Cognitive biases in children and adolescents with chronic pain: A review of findings and a call for developmental research

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Abstract

Cognitive biases that emphasise bodily harm, injury, and illness could play a role in the maintenance of chronic pain, by facilitating fear and avoidance. Whereas extensive research has established attention, interpretation, and memory biases in adults with chronic pain, far less is known about these same biases in children and adolescents with pain. Studying cognitive biases in attention, interpretation, and memory in pain that occurs in youth is important because youth is a time when pain can first become chronic, and when relationships between cognitive biases and pain outcomes emerge and stabilise. Thus, youth potentially offers a time window for the prevention of chronic pain problems. Here, we summarise the growing corpus of data that has measured cognitive biases in relation to paediatric pain. We conclude that although biases in attention, interpretation and memory characterise children and adolescents with varying pain experiences, questions regarding the direction, magnitude, nature and role of these biases remain. We call for independent extension of cognitive bias research in children and adolescents, using well-powered longitudinal studies with wide age ranges and psychometrically-sound experimental measures to clarify these findings and any developmental trends in the links between cognitive biases and pain outcomes.

Perspective: This article provides a rationale for the theoretical and practical importance of studying the role of cognitive biases in children and adolescents with chronic pain, which has to date, been relatively under-studied. Existing findings are reviewed critically, and recommendations for future research are offered.

Key words: child and adolescent, paediatric pain, cognitive bias, information-processing, cognitive distortions

Chronic pain is common in children and adolescents, with a systematic review of over 40 epidemiological studies reporting median prevalence rates of 11-38% for different types of chronic pain[41]. As with adults, chronic pain in children and adolescents can incur long-term suffering and huge economic burden[2]. A significant number of children and adolescents with chronic pain report a devastating effect of their pain on many domains of life[17]. Pain can affect engagement with age-typical social, educational and recreational activities, sleep, mood and appetite, as well as the emergence of key self-concepts and self-esteem[17; 25; 36]. Unsurprisingly, pain in children and adolescents places huge and continuous emotional and financial strains on family life[37; 63], and affects the mental well-being of parents[7]. Yet, current treatments for chronic pain in children and adolescents are unsatisfactory. The evidence-base for pharmacotherapy in children and adolescents is generally poor[11-13; 18]. Psychological interventions have a growing potential but meta-analyses reveal that most treatment gains (relative to control conditions) are not sustained at follow-up[23]. Evidence for treatment effects on disability and other indices of psychological functioning such as distress, anxiety and depression are less definitive. Thus, more can be done to improve treatment effects, with recent calls for continuous treatment innovation[20].

In this paper, we propose that the study of cognitive biases in relation to paediatric chronic pain could inform our current understanding of how these early-emerging conditions are maintained. If biases are consistently associated with pain outcomes, then eventually, this body of work could inform treatment efforts, for example, cognitive biases could be used to predict responsiveness to treatment and tentatively, to guide new strategies for enhancing current psychological treatments. Although cognitive biases in attention, interpretation and memory have been studied extensively in adult chronic pain[53], they have been studied to a much lesser extent in paediatric populations. Independent extension of this work to samples of children and adolescents may be important. This is because substantial developmental changes in experience and neurocognitive maturation might mean that cognitive biases only

emerge to influence pain outcomes at particular developmental periods. Therefore, the extent to which they predict pain outcomes could also vary across childhood, adolescence, and adulthood. This paper is divided into four sections. First, we provide a definition of cognitive biases, explain how these are assessed, and briefly discuss data in support of their relationship with chronic pain conditions in adults. Next, we discuss why developmental extension of these biases in child and adolescent pain experiences is important for both scientific and clinical purposes. Third, we present an overview of research measuring cognitive biases in relation to paediatric pain experiences. As there have been no prior reviews of this growing literature, in our final section, we highlight overarching themes and questions for future research to address.

Cognitive biases and chronic pain in adults

Cognitive biases are an umbrella term for the tendency to preferentially process information that matches the current interests and concerns of a particular individual. Biases can occur in attention focus, interpretation of ambiguous information, and retention and recall of past (and future) information[45]. While their content is different, biases are now thought to characterise, maintain and even precede many psychiatric [4; 26; 45]. For example, emotional disorders such as anxiety and depression have been associated with biases in attention, interpretation and memory [45], with psychosis associated with biased reasoning and appraisal (interpretation) [26]. More recent extensions of cognitive bias work in eating disorders reveal biased patterns of attention focus [4]. Biased information-processing has also been demonstrated in many non-psychiatric conditions such as chronic fatigue, autoimmune diseases such as systemic lupus erythematosus and developmental conditions such as stuttering, to name but a few [15; 35; 46]. Because pain is a threat signal, in chronic pain, cognitive biases manifest as preferential processing of information that highlights the primacy of bodily threat and harm. Furthermore, cognitive-affective models of chronic pain suggest

that these biases in information-processing contribute to the mechanisms by which acute pain becomes chronic or disabling. Specifically, by enhancing the salience of these harmful stimuli, cognitive biases can increase fear and anxiety. In turn, this could a) amplify biases in information-processing and promote a vicious cycle, and b) facilitate avoidant tendencies that maintain the maladaptive processing styles (i.e. by preventing contact with counter-factual evidence). Thus biases are hypothesized to facilitate fear and avoidance, and exacerbate the impact of pain on functioning and disability [19; 53], although these association await empirical verification.

Given the hypothesized key role that cognitive biases are hypothesised to play in maintaining pain intensity and disability, a large body of research has measured these biases in adults with chronic pain. Studies have compared patients with chronic pain with various control participants in the magnitude and direction of biases. Some studies have investigated how well these biases associate with variability in the experience and impact of pain amongst patients. This rich body of research has been summarised in various meta-analyses and qualitative reviews [14; 53; 60], and will only be briefly presented here. To lay the groundwork for later sections, we describe how each bias is typically measured using experimental paradigms.

Attention biases

A large number of studies has focused on attention biases. Attention bias refers to the degree to which participants involuntarily or voluntarily attend towards stimuli representing or symbolising pain (e.g., pain words, facial expressions, or body images) at the cost of other information/stimuli. Most studies have used the modified Stroop task or the visual dot-probe task. These tasks infer attention biases for pain-relevant stimuli from differences in response times (RT) to a primary task, under conditions where a pain-relevant stimulus is present, to conditions where a neutral stimulus is present. In the modified Stroop task, this primary task is naming the colour of different words; slower RTs on pain-relevant

words relative to neutral words index biased attentional processing of the pain-relevant word. During the visual dot-probe task, participants view two stimuli presented simultaneously, with one of the stimuli being a pain-relevant stimulus (word or picture) and the other a neutral stimulus (also word or picture). Both stimuli disappear after a brief time period, and participants are then instructed to respond to a probe that replaces one of the stimuli on each trial. Faster RTs on trials in which the probe replaces the pain-relevant threat stimulus (known as congruent trials) over RTs on trials where the probe replaces the neutral stimulus. Unlike the Stroop task, the exposure time of the stimulus in the visual dot-probe task can be manipulated such that briefer presentation times (for example, those under 500ms) are thought to tap more involuntary attention processes, and longer presentation times (for example those over 1000ms), reflect more voluntary processes.

Two earlier meta-analyses reported significant differences in attentional bias between individuals with chronic pain and those who were pain-free[58; 61]. However a more recent meta-analysis (that included more studies) reported only partial support for attention biases for pain-relevant information[14]. Whereas an overall significant attention bias for pain-relevant information in patients with chronic pain was found, the effect size was small. Moreover, the only studies to report a significant group difference with comparison participants were those using the visual dot-probe in conjunction with sensory pain words. Under these conditions, patients with chronic pain showed greater attention towards sensory pain words when these words were presented for long durations, suggestive of biases at voluntary stages of attention. Of further note, biases in attention did not relate to other aspects of the pain experience (pain severity, pain-related fear, anxiety or depression). These results may emerge from poor psychometrics of current attention tasks, including their reliability and validity. These tasks have been criticised for failing to capture the real-life situations under which biased attention patterns emerge. For example, clinically, patients

with chronic pain are seen to fluctuate from patterns of vigilance to avoidance to no-bias. Such dynamic shifts across time and context may not be as well implemented in the simple index derived from response-time based tasks that characterise most of the studies published[73]. Alternatively, it could be that biases in selective attention for painful words only weakly contribute to the chronicity of pain in adults.

Interpretation biases

More promising findings have been reported for studies assessing biased interpretation of ambiguous information in relation to chronic pain. Biases in interpretation refer to the generation and endorsement of explanations of ambiguous or innocuous cues and situations that highlight bodily threat (pain or illness). Most studies have used homographs (words that are spelled the same but which have two meanings, one of which is pain-, threat- or illness-relevant; e.g. patient), or homophones (words which sound the same, again where one of which is pain-, threat- or illness-relevant; e.g. die/dye). Participants are typically asked to generate an associate word or sentence to a homograph/homophone. Their responses are then coded as threatening, if they are congruent with bodily threat, or benign, if they are words with neutral or positive connotations. An interpretation bias is quantified as the relative difference in selection of threatening over benign words. Another commonly used task is the word-stem completion task. Participants complete a word stem with the first word that comes to mind. Responses are then rated for words that have connotations of bodily threat, or are benign. As it is difficult to determine whether interpretations from these tasks are generated involuntarily (automatically), or generated through voluntary (controlled) processes, other methods to measure biases more indirectly have been developed[40; 70].

A meta-analysis of 7 studies on biased interpretations comprising 445 individuals with chronic pain and 407 pain-free comparison participants found significant group differences of moderate-to-large effect size[60]. Patients with chronic pain were more likely to endorse bodily threat interpretations of ambiguous cues than pain-free participants. Relationships

between interpretative bias and individual differences in the experience of pain amongst patients were not explored in this meta-analysis. However, across individual studies (within the meta-analysis), findings were mixed: two reported significant positive associations between interpretation bias and pain intensity[54; 56] whereas one reported a significant inverse correlation, such that greater bias for bodily threat interpretations was associated with less severe pain in the preceding week[40]. These inconsistent findings around associations with variability in the pain experience call for further clarification. Moreover, as only one study investigated interpretation biases using a more indirect method, it is unclear whether these biases emerge during the involuntary or voluntary stages of ambiguity resolution.

Memory biases

A small yet rather dated body of work has investigated memory biases, the selective retrieval of pain- and illness-associated, or broadly negative, information from memory. Participants are commonly presented with word lists containing sensory-pain and/or affective-pain descriptors, or words with illness-related or broadly negative connotations. Encoding instructions vary, but a powerful manipulation to probe pain-related differences has been to ask participants to rate words in reference to the self or in reference to others. Retrieval instructions also vary from free recall possibly followed by a recognition test, to 'indirect' measures where participants are not explicitly asked to remember, such as word completion. Although there has been no meta-analysis on memory biases in patients with chronic pain, robust data from both direct and indirect methods suggest that adults with chronic pain have a tendency to retrieve sensory pain words[21; 51] [22; 59; 62] (although there are some exceptions[6; 24; 39]). Interestingly, stimuli encoding instructions appear to affect recall[55]: Under self-referential conditions patients with pain, particularly those with concurrent depression or distress, not only recall more pain sensory words, but also more

negative personal and health-related descriptors[9]. These studies have not assessed whether memory correlated with patients' pain experiences. However, one study comparing patients with adaptive versus maladaptive coping responses to pain found that greater recall bias for pain-related material relative to neutral material characterized patients who responded to pain by thought suppression[39]. Contrastingly, those with fear-avoidance tendencies showed reduced recall for pain material. Studies examining the link between memory biases and patient pain experiences are clearly crucial.

Summary

Adult data provide evidence for biases in interpretation and memory among individuals with chronic pain relative to comparison participants, but only weak support for biases in attention. Of further interest to theory and clinical practice is whether these biases relate to variability in the pain experience and its impact on functioning. Yet few adult studies have empirically assessed these questions and in those that have, findings are mixed.

The need for developmental research in cognitive biases and pain

A growing number of studies have measured cognitive biases in relation to child and adolescent pain experiences. Before we summarise these data, we highlight four reasons why developmental extensions of adult findings to children and adolescents are important.

Addressing a major public health issue

Prevalence rates of pain sharply increase from childhood to adolescence, such that by the end of adolescence, these rates approach those of adults[38]. Many of these adolescents become adults with chronic pain. Pain in youth incurs other social and health costs. Young people with chronic pain have reduced educational opportunities[44], which could affect long-term job opportunities and financial prospects. Furthermore, unhealthy lifestyle habits that may become entrenched in youth[66], can place the young person at risk for other chronic physical and mental health problems such as obesity[50] and depression[34]. The high prevalence rates and the widespread and long-term functional impact of early chronic pain warrant understanding the causes and correlates of child and adolescent pain experiences to tackle a key public health issue.

An opportunity to address early risk factors contributing to the onset of chronic pain

Although adult data are useful in addressing theoretical predictions of how pain is maintained and could be managed, there are limitations. Most notably, the presence and effects of cognitive biases in adult chronic pain could be confounded by recurrent episodes of pain and attempted pain management. These prior pain experiences could bias informationprocessing, making it difficult to decipher whether biases are pre-existing vulnerability factors on early pain trajectories, or whether they are consequences of pain. Differentiating between these roles may have important implications for early detection and prevention. Extending research to child and adolescent pain experiences provides insights into *earlier* stages of pain onset and maintenance.

Developmental changes could alter the expression of cognitive biases on pain outcomes

Across childhood and adolescence, age-related developments occur in many cognitive domains, including abstract reasoning, attentional shifting, response inhibition and processing speed[72]. Continuous improvements in emotional understanding and regulation also occur, enabling the young person to respond to stressful situations independently, and to navigate more complex, multi-layered social situations and peer interactions[5; 52]. These 'typical' cognitive-affective changes could mean that individual differences in selective attention, interpretation of ambiguity and selective memory only emerge once certain developmental milestones are reached. For example, the ability to select one interpretation of the same situation over another may only emerge once children have developed abstract thinking, are able to hold two alternative options in working memory, and can inhibit one response over another. Similarly, the ability to use voluntary strategies to focus attention away from threatening/pain-relevant stimuli may only emerge once mature attentional-

shifting and inhibition are attained. Thus, individual differences may possibly be observed once abilities have emerged and only consistently link with pain outcomes once these differences stabilize.

Indeed, data from the psychopathology literature suggest that age can moderate the expression and impact of cognitive biases in relation to child and adolescent anxiety and depression[43]. Meta-analyses in this literature have shown that the association between attention bias and anxiety, and interpretation bias and anxiety, increases with age[16; 65]. Qualitative reviews suggest similar developmental trends in the association between explicit memory biases and depression[57]. These developmental patterns could be methodological; the tasks used to measure cognitive biases in children may not typically be age-appropriate and may not accurately measure these biases in younger age ranges[43]. However, it could be that some cognitive processes take time to mature, only becoming more stable and consistent in their associations with behaviour with development. Such development-by-painby-cognitive bias interactions could also apply to pain outcomes. Speaking in support of this, a recent study reported age dissociations with the effects of pain catastrophizing (a cognitive factor) on pain interference, such that this predictive association was greatest in adolescent patients with chronic pain[67]. Tentatively, these data suggest that the expression of some cognitive factors on pain outcomes could vary, depending on maturational and/or experiential changes during development (although very few studies have assessed these developmental-age-by-cognitive-bias-by-pain-symptom interactions).

An opportunity to implement preventative interventions

The last two decades of research from developmental cognitive neuroscience have shown significant brain reorganization in the transition to and across youth, consistent with structural and functional maturation, and heightened plasticity [10]. This may mean that administering external interventions that target cognitive biases during childhood and adolescence could be more powerful. However, current data comparing the effects of

psychological interventions such as cognitive behavioural therapy have not revealed greater therapeutic improvements in children and adolescents compared to adults (probably because not all techniques used in CBT are developmentally-appropriate), and there are yet to be studies comparing more targeted interventions for modifying biases in different age groups. Regardless, if cognitive biases do contribute to pain chronicity, targeting these biases before they become habitual may help attenuate the short- and long-term impact of pain.

Summary

In summary, developmental extensions of cognitive bias research could be helpful in uncovering the early processes of pain chronicity as they emerge across development, and provide unique preventative opportunities.

Cognitive biases and child and adolescent pain: A review of findings and research gaps

Research in children and adolescents has largely focused on biases in the same stages of information-processing as those in adults. Here, we review findings for each bias. Because there are only a handful of studies comparing child and adolescent patients with chronic pain against pain-free comparison participants, we have also included studies that have assessed the bias in relation to pain-related vulnerability factors such as pain catastrophising within community samples.

Attention biases

A handful of studies has assessed young people's selective attention for pain-related information. Mirroring the methodology of the adult literature, these studies have largely employed visual dot-probe tasks to infer attention bias based on RTs to probes replacing pain-relevant and neutral stimuli. One study has used eye movements (initial fixations and total dwell time) to pain versus non-pain stimuli as a more continuous assessment of attention. Across the small number of studies of young people with chronic pain, conclusions are mixed. An early study of patients with recurrent abdominal pain (aged 9-17 years)

reported significant attention biases for pain-relevant and social threat information relative to neutral words at brief (20ms) and long (1250ms) presentation times. However, the absence of a control group in this study makes it difficult to benchmark the magnitude of this 'threat bias'[3]. A second study, which did use a pain-free comparison group[1], reported greater attention for pain-related words in patients with functional abdominal pain (aged 10-16 years) at both brief (20ms) and long (1250ms) presentation times, but only after a laboratory stressor (failure versus success feedback regarding their performance on a challenging computer game). A subsequent study, also of patients (aged 8-17 years) with functional abdominal pain reported no attention biases for pictorial stimuli depicting pain in either group[69] at either brief (20ms) or long (1250ms) presentation times. Most recently, a study assessed selective attention bias for pain-related faces (presented for 500ms) amongst patients with chronic pain aged 10-18 years in the context of a larger attention training controlled trial (for the reduction of pain symptoms)[30]. At baseline, there was no evidence for an attention bias towards or away from pain-related stimuli. Importantly, this study also found no evidence for the efficacy of attention training on the young patients' pain symptoms, disability, or psychological outcomes beyond placebo training or waitlist. Only one of these studies assessed relationships between attention biases for pain words and indices of pain severity in patients; attention for pain words presented at long durations correlated negatively with parent reports of their child's pain but not child reports [3].

Attention biases have also been found to correlate with pain-related vulnerability factors within community samples, though findings are inconsistent across studies. One study reported biases away from pain (presented for 500ms) in children and adolescents (aged 10-16 years) with high levels of pain magnification, an aspect of pain catastrophising[71]. Furthermore, attention avoidance and pain magnification interacted to influence pain tolerance: participants who showed a tendency to attend away from pain-related information and had high magnification levels had lower pain tolerance. In another study of 16-18 year

olds, biases towards pain-related pictures were found in those with high pain catastrophising scores (across brief, 100ms and long, 1250ms presentation times) but only if they also had weak attention control[33]. Finally, in an eye-tracking study of young people aged 8-17 years, with arguably more direct measures of attention-orienting/disengagement (via continuous eye movements and gaze data), all participants showed a bias towards pain-relevant stimuli over neutral stimuli (both presented for 3500ms) but these were not correlated with individual differences in pain catastrophising (or anxiety) scores. As in the previous study there was also a moderating role of attention control, but this time biases towards pain-related pictures were found in those with low anxiety and low attention control[32].

The reasons for these inconsistences are unclear and may be methodological, as consistent with the adult literature. As discussed, current paradigms assessing attention biases may lack ecological validity, as they are unable to capture the fluctuating nature of biases as they emerge in response to different situations and contexts. Alternatively, consistent with findings in developmental psychopathology, attention biases for pain in children and adolescents could become increasingly linked with pain vulnerability across development. Thus, they may only associate with pain outcomes in later adolescence. However, because most of the studies used similar age ranges, it is difficult to attribute differences in results across studies to differences in age. However, where studies did investigate the main effects of age on bias [3, 69], these effects were non-significant. A final possibility is that attention biases are as weak in this age range as they are in adults, and may not contribute to pain outcomes.

Interpretation biases

Two studies have investigated the role of biased interpretations in young people's pain experiences, one in community participants aged 16-18 years[31] and one in patients with chronic musculoskeletal pain aged 10-18 years[29]. Neither study used tasks typically employed in adult studies of chronic pain, but instead administered the computerised

Adolescent Interpretation of Bodily Threat (AIBT) task[28]. This task was based on similar measures from the developmental psychopathology literature, and presents 8 vignettes describing ambiguous body-related situations that could have either injury/illness-related or benign interpretations. The task also presents a further 8 vignettes describing ambiguous social situations to assess whether chronic pain is associated with biased interpretations towards body-specific situations or towards ambiguous situations in general. Whereas both studies reported evidence of biased interpretations in relation to pain, the nature of the bias varied across community and patient samples. In community adolescents[31], experiences of pain were associated with both biased interpretations of bodily threat situations and social situations. In the patient study[29], group differences in biases emerged to bodily threat situations only, and were characterised by reduced endorsement of benign interpretations with no differences in negative interpretation ratings.

These preliminary studies are largely consistent with adult findings[60], and raise interesting questions around the nature of these biases. As the AIBT task is likely to tap biases at a more voluntary, strategic stage of ambiguity resolution, an outstanding question is whether interpretation biases also emerge at earlier, more involuntary stages when using less direct tasks[40; 70]. Finally, it is unknown whether similar biases characterise pre-adolescent children experiencing pain as both existing studies focused on adolescents only. Indeed, there are developmental reasons for expecting that these inferential biases emerge with the maturation of particular cognitive abilities. Consequently, stronger linkages between interpretation biases and pain are to be expected across development, as they are in relation to anxiety outcomes[27; 65].

Memory biases

Considerable research has measured biases in pain memories in children and adolescents. However, only one study has, to our knowledge, used similar methods as those in adults, namely free recall of pain and non-pain words. Consistent with adult findings,

patients with juvenile arthritis showed a memory bias for sensory words compared to comparison participants, only when these words were self-referentially encoded[42].

More recent studies of memory bias have deviated from this experimental procedure and measured affective memories (such as pain intensity or fear) of actual sensory/painful experience induced in the lab (e.g. cold pressor task) or in real-life (e.g. surgical procedures), comparing these to ratings taken during the initial experience[48]. Over- or under-reporting of pain or fear during the recollection phase relative to the actual experience are then thought to index memory biases. Studies using this approach have reported mixed findings. One study of participants aged 9-16 years who experienced headache at least weekly found a tendency to over-report pain intensity and duration in retrospective compared to daily ratings of the experience[68]. Two other studies recruiting patients of similar age range (8-17 year olds[8] and 9-18 year olds[64]) but different diagnoses (chronic abdominal pain[8] and juvenile idiopathic arthritis[64]) found an under-reporting of pain using similar designs. However, in all these studies, the absence of comparison participants precludes benchmarking of these distorted retrieval patterns.

In terms of predictors of the bias, one study reported that greater pain severity was associated with more exaggerated recall of pain[68], but another found no such relationship[8]. Other studies have investigated biased retrieval in individuals with high levels of pain-vulnerability factors. One study showed that amongst 10-18 year olds undergoing surgery, the children and young people's tendency to catastrophise about pain was not associated with affective-pain memories[49]. However, both this study, and another study of 5-10 year old children following venipuncture[47] found that greater reporting of pain intensity shortly after the time of the actual pain experience was a significant predictor affective pain memories.

Thus, although young patients with chronic pain appear to show memory distortions of pain, data from pain-free participants will be needed to clarify the direction of this bias.

Data that children and adolescents with persistent pain, or high levels of pain-related fear and catastrophizing, show distorted memories for pain-related information is still mixed and requires further clarification.

Summary

Preliminary data indicates the presence of pain-related cognitive biases in children and adolescents with chronic pain and pain-related vulnerability. Further research is needed to clarify the nature of these biases, particularly the presence and direction of attention and memory biases, and the magnitude of interpretation biases.

Overarching research directions and conclusions

While specific research directions for each bias type have been discussed, there are some overarching research challenges, which will be explored in the final section. *Methodological issues in translation of adult measures for use in children and adolescents*

A priority in establishing associations between cognitive biases and pain outcomes is to ensure that the current experimental paradigms used in child and adolescent studies are age-appropriate. Questions over age-appropriateness can be considered on various levels. First, are the task stimuli relevant for the particular age group? On the one hand, it may be argued that faces rather than words are more accessible for children and adolescents in attention tasks, due to poorer reading abilities. On the other hand prior studies have tended to report effects for linguistic but not pictorial studies in this age group[16], suggesting careful consideration of the type of stimulus is needed. Two of the four studies of attention bias used in paediatric patients with chronic pain employed words. Second, is task performance reflective of the cognitive process of interest, or are scores affected by other cognitive skills and abilities that may not yet be mature? As an example, measuring memories of actual pain experiences (whether induced in the lab or following real-life medical/dental procedures) are likely concrete and accessible models for paediatric populations. Remembering word lists likely require more mature working memory capacities, and relies on abstract notions of what symbolises pain. Similarly, presenting children with scenarios describing ambiguity could again be more concrete than measuring sentence generation of homophones/homographs, which relies on a broader vocabulary. Third, is the outcome variable meaningful for a particular age group? While the AIBT asks participants to rate the likelihood of an interpretation actually occurring, this may be inappropriate for younger children. For younger children, it may be more meaningful to ask about expectations of outcome. Finally, are task instructions appropriate for the particular population? There is of course extensive variability in comprehension and reading ability levels even within a relatively narrow paediatric age range, and this should be considered when developing task instructions.

Once the experimental stimuli and procedures are deemed appropriate for particular age groups, researchers need to consider the psychometric properties of their measures. In efforts to improve the replicability of findings in psychological science, the reliability and validity of experimental tasks have become increasingly scrutinized. Consequently, establishing the inter-time stability of a task and its validity against other similar constructs has become quintessential to its further application in understanding individual differences. Even when the psychometric properties of particular tasks have been established in adults, extension to new populations such as children and adolescents requires similar systematic attempts to establish reliability and validity.

Applying measures of cognitive biases to test theoretical gaps in our understanding of pain experiences and outcomes

A gap in our existing knowledge of the chronicity of pain is how psychological factors contribute to pain effects on functioning and disability. Consistent with many cognitiveaffective models of chronic pain, here, we propose that biased information-processing can contribute to the mechanisms by which acute pain becomes chronic and disabling. More

particularly, we suggest that cognitive biases may enhance the threat value of pain, shaping trajectories of approach (and positive outcomes to recovery) versus avoidance (and negative outcomes to recovery and rehabilitation). Yet, despite these hypotheses, little research in children and adolescents, nor in adults, has focused on these 'individual difference' questions beyond establishing whether cognitive biases differentiate individuals with and without pain. The little research that has investigated individual differences in pediatric populations is somewhat inconsistent, for example with evidence that pain catastrophizing both increases and decreases selective attention to pain. There are also few data measuring whether cognitive biases explain variability on pain outcomes beyond catastrophizing. These could include pain intensity, distress, and disability, as well as intermediate psychological variables such as fear and avoidance, which may be key mediating mechanisms linking cognitive biases with pain chronicity. Ideally, collecting data on these dependent, intermediate, and independent variables in longitudinal designs would enable mediating pathways to be examined, enabling us to decipher how biases maintain pain in those suffering from chronic pain, and how they come to predict disability in youth. Addressing such questions will require large samples with adequate power to detect individual differences, and the use of ageappropriate, psychometrically-sound experimental measures of cognitive bias.

There has also been a call in adult psychopathology for investigating the combined effects of biases and considering their interactions and correlations in explaining key outcomes. The same principle is likely to apply in order to understand the compound effect of biases on pain outcomes in children and young people. We therefore encourage researchers to consider multiple biases in prediction of pain conditions in childhood and adolescence. A related set of questions concerns the remit of biased information-processing; whether other cognitive factors such as dysfunctional attitudes and automatic thinking errors, and cognitivelearning processes such as threat-safety discrimination learning should be considered; and how these, and also pain catastrophizing, fit in together with biases in attention, interpretation and memory in maintenance pathways. Clearly, there is potential for more elaborated and integrated models of cognition within chronic pain.

Testing developmental moderation of cognitive bias-pain relationships

A final overarching question concerns interactions between developmental factors and cognitive biases on pain outcomes. We have argued here that neurocognitive maturation and environmental experience may 'bring out' or enable biases to be elicited[27] in relation to behavioural outcomes such as pain. To test whether development moderates bias-pain associations, future studies should consider recruiting larger samples with wider age ranges to assess three-way interactions between developmental maturation (either using chronological age or puberty), cognitive biases and pain symptoms. These questions could also be considered in the context of longitudinal designs, allowing cross-sectional age differences and temporal age changes to be examined simultaneously.

Closing remarks

This paper has reviewed the presence and nature of cognitive biases in relation to child and adolescent pain. If these biases are indeed found to be involved in the maintenance of pain and disability as theoretical models would suggest, then eventually they may inform pain management strategies. For example, cognitive biases could be used to predict responsiveness or adherence to treatment, consistent with their hypothesized role in predicting natural recovery from acute pain. If specific cognitive biases are consistently linked with pain outcomes, this could open up novel methods for optimising current treatments. Although research into the modification of biases using computerised training intervention programmes has revealed null effects in reducing pain symptoms in children and adolescents [30] and weak effects on other developmental psychopathology conditions, targeting biases could also be implemented using other well-used cognitive techniques such as re-appraisal and re-structuring. However, before these clinical implications are considered further, we

require convincing data to establish the presence and role of cognitive biases in explaining variability in the experience and impact of pain in children and adolescents.

References

- [1] Beck JE, Lipani TA, Baber KF, Dufton L, Garber J, Smith CA, Walker LS. Attentional bias to pain and social threat in pediatric patients with functional abdominal pain and pain-free youth before and after performance evaluation. Pain 2011;152(5):1061-1067.
- [2] Bennett SM, Huntsman E, Lilley CM. Parent perceptions of the impact of chronic pain in children and adolescents. Child Health Care 2000;29(3):147-159.
- [3] Boyer MC, Compas BE, Stanger C, Colletti RB, Konik BS, Morrow SB, Thomsen AH. Attentional biases to pain and social threat in children with recurrent abdominal pain. Journal of pediatric psychology 2006;31(2):209-220.
- [4] Brooks S, Prince A, Stahl D, Campbell IC, Treasure J. A systematic review and meta-analysis of cognitive bias to food stimuli in people with disordered eating behaviour. Clinical psychology review 2011;31(1):37-51.
- [5] Burnett Heyes S, Jih YR, Block P, Hiu CF, Holmes EA, Lau JY. Relationship Reciprocation Modulates Resource Allocation in Adolescent Social Networks: Developmental Effects. Child development 2015;86(5):1489-1506.
- [6] Busch H, Montgomery W, Melin B, Lundberg U. Visuospatial and verbal memory in chronic pain patients: an explorative study. Pain practice : the official journal of World Institute of Pain 2006;6(3):179-185.
- [7] Campo JV, Bridge J, Lucas A, Savorelli S, Walker L, Di Lorenzo C, Iyengar S, Brent DA. Physical and emotional health of mothers of youth with functional abdominal pain. Archives of pediatrics & adolescent medicine 2007;161(2):131-137.
- [8] Chogle A, Sztainberg M, Bass L, Youssef NN, Miranda A, Nurko S, Hyman P, Cocjin J, Di Lorenzo C, Saps M. Accuracy of pain recall in children. Journal of pediatric gastroenterology and nutrition 2012;55(3):288-291.
- [9] Clemmey PA, Nicassio PM. Illness self-schemas in depressed and nondepressed rheumatoid arthritis patients. Journal of behavioral medicine 1997;20(3):273-290.
- [10] Cohen Kadosh K, Linden DE, Lau JY. Plasticity during childhood and adolescence: innovative approaches to investigating neurocognitive development. Developmental science 2013;16(4):574-583.
- [11] Cooper TE, Fisher E, Anderson B, Wilkinson NM, Williams DG, Eccleston C. Paracetamol (acetaminophen) for chronic non-cancer pain in children and adolescents. The Cochrane database of systematic reviews 2017;8:CD012539.
- [12] Cooper TE, Heathcote LC, Clinch J, Gold JI, Howard R, Lord SM, Schechter N, Wood C, Wiffen PJ. Antidepressants for chronic non-cancer pain in children and adolescents. The Cochrane database of systematic reviews 2017;8:CD012535.
- [13] Cooper TE, Wiffen PJ, Heathcote LC, Clinch J, Howard R, Krane E, Lord SM, Sethna N, Schechter N, Wood C. Antiepileptic drugs for chronic non-cancer pain in children and adolescents. The Cochrane database of systematic reviews 2017;8:CD012536.
- [14] Crombez G, Van Ryckeghem DM, Eccleston C, Van Damme S. Attentional bias to pain-related information: a meta-analysis. Pain 2013;154(4):497-510.

- [15] Denton FJ, Sharpe L, Schrieber L. Cognitive bias in systemic lupus erythematosus. European journal of pain 2005;9(1):5-14.
- [16] Dudeney J, Sharpe L, Hunt C. Attentional bias towards threatening stimuli in children with anxiety: A meta-analysis. Clinical psychology review 2015;40:66-75.
- [17] Eccleston C, Clinch J. Adolescent chronic pain and disability: A review of the current evidence in assessment and treatment. Paediatrics & child health 2007;12(2):117-120.
- [18] Eccleston C, Cooper TE, Fisher E, Anderson B, Wilkinson NM. Non-steroidal antiinflammatory drugs (NSAIDs) for chronic non-cancer pain in children and adolescents. The Cochrane database of systematic reviews 2017;8:CD012537.
- [19] Eccleston C, Crombez G. Pain demands attention: a cognitive-affective model of the interruptive function of pain. Psychological bulletin 1999;125(3):356-366.
- [20] Eccleston C, Crombez G. Advancing psychological therapies for chronic pain. F1000Research 2017;6:461.
- [21] Edwards L, Pearce S, Collett BJ, Pugh R. Selective memory for sensory and affective information in chronic pain and depression. The British journal of clinical psychology 1992;31 (Pt 2):239-248.
- [22] Edwards LC, Pearce SA. Word completion in chronic pain: evidence for schematic representation of pain? Journal of abnormal psychology 1994;103(2):379-382.
- [23] Fisher E, Heathcote L, Palermo TM, de CWAC, Lau J, Eccleston C. Systematic review and meta-analysis of psychological therapies for children with chronic pain. Journal of pediatric psychology 2014;39(8):763-782.
- [24] Flor H, Knost B, Birbaumer N. Processing of pain- and body-related verbal material in chronic pain patients: central and peripheral correlates. Pain 1997;73(3):413-421.
- [25] Forgeron PA, Evans J, McGrath PJ, Stevens B, Finley GA. Living with difference: exploring the social self of adolescents with chronic pain. Pain research & management 2013;18(6):e115-123.
- [26] Garety PA, Kuipers E, Fowler D, Freeman D, Bebbington PE. A cognitive model of the positive symptoms of psychosis. Psychological medicine 2001;31(2):189-195.
- [27] Haller SP, Cohen Kadosh K, Scerif G, Lau JY. Social anxiety disorder in adolescence: How developmental cognitive neuroscience findings may shape understanding and interventions for psychopathology. Developmental cognitive neuroscience 2015;13:11-20.
- [28] Haller SP, Raeder SM, Scerif G, Cohen Kadosh K, Lau JY. Measuring online interpretations and attributions of social situations: Links with adolescent social anxiety. Journal of behavior therapy and experimental psychiatry 2016;50:250-256.
- [29] Heathcote LC, Jacobs K, Eccleston C, Fox E, Lau JY. Biased interpretations of ambiguous bodily threat information in adolescents with chronic pain. Pain 2017;158(3):471-478.
- [30] Heathcote LC, Jacobs K, Van Ryckeghem DML, Fisher E, Eccleston C, Fox E, Lau JYF. Attention bias modification training for adolescents with chronic pain: a randomized placebocontrolled trial. Pain 2017.

- [31] Heathcote LC, Koopmans M, Eccleston C, Fox E, Jacobs K, Wilkinson N, Lau JY. Negative Interpretation Bias and the Experience of Pain in Adolescents. The journal of pain : official journal of the American Pain Society 2016;17(9):972-981.
- [32] Heathcote LC, Lau JY, Mueller SC, Eccleston C, Fox E, Bosmans M, Vervoort T. Child attention to pain and pain tolerance are dependent upon anxiety and attention control: An eye-tracking study. European journal of pain 2017;21(2):250-263.
- [33] Heathcote LC, Vervoort T, Eccleston C, Fox E, Jacobs K, Van Ryckeghem DM, Lau JY. The relationship between adolescents' pain catastrophizing and attention bias to pain faces is moderated by attention control. Pain 2015;156(7):1334-1341.
- [34] Holley AL, Law EF, Zhou C, Murphy L, Clarke G, Palermo TM. Reciprocal longitudinal associations between pain and depressive symptoms in adolescents. European journal of pain 2013;17(7):1058-1067.
- [35] Hughes A, Hirsch C, Chalder T, Moss-Morris R. Attentional and interpretive bias towards illness-related information in chronic fatigue syndrome: A systematic review. British journal of health psychology 2016;21(4):741-763.
- [36] Hunfeld JA, Perquin CW, Duivenvoorden HJ, Hazebroek-Kampschreur AA, Passchier J, van Suijlekom-Smit LW, van der Wouden JC. Chronic pain and its impact on quality of life in adolescents and their families. Journal of pediatric psychology 2001;26(3):145-153.
- [37] Hunfeld JA, Perquin CW, Hazebroek-Kampschreur AA, Passchier J, van Suijlekom-Smit LW, van der Wouden JC. Physically unexplained chronic pain and its impact on children and their families: the mother's perception. Psychology and psychotherapy 2002;75(Pt 3):251-260.
- [38] Kamper SJ, Henschke N, Hestbaek L, Dunn KM, Williams CM. Musculoskeletal pain in children and adolescents. Brazilian journal of physical therapy 2016;20(3):275-284.
- [39] Karimi Z, Pilenko A, Held SM, Hasenbring MI. Recall Bias in Patients with Chronic Low Back Pain: Individual Pain Response Patterns Are More Important Than Pain Itself! International journal of behavioral medicine 2016;23(1):12-20.
- [40] Khatibi A, Sharpe L, Jafari H, Gholami S, Dehghani M. Interpretation biases in chronic pain patients: an incidental learning task. European journal of pain 2015;19(8):1139-1147.
- [41] King S, Chambers CT, Huguet A, MacNevin RC, McGrath PJ, Parker L, MacDonald AJ. The epidemiology of chronic pain in children and adolescents revisited: a systematic review. Pain 2011;152(12):2729-2738.
- [42] Koutantji M, Pearce SA, Oakley DA, Feinmann C. Children in pain: an investigation of selective memory for pain and psychological adjustment. Pain 1999;81(3):237-244.
- [43] Lau JYF, Waters AM. Annual Research Review: An expanded account of information-processing mechanisms in risk for child and adolescent anxiety and depression. J Child Psychol Psyc 2017;58(4):387-407.
- [44] Logan DE, Simons LE, Stein MJ, Chastain L. School impairment in adolescents with chronic pain. The journal of pain : official journal of the American Pain Society 2008;9(5):407-416.

- [45] Mathews A, MacLeod C. Cognitive vulnerability to emotional disorders. Annual Review of Clinical Psychology 2005;.1(1):pp.
- [46] McAllister J, Kelman E, Millard S. Anxiety and cognitive bias in children and young people who stutter. Procd Soc Behv 2015;193:183-191.
- [47] Noel M, McMurtry CM, Chambers CT, McGrath PJ. Children's Memory for Painful Procedures: The Relationship of Pain Intensity, Anxiety, and Adult Behaviors to Subsequent Recall. Journal of pediatric psychology 2010;35(6):626-636.
- [48] Noel M, Pavlova M, Mccallum L, Vinall J. Remembering the Hurt of Childhood: A Psychological Review and Call for Future Research. Can Psychol 2017;58(1):58-68.
- [49] Noel M, Rabbitts JA, Tai GG, Palermo TM. Remembering pain after surgery: a longitudinal examination of the role of pain catastrophizing in children's and parents' recall. Pain 2015;156(5):800-808.
- [50] Paulis WD, Silva S, Koes BW, van Middelkoop M. Overweight and obesity are associated with musculoskeletal complaints as early as childhood: a systematic review. Obesity reviews : an official journal of the International Association for the Study of Obesity 2014;15(1):52-67.
- [51] Pearce SA, Isherwood S, Hrouda D, Richardson PH, Erskine A, Skinner J. Memory and Pain - Tests of Mood Congruity and State Dependent Learning in Experimentally Induced and Clinical Pain. Pain 1990;43(2):187-193.
- [52] Pfeifer JH, Blakemore SJ. Adolescent social cognitive and affective neuroscience: past, present, and future. Social cognitive and affective neuroscience 2012;7(1):1-10.
- [53] Pincus T, Morley S. Cognitive-processing bias in chronic pain: a review and integration. Psychological bulletin 2001;127(5):599-617.
- [54] Pincus T, Pearce S, McClelland A, Farley S, Vogel S. Interpretation bias in responses to ambiguous cues in pain patients. Journal of psychosomatic research 1994;38(4):347-353.
- [55] Pincus T, Pearce S, McClelland A, Turner-Stokes L. Self-referential selective memory in pain patients. The British journal of clinical psychology 1993;32 (Pt 3):365-374.
- [56] Pincus T, Pearce S, Perrott A. Pain patients' bias in the interpretation of ambiguous homophones. The British journal of medical psychology 1996;69 (Pt 3):259-266.
- [57] Platt B, Waters AM, Schulte-Koerne G, Engelmann L, Salemink E. A review of cognitive biases in youth depression: attention, interpretation and memory. Cognition & emotion 2017;31(3):462-483.
- [58] Roelofs J, Peters ML, Zeegers MP, Vlaeyen JW. The modified Stroop paradigm as a measure of selective attention towards pain-related stimuli among chronic pain patients: a meta-analysis. European journal of pain 2002;6(4):273-281.
- [59] Rusu AC, Pincus T, Morley S. Depressed pain patients differ from other depressed groups: examination of cognitive content in a sentence completion task. Pain 2012;153(9):1898-1904.
- [60] Schoth DE, Liossi C. Biased interpretation of ambiguous information in patients with chronic pain: A systematic review and meta-analysis of current studies.

Health psychology : official journal of the Division of Health Psychology, American Psychological Association 2016;35(9):944-956.

- [61] Schoth DE, Nunes VD, Liossi C. Attentional bias towards pain-related information in chronic pain; a meta-analysis of visual-probe investigations. Clinical psychology review 2012;32(1):13-25.
- [62] Schoth DE, Parry L, Liossi C. Combined cognitive biases for pain and disability information in individuals with chronic headache: A preliminary investigation. Journal of health psychology 2016:1359105316664136.
- [63] Sleed M, Eccleston C, Beecham J, Knapp M, Jordan A, Id, Eccleston COhoo. The economic impact of chronic pain in adolescence: Methodological considerations and a preliminary cost-of-illness study. Pain 2005;.119(1-3):pp.
- [64] Stinson JN, Jibb LA, Lalloo C, Feldman BM, McGrath PJ, Petroz GC, Streiner D, Dupuis A, Gill N, Stevens BJ. Comparison of average weekly pain using recalled paper and momentary assessment electronic diary reports in children with arthritis. The Clinical journal of pain 2014;30(12):1044-1050.
- [65] Stuijfzand S, Creswell C, Field AP, Pearcey S, Dodd H. Research Review: Is anxiety associated with negative interpretations of ambiguity in children and adolescents? A systematic review and meta-analysis. Journal of child psychology and psychiatry, and allied disciplines 2017.
- [66] Swinburn BA, Sacks G, Hall KD, McPherson K, Finegood DT, Moodie ML, Gortmaker SL. The global obesity pandemic: shaped by global drivers and local environments. Lancet 2011;378(9793):804-814.
- [67] Tran ST, Jastrowski Mano KE, Hainsworth KR, Medrano GR, Anderson Khan K, Weisman SJ, Davies WH. Distinct Influences of Anxiety and Pain Catastrophizing on Functional Outcomes in Children and Adolescents With Chronic Pain. Journal of pediatric psychology 2015;40(8):744-755.
- [68] van den Brink M, Bandell-Hoekstra EN, Abu-Saad HH. The occurrence of recall bias in pediatric headache: a comparison of questionnaire and diary data. Headache 2001;41(1):11-20.
- [69] van der Veek SM, Derkx BH, Plak RD, Benninga MA, Boer F, Lindauer RJ, de Haan E. Attentional bias to activity of different parts of the body in children with functional abdominal pain: an experimental study. Journal of pediatric psychology 2014;39(4):438-449.
- [70] Vancleef LM, Peters ML, De Jong PJ. Interpreting ambiguous health and bodily threat: are individual differences in pain-related vulnerability constructs associated with an on-line negative interpretation bias? Journal of behavior therapy and experimental psychiatry 2009;40(1):59-69.
- [71] Vervoort T, Trost Z, Van Ryckeghem DM. Children's selective attention to pain and avoidance behaviour: the role of child and parental catastrophizing about pain. Pain 2013;154(10):1979-1988.
- [72] Yurgelun-Todd D. Emotional and cognitive changes during adolescence. Current opinion in neurobiology 2007;17(2):251-257.
- [73] Zvielli A, Bernstein A, Koster EH. Dynamics of attentional bias to threat in anxious adults: bias towards and/or away? PloS one 2014;9(8):e104025.