The cyclical relation between chronic pain, executive functioning, emotional regulation and self-management

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Abstract

Objective: To propose a new model outlining a hypothesized cyclical relation between executive functioning, emotional regulation and chronic pain in adolescence and to highlight the likely importance of such a relation for self-management behavior and pain-related disability.

Methods: A review of the existing literature that critically explores the role of executive functioning in understanding chronic pain experiences and self-management in adolescence in order to develop the Cyclical model Of Pain, Executive function, emotion regulation and Self-management (COPES).

Results: Growing evidence points towards a potential cyclical relation between chronic pain and impaired executive functioning, which forms the basis of COPES. The COPES model proposes that the relative immaturity of executive functioning in adolescence negatively influences their ability to engage with self-management, which in turn increases adolescents' disability due to pain and contributes to the maintenance of chronic pain, which perpetuates the reduced capacity of executive functioning. The moderating influence of flexible parental support is hypothesized to offset some of these influences. However, the available evidence is limited due to methodological shortcomings such as large variety in executive functioning operationalization, reliance on self-report and cross-sectional designs.

Conclusions: It is anticipated that the COPES model will stimulate more systematic, theory-driven research to further our understanding of the links between executive functioning, chronic pain, self-management and wellbeing. Such enhanced understanding has the potential to drive forward intervention development and refinement aimed at improving self-management uptake and adherence amongst adolescents with chronic pain.

Pediatric chronic pain [i.e. continuous or recurrent pain lasting longer than three months (American Pain Society, 2001)] represents a major public health problem, as it interferes with daily functioning across a broad range of domains including sleep, academic, emotional, and social functioning (e.g., Gauntlett-Gilbert & Eccleston, 2007). Treatment for pediatric chronic pain ranges from pain medication and general management advice to enrolment in specialized, evidence based programs such as Intensive Interdisciplinary Pain Treatment (IIPT), which work across all aspects of the pain process with input from at least three disciplines (e.g., medicine, physiotherapy, psychology; Hechler et al.,2015).). Integral to the success of chronic pain treatment is the ability of treatment participants to engage effectively in some level of self-management. Self-management can be defined as "*the individual's ability to manage the symptoms, treatment, physical and psychological consequences, and lifestyle changes inherent in living with a chronic illness*" (Barlow, Wright, Sheasby, Turner, & Hainsworth, 2002, p.178). For chronic pain, this involves increasing and modulating physical activity, engaging in relaxation (reducing physiological arousal), problem solving, regulating emotions and mood, health-related stress-management, attention modulation, acceptance-based strategies, and adhering to a recommended medical treatment plan. Adolescence is a crucial stage in development where individuals increasingly take responsibility for key domains of chronic pain self-management. Successful execution of this self-management is crucial to offset potential lifelong pain-related disability. However, adherence to pain treatment regimens and associated relevant self-management tasks is highly variable amongst adolescents with chronic pain (Simons, Logan, Chastain, & Cerullo, 2010). Although not pain-specific, evidence across pediatric chronic illnesses suggests that adolescents' adherence to self-management is worse compared to younger children and adults (e.g., Costello et al., 2016). To date, little is known about factors that may exacerbate or ameliorate this lack of adherence. One factor, which is

under-investigated but highly likely to be relevant, is the role of executive functioning skills, including their effect on emotional regulation.

Executive functions - cognitive processes that underpin the ability to work towards goals and effortfully self-regulate behavior (Miyake & Friedman, 2012) - display erratic growth during adolescence (Sawyer, Azzopardi, Wickremarathne, & Patton, 2018). While executive functioning improves throughout childhood, some aspects (e.g., working memory) show a dip in performance during early adolescence due to rapid changes in brain structure and functioning (Blakemore & Choudhury, 2006) and most executive processes continue to develop into early adulthood (Taylor et al., 2013). The implications of this cognitive immaturity on adolescents' capacity to effectively self-manage their chronic pain remains unknown and forms the basis of the present topical review.

Executive functioning

For the purpose of this review, we focus on three generally accepted core components of executive functions (EF): inhibition (the ability to ignore irrelevant information and suppress automatic/inappropriate responses), working memory (the ability to monitor and update information in your mind), and cognitive flexibility (the ability to shift readily between tasks and mental sets, and to adapt behaviors to changing demands) (Diamond, 2013; Miyake et al, 2000). As more efficient EF is associated with an increased likelihood of goal attainment, adequate development of EF has wide-spread beneficial impacts across academic, career, health and social domains (Diamond, 2013; Pandey et al., 2018).

EF skills also are particularly relevant to the development of efficient emotional regulation (ER), such as positive reframing of negative emotions (Lantrip et al., 2016). Successful ER reflects the capacity to inhibit, delay, or modify emotions or emotional expression consistent with social norms to avoid negative consequences (Steinberg, 2005). This ability is essential in forming durable social relations and modulating one's emotional state and may in turn,

enhance EF skills (such as decision-making) by increasing expression and experience of positive emotions and broadening perceptions of interconnections among thoughts and ideas (Bandura, Caprara, Barbaranelli, Gerbino & Pastorelli, 2003). Consequently, the development of EF and ER cannot be investigated in isolation (Steinberg, 2005) and needs to be considered in tandem for a comprehensive understanding of how developmental challenges in regulation skills influence adolescent self-management.

Executive functioning and emotional regulation in the context of pain

In the context of pediatric chronic pain, preliminary findings in adolescents with sickle cell disease illustrate that general parent-reported EF levels play a key role in how adolescents cope with pain, for example by enabling effective shifting of attention away from pain, and thus improving adolescents' wellbeing (Ludwig et al., 2018). Optimal working memory is also required for other self-management tasks, like remembering to take pain medications and keeping up with schoolwork despite frequently missing school (Mifflin et al, 2016). Furthermore, in adolescents with Juvenile Idiopathic Arthritis, adaptive regulation of intense negative emotions (i.e., effective ER) was related to reduced functional disability*;* adolescents who were more able to regulate their emotional response to pain were less likely to avoid or reduce activity (Connelly et al., 2012). Consequently, optimal cognitive flexibility, inhibition and ER skills are each likely to be of importance for successful implementation of different non-pharmacological coping strategies (e.g., relaxation, controlling thoughts, and goal setting). Continued engagement with more general health behaviors (e.g., exercising regularly) on the other hand, may require multiple components of EF (Allan et al., 2015).

Although EF and ER likely play a key role in supporting successful pain self-management, research suggests that about half of adolescents with chronic pain, who seek treatment at a tertiary pain clinic, struggle with EF tasks, such as sustained attention and working memory (Mifflin et al., 2016; Weiss et al., 2018). This aligns with findings in adults with chronic pain

who demonstrate deficits across all three components of EF, and associated difficulties in the completion of everyday tasks (Berryman et al., 2014; Moriarty, McGuire & Finn, 2011). However, the exact relation between chronic pain and EF deficits is unclear. When pain is experimentally induced in healthy adults, low inhibitory capacity (i.e., weak EF) is related to slower extinction of pain-related fear and pain expectancy. These slower extinction rates, due to pre-existing weaker inhibition skills, could motivate widespread avoidance of activities anticipated to induce pain and thereby contribute to the development of pain-related disability (Niederstrasser et al., 2017). Furthermore, pre-existing difficulties with cognitive flexibility and working memory have also been linked to the development of post-surgical chronic pain in adults (Attal et al., 2014).

In sum, the available evidence across pediatric and adult pain literature points to a potential circularity between EF and chronic pain where impaired, immature or less efficient EF can be a predisposing factor to the development chronic pain; and chronic pain can reduce an individual's ability to effectively engage EF and associated ER skills. That in turn perpetuates chronic pain via reduced engagement in helpful, and increased engagement in unhelpful, self-management behaviors. Despite this accumulating evidence, our theoretical understanding of the mechanisms is lacking (Berryman et al., 2014). It is unknown to what extent, how, and which aspects of EF predispose the development of or are affected by chronic pain or when these impairments become apparent. Although adolescence is a sensitive period in the development of EF and a time which increasingly requires successful self-management, few studies have investigated EF in adolescents with chronic pain. Furthering understanding of the relation between EF and chronic pain will be crucial to optimize self-management support and provide insight into the etiology and maintenance of chronic pain symptoms and disability (Berryman et al., 2014). To advance this field, a guiding theoretical framework and awareness of the methodological challenges will be fundamental.

Cyclical model Of Pain, Executive function, emotion regulation and Self-management (COPES)

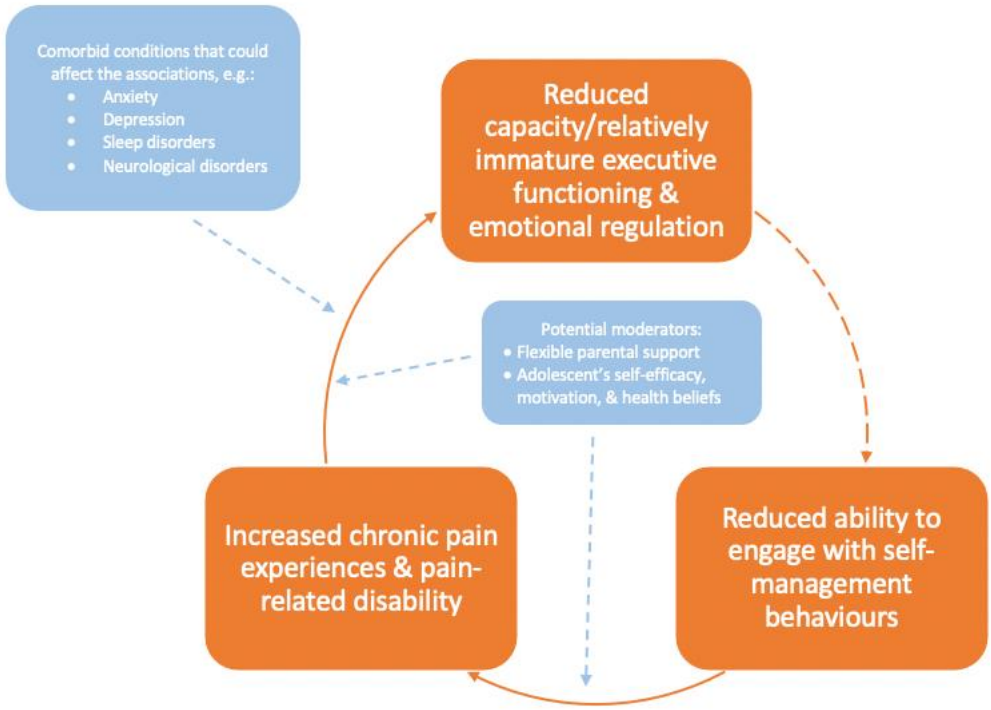
The preliminary evidence highlighting the circularity between EF and chronic pain resembles the "Cyclical Model of EF and Health" proposed by Allan and colleagues (2015). This model postulates that individuals with stronger EF across all three core domains are more likely to successfully engage in effortful health behaviors (e.g., physical activity, healthy eating), which in turn further improves EF and the chances of continued engagement in health behaviors. Our proposed model, the "Cyclical model Of Pain, Executive function, emotion regulation and Self-management" (COPES, see Figure 1, full lines represent associations with established evidence, while dotted lines represent hypothesized relations) applies the cyclical principals of Allan and colleagues' (2015) model to the context of pediatric chronic pain. Based on the evidence summarized above (e.g., Ludwig et al., 2018), the COPES model proposes that any deficit in EF and associated ER in adolescence (whether resulting from developmental immaturity, impairment or natural interpersonal variation) will negatively influence the ability of adolescents with chronic pain to engage with appropriate self-management. While suboptimal EF/ER is not inevitable, reduced functioning is more likely experienced in this group given the developmental stage and chronic exposure to pain. In the proposed model, EF/ER efficiency is conceptualized to be on a continuum from impairment through 'normal' to optimal functioning. Any progression along this continuum, regardless of starting point would be hypothesized to have an impact on self-management. For instance, reduced working memory or attention skills have been found in adolescent chronic pain, which is anticipated to negatively impact their ability to engage in coping strategies to reduce the impact of pain on academic achievements (Mifflin et al., 2016; Weiss et al., 2018). As evidence supports the efficacy of IIPT in improving functional recovery (Hechler et al., 2015), we assume that this reduced ability to engage in self-management will in turn increase adolescents' disability due

to pain (e.g., social isolation, reduced wellbeing), thereby contributing to the maintenance of chronic pain. Furthermore, given the important role of EF in ER, poorer EF skills in adolescents with chronic pain could also reduce the ability to cope emotionally with challenges, thereby contributing to the common comorbidity of anxiety and depression (Asmundson & Katz, 2009). Lastly, despite limited evidence in adolescence, evidence within adults (e.g., Moriarty et al., 2011) suggests that persistent experience of chronic pain has itself the ability to perpetuate the reduced capacity of EF skills by draining cognitive resources, introducing a cyclical element to the model.

Because the family social context cannot be overlooked throughout childhood development, the model includes a moderating influence of flexible parental support that is hypothesized to offset some of these influences. Despite increased adolescent autonomy, the family environment continues to influence the adolescent's pain management decisions (Palermo, Valrie, & Karlson, 2014). Evidence across various chronic illnesses (i.e., sickle cell disease and diabetes) indicates that overinvolvement of parents is related to more functional disability (Oliver-Carpenter, Barach, Crosby, Valenzuela, & Mitchell, 2011), while appropriate parental involvement, in the form of shared responsibilities and decision making, seems optimal (Helgeson, Reynolds, Siminerio, Escobar, & Becker, 2008). For example, in the context of diabetes, parent-child agreement on who takes responsibility for condition-related tasks and increased levels of EF were associated with greater self-management and adherence, which, considerably improved quality of life (Smith, Kugler, Lewin, Duke, Storch & Geffken, 2014). It is reasonable to assume that parental support may moderate the relations between relatively immature EF and engagement with/adherence to self-management tasks by acting as their child's "frontal lobe". However, at present, no evidence on the potential buffering role of flexible parental support is available in the context of adolescents' pain self-management,

preventing us from identifying which other associations outlined within the COPES model are moderated by parental flexible support.

Figure 1: Graphical representation of the Cyclical model Of Pain, Executive function, emotion regulation and Self-management (COPES). Full lines represent associations with established evidence, while dotted lines represent hypothesized relations.



Future research agenda & Methodological challenges

The present review highlights several priorities for future research: 1) clarification of the bidirectional relationship between chronic pain and impaired EF/ER; 2) identification of the specific EF/ER skills that are crucial for adolescents to effectively self-manage chronic pain; 3) exploration of the associations between EF/ER and pain in various sub-populations of adolescents with chronic pain and comorbidities known to influence EF/ER capacity, such as adolescents with anxiety, depression, sleep impairments and neurological deficits (e.g., ADHD, ASD); 4) further investigation of the moderating effect of parental support in the

successful self-management of chronic pain in adolescence; and, 5) exploration of other potential moderators (e.g., factors or processes such as self-efficacy, motivation, and health beliefs) in future research to further refine the COPES model.

In addition, several methodological challenges need to be overcome to advance our understanding of the cyclical relationship between EF/ER and chronic pain and how this in turn impacts self-management behaviors.

First, while it is generally agreed that EF encompasses three distinct but overlapping domains, definitions and measures of EF vary from study to study (Allan et al., 2015; Miyake et al., 2000), making it difficult to compare findings. For example, a recent scoping review identifies more than 300 different EF measures in studies of adolescents since 2002 (Nyongesa et al., 2019). Moving forward, a focus on utilizing common measures to allow evidence synthesis and within this, prioritize measures which: 1) assess multiple executive components; 2) are available in a standardized form; and 3) report adequate validity and reliability, is necessary. For self-report, the Behavior Rating Inventory of Executive Function (BRIEF; Gioia, Isquith, Guy & Kenworthy, 2000) is a comprehensive and psychometrically robust scale assessing both general EF and specific sub-domains of interest. Performance-based measures, while objective, are typically more challenging and time-consuming to administer, and (due to their reliance on novelty and speeded tasks) often display less robust reliability and validity over repeated administrations. However, such measures do enable comprehensive assessment of all facets of EF. Two of the best validated and most frequently used batteries of performance-based measures are the Delis-Kaplan Executive Function System (Delis, Kaplan & Kramer, 2001) and the executive function module of the Cambridge Neuropsychological Test Automated Battery (De Luca et al., 2013). Similarly, while there are a wide variety of adherence measures available across pediatric chronic illnesses (Plevinsky et al., 2020), there is a lack of a validated and reliable assessment for adherence to pain self-management tasks

and behaviors. There is an urgent need to reach a consensus on the key tasks and behaviors that compose pain self-management and a standardized tool to assess them. While self-management is primarily considered to reflect specific self-management skills and behaviors, we posit that it is also important that self-management research includes a focus on broader variables related to the implementation of these behaviors including behavioral activation, motivation, and self-efficacy.

Second, despite adolescence being recognized as a critical stage for the development of EF/ER, studies examining EF/ER in adolescents with chronic pain are scarce. Interpretation and generalization of existing findings is hampered by small sample sizes, lack of comparison with a pain-free sample and focus on one or two aspects of EF (an inherently multi-faceted construct). Of the known facets of EF, attention and working memory have received the most scrutiny to date within the context of pain. In contrast, there has been little research attention on facets of EF such as inhibition and cognitive flexibility, despite their likely relevance to adolescent pain self-management (e.g., their involvement in suppressing unhelpful thoughts and emotional responses to pain, and in the ability to deal flexibly with challenges as they arise). Comprehensive assessment across the full EF construct and comparison with a pain-free control group is needed to identify which EF skills are most affected by chronic pain yet necessary for appropriate engagement in self-management.

Third, a lack of longitudinal studies of EF and chronic pain results is limiting insight into the time course and directionality of reported associations. Prospective investigations early in adolescence will be important to test the proposed cyclical model and provide clarification on whether chronic pain reduces the capacity of EF skills and/or whether relatively immature or impaired EF skills are a risk factor to develop chronic pain. Early adolescence presents an ideal timepoint to explore these associations, as it represents a sensitive period for the onset of chronic pain and the development of EF skills.

Implications

It is anticipated that the COPES model will stimulate more systematic, theory-driven research to further our understanding of the links between EF/ER, chronic pain, self-management and wellbeing. Such enhanced understanding has the potential to drive forward intervention development and refinement aimed at improving self-management uptake and adherence amongst adolescents with chronic pain. The COPES model is ideally suited to foster such theoretical and clinical research as cyclical models open up the possibility for exploring vicious cycles (when we do not intervene) and virtuous cycles (when an intervention prevents negative impact). The description of the COPES model above illustrates the likely vicious cycle, however, an alternative virtuous cycle can be identified, whereby interventions may interrupt the negative impact of immature EF/ER, thereby improving engagement with self-management behaviors and associated functioning, and in turn further improve EF/ER impairments.

Interventions could either be targeted at improving EF and associated ER relevant for self-management or at reducing the EF/ER demands associated with self-management by adjusting the tasks or the environment (e.g., supportive parental involvement). Recent preliminary evidence shows that intensive cognitive training can improve EF skills in a small sample of adults with chronic pain (Baker et al., 2018). However, improved EF did not translate into a significant immediate impact on clinical and functional outcomes (e.g., pain interference, self-efficacy) and the underlying mechanisms of change were unclear. Furthermore, a case series study in adolescents with chronic pain highlighted that treatment approaches focused on enhancing ER reduced their functional disability (Allen et al., 2012). It would be worthwhile to further investigate, whether self-management and improved functioning could be better facilitated through incorporating cognitive training aimed at specific EF skills (e.g. attention regulation), emotional regulation (e.g., mindfulness training) or approaches to reduce the

cognitive demands of self-management tasks (e.g., structuring the tasks differently; Diamond, 2013) within the early phases of an IIPT approach.

In conclusion, we propose the COPES model as a means to encourage more systematic research on the potentially cyclical relationship between chronic pain and executive function in adolescence. The model can be used to generate testable hypotheses about pain-related determinants and consequences of changes in the executive skills that underpin successful self-regulation.

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