was used to analyse all data. Normality and homogeneity of variance were assessed using Shapiro-Wilk and Levene's test, respectively. Data from the two behavioural groups were analysed using unpaired t-tests, and CPS in the formalin test was assessed using repeated measures analysis of variance (ANOVA). Endocannabinoid levels and gene expression were assessed using one-way ANOVA with post-hoc Fisher LSD tests. If data were found to be non-parametric, three transformations were applied, in this order: square root of the data values, log of the data values, and ranking of the data values. Also, it was checked if the highest standard deviation was less than or equal to 2 times the smallest standard deviation for the particular data set being analysed (Moore, McCabe et al., 2012). All data was parametric prior to or following these transformations. Statistical significance was set at $p \leq .05$. All graphs were constructed using GraphPad Prism and data are presented as group mean ± standard error of the mean (SEM).

**Results**

**Isolated juvenile female rats exhibit thermal and mechanical hypoalgesia and cold allodynia when compared to pups tested in the presence of the dam**

The effect of acute isolation versus social support (presence of dam) of juvenile rat pups on nociceptive responding to heat, cold and mechanical stimuli was examined. There was a significant difference on latency to respond in the hot plate test, with isolated juvenile pups demonstrating longer withdrawal latencies than dam-paired counterparts; $t(18) = 2.29$, $p = .034$ (Figure 4.1a, *overleaf*). During the acetone drop test, isolated juvenile pups demonstrated significantly reduced withdrawal latencies compared to dam-paired juveniles; $t(16) = 2.33$, $p = .033$ (Figure 4.1b). Analysis of the sensitivity to mechanical stimuli during Von Frey testing revealed that isolated juvenile pups required heavier filaments to provoke a withdrawal

response; t(18) = 3.74, $p$ = .002 (Figure 4.1c), and demonstrated a significantly increased paw withdrawal threshold compared to dam-paired juvenile pups; t(18) = 4.15, $p$ < .001 (Figure 4.1d).

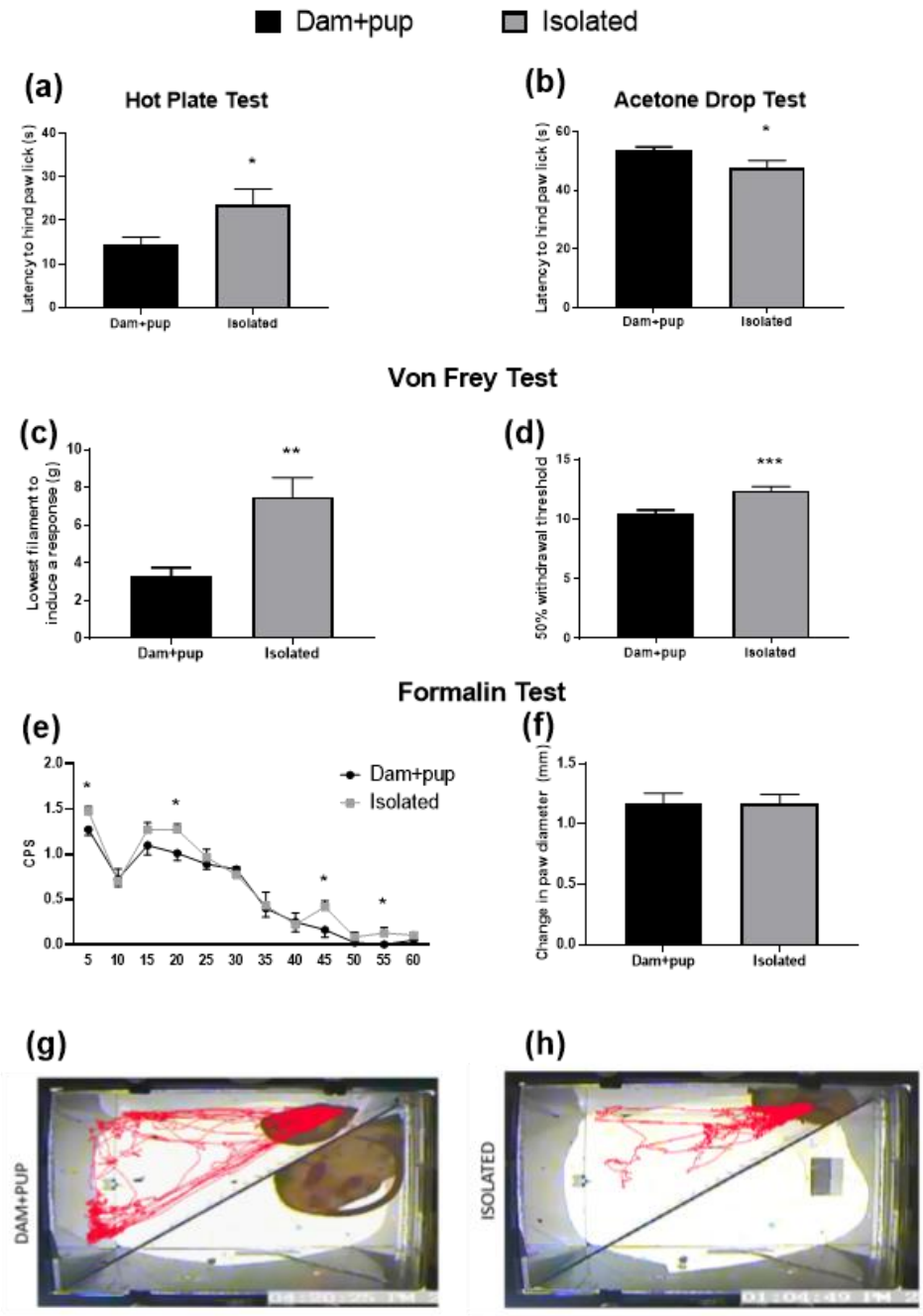


**Figure. 4.1: The effect of acute isolation vs maternal support on nociceptive responding of juvenile female pups. (a) Latency to respond in the hot plate test. (b) Latency to hind paw lick in the acetone drop test. (c-d) Mechanical withdrawal thresholds in the Von Frey test. (e) CPS (*composite pain score*) over the 60-minute formalin trial (5-minute bins). (f)**

**Change in paw diameter following formalin administration. (g-h) Representative images of the distance moved during the formalin test. Data expressed as mean ± SEM (n= 8-10 per group). *** p < .001; ** p < 0.01; * p < 0.05 vs dam-paired pups. #represents phase 1 and 2 of the formalin test.**

**Nociceptive responding to an inflammatory stimulus is increased in isolated juvenile female rat pups compared to pups tested in the presence of the dam**

Prior to formalin administration, rats were exposed to a novel Perspex arena for 10 minutes. Analysis of this habituation period revealed no significant difference between isolated and dam-paired juvenile pups in relation to distance moved, rearing or grooming behaviour (Table 4.1). During the 60 minute formalin trial, isolated juvenile pups moved significantly less, $t(16) = 4.62$, $p < .001$, and reared less, $t(16) = 3.30$, $p < .001$, than dam-paired pups but there was no significant difference between the groups in duration of grooming during the trial; $t(16) = .32$, $p > .05$ (Table 4.1, *overleaf*).

In order to examine the effect of isolation vs social support on inflammatory nociceptive responding, juvenile rats received an intra-plantar formalin administration and behaviour was assessed over a 60-minute period. Repeated measures ANOVA revealed a significant effect of time, $F_{(11, 176)} = 83.61$, $p < .001$, on the composite pain score (CPS) per 5 min time bin over the course of the 60-minute formalin trial (Figure 4.1e). Further discrete analysis of the two main phases of the formalin test revealed that isolated pups exhibited a significant increase in CPS during the first phase of the formalin trial ($p = .035$), with a trend for an increase in responding in the second phase, which just failed to reach statistical significance ($p = .06$) (Figure 4.1e). There were no differences between dam-paired and isolated pups in relation to paw oedema at 60 mins post-formalin administration; $t(16) = .06$, $p > .05$ (Figure 4.1f). Examination of the movement tracking data revealed that dam-paired pups moved significantly more and explored a wider area of the novel arena compared to isolated pups (Figure 4.1g-h; see Appendix S).

**Table 4.1: Distance moved, rearing, and grooming during habituation and formalin trial. Data expressed as mean ± SEM (N = 8-10 per group); *** $p < .001$; ** $p < .01$; ns= not significant.**

| **Habituation (10 mins)** | | | | |
|---|---|---|---|---|
| | **Dam-pup** | **Isolated** | **Sig.** | |
| **Distance moved (cm)** | 1038 ± 60 | 868 ± 68 | t(18) = 1.89; *p = .07* | *ns* |
| **Rearing (s)** | 95.45 ± 6.19 | 87.95 ± 14.93 | t(18) = 0.46; *p = .65* | *ns* |
| **Grooming (s)** | 128.60 ± 11.11 | 117.23 ± 15.78 | t(18) = 0.59; *p = .56* | *ns* |
| **Formalin trial (60 mins)** | | | | |
| | **Dam-pup** | **Isolated** | **Sig.** | |
| **Distance moved (cm)** | 1523 ± 122 | 822 ± 73 | t(16) = 4.62, *p = .001* | *** |
| **Rearing (s)** | 69.17 ± 11.57 | 20.63 ± 7.69 | t(16) = 3.30, *p = .004* | ** |
| **Grooming (s)** | 60.60 ± 7.18 | 73.00 ± 13.50 | t(16) = 0.86; *p = .40* | *ns* |

**PFC anandamide levels are reduced in pups with dam present during nociceptive testing**

Endocannabinoid levels were assessed in the prefrontal cortex (PFC) following nociceptive testing and in a behaviourally-naïve control group. Analysis revealed a significant effect of nociceptive testing on levels of the endocannabinoid anandamide (AEA) in the PFC; $F_{(2,28)} = 5.18$, $p = .013$ (Figure 4.2a). *Post-hoc* analysis revealed that levels of AEA were significantly lower in the PFC of dam-paired pups following nociceptive testing, compared to control ($p = .010$), an effect not observed in isolated pups (Figure 4.2a). There was no significant difference in 2-AG levels in the PFC between any of the groups; $F_{(2,28)} = 1.32$, $p > .05$ (Figure 4.2b).

**Nociceptive testing is associated with decreased in $CB_2$ receptor expression in the PFC**

Fatty acid amide hydrolase (FAAH) is the enzyme primarily responsible for the catabolism of anandamide, while monoacylglycerol lipase (MAGL) preferentially metabolises 2-AG. There were no significant difference between the groups in mRNA expression of FAAH [$F_{(2,27)} = 0.01$, $p > .05$], MAGL [$F_{(2,27)} = 2.16$, $p > .05$] or the $CB_1$ receptor [$F_{(2,27)} = .73$, $p > .05$] in the PFC (Figure 4.2c-e). Analysis revealed a significant effect group on the mRNA expression of $CB_2$ in the PFC [$F_{(2,27)} = 18.84$, $p < .001$]. Post-hoc analysis revealed that levels of $CB_2$ were significantly lower in both isolated ($p < .001$) and dam-paired pups ($p < .001$), compared to the behaviourally-naïve control group (Figure 4.2f, *overleaf*).

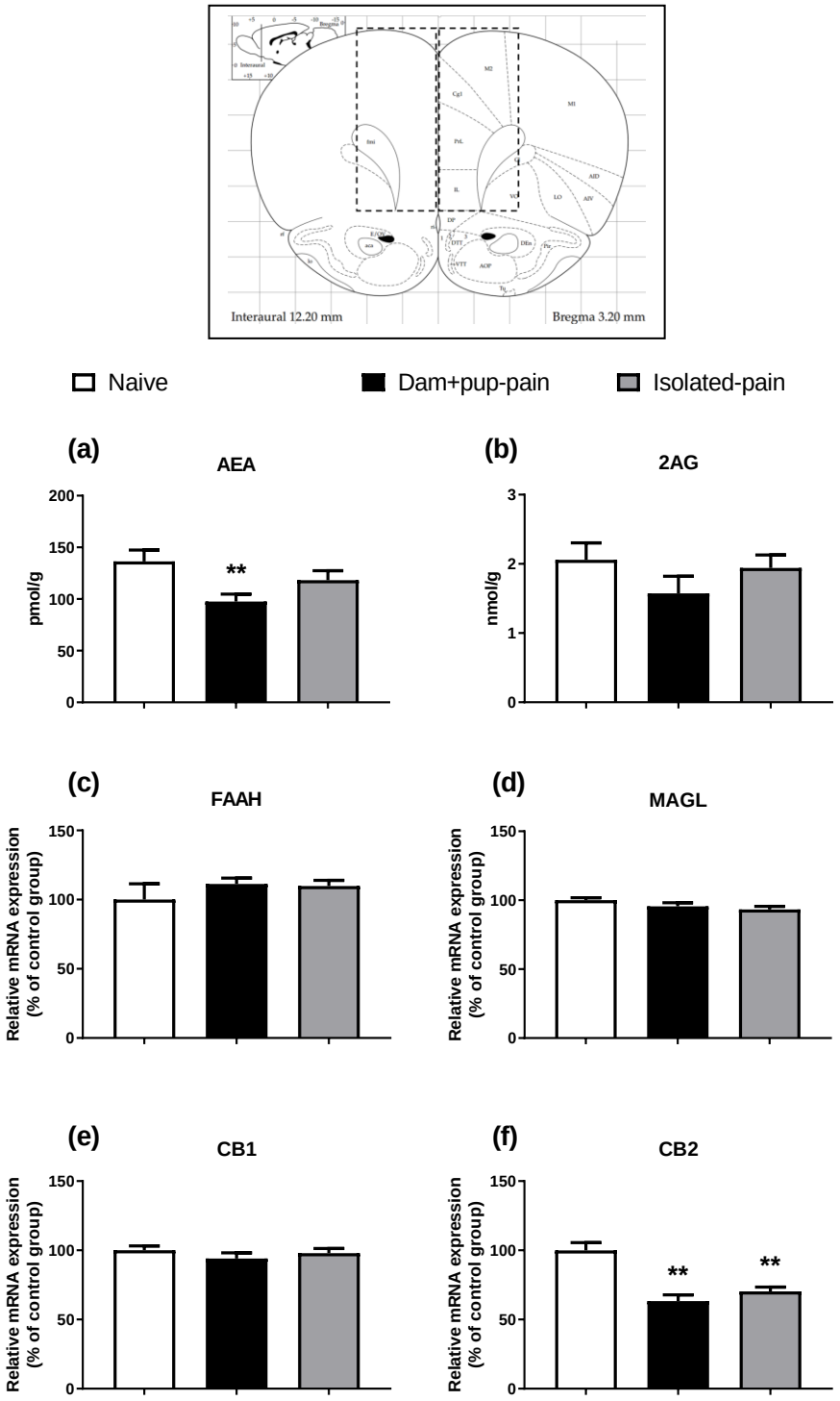


**Figure 4.2: The effect of intra-plantar formalin injection on endocannabinoid levels, enzyme, and receptor expression in the PFC of juvenile female pups. (top) Schematic of areas of PFC dissected for analysis; (bottom) (a-b) Expression of the endocannabinoids AEA and 2-AG levels; (c-d) Expression of the catabolic enzymes FAAH and MAGL; (e-f) Expression of the cannabinoid receptors $CB_1$ and $CB_2$. Data expressed as mean ± SEM (N = 8-10). ** p < .01 vs behaviourally-naïve control group.**

**Discussion**

The data presented here demonstrate that nociceptive responding of juvenile female rat pups is altered depending on maternal presence or acute isolation. Specifically, isolated juvenile pups exhibited enhanced inflammatory and cold nociceptive responding and reduced mechanical and heat nociceptive responding, when compared to pups tested in the presence of a dam. Conversely, the presence of the dam resulted in cold and inflammatory hyperalgesia, and mechanical and heat hypoalgesia in juvenile pups, when compared to pups tested in isolation. Taken together, the data indicate that maternal presence/isolation modulates nociceptive responding of juvenile female rat pups depending on the modality being examined.

To date, studies examining the effects of short-term isolation and/or maternal support on nociceptive responding have been carried out in the early postnatal period and have only examined heat nociceptive thresholds. For example, 6 day old rats isolated from the dam for 30 minutes exhibit increased tail flick latencies (Spear et al., 1985) and 10-12 day old rat pups isolated for 5-8 minutes exhibit longer latencies in the hot plate test (i.e. hypoalgesia), (Kehoe & Blass, 1986a; Kehoe & Blass, 1986b; Kozlov et al., 2013; Kozlov et al., 2012; Nizhnikov et al., 2014). Longer-term pup isolation (4-6 hr) has been associated with either no change (Kozlov et al., 2013) or reduced (Blass et al., 1995) latency to respond in the hotplate test. Thus short, but not long term, isolation induces a decrease in nociceptive responding to noxious heat stimuli in the early neonatal period. The current data expand on this data demonstrating that juvenile pups (PND21-24) isolated from the dam and siblings for a 1hr period also exhibit an increase in nociceptive thresholds to a thermal noxious stimulus and expand this to include an increase in thresholds to mechanical noxious stimuli. Although this is the first study to examine effects in the juvenile period, it has been demonstrated that mice isolated for 1 hour at 6-8 weeks of age exhibit increased mechanical thresholds and paw withdrawal latencies compared to non-isolated cage mates (Han, Lee et al., 2016). The precise mechanisms mediating

isolation-induced thermal and mechanical hypoalgesia remain to be determined, however effects may be due to isolation stress-induced engagement of the descending pain pathway and resultant analgesia (stress-induced analgesia) (Butler & Finn, 2009; Corcoran et al., 2015). Stress-induced analgesia is an important survival mechanism which results in reduced nociceptive responding to demanding acute internal and/or external stressors. However, stress-induced analgesia can be modality specific and effects are dependent on the type and intensity of the stressful event (psychological vs physical; conditioned vs unconditioned) (Butler & Finn, 2009; Olango & Finn, 2014). Accordingly, while acute isolation results in inhibition of nociceptive responding to heat and mechanical noxious stimuli, our data demonstrated that rat pups tested in isolation exhibited enhanced responding to a cold innocuous stimulus (cold allodynia) compared to dam-paired counterparts. Thus, the effects of acute isolation on nociceptive responding of juvenile female pups depends on the modality under investigation, which may reflect the involvement of the different spinal and/or supraspinal mechanisms mediating the nociceptive responses to these varying heat, cold and mechanical stimuli.

During the formalin test, pups tested in isolation exhibited increased inflammatory nociceptive responding when compared to those tested in the presence of the dam. The increase in nociceptive responding occurred during the first phase, with a tendency for an increase during the second phase also noted. Furthermore, isolated rats exhibit reduced locomotor activity and rearing during the formalin test which may reflect indirect behavioural responses to pain (i.e., less movement due to greater pain). These data highlight effects of brief isolation on nociceptive responding on both the initial somatosensory processing and the longer term supraspinal modulation of the inflammatory pain response. Although the mechanism mediating these effects remains to be determined, it is possible that the presence of the dam may act as a distractor from the inflammatory pain (distraction-induced analgesia). This is supported by the data demonstrating that rats tested in the presence of the dam exhibited greater distance moved

and rearing during the formalin trial, primarily directed towards the partition separating the dam and pup (see: Figure 4.1.2). Previous studies have demonstrated that the presence of a confined conspecific does not alter formalin-induced inflammatory nociceptive responding (Ford, Moriarty et al., 2008) or results in hyperalgesia to visceral inflammatory pain (acetic acid) (Langford, Tuttle et al., 2011). However, the conspecifics used in the aforementioned studies were unfamiliar to the test animal and testing was conducted using adult rodents. Furthermore, Langford et al demonstrated that mild social threat produces hyperalgesia (Langford et al., 2011). Thus, the presence of the dam may result in a distraction that promotes engagement of social circuits and descending pain pathways to modulate nociceptive responding. It should be noted that isolated animals exhibited hypoalgesia the first two nociceptive tests conducted (hot plate and Von Frey tests) and hyperalgesia in the subsequent two tests (acetone and formalin tests). We cannot rule out that the heat and mechanical hypoalgesia was a transient effect of acute isolation or whether sequential testing of the animals impacted on subsequent nociceptive responses. Regardless of the direction of change, acute isolation or maternal support each alter nociceptive responding in female juvenile rat pups.

The endocannabinoid system (ECS) is a key modulator of stress- and distraction-induced analgesia (Butler & Finn, 2009; Ford, Moriarty et al., 2015) and plays an important role in the prefrontal cortex (PFC) in mediating and modulating nociceptive responding (Fuchs et al., 2014; Okine, Madasu et al., 2016; Rea et al., 2019). The data herein demonstrate that AEA, but not 2-AG, levels were reduced in dam-paired, but not isolated, pups that underwent nociceptive testing. The decrease in AEA was not associated with a change in the expression of the metabolic enzyme FAAH, although activity of that enzyme may be altered. Recent data from our laboratory has demonstrated that increasing AEA tone within subregions of the prefrontal cortex modulates inflammatory nociceptive responding only under conditions of stress (attenuates fear-conditioned analgesia) (Rea et al., 2019). Thus, a decrease in AEA levels

in the PFC may mediate stress- and/or distraction-induced analgesia. However, given the time at which the tissues were collected, it is possible and even likely that the decrease in AEA reflects an earlier increase in release, mobilisation and utilisation. Accordingly, Ford et al demonstrated that distraction-induced analgesia was associated with an increase in AEA (and 2-AG) levels and could be attenuated by $CB_1$ antagonism (Ford et al., 2015). Thus, while additional studies are required to determine the precise mechanisms underlying the changes in nociceptive responding the presence or absence of the dam in juvenile rats, the data here suggest a possible role for AEA signalling in the PFC in mediating or modulating these effects. Interestingly both dam-paired and isolated juvenile rats that underwent nociceptive testing exhibited a decrease in $CB_2$ expression in the PFC. It is unknown if this effect is due to exposure to any one particular nociceptive test, removal from the home-cage during testing, or an effect of cumulative nociceptive testing over a 3hr period. $CB_2$ receptors are expressed on glia and discrete populations of neurons within the brain, and increasing data suggests an important role for $CB_2$ receptors in the mediation and modulation of pain (Starowicz & Finn, 2017) Accordingly, recent data from our laboratory has demonstrated that enhancing 2-AG tone within the PFC attenuates fear-conditioned analgesia via $CB_2$ receptor activation (Corcoran et al., 2020). However, the expression of $CB_2$ receptors are low under non-pathological conditions, which was confirmed in the current study ($CB_1$: average CT = 21 vs $CB_2$ average CT = 30). Future studies will be required determine if the decrease in $CB_2$ receptor expression following nociceptive testing translates into a change in protein expression, the location of such changes (neurons and/or glia, discrete areas of the PFC) and the physiological significance.

**Overall conclusions**

This study provides key insight into the effects of maternal presence vs acute isolation on nociceptive responding in juvenile female rat pups, effects which are dependent on the

modality under investigation. The data also demonstrate that anandamide levels are altered in the prefrontal cortex, a key brain region involved in both affect and nociception, and thus provides further support for the endocannabinoid system as a mediator and/or modulator of social support on nociceptive responding. This may provide a framework for evaluating the role of the endocannabinoid system in sociobehavioural responding during painful experiences in the key preschool period of development. These data further enrich the findings regarding the psychosocial impact of parental support from Studies 1 and 2 and contributes to our limited understanding of parent-child interactions during acute pain experiences.

# CHAPTER V

# DISCUSSION

## Chapter overview

Pain is both an intra- and interpersonal experience, and we require an understanding of both elements if we are to fully understand pain (Karos, 2017). This is of particular relevance to the context of childhood pain experiences, as children highly depend on others (mostly their parents) for help and care. As demonstrated extensively within empirical literature, the availability of parental social support during painful experiences in clinical settings (such as immunisations and post-procedural pain) and their behaviour and responses towards their child are strong predictors of their child's responses to pain. For example, parental protective behaviours such as discouragement or reassurance may magnify distress and anxiety in their child (Birnie et al., 2013; Boerner et al., 2017; Cohen et al., 2015; Jacobsen et al., 1990), while parental coping-promoting behaviours such as distraction or breathing techniques can produce more positive outcomes, including reduced parent and child distress, reduced pain sensitivity, and enhanced pain tolerance (for review, see: Brown et al., 2018; Campbell et al., 2017; Chambers et al., 2009; Piira et al., 2005). Comparatively, literature which has specifically explored bidirectional parent-child influences during naturalistic pain experiences is scarce, and it remained unclear whether the compelling evidence from clinical settings would translate to understanding how parents and children respond to pain in other settings. Therefore, the primary focus of this compendium of research was to explore the mutual social influences between parent and child during "everyday" (i.e., non-clinical) pain events, and to examine the role of parental social support in altering the child's pain experience, through three empirical studies. In the first study, two novel means of capturing everyday pains were assessed and validated, in comparison to an existing method. The second study described the use of a novel diary measure for capturing parent impressions of their child's pain, and a real-time digital

assessment of parent-child pain ratings was trialled. Finally, a laboratory study explored the biological underpinnings of pain experienced in the presence or absence of social support. Consistent with theory and empirical literature, significant relationships were identified between social support and child and parent responses to child pain across all three studies.

This chapter will present a summary of the findings from each study and evaluate the contribution of each study to improving the understanding of parent-child bidirectional influences during minor, "everyday" pain experiences, with reference to existing literature. While being mindful of the limitations associated with each study, the methodological, theoretical, and clinical implications of this research will be considered. Based on these implications, suggestions for future research will be highlighted. Finally, this chapter will present concluding remarks.

## Integrated summary of studies

### *Overview of Study 1*

***Study 1*** observed parent, child, and researcher interactions during everyday pain events within the family home and compared the robustness of this home-based methodology to the more established method of observing everyday childhood pain experiences within day-care settings. These observations illustrated that social influences play a role in our interpersonal "performance" during minor pain events: children who experienced pain in front of researchers cried for shorter periods of time, gave lower ratings for their pain and received lower pain estimates from researchers, compared to children who experienced pain in front of their parents only. These findings may indicate that the child was trying to "put on a brave face", to discourage unfamiliar persons from intervening or offering comfort. This is consistent with previous literature that children readily regulate their responses to pain depending on who is

watching them, in order to continue playing with and/or avoid embarrassment in front of peers, or to avoid reprimands from caregivers (Larochette et al., 2006; Liossi et al., 2012; Zeman & Garber, 1996). The findings also support the underlying assumptions of the Actor-Partner Interdependence Model (APIM; Cook & Kenny, 2005), which proposes that dyadic interpersonal relationships are bidirectional: i.e., the behaviour of one person (in this case, a child) can influence the behaviour of a second person (i.e., their parent), which will influence their child's subsequent behaviour in return. However, ***Study 1*** also found that parents tended to give lower estimates for pain ratings than the child themselves, perhaps indicating that the intra- versus interpersonal experiences of pain do not necessarily converge. Previous evidence from clinical settings has demonstrated that pain ratings are often incongruous with the child's own rating, with both parents and nurses consistently giving lower pain estimates than the child (Manne et al., 1992; Zhou, Roberts et al., 2008). The findings from ***Study 1*** appear to extend this phenomenon to natural settings. These findings begin to partly address a wider issue within paediatric pain research, which is that much of what we currently know about parent-child interactions has been extrapolated from clinical settings. There is still a relative paucity of studies exploring everyday pains, and each relied on the same measure, the *Dalhousie Everyday Pain Scale (DEPS)*, which looks at caregiver (but not necessarily parent) behaviours within day-cares and play centres (Fearon et al., 1996; Gilbert-MacLeod et al., 2000; Noel, Chambers, et al., 2018; von Baeyer et al., 1998). One limitation of ***Study 1***, therefore, was that the DEPS scale had not previously been used within family homes, and as such, some items did not accurately depict the situations or behaviours that were observed. Furthermore, the recording measures that accompanied this scale were somewhat burdensome: in families who had participated without a researcher present, a small number of parents admitted afterwards that they felt uncomfortable at having private interactions with their family recorded by video-cameras, and that without researchers present, the experience felt slightly more intrusive and

this reduced their overall experience of participation. This – combined with the need to be constantly available to attend every one of their child's pain events – left parents feeling unable to act completely naturally. This represented a considerable shortcoming in this research and led to the implementation and evaluation of alternative methodologies, such as diary methodology, in Study 2.

### *Overview of Study 2*

Building from the findings in Study 1, ***Study 2*** sought to investigate the psychosocial impact on parents observing their child's everyday pain experiences. A parental daily diary was used to give valuable insight into the context surrounding "everyday" pains within the home. Pains were a near-daily occurrence, and injuries were mostly minor (e.g., bumps on the head, scrapes on the hands or knees; etc.). Discrepancies emerged in pain intensity estimates wherein parents consistently underestimated their child's pain, reaffirming the findings from *Study 1* and previous clinical reports of incongruent pain estimates (Manne et al., 1992; Zhou et al., 2008). Contextual factors were a significant influence on parental responses to their child's pain experience. Where Study 1 confirmed that children respond differently in front of their parents than with strangers, ***Study 2*** confirmed that parents themselves respond differently based on the situational context and other moderating factors (such as the age, sex, and birth order of the child, and the level of supervision by the parent prior to the pain event). In turn, parental responses, such as the level of distress and catastrophizing they exhibited during pain events, were significantly associated with higher estimates of pain severity and child distress. Importantly, the findings also highlighted how parental trait-level *expectations* of their behaviours and thoughts during their child's pain experiences were not a strong predictor of their state-level behaviours and thoughts during the *actual* events, which is in line with recent parental pain catastrophizing literature (Caes, Vervoort, Eccleston, et al., 2012; Durand et al.,

2017; Goubert et al., 2012). The design of the diary in ***Study 2*** limited us from examining *all pain events* within the reporting period, which raised questions around potential selection bias (i.e., if parents chose to only report events which were more socially acceptable). Despite this, ***Study 2*** represents the first use of the DEPS-R within the family home as an ecologically valid environment in which childhood pains occur and the first use of the scale by parents (or other untrained observers). In doing so, our use of the DEPS-R in this context offers additional validation of a relatively new measure and strengthens confidence in its viability to measure parental responses to minor child pains in naturalistic settings. Given the paucity of literature on everyday pains, the contributions made by ***Study 2*** to the wider field of paediatric pain are modest but significant.

Collectively, Studies 1 and 2 proposed and tested new methods to capture the psychological and social (interpersonal) context surrounding everyday pain experiences. These studies presented evidence that the effectiveness of social support during pain experiences is dependent on who is present to offer support (i.e., parents or strangers), and that parental behaviour and thoughts surrounding pain are a particularly powerful influence on both their child's experience of pain and their own interpretations of their child's pain. However, pain experiences can best be described as the confluence of psychological, social, and biological factors (Engel, 1977; Hadjistavropoulos et al., 2011). Therefore, questions remained as to precisely how the biological (intrapersonal) mechanisms that underpin pain processing are associated with the psychosocial (interpersonal) context of a pain event. More specifically, we wanted to explore whether the presence or absence of maternal social support during pain would expose differences in pain processing at a biological level, to reflect the behavioural differences in pain responding that we had observed in the previous studies.

***Overview of Study 3***

The neurobiological changes associated with social support during pain cannot be readily investigated within clinical or family settings. Instead, this thesis employed a translational approach and utilised both clinical and preclinical methods to clarify the role of social support during pain. Specifically, ***Study 3*** employed preclinical laboratory methods to investigate behavioural and neurobiological changes in juvenile rodents exposed to pain either while isolated or in the presence of their mother. Behavioural testing revealed that experiencing pain while isolated resulted in increased sensitivity and reduced reaction times to withdraw from cold stimuli, but blunted responses to mechanical stimuli. Isolated rodents also demonstrated increased pain behaviours to noxious inflammatory stimuli (e.g., formalin exposure) while rodents paired with their mother did not, suggesting that isolation results in aberrant pain responding while social support may be somewhat protective against pain. This correlated with previous data on pain thresholds following brief isolation (5-30 mins) (Kehoe & Blass, 1986a; Kehoe & Blass, 1986b; Nizhnikov et al., 2014), and highlighted that similar effects also occur during longer periods of isolation (1-5 hours). These behavioural differences were associated with alterations to key neurobiological substrates in the prefrontal cortex. Specifically, social support was associated with reduced levels of anandamide (AEA), while noxious pain experience was associated with reduced expression of cannabinoid $CB_2$ receptors in both isolated and mother-paired rats. This echoed previous findings that isolation of 2-3 hours resulted in blunted nociceptive responding in adolescent mice (Han et al., 2016) and social support or isolation alters pain sensitivity and endocannabinoid signalling in infant and adolescent rats (Marco et al., 2011; Schneider, Bindila, et al., 2016). However, ***Study 3*** is – to the author's knowledge – the first such work to examine the impact of social support during pain in *juvenile* rats, and one of a scant number of studies to specifically examine pain behaviours in female rats (where the predominant literature features male rats only). When

combined with the findings from Studies 1 and 2, Study 3 provides strong evidence that social support is essential to adaptive function during painful or uncomfortable experiences in early life and represents a modest but valuable contribution to the understanding of the role that social support provides during mild pain experiences during this period.

**Methodological implications**

The focus on everyday pains is still relatively recent within the field of paediatrics, with most of the research emerging only within the last two decades (Fearon et al., 1996; Noel, Chambers, et al., 2018; O'Sullivan et al., 2019; von Baeyer et al., 1998). Since the inception of this thesis alone, significant methodological improvements have emerged to further facilitate the study of everyday pains. For example, each study on everyday pains which we originally reviewed had utilised the Dalhousie Everyday Pain scale (DEPS; Fearon et al., 1996), and primarily captured the tone and behaviours of children and staff within day-care centres. While undoubtedly valuable, this approach left everyday pain events in *other* naturalistic settings mostly undocumented and excluded meaningful data from parents and other caregivers during everyday pain events. More recently, the Revised DEPS was developed (DEPS-R; Noel, Chambers, et al., 2018), to include an objective record for parental responses to pain, and was initially validated through observations of everyday pains within a play activity centre. Therefore, while ***Study 1*** of this thesis utilised the original DEPS, ***Study 2*** could take advantage of the newer DEPS-R and allow the parent to better capture everyday pain interactions with their child. Crucially, both studies centred on the family home as the focal environment. The family home represents potentially the most significant ecologically valid environment for studying everyday pains, and these works are the first reported use of either the DEPS or DEPS-R within this context, to the author's knowledge.

For research on everyday pains to flourish, it is essential that methods continue to be developed which are suitable and acceptable for children and their parents. It must also be acknowledged that not all methods will be feasible, and transparency in reporting such "failures" is vital to advancing feasible developments. For example, in ***Study 1***, the use of video-cameras presented significant barriers to recruitment and the comfortable participation of parents during the study and disrupted the natural family environment. Subsequently, another study reported technological difficulties with video-recording, and the data was discarded (Noel, Chambers, et al., 2018), Thus, in ***Study 2***, an electronic diary method was chosen to replace the video-cameras, to reduce the potential impact of these barriers. This change to a diary format enabled us to include elements from the DEPS-R (Noel, Chambers, et al., 2018), which were completed solely by parents. The further validation of this measure represents a modest contribution to the field, but further studies will be needed to confirm the validity and reliability of the various adaptations of the DEPS-R, and other pain measurement scales, in naturalistic environments and completion by parents versus trained professionals.

Within paediatrics, the use of pain measurement scales by a wider range of observers (e.g., clinicians, researchers, and more recently, parents) is generally considered as beneficial to providing greater insight into the potential difference in viewpoints among those witnessing a child's pain event. However, the use of self-report measures by the children themselves has long been contested and this has resulted in two conflicting positions (Emmott et al., 2017; Stanford et al., 2006; von Baeyer, 2009; von Baeyer, Chambers et al., 2013; von Baeyer et al., 2017). On one hand, the child's self-report is crucial to our understanding of their experience of pain, and should complement parental observation wherever possible (von Baeyer, 2009; von Baeyer et al., 2013). Conversely, opposition to the use of child self-report rests on the concerns that younger children cannot accurately judge the discrete increases in pain on existing scales, and though newer, more age-appropriate scales are continually being

developed, the evidence from such scales is currently too limited to entirely refute existing concerns (von Baeyer, Forsyth et al., 2009; von Baeyer et al., 2017). In this dissertation, we opted for aligning with the first position and included, where possible, child self-reports of their pain experiences. In ***Study 1***, the *Faces Pain Scale–Revised* (FPS-R) scale was chosen for the parent and child ratings as it was the most reliable validated tool available at that time (Hicks et al., 2001), and would allow us to relate our findings to previous literature within the field and close some of the knowledge gaps. However, the possibility remains that the scale was not suitable for our cohort (given their young age of 3-5 years) and did not reliably capture the insights we intended it to. This is notable as, since Study 1 was conducted, the reliability of the FPS-R and facial rating scales have been further questioned even in the 4-5-year age range, much less for the younger children we observed. This limitation reduces the wider applicability of the findings from Study 1. As such, within ***Study 2***, the recent publication of the *Simplified Faces Pain Scale* (S-FPS) offered a more suitable choice for the EMA, as it is specifically adapted to the cognitive abilities of young children and more reliable for younger cohorts (Emmott et al., 2017). While concerns about using child self-report may remain even with these newer scales, their validity for use with younger cohorts is more assured than for their predecessors and they now represent the best option at the current time. Within ***Studies 1 and 2***, both scales demonstrated clear disparities between parent ratings and child ratings, reaffirming findings from clinical settings (Manne et al., 1992; Zhou et al., 2008), and highlighting that the disparity also occurs in natural settings. What remains unclear from these findings, however, is whether such discrepancies result from the unreliability of child reports or from parents assuming a natural tendency to underestimate their child's pain (or perhaps some combination of the two phenomena), and further research is needed to explore these discrepancies between parent and child ratings of pain. As with the validation of the DEPS-R, continued use of newer self-report measures such as the S-FPS will contribute to their increased

validity for naturalistic settings, and provide evidence to address concerns regarding the inclusion of child self-reports.

The availability of appropriate measures and the reporting of data from both parent and child contributed significantly to the robustness of the findings in the presented studies; however, the samples used within each of the studies varied and the potential for some findings to be underpowered cannot be ruled out. For example, the final sample in ***Study 1*** was small but acceptable, and was within previously-suggested guidelines for pilot studies (Hertzog, 2008). While ***Study 2*** contained a larger sample and the quality of the findings was further strengthened by the repeated nature of the measurements, it must be acknowledged that the final sample suffered from high attrition rates, and an increased sample size could have increased the power to detect small effects. Regarding ***Study 3***, as is common for animal studies, sample calculations are concerned less with obtaining sufficient power to generalise findings to the wider population, and instead intended to sufficiently answer the research objectives while adhering to the "*Three R's*" of animal research: "*Replace, Reduce, Refine*" (Animals (Scientific Procedures) Act, 1986). This governs that research should not make unnecessary use of animals, and that every attempt should be made to replace and/or refine research methods to reduce animal involvement and suffering as much as possible. In respects of these requirements, Study 3 answered its research objectives, and the findings can be considered robust. In general summation of the three studies, continued use and validation of novel methodologies in naturalistic environments will enhance our understanding of everyday pains, while larger sample sizes may improve some findings. Finally, greater emphasis should be placed on translational research, in order to more adequately investigate childhood pains as both a psychosocial and biological experience.

While Studies 1 and 2 largely devoted themselves to the validation of novel methods to explore the psychosocial impact of everyday pains, ***Study 3*** explored the biological

mechanisms of pain using well-established and validated methods, albeit from beyond the realm of clinical practice. By establishing a means of conducting comparative pain research in rodents, this created the possibility of examining the associated neurobiology of the effects of related stressors or treatments during painful experiences, including social support. Pain is common to all species, and the protective behaviours exhibited by the children we observed (such as holding or favouring the injured site) and attempts to gain their parent's attention for comfort were not dissimilar from the limb elevations and attempts to reach their mother observed in the rats in our laboratory tests. Without attempting to anthropomorphise the rodents, the presence of the mother appeared to exert similar effects to parental presence in our home studies, with both groups reducing distress and providing distraction to their offspring. This is in line with previous evidence that the availability of social support during pain modulates pain and provides analgesia in certain contexts (Krahé et al., 2013), and that the experience of pain and the mannerisms that convey it are not uniquely human (Hadjistavropoulos et al., 2011; Mogil, 2015). For example, similar non-verbal facial "action units" which indicate pain are observed in humans (Ekman & Friesen, 1978; Grunau & Craig, 1987) and in rodents, rabbits, horses, and several other species (Dalla Costa et al., 2014; Dolensek et al., 2020; Mogil et al., 2020; Sotocina et al., 2011). In this example, the clinical pain measurement was developed first, and was shared across the disciplines to advance preclinical pain measurement of pain indicators. However, as demonstrated in ***Study 3***, it is equally possible that clinical pain expertise can advance through engaging with preclinical measures to generate translational research that benefits both disciplines, and future studies should also consider adopting a translational approach. The examination of the neurobiological underpinnings of pain in ***Study 3*** simply could not be achieved without adopting established pre-clinical methods, and the research objectives would have remained either unanswered or concealed within a knowledge silo that clinicians may not necessarily have considered

accessing. Taken together, the studies in this thesis have made several methodological contributions to advance the understanding of parent-child interactions during everyday pains, as well as to the wider literature on social support during painful experiences.

## Theoretical implications

The theoretical basis for this thesis was drawn from social learning theory and the biopsychosocial model (Craig, 2009; Engel, 1977; Hadjistavropoulos et al., 2011). The experience of pain depends on a myriad of biological, psychological and social influences, and the encoding of pain into behaviour and the decoding of these pain behaviours by others involves an elaborate social process of communication (Karos, 2017). Social learning is particularly evident during the preschool stage of development, where parents offer guidance and model appropriate pain responding for their child to mimic (Goubert et al., 2011; Langford, 2005) and children develop self-regulation of pain through social cues (Larochette et al., 2006; Liossi et al., 2012; Zeman & Garber, 1996). As a result, the social communication of pain is relevant during the preschool period, as pain experiences are relatively frequent, but young children are often ill-equipped to cope with pain alone and must rely on caregivers to provide comfort (Hadjistavropoulos et al., 2011; Harbeck & Peterson, 1992). Through the study findings reported in this thesis, robust evidence has been presented that provides further support for the application of the biopsychosocial model of pain to naturalistic contexts; namely, mutual social influences between parent and child, the impact of psychological distress on parents responding to their child's pain, and the biological underpinnings associated with pain in different social contexts.

Everyday pains are spontaneous and often unremarkable events in the daily life of a child. The existing body of literature which explores everyday pains is scant, and those specifically featuring the involvement of parents are relatively rare. As a result, much of the

theoretical evidence which created the foundations for this thesis was drawn from clinical pain research, in which parents are routinely involved. For example, evidence that video-recording during clinical procedures did not alter patient behaviour was hugely informative when considering methods to capture parent-child interactions during everyday (non-clinical) pain experiences (Albrecht, Ruckdeschel et al., 2005; Newell, Keane et al., 2018), while evidence that parental presence reduced child distress was decisive in including supervision as a factor in our studies (Piira et al., 2005; Wolfram & Turner, 1996). Indeed, the clinical evidence supporting parental presence during procedures was so robust that it sparked a reassessment of conduct during needle-pain procedures, and a flurry of new policy recommendations for paediatric practice within clinical settings (Taddio et al., 2013; WHO & HELPinKids, 2015). However, though this thesis shared a foundation with clinical interventions, the theoretical implications are not transferrable. This thesis was primarily interested in exploring and understanding the natural context surrounding "unremarkable" everyday pains, and its findings were never intended to intervene in parent or child behaviours or change the child's experience of everyday pain. Perhaps unsurprising, when the subject matter of this thesis has focused on understanding the "unremarkable", the theoretical contributions that emerged are less concerned with advancing the knowledge of clinicians and paediatricians, or with reinventing our conceptualisations of social support during pain. Rather, our ambition was to examine these concepts in practice, and gain a better understanding of the lived experience of parents and children during everyday pains. This thesis has contributed strong evidence to demonstrate that social support presents a valuable protective factor during everyday pain experiences, which has extended our prior understanding of social support during painful experiences beyond clinical settings. As our research findings are embedded in the mundane experience of pain in natural environments, their theoretical offerings carry significant *practical* applications which could be of immense value to families and child-care practitioners. For example, it may be

useful for parents and childcare staff to know that most everyday pain events are minor and last only a few seconds, that children respond differently in front of different people, and that other children rarely intervene when a child experiences an everyday pain (***Study 1***). Furthermore, parents may benefit from the knowledge that their own distress influences how they respond to their child's pain, which can negatively impact their child's response, or that parents *think* they will react to their child's pain a certain way, but this may not always match how they act "in the moment" (***Study 2***). Finally, parents, childcare practitioners, and medical and academic scientists may all hold interest in the findings that social support during pain in early life is associated with behavioural differences and biochemical alterations within the brain (***Study 3***). Each of these studies has advanced our understanding of the biopsychosocial experience of everyday pain, which can stimulate future avenues of research.

For instance, the findings from Study 1 and 2 provide evidence on how the influence of parental catastrophic thoughts about their child's pain is not limited to clinical and experimental settings. In both ***Study 1*** and ***Study 2***, parental 'catastrophizing' has been presented as a proxy for how parental psychological and emotional status might influence how they respond to their child's pain (Goubert et al., 2006). The assessment of catastrophizing was supported by extensive clinical and experimental research demonstrating that parents with high tendencies to catastrophize their child's pain often negatively impact on their child's experience of pain, such as restricting their child's activities to prevent further potential pain (Caes, Vervoort et al., 2004; Caes, Vervoort, Eccleston, et al., 2012; Caes et al., 2011; Caes, Vervoort, Trost, et al., 2012; Vervoort et al., 2011; Vervoort, Goubert et al., 2010). Both Study 1 and 2 demonstrated that parental catastrophizing significantly influences how parents respond to their child during everyday pains and how parental behaviours influence their child's response to pain. However, the chosen measure for these studies (PCS-P; Goubert et al., 2006) was originally designed and validated to assess catastrophizing in parents of school-aged

children and parents of children with chronic pain. The PCS-P had not been previously used with parents of preschool children experiencing mild, acute pains at home. As we have seen with the other measures, the validity of capturing pain responses to one type of pain may not translate to capturing responses to other types of pain or pain in other contexts. As such, everyday pains – by virtue of them being fleeting, acute experiences – may not fully evoke the hallmark behaviours associated with catastrophizing (rumination, magnification, and helplessness). Thus, it is possible that the PCS-P did not capture parental catastrophizing within the home as adequately as a purposely designed measure may have done. More recently, it has been further suggested that existing measures of pain catastrophizing do not capture the construct accurately, regardless of the type of pain involved, and that catastrophizing may fit better if reclassified as pain-related "worry" (Crombez, De Paepe et al., 2020). The theoretical implications of this reclassification may ultimately affect how catastrophizing is conceptualised within paediatric literature. In the studies presented here, data on parental catastrophizing was presented within the context of the family home, an ecologically valid but rarely studied environment within pain catastrophizing literature. As such, this thesis contributes a novel viewpoint to the ongoing discussion regarding the relevance of studying (or reclassifying) parental catastrophizing and the impact this may have on the conceptualisation of catastrophizing in future studies.

## Clinical implications

Considering the potential practical benefit of the findings reported in this thesis, novel opportunities for information and knowledge exchange about everyday pains should be explored (i.e., beyond traditional academic publishing routes). For example, ***Study 2*** reported the promising use of smartphone technology to allow parents and children to engage in conversations about their child's everyday pain experiences, and suggested the wider use of

other measures (such as colouring tools) to draw younger children into informal discussions around their own pain (Mahon et al., 2015). The use of smartphone apps has already been successfully demonstrated as a means of educating parents and children about managing procedure-related anxiety or post-operative pain (Birnie, Campbell et al., 2019; Morrow, Burton et al., 2018). Similar technologies could be explored as a method of sharing pain research findings with children in an engaging and age-appropriate way; for example, through an educational app to teach children ways of managing everyday pains, which in turn may make subsequent clinical visits less daunting for children if they feel more confident about managing their pain.

For parents, a multitude of clinical studies have demonstrated that focused educational interventions can improve their knowledge on how to respond appropriately during their child's needle-pain procedures (Chambers et al., 2009; Cohen et al., 2015; Pillai Riddell et al., 2015; Taddio et al., 2009). In particular, there has been an increase in the use of Internet-led information campaigns to instruct parents in managing aspects of their child's pain, such as the 'It Doesn't Have to Hurt' video series which demonstrates child-friendly coping techniques to reduce procedural pain and anxiety (Centre for Pediatric Pain Research, 2015). It is possible that some of the coping techniques (e.g., distraction, deep breathing) could also be suitable for managing aspects of everyday pains, and with smartphone technology readily available, similar information campaigns could focus on providing parents with the tools to guide their child during everyday pains. Such campaigns represent a practical and accessible means of sharing knowledge with parents and can equip them to better manage their child's everyday pain experiences and help them to develop more adaptive coping strategies for other pains (such as clinical procedures) in turn.

**Suggestions for future research**

Naturally, though this thesis presents the findings of a small number of focused research objectives, gaps in our understanding of everyday pains will remain. ***Study 1*** was devoted to capturing specific naturally occurring pains, such as bumps and scrapes, and though we gained a clearer understanding of how parents and children rate certain everyday pains, this approach potentially left a wide range of everyday pains unexplored. Therefore, ***Study 2*** allowed parents to report on whichever pain events they found memorable, which resulted in a wider range of pains and injuries being included. This gave a better insight into how parents perceive the severity of everyday pain events, but even this approach potentially left some types of pain unreported. Given that both Studies 1 and 2 demonstrated that parents responded differently to minor pain events when the severity of incidents was perceived as high versus low, it is worth examining how parent and child categorise *different types* of everyday childhood pains, such as bee stings, toothaches and sunburns (McGrath, Speechley et al., 2000). These could highlight variations in how parents and children distinguish and respond to high versus low severity everyday pain experiences, which would contribute further to understanding of naturally adopted pain management strategies across the wide variety of everyday pain experiences. Moreover, it is essential that we understand how children respond to pains in *different settings*. Given that the bulk of our understanding of how children cope during painful experiences has been derived from clinical settings, and we have presented evidence demonstrating that everyday pains may play a role in shaping the pain management skills of children, a strong recommendation for future research is to *compare* the child's experience of pain in both settings. For example, by comparing the reports and behaviours of parents and children during both a clinical pain experience and an everyday pain experience. If these comparison studies were conducted longitudinally, they could also reveal differences in how children shape strategies to manage different pain experiences more effectively as they grow

older, which could give greater insight into the motor and cognitive changes that occur during the preschool stage of development (Noel, Chambers, et al., 2018; Schinkel et al., 2017).

Furthermore, by studying developmental shifts in child pain behaviours within the "everyday" context in which they occur, future research could unravel the potential impact of behaviours related to *parental sex* or *cultural values*. It has been demonstrated that mothers and fathers respond differently to their child in experimental pain situations (Damashek & Kuhn, 2013; Evans & Keenan, 2007; Goubert et al., 2012; Moon, Chambers et al., 2011; Noel et al., 2019; Schinkel et al., 2017), yet questions remain as to whether mothers and fathers respond differently to *everyday* pain situations. More widely, the majority of pain studies reporting on parent-child pairs obtained data from only the child's mother, and paediatric research across all settings has reported significant challenges in recruiting fathers into study samples (Macfadyen, Swallow et al., 2011; Phares, Lopez et al., 2005). In this thesis, ***Study 1*** recruited 5 fathers in 12 families (where fathers provided ratings in addition to those provided by the child's mother), while ***Study 2*** only attracted 1 father in the sample of 21. Future studies must continue attempting to recruit fathers to ensure better representation within samples. To an extent, the seeming lack of involvement of fathers may result from *cultural values*, which govern how parents interact with their children. Just one study to-date has examined the association between cultural values and caregiver responses to child pain (Kristjansdottir, McGrath et al., 2018). In both "individualistic" (Canada; Iceland) and "collectivistic" cultures (Thailand), caregiving duties predominantly fell to female family members: approximately 80% of caregivers were female and included a wide range of female relatives (mothers, stepmothers, female guardians, grandmothers). Cultural and societal norms appeared to dictate the involvement of female versus male caregivers: in the Thai sample, mothers and grandmothers represented 77% of caregivers, with fathers accounting for 18% and grandfathers representing up to 6% of the remaining sample. In contrast, just 14% of the total Canadian

sample (and 19% of the Icelandic sample) was comprised of fathers, and no Canadian or Icelandic grandfathers assumed any caregiving duties at all (Kristjansdottir, McGrath et al., 2018). In attempting to resolve knowledge gaps in our understanding of parent-child behaviours in their natural environment, we must consider those unchangeable contextual factors which exert top-down influences and may be shared from parent to child. Indeed, this highlights a considerable limitation of the evidence we have presented from the few available studies on everyday pains, in that they have all been conducted in Western cultures. We do not currently have insight into how parents and children in other cultures respond to everyday pains, and future studies should consider exploring everyday pain interactions in families from other cultural contexts.

Finally, this thesis represents a multi-disciplinary approach to the study of minor child pains, through the integration of methods from both preclinical and clinical research to answer the primary research question more adequately. Previous literature has robustly demonstrated that pain is common to all species, and there are considerable similarities in how social support can modulate pain in humans and other mammals (Hadjistavropoulos et al., 2011; Krahé et al., 2013; Mogil, 2015). Knowledge translation between these disciplines can provide a more unified approach and enrich our understanding of pain. The entire experience of pain can only be elucidated if preclinical and clinical researchers continue to collaborate and "borrow" from each other's knowledge bases. For example, future studies investigating the impact of stress during pain could implement a "back-translational" approach, wherein the clinical literature informs the preclinical development and testing of new strategies to provide evidence for interventions to modulate adversity or stress, and these findings can then be brought forward into clinical settings. In short, future studies into childhood pains – and particularly those intending to explore the effects of social context on pain processing – should consider utilising multidisciplinary teams of preclinical and clinical researchers to examine the underlying

mechanisms associated with aspects of pain and the overall experience of pain at an individual or social level.

## CONCLUSIONS

The central objective of this thesis was to explore mutual parent-child influences during "everyday" pain experiences and establish evidence for the role of parental social support in influencing pain experiences in different contexts. Findings across all studies confirmed that children exhibit different pain behaviours when in the presence of their parent compared to when alone or in the presence of strangers or peers, and that parent behaviours are a significant influence on their child's experience of pain. These findings are consistent with previous literature which confirmed the existence of bidirectional parent-child influences within clinical settings; moreover, these findings also confirm the existence of parent-child influences in natural settings such as the family home. However, gaps remain in our understanding of several other aspects of a child's experience of "everyday" pains, and further research is needed. In conclusion, this thesis represents a preliminary foray into the study of everyday pains and highlights the relevance of exploring everyday pains as distinct experiences than clinical, chronic, or experimental pains.

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# APPENDICES

## Appendix A: Parent Information Sheet (Study 1)

### Title of Study

Parent-child mutual interactions during pain experiences

You and your child are invited to take part in a research study to increase our understanding of how children and their parents react to the everyday experience of pain as they get older. We are asking 24 families with a child between the ages of 2.5 and 5 years to take part in this study. This Information Sheet will help you decide if it is in your and your child's best interest to take part in this study. If there is anything you are not clear about, we will be happy to explain it to you. Please take as much time as you need to read this information.

### What is the research about?

Pain is an integral part of children's everyday experience and children mainly depend upon their parents for help and care. We need to better understand how parents and their children react to each other during and after their child goes through one of those everyday tumbles or short painful experiences that happen while playing at home. This will help us understand better how children learn to cope and recover from pain. But we don't know how to best observe children and parents in these situations and want to try two different ways of going about it. That is where you and your child come in!

### Do I or my child have to take part?

It is your choice and your child's choice whether to take part in this research. You and your child do not have to take part in this study; participating is entirely voluntary. Children can only take part if their parent has first given permission for them to do so. If you decide to allow your child to take part in the research, you will be asked to sign a consent form. It is important to understand that both you and your child are free to withdraw from this research at any time and without giving any reason. This will not affect your or your child's rights. It will also not affect the care you receive in the participating child-care centres. You and your child's participation in the study may be ended if, in the opinion of the study staff, it is not safe or reasonable for you and/or your child to continue. Materials (including video/audio tapes) from those who withdraw from the study or who do not participate will be destroyed if you tell us to do so.

### What will be involved if my child and I take part?

First: You will be asked to complete a questionnaire, which will include some questions on how you typically react to your child when they are in pain.

Second: Each family will be observed at home for a maximum of 3 hours per session. During the observation your family will be asked to behave and do what you would normally do around the house

with some restrictions (i.e. no television watching, no outgoing phone calls or visitors, being restricted to two rooms of your choice). You will be randomly allocated to one of two observational methods:

1) For one method, a researcher will observe your family interactions for a maximum of 3 hours and the interactions will be recorded on tape. Every time your child hurts him/herself or experiences pain, we will ask you and your child a few questions about this painful experience, as soon as your child is soothed.
2) The second method is similar but does not involve a research assistant to be present during the observation. You will be shown how to set up the camera yourself and asked to set up the video camera at a time convenient for you to videotape a normal family interaction for approximately 3 hours. Similar to the first method, every time your child hurts him/herself or experiences pain, you and your child will answer a few questions about this painful experience as soon as your child is soothed.

Third: After the observations we would like you to complete some questions on how you felt about being watched, either by the researcher or the video camera. You can be completely honest on this evaluation sheet as it will not include your participant number; therefore, your answers on this evaluation sheet will be anonymous and not connected to you or your child's participant number or names.

Your total participation time for this study is 3 hours. To thank you for your participation, we will give you a €50 One-4-All voucher after the session and your child will receive a junior scientist certificate.

## Are there any potential risks to me or my child taking part?

Although no harms are anticipated from your participation in this study, we do realize that sometimes issues may arise. In the unlikely event that completing the questionnaires or observations at home make you or your child feel uncomfortable, you are free to withdraw at any time from the research or you can also choose not to answer those specific questions. Should you or your child experience distress, and wish to discuss this with Dr Caes, you can indicate this to Grace, the research assistant.

## What are the benefits to me and my child taking part?

In being part of this research, you and your child will be helping to increase our knowledge about how children and parents deal with everyday painful experiences. In the past, children and parents have enjoyed participating in studies like this one and have reported that they liked the idea of helping others through research. We plan to publish our group results in academic journals and present it at conferences so that others can learn from this and so that in the future we can improve pain management for children.

## What will happen with the information collected?

The information we collect will be used to inform the research questions, which may be presented at an academic conference or published in a journal. However, anything that is learned about you and your child will be kept private. We will never use your or your child's name in any publications of the completed study. Only group results will be given in presentations/talks or reports.

## How will the information be kept confidential?

All children and families participating in this study will be given a participant number (e.g. 001). This number will be used to identify all information we get so your name will not be on any of the data forms. The participation evaluation form you complete at the end of the study will not include your participant number; therefore, your answers on these questionnaires will be anonymous and not connected to you or your child's participant number or names. Only the consent form will have your name and signature and this form will be kept separate from all the other materials.

All study records will be stored in a locked/secure area. Electronic data records (including video/audio tapes) will be kept on the NUI Galway secure servers where only authorized members of the research team will have access to them. Members of the research team may use group datasets without identifying outside of the university on password-protected computers.

## Who are the study researchers?

Grace is a PhD researcher on this project in the Centre for Pain Research at NUI Galway, supervised by Dr Line Caes (University of Stirling, Scotland). Grace has been trained for the study and subject to security vetting by An Garda Siochána, for the protection of your child.

## Where can I get further information?

If you have any queries relating to the research, you can contact Dr Line Caes at 091-493457 or line.caes@nuigalway.ie. If you have any concerns about the research and wish to speak to someone in confidence, you can contact the Head of School, Dr Annmarie Groarke at 091-493101.

A report with the research findings will be available from the researcher following the research's completion. You may choose to be included on a mailing list to receive a copy of this report.

*Thank you for taking the time to read this information sheet.*

**Appendix B: Recruitment flyer (Study 1)**

## Appendix C: Parent Consent Form


Section A (to be completed by the researcher)

_____

Participant ID

_____ _____ _____

Name of Researcher Date Signature

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Section B (to be completed by parents)

Title of Study: Parent-child mutual interactions during pain experiences

Please initial the boxes below to indicate whether you agree to allow your child to take part in the research and sign the form at the end.

1. I confirm that I have read the information sheet for the above research. ☐

2. I am satisfied that I understand the information provided and have had enough time to consider the information. ☐

3. I understand that my own and my child's participation is voluntary and that we are free to withdraw from the study at any time without our rights being affected. ☐

4. I agree to take part in this research. ☐

5. I agree to allow my child to take part in this research. ☐

6. I agree for myself and my child(ren) to be videotaped during the procedure so that the researchers can examine children's distress and how parents and their child interact during a painful event. I understand this footage will be confidential and anonymous. ☐

| _____ | _____ | _____ |
|---|---|---|
| Name of Parent/Guardian | Signature | Date |
| _____ | _____ | |
| Name of Child | Parent email address | |

Please include your email address if you wish to receive information in future on the findings of this study.

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Section C (to be completed by parents)

Videotape/Audiotape Release Form

Title of Study: Parent-child mutual interactions during pain experiences

Occasionally, we may want to use study video/audio tapes for research and educational purposes (i.e., using clips of videos in presentations to researchers and health professionals; or to provide training data when training students in video-coding practices). If you would like to allow the videotape/audiotape from this research to be used for these purposes, please sign below. If you later decide that you do not want us to use the video/audio tapes for educational purposes, you may call us at 091-493457 at any time to withdraw the tapes.

By checking the "Yes" box, I agree to allow videotape/audiotape from this research to be used for educational purposes. I understand that I can refuse the use of the video/audio tape for educational purposes at any time.

YES ☐ NO ☐

_____

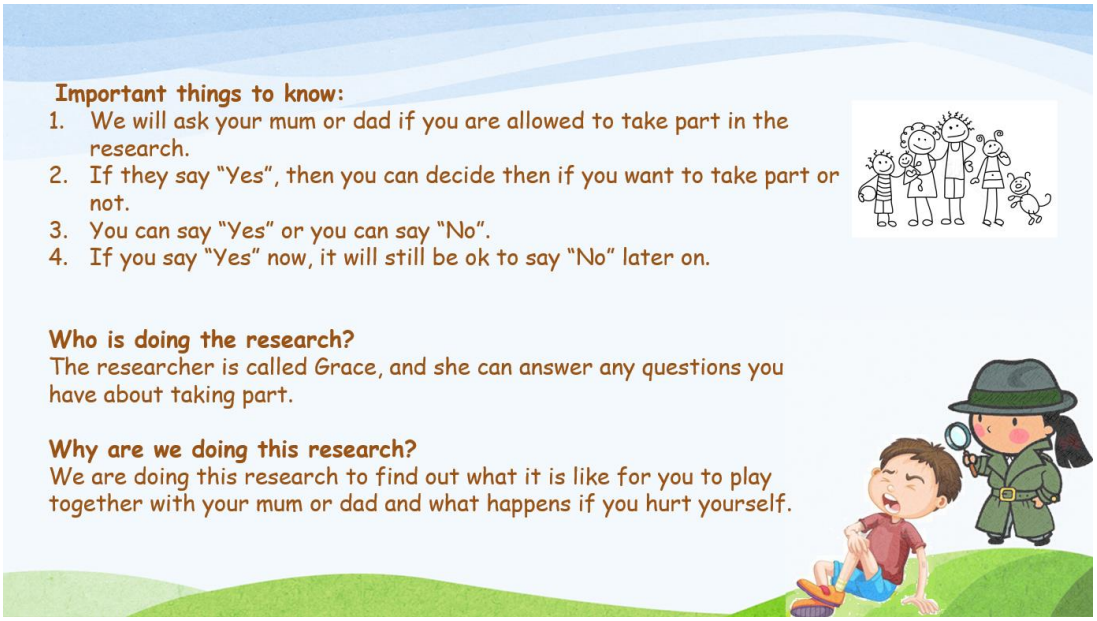
Name of Child (Print)

| _____ | _____ |
|---|---|
| Name of Parent (Print) | Parent signature |

_____

Date

**Appendix D: Assent forms for participating children and their siblings (note: these were full-page A4 booklets)**

## If you decide to take part- what will happen?

**1. watching**:
We will ask you to play with your mum or dad during one entire morning or afternoon. We will watch you while you are playing.

**2. questions:**
If you hurt yourself while playing, we will ask you some questions to find out how much it hurts.

**What could happen if I take part in this research?**
You might not like some of the questions we ask. You don't have to answer any questions you don't want to. You might also not like that we are watching you and your mum or dad while you play. If you don't want us to watch you, that is fine, we will NOT be mad.

**Could this research help me?**
Doing this research will help us learn about how to make other children feel good when they are hurt themselves while playing.

**If you would like to take part you can colour the box:**

☐

Name of child: _____

Researcher's Signature: _____

Date: _____

Assent form for siblings

# What is research?

Research means collecting information to find out something. People ask questions and find out answers.

This sheet tells you about our research and your choice to be part of it. You can ask us any questions you want about it, at any time.

**Important things to know:**

1. We will ask your mum or dad if you are allowed to take part in the research, with your brother or sister.
2. If they say "Yes", then you can decide then if you want to take part or not.
3. You can say "Yes" or you can say "No".
4. If you say "Yes" now, it will still be ok to say "No" later on.

**Who is doing the research?**
The researcher is called Grace, and she can answer any questions you have about taking part.

**Why are we doing this research?**
We are doing this research to find out what it is like for your brother or sister to play together with your mum or dad, and what happens if they hurt themselves.

## If you decide to take part- what will happen?

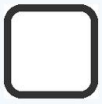
**1. watching**:
- We will ask you to play with your brother or sister and your mum or dad during one entire morning or afternoon.
- We will watch while you are playing with them.

**2. questions:**
If your brother or sister hurts themselves while playing, we will ask them some questions to find out how much it hurts.

**What could happen if I take part in this research?**
You might not like some of the questions we ask. You don't have to answer any questions you don't want to. You might also not like that we are watching you and your mum or dad while you play. If you don't want us to watch you, that is fine, we will NOT be mad.

**Could this research help me?**
Doing this research will help us learn about how to make other children feel good when they are hurt themselves while playing.

**If you would like to take part you can colour the box:**



Name of child: _____

Researcher's Signature: _____

Date: _____

## Appendix E: Demographic information Sheet


Please fill in the information below

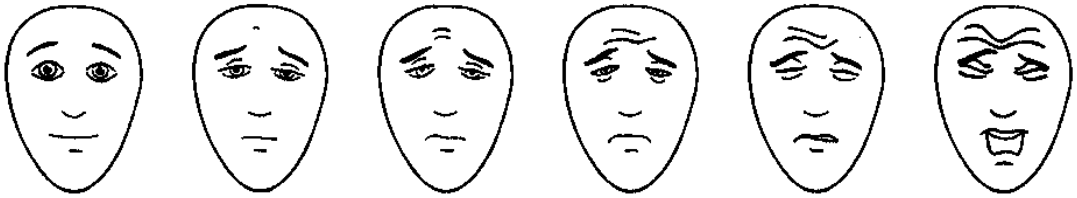
1. Your Relationship to the Child (tick one):
   ☐ Mother ☐ Father ☐ Stepmother ☐ Stepfather
   ☐ Other _____
2. Your Current Age: _____ years
3. Child's date of birth: _____
4. Gender of child: ☐ Male ☐ Female
5. Current marital status:
   ☐ Married ☐ Divorced ☐ Remarried
   ☐ Widowed ☐ Never Married ☐ Other: _____
6. What is the highest level in school that you have completed? _____
7. Have you completed any post-secondary education? ☐ Yes ☐ No
8. How many children live in your household who are...
   less than 5 years old? _____
   5 through 12 years old? _____
   13 through 17 years old? _____
9. Has your child been diagnosed with any chronic condition?
   ☐ Yes ☐ No
   If yes, please indicate which condition: _____

## Appendix F: FPS-R (Faces Pain Scale - Revised) (Hicks, von Baeyer, et al., 2001)

### *F.1: Version for children (presented on a laminated card)*

FPS-R

These faces show how much something can hurt. This face *(point to the left-most face)* shows no pain/hurt. The faces show more and more pain/hurt *(point to each from left to right)* up to this one *(point to right-most face)* – it shows very much pain/hurt. Point to the face that shows how much pain or hurt you had.

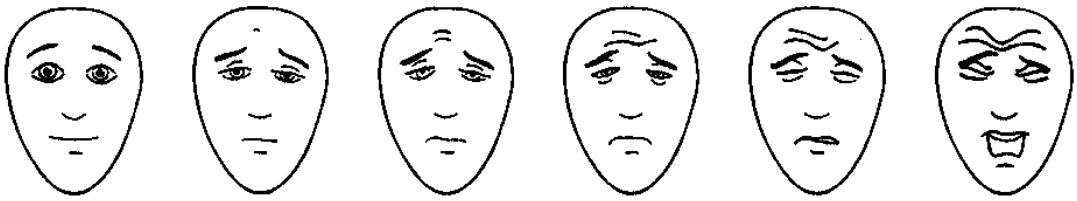


### *F.2: Version for parents*

Parent questions

FPS-R

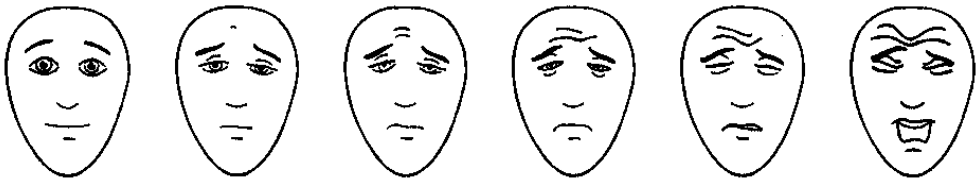
These faces show how much something can hurt. The face on the left shows no pain/hurt. The faces show more and more pain/hurt up to the face on the right – it shows a lot of pain/hurt. Circle the face that shows how much pain or hurt you think that your child felt.



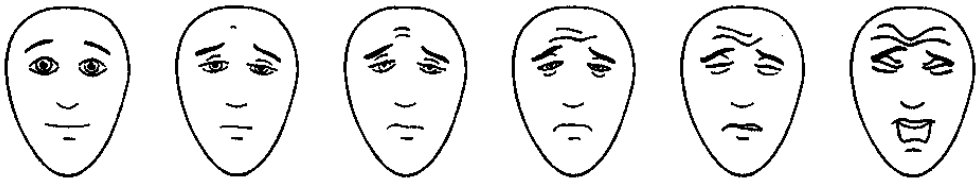
## Appendix G: FPS-R report sheet (for parents to record the child pain responses)

Ask your child whether they are in pain (Yes/No). If they say 'Yes', tick the box and then ask them to 'Point to the face that shows how much pain or hurt you had just now'. Circle the same face that the child points to on the graph below. (If they say 'No', you don't need to ask them to point to a face).

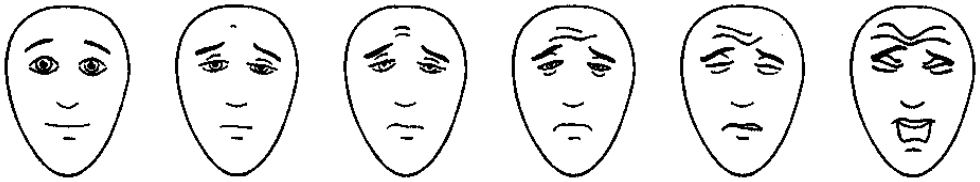
Pain episode 1: Child's answer to question "Are you sore/in pain?" YES ☐ NO ☐



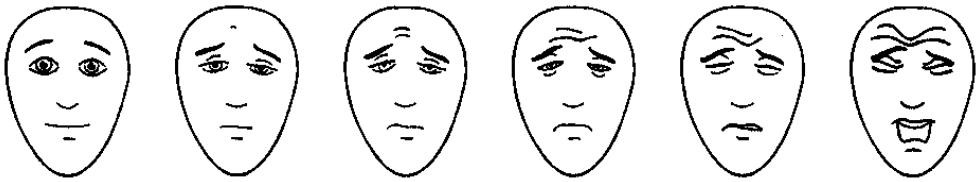
Pain episode 2: Child's answer to question "Are you sore/in pain?" YES ☐ NO ☐



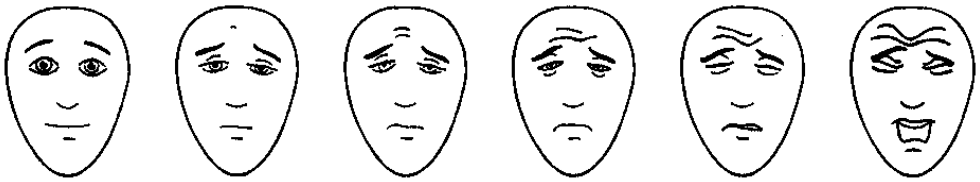
Pain episode 3: Child's answer to question "Are you sore/in pain?" YES ☐ NO ☐



Pain episode 4: Child's answer to question "Are you sore/in pain?" YES ☐ NO ☐



Pain episode 5: Child's answer to question "Are you sore/in pain?" YES ☐ NO ☐



**Appendix H: PDSQ (Parent Distress and Sympathy Questionnaire) (Caes et al. 2011)**

At this moment, to what extent are you experiencing the following emotions:

1) Worried

| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|
| not at all | | | | | | | | | | extremely |

2) Understanding

| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|
| not at all | | | | | | | | | | extremely |

3) Upset

| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|
| not at all | | | | | | | | | | extremely |

4) Compassionate

| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|
| not at all | | | | | | | | | | extremely |

5) Anxious

| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|
| not at all | | | | | | | | | | extremely |

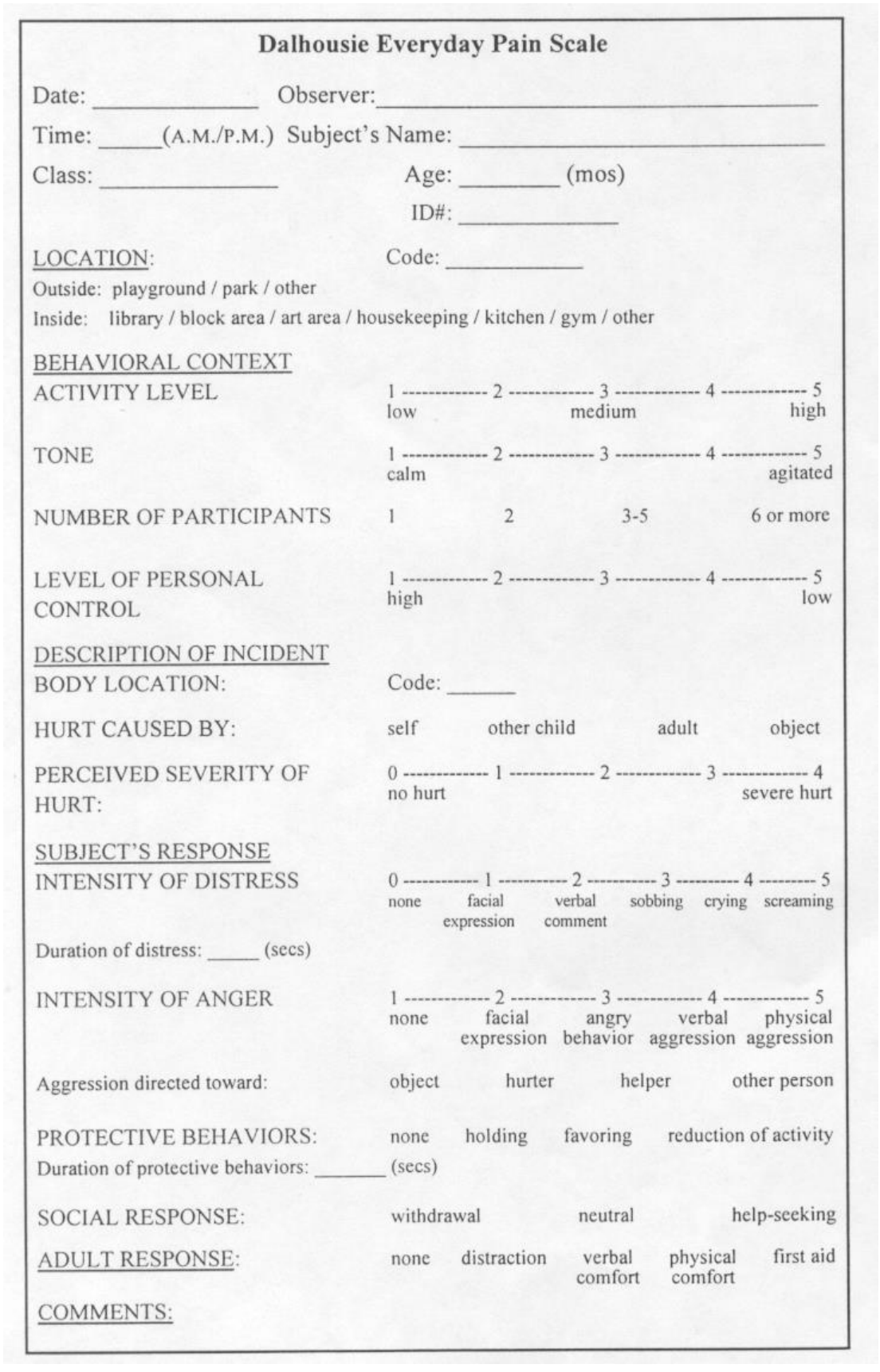
6) Sympathizing

| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|
| not at all | | | | | | | | | | extremely |

7) Sad

| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|
| not at all | | | | | | | | | | extremely |

**Appendix I: Dalhousie Everyday Pain Scale (Fearon et al., 1996)**



**Dalhousie Everyday Pain Scale**

Date: _____ Observer: _____

Time: _____(A.M./P.M.) Subject's Name: _____

Class: _____ Age: _____ (mos)

ID#: _____

LOCATION: Code: _____

Outside: playground / park / other

Inside: library / block area / art area / housekeeping / kitchen / gym / other

BEHAVIORAL CONTEXT

ACTIVITY LEVEL 1 ---------- 2 ---------- 3 ---------- 4 ---------- 5
low medium high

TONE 1 ---------- 2 ---------- 3 ---------- 4 ---------- 5
calm agitated

NUMBER OF PARTICIPANTS 1 2 3-5 6 or more

LEVEL OF PERSONAL CONTROL 1 ---------- 2 ---------- 3 ---------- 4 ---------- 5
high low

DESCRIPTION OF INCIDENT

BODY LOCATION: Code: _____

HURT CAUSED BY: self other child adult object

PERCEIVED SEVERITY OF HURT: 0 ---------- 1 ---------- 2 ---------- 3 ---------- 4
no hurt severe hurt

SUBJECT'S RESPONSE

INTENSITY OF DISTRESS 0 ---------- 1 ---------- 2 ---------- 3 ---------- 4 ---------- 5
none facial expression verbal comment sobbing crying screaming

Duration of distress: _____ (secs)

INTENSITY OF ANGER 1 ---------- 2 ---------- 3 ---------- 4 ---------- 5
none facial expression angry behavior verbal aggression physical aggression

Aggression directed toward: object hurter helper other person

PROTECTIVE BEHAVIORS: none holding favoring reduction of activity

Duration of protective behaviors: _____ (secs)

SOCIAL RESPONSE: withdrawal neutral help-seeking

ADULT RESPONSE: none distraction verbal comfort physical comfort first aid

COMMENTS:

## Appendix J: Research participation evaluation form

1) Overall, how would you rate your participation experience? (Circle response)

| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|
| very negative | | | | | neutral | | | | | very positive |

2) What was the most positive (or best) aspect of your participation?

_____

_____

_____

3) What was the most difficult (or worst) part of your participation?

_____

_____

_____

4) Think about how your child usually acts when he/she is in pain. Was your child acting the same as usual today or differently than usual when the observation took place? (Circle one).

| 0 | 1 | 2 | 3 | 4 |
|---|---|---|---|---|
| Not at all different | A little different | Somewhat different | Quite different | A whole lot different |

5) To what extent did the observation and videotaping of your interactions with your child feel intrusive? (Circle one).

| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|
| not at all | | | | | neutral | | | | | a lot |

6) To what extent were things different because you knew you were being videotaped? (Circle one)

| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|
| not at all | | | | | neutral | | | | | a lot |

7) To what extent did you feel comfortable with the duration of the recording (i.e. maximum 3 hours)?

| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|
| not at all comfortable | | | | | | | | | | extremely comfortable |

Please provide any reasons as to why you felt comfortable or not comfortable with the duration of the observation:

_____

_____

_____

8) Did you feel that the study was explained well enough to you?

☐ Yes ☐ No

9) Did the researcher use language that you could easily understand?

☐ Yes ☐ No

10) Did you feel that the study was explained well enough to your child?

☐ Yes ☐ No

11) Did the researcher use language that your child could easily understand?

☐ Yes ☐ No

12) Were you given the opportunity to ask the researcher questions?

☐ Yes ☐ No

13) Is there anything that would have made it easier for you and your child to participate?

_____

_____

_____

14) We value your opinion, so please feel free to make any comments or suggestions on any aspect of your research participation experience:

_____

_____

_____

## Appendix K: Parent Information Sheet (Study 2)

Information Sheet for Parents

NUI Galway
OÉ Gaillimh

Title of Study

Parent-child mutual interactions during pain experiences

You and your child are invited to take part in a research study to increase our understanding of how children and their parents react to the everyday experience of pain. We are asking families with a child between the ages of 2.5 and 5 years to take part in this study. This Information Sheet will help you decide if it is in your and your child's best interest to take part in this study. If there is anything you are not clear about, we can explain it to you. Please take as much time as you need to read this information.

### What is the research about?

Pain is an integral part of children's everyday experience and children mainly depend upon their parents for help and care. We need to understand how parents and their children react to each other during and after their child goes through one of those everyday tumbles or short painful experiences that happen while playing. Specifically, we want to understand how parents and children respond to pain, by asking parents to keep a pain diary for two weeks, of one pain event that their child experiences each day. This will help us understand better how children learn to cope and recover from pain. That is where you and your child come in!

### Do I or my child have to take part?

It is your choice and your child's choice whether to take part in this research. You and your child do not have to take part in this study; participating is entirely voluntary. Children can only take part if their parent has first given permission for them to do so. If you decide to allow your child to take part in the research, you will be asked to complete a consent form (as part of the participant details form at the start). It is important to understand that both you and your child are free to withdraw from this research at any time and without giving any reason. This will not affect your or your child's rights. You and your child's participation in the study may be ended if, in the opinion of the study staff, it is not safe or reasonable for you and/or your child to continue. Materials from those who withdraw from the study or who do not participate will be destroyed if you tell us to do so.

### What will be involved if my child and I take part?

1. Parents will be asked to complete a short pain diary each day for two consecutive weeks, to report on a pain event that their child experienced that day (14 pain entries in total). This will be completed online, and should not take longer than 5 minutes each day.

2. If families so choose, they can also complete a short assessment immediately after any pain event that occurs. This involves the child answering 2 questions about their pain, and the parent answering 3 questions about their child's pain (up to a maximum of 5 assessments during the two week period). This will be completed online via the parent's smartphone, and should take 2-3 minutes to complete each time.

Your total participation time for this study is 1.5 hours for the diary across the two week reporting period (plus 15 minutes for the assessments if also completing those).

To thank you for your participation, your child will receive a Junior Scientist certificate, and you will have the option to enter a draw for a €50 One4All voucher, with separate entries for completing the diary and the assessments (UK participants who win a prize will be offered their prize in Pound Sterling instead of Euro).

## Are there any potential risks to me or my child taking part?

Although no harms are anticipated during your participation in this study, we realize that sometimes issues may arise. In the unlikely event that completing the questionnaires or observations at home make you or your child feel uncomfortable, you are free to withdraw at any time from the research or you can choose not to answer those specific questions. Should you or your child experience distress, you may wish to discuss this with Grace (the researcher) or with her supervisor, Line Caes (contact details below).

## What are the benefits to me and my child taking part?

In being part of this research, you and your child will be helping to increase our knowledge about how children and parents deal with everyday painful experiences. In the past, children and parents have enjoyed participating in studies like this one and have reported that they liked the idea of helping others through research. We plan to publish our group results in academic journals and present it at conferences so that others can learn from this and so that in the future we can improve pain management for children.

## What will happen with the information collected?

The information we collect will be used to inform the research questions, which may be presented at an academic conference or published in a journal. However, anything that is learned about you and your child will be kept private. We will never use your or your child's name in any publications of the completed study. Only group results will be given in presentations/talks or reports.

## How will the information be kept confidential?

All children and families participating in this study will be given a participant number (e.g. 001). This number will be used to identify all information we get so your name will not be on any of the data forms. The participation evaluation form you complete at the end of the study will not include your participant number; therefore, your answers on these questionnaires will be anonymous and not connected to you or your child's participant number or names. Only the consent form will have your name and signature and this form will be kept separate from all the other materials.

In line with the University's video recording policy, electronic data (including video recordings) will be uploaded onto a secure computer within the University, which will only be accessible to the research team for research purposes. Video recordings will be destroyed after 10 years, in accordance with University guidelines on data retention and GDPR recommendations. Members of the research team may use group datasets without identifying outside of the university on password-protected computers.

## Who are the study researchers?

Grace O'Sullivan is a PhD researcher on this project in the Centre for Pain Research at NUI Galway, supervised by Prof Brian McGuire (NUI Galway) and Dr Line Caes (University of Stirling, Scotland). Several final year Psychology undergraduate students from the University of Stirling will also be assisting with data collection, under the supervision of Dr Line Caes. Grace has been trained for the study and subject to security vetting by *An Garda Siochána* (national police force in Ireland), for the protection of your child. Dr Caes and all the Psychology undergraduate students are approved by the Scottish PVG scheme.

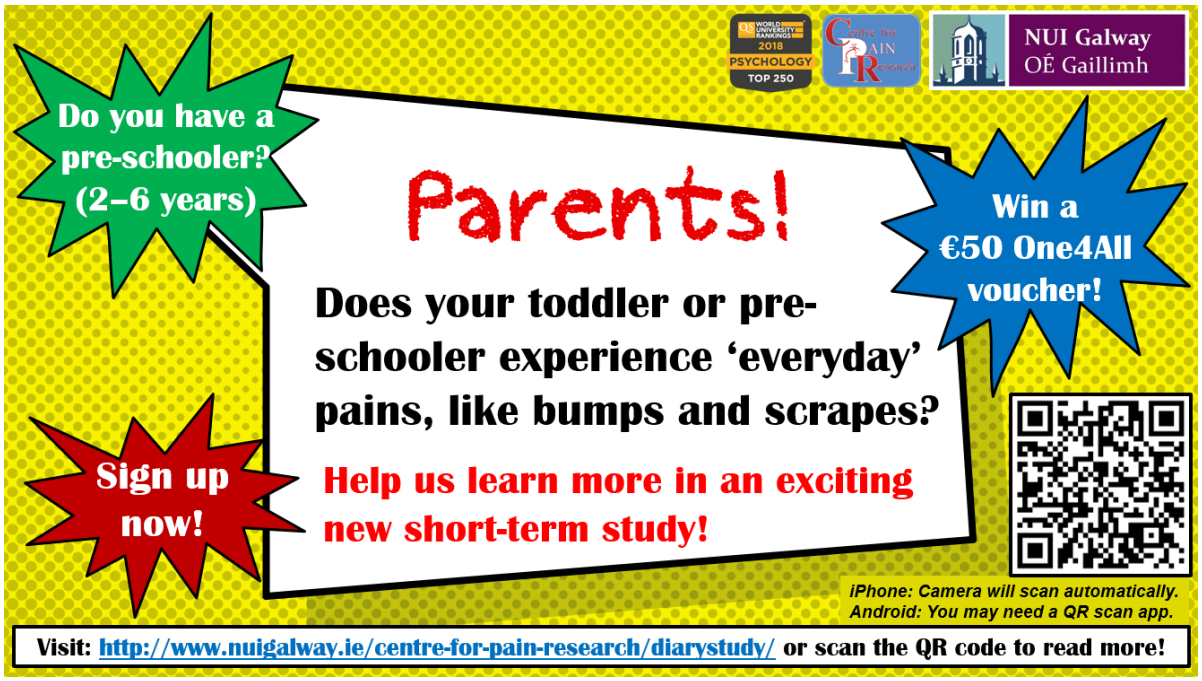
## Where can I get further information?

A report with the research findings will be available from the researcher following the research's completion. You may choose to be included on a mailing list to receive a copy of this report.

If you have any queries relating to the research, you can contact Grace O'Sullivan at g.osullivan6@nuigalway.ie; Dr Line Caes at line.caes@stir.ac.uk / +44 (0)1786 467639; or Prof Brian McGuire at brian.mcguire@nuigalway.ie. If you have any concerns about the research and wish to speak to someone in confidence, you can contact the Head of Psychology at NUI Galway, Dr John Bogue, at john.bogue@nuigalway.ie.

*Thank you for taking the time to read this information sheet.*

**Appendix L: Recruitment flyer (Study 2)**



## Appendix M: Demographics information sheet

*The following questions will relate to you and your family. There are 13 questions in this survey.*

Please fill in the information below

1. Your Relationship to the Child (tick one):

   ☐ Mother ☐ Father ☐ Stepmother ☐ Stepfather

   ☐ Other _____

2. Your Current Age: _____ years

3. Child's date of birth: _____

4. Gender of child: ☐ Male ☐ Female

5. Current marital status:

   ☐ Married ☐ Divorced ☐ Remarried

   ☐ Widowed ☐ Never Married ☐ Other: _____

6. Country of residence: _____

7. What is the highest level of education you have completed? _____

8. How many children live in your household who are:
   - Less than 5 years old? _____
   - 5 through 12 years old? _____
   - 13 through 17 years old? _____

9. Has your child been diagnosed with any chronic condition?

   ☐ Yes ☐ No

   If yes, please indicate which condition: _____

10. Please enter your email address (this will be used to match your answers together, and to enter you into the prize draw if you wish; it won't be used for any other purpose):

    _____

## Appendix N: IRPEDNA (Huguet et al., 2008)

We would like to know what you do when your child is in pain. Below you will find a list of things that you might do. Circle one number to show how often you do each of the things below when your child is in pain.

0= **Never** It means that you never do this

1= **Hardly ever** It means that you hardly ever do this

2= **Sometimes** It means that you sometimes do this

3= **Often** It means that you normally do this

4= **Always** It means that you always do this

| WHEN YOUR CHILD IS IN PAIN... | Never | Hardly ever | Some times | Often | Always |
|---|---|---|---|---|---|
| I think that it cannot really be so bad. | 0 | 1 | 2 | 3 | 4 |
| I tell him/her that he/she can cope with the problem using expressions such as “you are strong”, “you can cope with this and more”. | 0 | 1 | 2 | 3 | 4 |
| I stay home from work to provide him/her with as much care and attention as possible. | 0 | 1 | 2 | 3 | 4 |
| I try to explain the reasons for his/her complaint so that he/she does not worry so much. | 0 | 1 | 2 | 3 | 4 |
| I wonder how he/she can complain so much. | 0 | 1 | 2 | 3 | 4 |
| I advise him/her to relax and breathe deeply. | 0 | 1 | 2 | 3 | 4 |
| I do not believe him/her. | 0 | 1 | 2 | 3 | 4 |
| I do not listen him/her. | 0 | 1 | 2 | 3 | 4 |
| I try to distract him/her by suggesting attractive activities (e.g. plans for the weekend). | 0 | 1 | 2 | 3 | 4 |
| I try to make his/her surroundings as comfortable as possible (for example, minimum noise and little light). | 0 | 1 | 2 | 3 | 4 |

| WHEN YOUR CHILD IS IN PAIN... | Never | Hardly ever | Some times | Often | Always |
|---|---|---|---|---|---|
| I monitor the evolution of the problem by regularly asking him/her how he/she feels. | 0 | 1 | 2 | 3 | 4 |
| I make him/her go to bed earlier. | 0 | 1 | 2 | 3 | 4 |
| I think it does not matter because I believe the suffering will make him/her stronger. | 0 | 1 | 2 | 3 | 4 |
| I try to entertain him/her so that he/she doesn't think about the problem | 0 | 1 | 2 | 3 | 4 |
| I try to make up for his/her suffering by paying him/her more attention. | 0 | 1 | 2 | 3 | 4 |
| I advise him/her to concentrate on other things (e.g. listen to music, watch the TV) so that he/she does not think about the pain. | 0 | 1 | 2 | 3 | 4 |
| I suggest that he/she stays at home, with a relative, or with someone else (for example, a child minder) while the problem lasts. | 0 | 1 | 2 | 3 | 4 |
| We arrange for others to take over his/her duties and responsibilities at home while he/she does not feel well. | 0 | 1 | 2 | 3 | 4 |
| I show him/her that I am very concerned. | 0 | 1 | 2 | 3 | 4 |
| I tell him/her that it is really not so bad. | 0 | 1 | 2 | 3 | 4 |
| I help him/her to do certain things. | 0 | 1 | 2 | 3 | 4 |
| I spend as much time with him/her as possible. | 0 | 1 | 2 | 3 | 4 |
| A little bit angry, I tell him/her not to complain so much. | 0 | 1 | 2 | 3 | 4 |
| I use humor to take his/her mind off the discomfort. | 0 | 1 | 2 | 3 | 4 |
| I tell him/her that adults don't complain. | 0 | 1 | 2 | 3 | 4 |
| I tell him/her not to worry because it will soon go away. | 0 | 1 | 2 | 3 | 4 |

| | | | | | |
|---|---|---|---|---|---|
| I stop what I am doing to do something that he/she likes (e.g. play). | 0 | 1 | 2 | 3 | 4 |
| I tell him/her that she/he think everything will be all right. | 0 | 1 | 2 | 3 | 4 |
| I tell him/her that he/she may be exaggerating | 0 | 1 | 2 | 3 | 4 |
| I try to get him/her to be optimistic about the pain (e.g. pain will go away soon). | 0 | 1 | 2 | 3 | 4 |
| I tell him/her not to be afraid. | 0 | 1 | 2 | 3 | 4 |
| I make light of the problem because I think he/she is exaggerating a little | 0 | 1 | 2 | 3 | 4 |
| I try to encourage him/her. | 0 | 1 | 2 | 3 | 4 |
| I do not do my leisure activities so that I can be with him/her. | 0 | 1 | 2 | 3 | 4 |
| I arrive home as early as possible. | 0 | 1 | 2 | 3 | 4 |

THANK YOU SO MUCH FOR YOUR ATTENTION

**Appendix O: PCS-P (Pain Catastrophizing Scale – Parent version) (Goubert et al., 2006)**

## PCS-P

## Thoughts and feelings when you child is in pain

We are interested in the thoughts and feelings you have when your child is in pain. Below are 13 sentences of different thoughts and feelings. Please put a circle around the word or phrase under each sentence that best reflects how strongly you have each thought when your child is in pain.

---

1. When my child is in pain, I worry all the time about whether the pain will end.

NOT AT ALL MILDLY MODERATELY SEVERELY EXTREMELY

2. When my child is in pain, I feel I can't go on like this much longer.

NOT AT ALL MILDLY MODERATELY SEVERELY EXTREMELY

3. When my child is in pain, it's terrible and I think it's never going to get better.

NOT AT ALL MILDLY MODERATELY SEVERELY EXTREMELY

4. When my child is in pain, it's awful and I feel that it overwhelms me

NOT AT ALL MILDLY MODERATELY SEVERELY EXTREMELY

5. When my child is in pain, I can't stand it anymore

NOT AT ALL MILDLY MODERATELY SEVERELY EXTREMELY

6. When my child is in pain, I become afraid that the pain will get worse

NOT AT ALL MILDLY MODERATELY SEVERELY EXTREMELY

7. When my child is in pain, I keep thinking of other painful events

NOT AT ALL MILDLY MODERATELY SEVERELY EXTREMELY

8. When my child is in pain, I want the pain to go away

NOT AT ALL MILDLY MODERATELY SEVERELY EXTREMELY

9. When my child is in pain, I can't keep it out of my mind

NOT AT ALL MILDLY MODERATELY SEVERELY EXTREMELY

10. When my child is in pain, I keep thinking about how much he/she is suffering

NOT AT ALL MILDLY MODERATELY SEVERELY EXTREMELY

11. When my child is in pain, I keep thinking about how much I want the pain to stop

NOT AT ALL MILDLY MODERATELY SEVERELY EXTREMELY

12. When my child is in pain, there is nothing I can do to stop the pain.

NOT AT ALL MILDLY MODERATELY SEVERELY EXTREMELY

13. When my child is in pain, I wonder whether something serious may happen

NOT AT ALL MILDLY MODERATELY SEVERELY EXTREMELY

**Appendix P: Daily diary - layout (completed on-screen on smartphones)**

## Daily pain diary

Every evening for the next two weeks, we would like you to complete these diary questions about <u>one</u> specific pain event that your child experienced that day (i.e., 14 pain events in total). This should take about 3-5 minutes per evening.

If there were no pain events on a given day, or if you missed a day, just fill it in the following day as normal.

*There are 12 questions in this survey.*

---

1) Did your child experience a pain event today: YES / NO

2) If yes, how many pain events took place? _____

## Please, think of the pain event that stood out the most to you today:

3) Can you describe the pain event?

*For example,*

*"Thomas has two pain events today. Scraped his knee while playing outside. Also bumped his head on the coffee table, and he was crying a bit"*

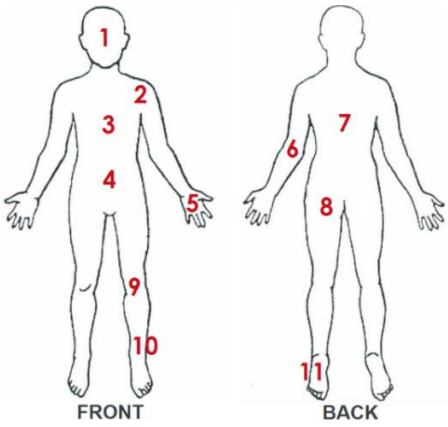
*"I heard Alice crying from the next room. I didn't see what happened, but she had a cut on her elbow, so I cuddled her until she calmed down, and then we got a plaster"*

_____

_____

_____

4) For that pain event, please indicate where your child's hurt/pain was located:
*(You can circle the location on the picture, or write in the area/zone if that is more convenient)*

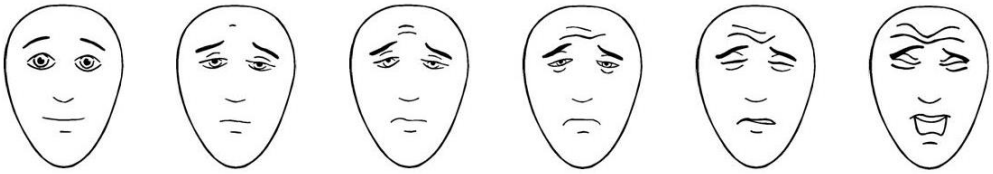



Write in: _____

5) For that pain event, how severe would you rate your child's hurt? (circle one):

| 0 | 1 | 2 | 3 | 4 |
|---|---|---|---|---|
| NO HURT | | | | SEVERE HURT |

6) Choose the face that shows how much your child hurt just after that pain event (circle one):



7) For that pain event, what level of distress did your child show when they got hurt? (circle one):

| 0 | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| NONE | FACIAL EXPRESSION | VERBAL COMMENT | SOBBING | CRYING | SCREAMING |

8) At the time of the pain event, were you nearby? (circle one):

a. *Yes, your child was in view (i.e., you were watching when he/she got hurt and saw the event)*

b. *No, your child was not in view but you were listening in*

   i. If so, were you listening in constantly or intermittently? (circle one):
   *CONSTANTLY / INTERMITTENTLY*

c. *No, you did not see or hear the event but another adult was present and saw the event*

d. *No, you did not see or hear the event but you had been checking on your child before that*

9) For that pain event, please indicate which answer most closely matches the response you had towards your child (circle one answer for <u>each</u> statement):

*a) When my child was in pain, I kept thinking about the pain he/she was experiencing*

NOT AT ALL MILDLY MODERATELY SEVERELY EXTREMELY

*b) When my child was in pain, I thought something serious might happen to him/her because of it*

NOT AT ALL MILDLY MODERATELY SEVERELY EXTREMELY

*c) When my child was in pain, I couldn't stand it any longer*

NOT AT ALL MILDLY MODERATELY SEVERELY EXTREMELY

*d) I stopped what I was doing to do something that my child likes (e.g. play)*

NOT AT ALL MILDLY MODERATELY SEVERELY EXTREMELY

*e) I tried to make up for my child's suffering by paying him/her more attention*

NOT AT ALL MILDLY MODERATELY SEVERELY EXTREMELY

*f) I monitored their pain afterwards by regularly asking my child how he/she felt*

NOT AT ALL MILDLY MODERATELY SEVERELY EXTREMELY

*g) I made light of the problem because I thought my child was exaggerating a little*

NOT AT ALL MILDLY MODERATELY SEVERELY EXTREMELY

*h) I tried to entertain my child so that he/she did not think about the problem*

NOT AT ALL MILDLY MODERATELY SEVERELY EXTREMELY

*i) I advised my child to relax and breathe deeply*

NOT AT ALL MILDLY MODERATELY SEVERELY EXTREMELY

*j) I told my child that I think everything will be all right*

NOT AT ALL MILDLY MODERATELY SEVERELY EXTREMELY

---

k) *I felt worried*

0 1 2 3 4 5 6 7 8 9 10

NOT AT ALL EXTREMELY

*l) I felt upset*

0 1 2 3 4 5 6 7 8 9 10

NOT AT ALL EXTREMELY

*m) I felt anxious*

0 1 2 3 4 5 6 7 8 9 10

NOT AT ALL EXTREMELY

*n) I felt sad*

0 1 2 3 4 5 6 7 8 9 10

NOT AT ALL EXTREMELY

10) Is there anything else that you want to share about today's pain incidents?

_____

_____

_____

**Appendix Q: EMA - layout (completed on-screen on smartphones)**

# My child just got hurt. What now?

This short survey looks at how you and your child rate everyday pain events as they happen.

For this, we would like families to complete this short survey as soon as possible following a pain event that their child has just experienced

If possible, we'd like you to complete this survey up to five times (but if you can only complete it 1-2 times, that's still great and will help a lot!)

WHAT TO DO:

If your child has just had one of those "everyday" pain events that often occur (like bumps, scrapes, cuts, etc.), first soothe your child and make sure they're okay.

When they're ready, your child should answer the first two questions on the next page, and then you should answer the remaining three questions.

*[This will take approximately 2-3 minutes to complete]*

*At the end of this study, there will be a prize draw for one of ten €50 One4All vouchers. This draw is open to all families who completed at least 4 out of 5 pain assessments.*

---

## 1. Ask your child: "Are you sore/in pain right now?" (Circle one)

*If your child answers* YES*, ask them the next question with the face picture.*

*If your child answers* NO*, you don't have to ask them the next question (If they want to answer it anyway, that's fine)*

| Yes | No |
|---|---|

## *2. CHILD estimate of pain:*

These faces show how much something can hurt. This face *(point to the left-most face)* shows no pain/hurt. The faces show more and more pain/hurt up to this one *(point to right-most face)* – it shows a lot of pain/hurt.

*Ask your child to indicate which face matches the pain they felt just now.*

Face 1 (no pain or hurt)

Face 2 (some pain or hurt)

Face 3 (a lot of pain or hurt)

---

## 3. PARENT estimate of pain:

*Please give an estimate for how bad YOU felt your child's pain was just now.*

Face 1 (no pain or hurt)

Face 2 (some pain or hurt)

Face 3 (a lot of pain or hurt)

## 4. *Parent ratings*: At this moment, to what extent are you experiencing the following emotions?

(mark one circle for each emotion, where 0= Not at all, and 5= Extremely/a lot):

| | 0 (Not at all) | 1 | 2 | 3 | 4 | 5 (Extremely) |
|---|---|---|---|---|---|---|
| Worried | ○ | ○ | ○ | ○ | ○ | ○ |
| Understanding | ○ | ○ | ○ | ○ | ○ | ○ |
| Upset | ○ | ○ | ○ | ○ | ○ | ○ |
| Compassionate | ○ | ○ | ○ | ○ | ○ | ○ |
| Anxious | ○ | ○ | ○ | ○ | ○ | ○ |
| Sympathising | ○ | ○ | ○ | ○ | ○ | ○ |
| Sad | ○ | ○ | ○ | ○ | ○ | ○ |

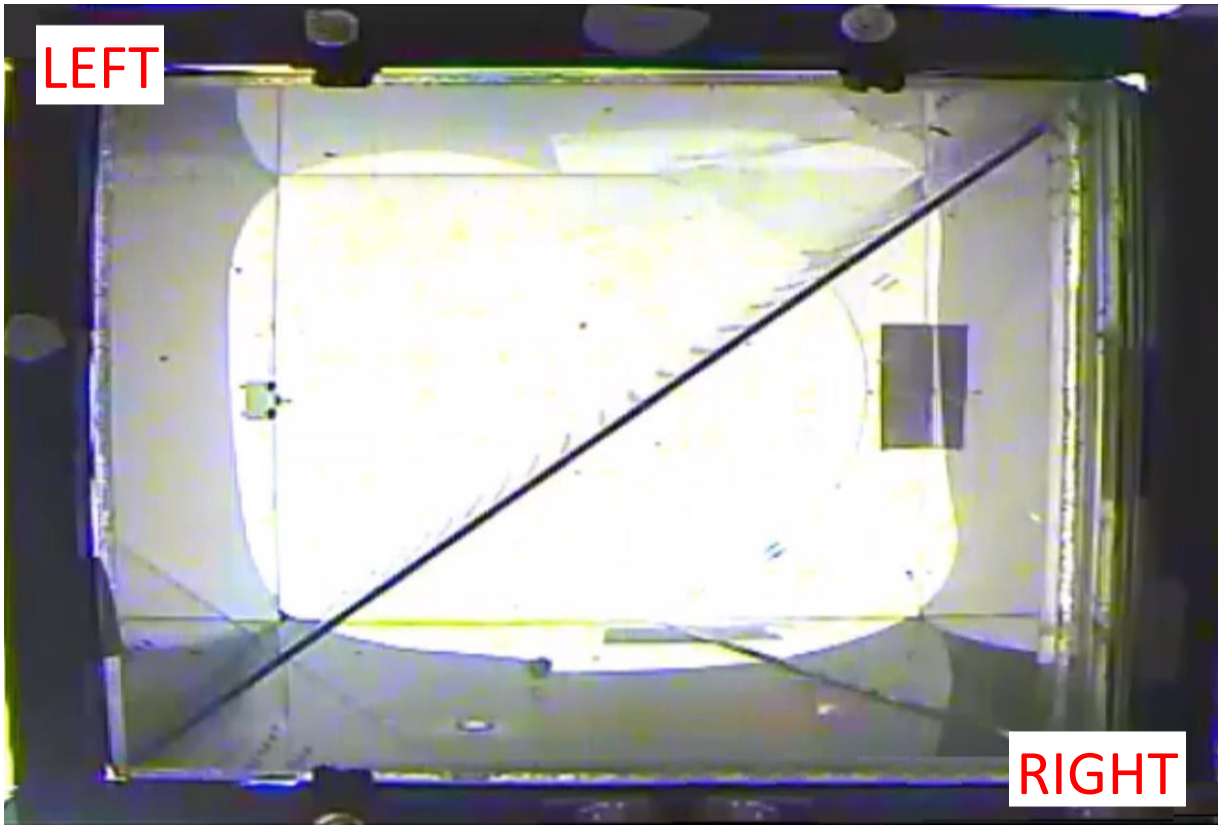
## 5. Please enter your email address:

(If you would like to enter in the prize draw for a €50 One4All voucher. It won't be used for anything else)

Email: _____

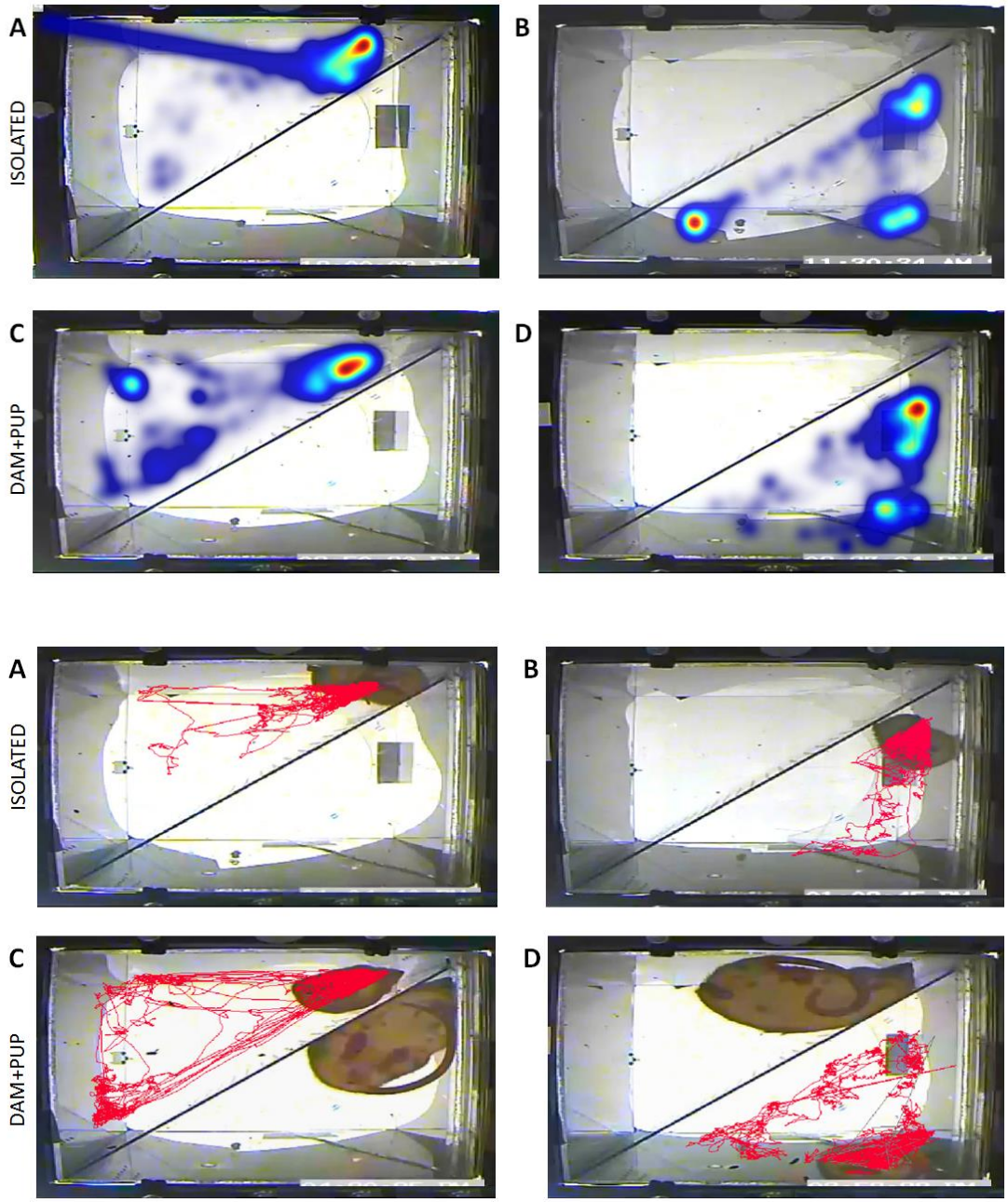
Thank you!

**Appendix R: Layout of the modified formalin arena**




Layout of the modified formalin arena, which was divided into two triangular (left and right) chambers. Dam-pup pairs were separated by the punched Perspex partition with one in each chamber. Pups were counter-balanced into either the left or right chamber for testing.

**Appendix S: Heat maps and tracking data (grouped) during the formalin trials**




**(top)** Heat-map visualisation of the mean movements of each group: (A) Isolated Left, (B) Isolated Right, (C) Dam-pup Left, and (D) Dam-pup Right; and **(bottom)** representative tracking visualisation of each group

## Appendix T: Ethics approval for research project


Leas-Uachtarán um Thaighde
Vice President for Research

26 June 2017

**Ref: 17-May-16**

Grace O'Sullivan
School of Psychology
NUI Galway

Dear Grace,

**Re: 'The influence of social context on childhood pain experiences: An investigation of psychological and neurobiological aspects'**

I write to you regarding the above proposal which was submitted for ethical review. Having reviewed your response to my letter, I am pleased to inform you that your proposal has been granted **APPROVAL.**

All NUI Galway Research Ethic Committee approval is given subject to the Principal Investigator submitting annual and final statements of compliance. The first statement is due on or before 25 June 2019. See annual and final statement of compliance forms below. Section 7 of the REC's Standard Operating Procedures gives further details, and also outlines other instances where you are required to report to the REC.

Yours sincerely

Kevin Davison

Chair, Research Ethics Committee

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