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## RESEARCH ARTICLE

# The Role of Executive Functioning in Understanding Chronic Pain Experiences in Adolescence: A Pilot Multi-Method Study

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## ABSTRACT

**Background:** Optimal executive functioning is pivotal to successful self-management of chronic pain (e.g., by being able to adapt self-management behaviours to changing situations), thereby contributing to improved health-related quality of life. However, preliminary evidence points to impaired executive functioning in people with chronic pain. Despite adolescence being identified as a sensitive period for the development of appropriate self-management and executive functioning skills, little is known about the associations between chronic pain and executive functioning performance in adolescents. The aim of the study was to pilot a multi-method approach to compare executive functioning, chronic pain, and quality of life between adolescents with and without chronic pain.

**Methods:** A sample of 22 adolescents with chronic pain (12-18 years, 82% female, mean chronic pain duration = 6.68 years) and 13 pain-free adolescents (age and sex matched) participated. All participants completed a battery of neuropsychological tasks to assess the three key executive functioning components (i.e., inhibition, working memory and cognitive flexibility) and provided self-report on their executive functioning, pain experiences and health-related quality of life.

**Results:** In addition to confirming the feasibility of the methods, data revealed that 23-62% of adolescents with chronic pain showed problematic performance, using normative scoring, in all three executive functioning components and showed significantly lower performance on all three executive functioning components compared to pain-free adolescents. Self-reported, but not neuropsychologically assessed, working memory and emotional control difficulties were associated with more pain-related interference and lower health-related quality of life.

**Conclusion:** These preliminary findings reveal the critical need to screen for and address any potential deficits in executive functioning in adolescents with chronic pain to optimise their self-management of pain and subsequent health-related quality of life. The findings also illustrate the feasibility of and need for future systematic, multi-method and prospective investigations in larger samples to further clarify the cyclical associations between chronic pain and executive functioning in adolescents.

**Keywords:** adolescent; chronic pain; executive function; emotion regulation; quality of life

## 1. Introduction

Executive functioning is defined as the capacity to coordinate our thoughts and behaviours, with three core components: *inhibition*, working memory and cognitive flexibility<sup>1</sup>. Inhibition is the ability to ignore irrelevant information and suppress automatic and/or inappropriate responses; *working memory* is defined as the ability to monitor and update information in your mind; and *cognitive flexibility* reflects the ability to shift readily between tasks and mental sets, as well as to adapt behaviours to changing demands<sup>1</sup>. Adequate development of executive functioning has widespread beneficial impact ranging from academic and career achievements, engaging in healthy behaviours, marital harmony, and optimal mental and physical health<sup>1,2</sup>. Of particular interest for the current study, optimal executive functioning skills are pivotal to successful self-management of chronic illness, such as chronic pain (i.e., pain lasting for more than 3 months), thereby contributing to improved health-related quality of life (HRQOL<sup>3,4</sup>). Adolescence has been identified as a sensitive and vulnerable period characterised by an erratic growth in executive functioning skills<sup>5</sup>: 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<sup>6</sup>. Furthermore, preliminary evidence indicates that this normative development of executive functioning can be impaired by chronic stressors, such as chronic pain<sup>7,8</sup>.

Chronic pain is a common, widespread, and costly public health concern across the lifespan, affecting 19% of adults<sup>9</sup> and up to 30% of children and adolescents worldwide<sup>10</sup>. Chronic pain has the potential to negatively affect the person's HRQOL due to associations with higher levels of depression, limited ability to work/attend school, sleep problems, difficulty to maintain relations and health care usage<sup>9,11</sup>. Despite the evidence of impaired executive functioning across all three domains in adults with chronic pain, a comprehensive understanding of the mechanisms underpinning these impairments is lacking<sup>12</sup>. It is unknown to what extent, how, and which aspects of executive functioning are affected by chronic pain experiences. Importantly, despite adolescence being crucial stage in development for both executive functioning and chronic pain, few studies have investigated the role of chronic pain on executive functioning performance in adolescents with chronic pain<sup>3,7</sup>. Indeed, prevalence of chronic pain increases from adolescence onwards<sup>10</sup>, which together with the observed erratic growth of

executive functioning skills across adolescence, further supports adolescence as a critical period to understanding the associations between chronic pain and executive functioning.

Based on this preliminary evidence, a theoretical framework, the Cyclical model Of Pain, Executive function, emotion regulation and Self-management (COPEs) was developed<sup>13</sup> to guide future research in this area. COPEs proposes a central role for executive functioning and associated emotional regulation abilities (i.e., capacity to control emotions) to explain the chronicity of pain and pain-related interference in adolescents. However, the limited available evidence is also hampered by methodological shortcomings: most available studies relied on self-report, rather than formal neuropsychological assessment, only assess one aspect of the inherently multi-faceted executive functioning construct and few studies compare with pain-free adolescents<sup>13</sup>. Consequently, there is a compelling need for a comprehensive comparison of the performance of adolescents with chronic pain with pain-free adolescents across all three core components of executive functioning, using standardised neuropsychological assessments. Such knowledge not only represents an important theoretical advancement (i.e., by either confirming or identifying a need for alteration of the proposed mechanisms in COPEs) but is also critical to provide targeted support aimed at preventing the potential negative consequences of impaired executive skills.

The aim of this pilot study was to evaluate the feasibility and utility of a multi-method approach to assess and compare the associations between executive functioning, chronic pain, and HRQOL in adolescents with and without chronic pain. The study aimed to answer the following research questions:

1. Is the multi-method approach to assess and compare executive functioning, pain experiences, and HRQOL between adolescents with and without chronic pain feasible and acceptable in terms of recruitment rate, participant's engagement, and burden?
2. Do adolescents with chronic pain **report** a tendency for more problems with executive functioning skills compared to adolescents without chronic pain?
3. Do adolescents with chronic pain **show** a tendency of lower executive functioning skills compared to adolescents without chronic pain?
4. How is executive functioning associated with the adolescent's chronic pain experience and HRQOL?

## 2. Materials and method

### 2.1 Participants

Adolescents with chronic pain were approached by their pain management consultant during their appointment at the Royal Hospital for Children, Glasgow. Any adolescent between the ages of 12 and 21 with an experience of pain rated at least  $>3/10$  on most days in the past 3 months was invited. Additional inclusion criteria included 1) having the capacity to give informed consent; 2) able to read, write, speak English to the level required to complete study tasks; 3) being unmarried and financially reliant upon parent(s); and 4) residing at home with parental caregiver(s) or attends college (living on- or off-campus). Exclusion criteria included having 1) a condition that would make taking part in the research too distressing or difficult; and 2) communication problems or diagnosed learning impairment that would make participation impossible. A total of 56 adolescents and their parents were approached by the pain consultants between August 2019 – February 2020, of which 46 families (82%) expressed an interest to receive more information about the study. A total of 8 families (17%) did not meet the eligibility criteria (e.g., needed an interpreter or adolescent had an impairment preventing participation) and 16 families (35%) declined to participate. Main reasons for non-

participation included lack of interest from either the adolescent or parent and difficulties to commit the time to the study. In addition, 4 adolescents with chronic pain found out about the study via advertisement through charities, such as [removed for blind review purposes], resulting in a final sample of 22 adolescents with chronic pain. The mean age of participants with chronic pain was 15.09 years (SD=1.72, range 12-18 years). Most participants were females (n=18; 82%). The mean duration of the chronic pain experience was 6.68 years (SD=4.14 years, range: 1-15 years). Participating adolescents were diagnosed with a range of pain conditions (see Table 1 for details), with 9 (41%) reporting more than one pain condition. Most adolescents lived with both of their parents at the time of the study (n=13; 59%) and identified with as “white” [n=19 or 86.4%; n=2 (9.1%) identified as “African” and n=1 (4.5%) identified with a mixed race]. Most participating parents of adolescents with chronic pain were mothers (n=18; 82%) with an average age of 44.63 years (SD=7.58 years, range: 33 – 59 years). Most parents had received at least an advanced higher diploma (n=13 or 59%; i.e., an upper secondary education programme designed to complete secondary education in preparation for tertiary education).

**Table 1:** Range of pain conditions

Pain condition	Frequency
Arthritis	4
Amputation pain	1
Inflammatory Bowel Disease	1
Headaches	5
Vascular Necrosis	1
Chronic constipation	2
Chronic recurrent multifocal osteomyelitis (CMRO)	1
Scoliosis	3
Complex Regional Pain Syndrome	2
Ehlers Danlos	1
Nerve damage	2
Hip dysplasia	1
Muscular dystrophy	1
Joint damage due to trauma	1
Neurofibromatosis	1
General pain syndrome	1
Unknown cause for pain	3

Pain-free adolescents were recruited through self-identification via posters in school/college settings and social media. Similar inclusion and exclusion criteria were used with the exception that this pain-free comparison group could not have had a pain rating of at least  $>3/10$  on most days in the

past 3 months. Furthermore, every pain-free participant was matched to a participant with chronic pain with the same sex and age ( $\pm 1$  year), resulting in a sample of 13 adolescents without chronic pain with the same sex distribution (n=9 females; 69.2%) and a mean age of 14.23 years

(SD=1.74; range 12-17 years). Recruitment of pain-free participants only started once 10 adolescents with chronic pain had taken part, as this allowed the research team to execute a targeted recruitment strategy to match on age and sex. However, during recruitment of the pain-free adolescent sample, the COVID-19 pandemic started. Any interested participants that had signed up for the study before the implementation of COVID-19 social restrictions (i.e., lockdowns) still took part remotely, using Microsoft Teams software. However, recruitment of new participants had to be halted, as any non-critical studies were paused due to social restrictions rules, and could not be resumed before the end of the grant period, resulting in a smaller sample of 13 adolescents without chronic pain. Most pain-free adolescents lived with both of their parents at the time of the study (n=9; 69.2%) and all identified as White. All but one participating parent were mothers (n=12; 92.3%), with an average age of 47.31 years (SD=4.19 years, range: 42-55 years). All parents had received at least an advance higher diploma.

### 2.3 Procedure

Ethical approval was obtained by the South East Scotland REC 01 [19/SS/0085]. When families of an adolescent with chronic pain expressed an interest in the study to their pain consultant (n=18), they briefly met with the principal researcher after their appointment to gain more information about the study and provide their contact details for a follow-up phone call. Families who saw the advertisement flyer (n=17) contacted the researcher directly via email or phone to express their interest. In either case, the researcher called families within two days of their expressing an interest. During the call, the researcher provided more information, checked their eligibility for participation and booked a study visit appointment.

The multi-method assessments took place during a single session (maximum duration=120 minutes) at the participant's home. Prior to starting the data collection, detailed study information was provided verbally to both the adolescent and their parents/carer, highlighting who is taking part, what they are committing to, and that they can withdraw at any time. Parents/carers and the adolescents were also provided with an information sheet to read through. The researcher answered any questions the adolescent and/or the parent/carer had at this time. After reading through the information sheet, all parents/carers and adolescents over the age of 16 years provided written consent for their participation in the study. Parents/carers of any participant under age 16

provided consent for their child to participate in the study, while adolescents younger than 16 provided written assent for their participation in the study. The results reported in this manuscript represent a selection of the data gathered as part of a larger project. The protocol of the full project can be found at <https://osf.io/zxy4i/#>.

During the multi-method assessment, adolescents and parents/carers were first asked to complete questionnaires on the adolescent's pain intensity and interference, executive functioning, and HRQOL. Following questionnaire completion, the adolescent completed four subtasks of the neuropsychological Dallas-Keplin Executive Functioning System (D-KEFS) battery assessing executive functioning, in a randomised order, and two subtests of the Wechsler Intelligence Scale for Children (WISC-V; for adolescents 12-15 years of age) or the Wechsler Adult Intelligence Scale (WAIS-IV; for adolescents >15 years of age) assessing working memory. Families received £20 to reimburse them for their time in participation in this home-based assessment phase.

For the 7 pain-free adolescents who participated during the COVID-19 lockdowns, a similar procedure was followed, but instead of going to the participant's home, participation took place remotely via Microsoft Teams. In advance of the participation date, participants were sent a paper copy of all the study materials (e.g., information sheet and consent form, questionnaires, D-KEFS work sheets) in a sealed envelope. Participants were instructed not to open the envelope until their participation session, during which the researcher walked through all the same steps as described above, using the screen sharing ability of Microsoft Teams when needed for the D-KEFS tasks (e.g., the Color-Word Interference booklet).

## 2.2 Measures

### 2.1 Executive functioning

Adolescents' executive functioning skills were assessed by both neuropsychological tasks and self-report. In terms of neuropsychological tasks, executive functioning was assessed by four subtests of the validated D-KEFS<sup>14</sup>. The D-KEFS is a battery of nine stand-alone tests to measure different manifestations of executive functioning, covering the three core components, across the lifespan<sup>14</sup>. Based on the D-KEFS factor structure and loadings identified by Latzman and Markon (2010)<sup>15</sup>, four subtests, with adequate internal consistency and test-retest reliability for participants aged 12-19 years<sup>14-16</sup> were selected to best represent the three core components: Trial Making Test, Verbal Fluency

Test, Color-Word Interference, and Sorting Test. For each of the subtests, the raw scores were converted to scaled scores (available for ages 12, 13, 14, 15 and 16-19) with a mean of 10 and standard deviation of 3 with a higher score reflecting better performance<sup>14</sup>. However, throughout data collection, it became apparent that many adolescents had difficulties understanding the instructions of the Sorting Test (e.g., the instructions still did not seem clear for various participants even after the example trial). In addition, the Sorting Task did not convert well into online assessment via Microsoft Teams. Consequently, to avoid confounding of the findings, we decided not to use the Sorting Test within the analyses, as we are confident that the remaining tasks still cover all three core components of executive functioning.

- The *Trail Making Test* is a visual motor sequencing task, measuring the flexibility of thinking and therefore represents both **inhibition**<sup>40</sup> and **cognitive flexibility** skills<sup>24</sup>. The Number-Letter Switching score was used in the analyses, which represents the time it takes for the participants to complete the task of alternating connecting numbers and letters in the correct order (i.e., 1 – A – 2 – B – 3 – C ...).
- The *Verbal Fluency Test*, which measures letter and category fluency as well as the ability to shift between learned categories, represents the ability to monitor information or consciously manipulate content in your mind. While this test is not originally intended to assess **working memory**, the monitoring ability is closely linked to working memory skills. The Category Switching Total Correct and Total Switching Accuracy scores were used in the analyses. Respectively, these scores reflect the number of correct words generated across two categories (e.g., hypothetically “animals” and “cities”) and the total number of times the respondent switched correctly between the two categories (i.e., naming an animal followed by a city and vice versa)
- The *Color-Word Interference Test* measures a person’s ability to inhibit a dominant verbal response, such as inhibiting reading a word to allow identifying the colour of the ink the word is printed in and therefore represents **inhibition skills**. The Inhibition and Inhibition/Switching scores were used in the analyses, with scores reflecting the time it takes participants to complete the task [i.e., read the ink colour (for Inhibition score) and switch between reading ink colour and word (for Inhibition/Switching score)].

As the D-KEFS does not have a specific task assessing working memory, adolescents also completed Digit Span and Letter-Number Sequencing Task subtests of the validated WISC-V (for participants younger than 16 years of age) or the WAIS-IV (for participants aged 16 years of age and older<sup>17,18</sup>). For each task, a scaled maximum span score (i.e., maximum digit span total score and maximum letter-number sequencing total score) was calculated and used in the analyses. Scaled scores range from 1 – 19, with a mean of 10, with higher scores reflecting better skills.

To assess adolescents’ perceptions of their executive functioning, they completed the validated Behavior Rating Inventory of Executive Functioning 2<sup>nd</sup> edition (BRIEF-2)<sup>19</sup>. The BRIEF-2 contains 55 items assessing inhibition, self-monitoring, shifting, emotional control, working memory, plan/organise and task completion. Age-based T-scores for the subscales reflecting the three core components of executive functioning, i.e., inhibition, shifting, and working memory, as well as the subscale emotional control were used in the analyses. We decided to include the emotional control subscale into the analyses given close interrelation between executive functioning and emotional regulation and the important role that emotional regulation plays in managing chronic pain. Higher T-scores on the BRIEF-2 reflect more impairment for that executive functioning skill. T-scores between 60-64 are mildly elevated, scores between 65-69 are potentially clinically elevated, and T-scores above 70 are deemed to be clinically elevated. Internal consistency within the current sample was adequate for all subscales ( $\alpha_{\text{inhibition}}=.69$ ;  $\alpha_{\text{shifting}}=.88$ ;  $\alpha_{\text{working memory}}=.75$ ;  $\alpha_{\text{emotional control}}=.89$ ).

## 2.2 Pain experiences

All adolescents completed the validated and reliable PROMIS Pediatric Profile Pain Intensity and Interference scales to assess their level of pain intensity and interference with social, cognitive, emotional, physical, and recreational activities<sup>20</sup>. Participants rated their average pain intensity in the past 7 days using a 11-point numerical scale ranging from 0 (no pain) to 10 (worst imaginable pain). The pain interference scale consists of 8 items assessing adolescents’ pain interference (e.g., “I had trouble doing schoolwork when I had pain”) in the past 7 days, using a 5-point Likert scale ranging from 1 (Never) to 5 (Almost always). A total score was created by summing all the item responses, which was in turn rescaled to a standardised T-score with a mean of 50 and standard deviation of 10. Higher scores reflect more pain interference.

Excellent reliability of the Pain Interference scale was observed in the current sample ( $\alpha=.97$ ).

### 2.3 Quality of Life

All adolescents completed the validated and reliable PedsQL General<sup>21</sup>, which assesses adolescents' general HRQOL across various domains (i.e., physical, emotional, social, and academic) in the past month. Each of the 23 items is rated on a 5-point Likert scale from 0 (Never) to 4 (Almost Always) A transformed total score, ranging from 0 to 100, was calculated across domains with higher scores reflected better HRQOL. The reliability of the total score was excellent in the current sample ( $\alpha= .95$ ).

### 2.4 Analysis plan

All analyses were carried out using IBM SPSS Statistics v.23. Descriptive analysis (i.e., frequencies, means and standard deviations) and correlation analyses were performed on all assessed variables. Differences between adolescents with chronic pain and pain-free adolescents on neuropsychological assessment scores and self-report of executive functioning were analysed using independent samples *t*-tests. Within the sample of adolescents with chronic pain only, hierarchical linear regression analyses were conducted to explore the associations between chronic pain experiences (i.e., intensity and interference), executive functioning, and HRQOL. Associations or differences were considered statistically significant if the unrounded *p*-value was smaller than .05.

## 3. Results

### 3.1 Descriptives

#### 3.1.1 Feasibility of multimethod assessment

With respect to recruitment rate, all adolescents with chronic pain were recruited within the anticipated timeframe (i.e., 6 months: September 2019 until February 2020) and recruitment of pain-free adolescents went equally smooth [with over half of the targeted participants ( $n=13$ ) recruited in 3 months: January – March 2020] until the COVID-19 pandemic forced the team to halt any recruitment efforts.

On average, participation required approximately 2 hours with none of the participants complaining that study completion was too lengthy, but rather reporting enjoying the mix of activities. While breaks were offered, only two participants took a short break. Participants also commented that taking part in their own home was 'easy,' 'comfortable' and 'familiar' and avoided the need to travel.

The data collection procedure also proved feasible with COVID-19 social distancing measures in place: 20% ( $n=7$ ) of families successfully participated during the COVID-19 lockdown, with slight adjustments to the study procedures (e.g., completing all assessments via Microsoft Teams), which did not affect the completion rate of the assessments, nor the duration of or perspective towards study participation. The only task that did not successfully transfer to online assessment was the D-KEFS Sorting Task and thereby potentially confounding the utility of this task by violating standardized protocol processes. Participants could not move the cards themselves and rather had to instruct the researcher how to sort the cards, thereby changing the integrity of inherent task components and importantly introducing a time delay.

#### 3.1.2 Pain experiences

See Table 2 for the descriptive statistics of all variables assessed within the study, separately for the adolescents with chronic pain and the pain-free adolescents. While there was a large variation in the levels of pain intensity, pain interference, and HRQOL, on average, our sample of adolescents with chronic pain reported high levels of pain intensity and interference and low levels of HRQOL. Adolescents with chronic pain also reported on their pain intensity on the day of data collection, which was on average 5.78 ( $SD=1.75$ , Range: 2.5 – 8.5). Furthermore, compared to the pain-free adolescents, the adolescents with chronic pain reported significantly higher levels of pain intensity ( $t(33)=15.14$ ,  $p < .001$ ), pain interference ( $t(33)=9.16$ ,  $p < .001$ ) and lower levels of HRQOL ( $t(32)=-6.09$ ,  $p < .001$ ).

#### 3.1.3 Association between self-reports and neuropsychological measures of executive functioning

See Table 3 for the correlations between adolescent self-report of executive functioning skills and neuropsychological assessment of executive function. Strong correlations (i.e., ranging from .61 - .78) can be observed between the self-report scales. There are also several significant negative correlations between the self-report scales and neuropsychological tasks, which reflects that participants who rate themselves as more impaired in their executive functioning (i.e., have a higher score on the BRIEF subscales) also perform worse (i.e., have a lower score) on the neuropsychological assessments of their executive functioning skills. However, the correlations between particular BRIEF subscales and neuropsychological tasks were not always as expected based on the concepts that the scales and tasks are meant to assess. For instance,

the self-report of Inhibit only showed a significant negative correlation with the D-KEFS tasks assessing inhibition (i.e., for Inhibition & Inhibition Switching  $r=-.37, p < .05$ ). Furthermore, the self-report of Working Memory shows a significant negative correlation with the D-KEFS task chosen to assess working memory (Category Switching Total Correct:  $r=-.37, p < .05$  and Total Switching Accuracy scores:  $r=-.42, p < .05$ ). However, there is no significant correlation observed between self-report of working memory and the Digit Span nor Letter Number Sequencing score, while there is a

significant negative correlation with the D-KEFS task scores assessing inhibition (Inhibition:  $r=-.46, p < .01$ , Inhibition Switching:  $r=-.39, p < .05$ ) and cognitive flexibility (Number Letter Switching:  $r=-.58, p < .01$ ). Lastly, the self-report of Shift is significantly negatively correlated with one of the D-KEFS task assessing cognitive flexibility (Number Letter Switching:  $r=-.51, p < .01$ ). However, a significant negative correlation was also found with the D-KEFS task assessing inhibition (Inhibition:  $r=-.46, p < .01$ ) and the Letter Number Sequencing score assessing working memory ( $r=-.38, p < .05$ ).

**Table 2:** Descriptive statistics of all assessed variables

Variable	Adolescents with chronic pain				Pain-free adolescents			
	N	M	SD	Range	N	M	SD	Range
Pain Intensity in past week	22	6.84	1.15	4.00 – 9.00	13	.69	1.18	0.00 – 4.00
Pain Interference in past week	22	64.03	8.59	45.40 – 78.00	13	39.38	5.79	34.00 – 49.10
HRQOL	22	43.35	19.80	15.22 – 88.04	13	82.70	13.91	55.43 – 98.91
BRIEF2 – Inhibit	22	57.59	10.26	45.00 – 77.00	13	51.85	10.79	37.00 – 72.00
BRIEF2 – Shift	22	60.77	13.79	37.00 – 84.00	13	52.69	10.49	41.00 – 75.00
BRIEF2 – Working Memory	22	64.14	12.06	38.00 – 82.00	13	54.15	10.66	38.00 – 69.00
BRIEF2 – Emotional Control	22	60.73	12.58	38.00 – 82.00	13	53.38	10.92	42.00 – 73.00
Number Letter Switching	22	6.32	3.77	1.00 – 13.00	13	10.92	3.35	1.00 – 14.00
Category switching – Total correct	22	10.64	4.70	2.00 – 19.00	13	15.77	3.44	9.00 – 19.00
Category switching – Total switching accuracy	22	10.86	3.85	4.00 – 18.00	13	15.77	2.68	11.00 – 19.00
Inhibition	21	8.14	4.27	1.00 – 13.00	13	12.46	1.71	8.00 – 14.00
Inhibition Switching	21	8.67	3.40	1.00 – 13.00	13	10.85	1.72	7.00 – 14.00
Digit Span	22	8.14	2.96	1.00 – 13.00	13	11.69	3.03	7.00 – 17.00
Letter Number Sequencing	21	7.19	2.34	4.00 – 12.00	13	10.00	2.92	6.00 – 16.00

**Table 3:** Correlations between adolescent self-report and neuropsychological assessment of executive function skills

	BRIEF2 - Shift	BRIEF2 - Emotional control	BRIEF2 - Working memory	Digit Span	Letter Number Sequencing	Category switching - Total correct responses	Category switching - Total switching accuracy	Inhibition	Inhibition switching	Number letter switching
BRIEF2 - Inhibit	.695**	.617**	.708**	-.209	-.276	-.273	-.332	-.373*	-.365*	-.208
BRIEF2 - Shift		.629**	.765**	-.219	-.380*	-.289	-.320	-.460**	-.314	-.509**
BRIEF2 - Emotional control			.605**	-.414*	-.323	-.165	-.272	-.311	-.310	-.365*
BRIEF2 - Working memory				-.224	-.292	-.367*	-.421*	-.459**	-.386*	-.573**
Digit Span					.637**	.380*	.419*	.443**	.545**	.446**
Letter Number Sequencing						.236	.330	.532**	.467**	.518**
Category switching - Total correct responses							.877**	.500**	.397*	.434**
Category switching - Total switching accuracy								.440**	.369*	.482**
Inhibition									.766**	.629**
Inhibition switching										.442**

\*p<.05; \*\*p<.01

### 3.2 Do adolescents with chronic pain report a tendency for lower executive functioning skills compared to adolescents without chronic pain?

In the sample of adolescents with chronic pain, an elevated score (i.e., T-score > 59; categorized as mildly elevated, potentially clinically elevated, or clinically elevated) for reported inhibition and shifting skills was observed in 45.5% (n=10) of the adolescents. In comparison, for the sample of pain-free adolescents, only 23.1% (n=3) had a similarly elevated score for inhibition and shifting skills.

An elevated score for working memory skills was observed for more half of the adolescents with chronic pain (63.5%, n=14). Lastly, elevated scores for emotional control skills were also observed in over half of the sample of adolescents with chronic pain (54.4%, n=12). In comparison, for working memory and emotional control, 30.8% (n=4) of pain-free adolescents had an elevated score. See Figure 1 for the percentage of elevated scores (including mildly, potentially clinically and clinically elevated scores) for adolescents with chronic pain.

Breaking the elevated scores further down, in the sample of adolescents with chronic pain, a clinically elevated score (i.e., score of >70) was observed in 13.6% (n=3) for inhibition, 27.2% (n=6) for shifting skills and emotional control, and in 36.4%, (or n=8) for working. In comparison, in the sample of pain-free adolescents, a clinically elevated score was only observed in 7.7% (n=1) for inhibition and shifting skills, as well as in 15.4% (n=2) for emotional control. None of the pain-free adolescents received a clinically elevated score for working memory.

With respect to mildly elevated or potentially clinically elevated scores, in the sample of adolescents with chronic pain, this was observed in 31.7% (n=7) for inhibition, 18.1% (n=4) for shifting

skills, and 27.2% (n=6) for both working memory and emotional control. In comparison, for pain-free adolescents, a mildly elevated or potentially clinically elevated score was observed in 15.4% (n=2) for inhibition, shifting skills and emotional control, and in 30.8% (n=4) for working memory.

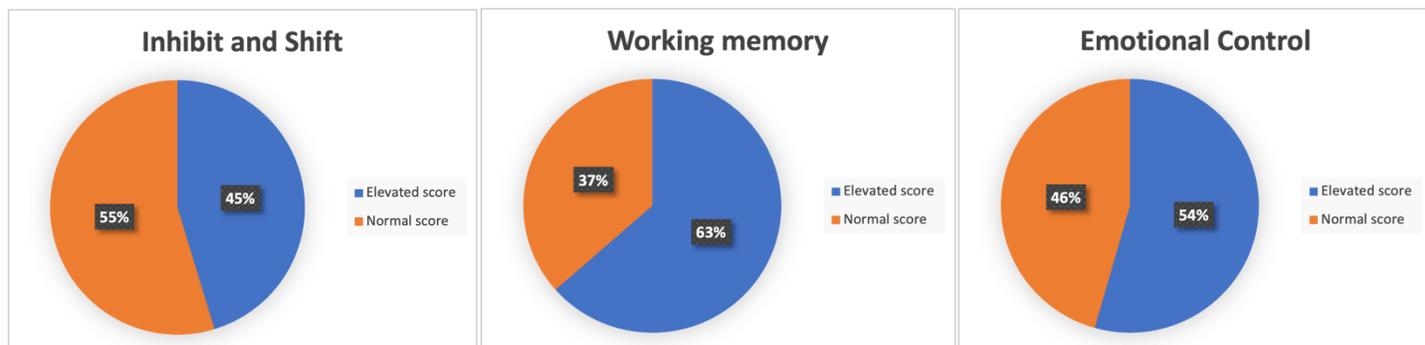
Direct comparison between the two samples, using independent sample *t*-tests, showed how only for working memory adolescents with chronic pain reported significantly more problems than the matched, pain-free adolescents ( $t(33)=2.47, p < .05$ ; see Table 2 for means and SD).

### 3.3 Do adolescents with chronic pain show a tendency for lower executive functioning skills compared to adolescents without chronic pain?

Using neuropsychological testing of adolescents' executive functioning skills, half of the sample of adolescents with chronic pain (50% or n=11) demonstrated a problematic performance (standardized norm score of 7 or lower), compared to only 7.7% (n=1) pain-free adolescent, for Number-Letter Switching component of the Trail-Making task, reflecting problems with both inhibition and cognitive flexibility skills.

For the Color-Word Interference task, reflecting inhibition skills, a problematic performance was observed for 38.1% (n=8) adolescents with chronic pain in the Inhibition component and 28.6% (n=6) of adolescents with chronic pain performed in the problematic range for the Inhibition Switching component. None of the pain-free adolescents received a problematic score for the Inhibition component, and only 7.7% (n=1) pain-free adolescent received a problematic score for the Inhibition Switching component.

**Figure 1:** Comparison of self-reported executive functioning of adolescents with chronic pain to norm scores.



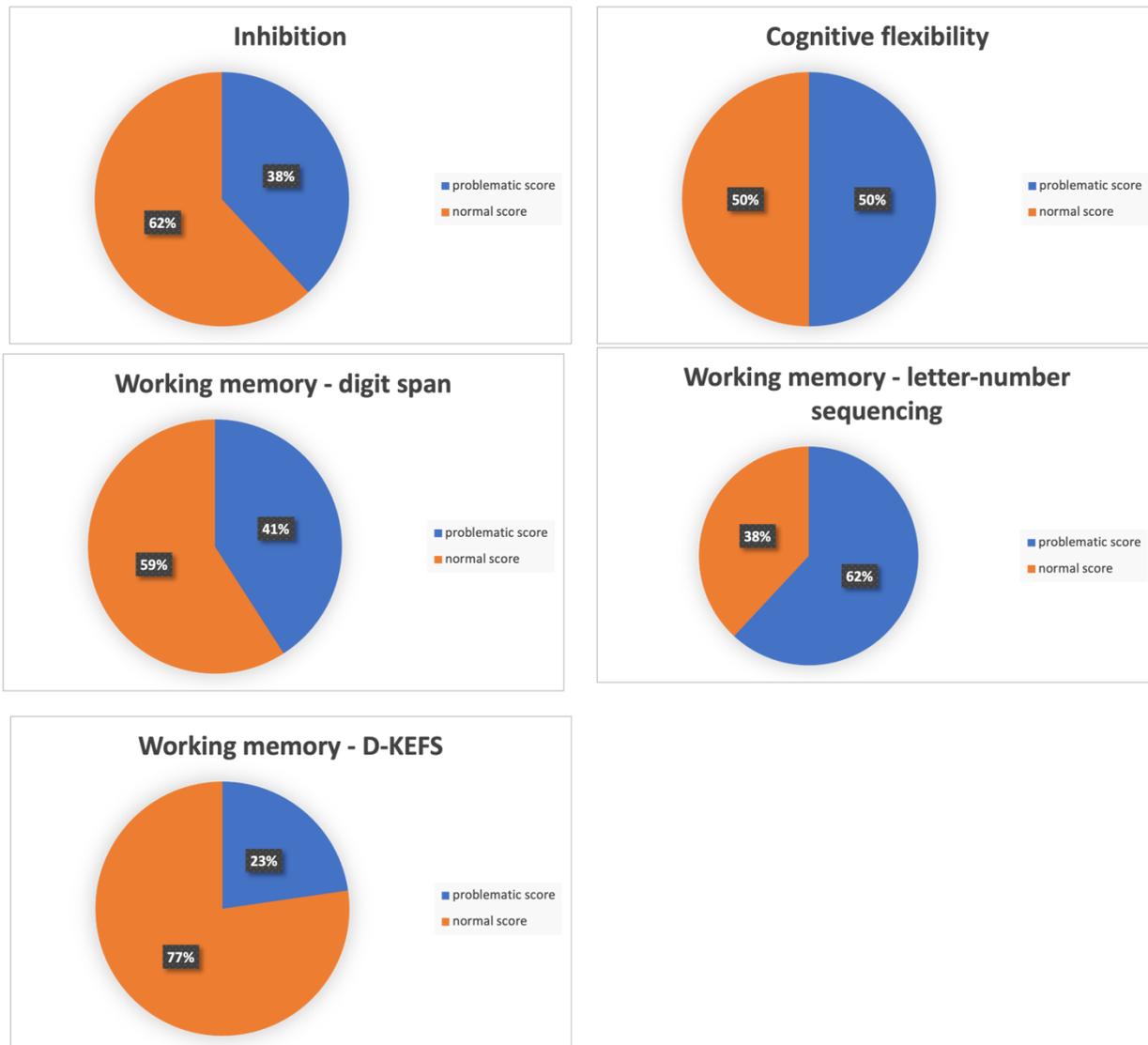
For the Verbal fluency task, reflecting monitoring skills, 22.7% (n=5) of the adolescents with chronic pain showed a problematic performance for both the total correct responses and accuracy of the Category Switching component. None of the pain-free adolescents received a problematic score for the total correct responses and accuracy of the Category Switching component.

Lastly, for the two tasks of the WISC-V/WAIS-IV reflecting working memory skills, a problematic score (standardized score of 7 or lower) was observed for 40.8% (n=9) of adolescents with chronic pain for the Digit Span task, while 61.9% (n=13) of adolescents with chronic pain received a problematic score for the Letter-Number Sequencing Task. In the sample of pain-free adolescents, only one adolescent (7.7%) obtained a problematic score for Digit Span and two

(15.4%) adolescents received a problematic score for the Letter-Number Sequencing Task. See Figure 2 for an overview of the scores for adolescents with chronic pain.

Direct comparison between adolescents with chronic pain and pain-free, matched adolescents, using independent sample *t*-tests, revealed that adolescents with chronic pain performed significantly worse on all the neuropsychological tasks assessing working memory [Digit span:  $t(33)=3.40, p < .001$ ; Letter-Number Sequencing Task:  $t(33)=3.10, p < .01$ ; Category Switching Total correct responses:  $t(33)=3.43, p < .01$ ; Category Switching Total accuracy:  $t(33)=4.04, p < .001$ ], inhibition [Inhibition:  $t(33)=4.13, p < .001$ ; Inhibition Switching:  $t(33)=2.14, p < .05$ ] and cognitive flexibility [Number Letter Switching:  $t(33)=3.63, p < .001$ ].

**Figure 2:** Comparison of neuropsychological scores for executive functioning of adolescents with chronic pain to norm scores.



### 3.4 How does executive functioning affects adolescent's chronic pain experiences and quality of life?

A total of six hierarchical linear regression analyses were conducted to evaluate the role of self-report or neuropsychological performance of executive functioning on adolescent's pain intensity, pain interference, and HRQOL. For all analyses, the control variable of adolescent age was included in the first step. For analyses with pain interference as an outcome, pain intensity scores were also controlled for in the first step. For analyses with HRQOL as an outcome, pain intensity and pain interference scores were additionally controlled for in the first step. Gender and pain duration were not included as control variables as exploration of the association of these variables highlighted that they did not make a significant contribution to the three outcome measures. In the second, and final step, either the self-reported executive functioning skills scores (i.e., BRIEF scores of Inhibit, Shift, Emotional Control or Working Memory) or the scores on the neuropsychological assessments (i.e., Category Switching Total Correct, Total Switching Accuracy, Inhibition, Inhibition/Switching, Number-Letter Switching, maximum digit span total score and maximum letter-number sequencing total score) were added. Below we report some trends of note here given that this is a feasibility study and recognize that these findings can only lead to speculation.

#### 3.4.1 Self-reported Executive Functioning

None of the variables showed a significant contribution to explaining *pain intensity* in the past 7 days (see Table 4), nor were the overall models tested significant.

For *pain-related interference*, beyond the contribution of pain intensity, a significant contribution was found for working memory ( $\beta=.51$ ,  $p < .05$ ), indicating that higher reported difficulties with working memory are related to more reported pain-related interference. A trend was found for self-reported emotional control ( $\beta=.42$ ,  $p = .055$ ), indicating that higher levels of self-reported problems with emotional control could be related to higher reports of pain-related interference (See Table 4).

Lastly, for *HRQOL* as an outcome, beyond the contribution of pain-related interference, a significant contribution was found for self-reported difficulties with emotional control ( $\beta=-.46$ ,  $p < .05$ ), indicating that adolescents with higher reports of difficulties with emotional control report lower levels of HRQOL. Self-reported working memory ( $\beta=-.37$ ,  $p = .066$ ), showed a trend towards explaining some variance in HRQOL, indicating that more self-reported problems with working memory could be related to lower reported HRQOL (see Table 4).

**Table 4:** Hierarchical linear regression analyses to evaluate the role of adolescent self-report or neuropsychological performance of executive functioning on adolescent's pain intensity, pain interference, and health-related quality of life.

Adolescent self-report of executive functioning					
Criterion variable	Step	Predictor	$\beta$	R <sup>2</sup> change	Adjusted R <sup>2</sup>
Pain intensity	1	Age	-.05	.01	-.04
	2	BRIEF2 -Inhibit	.01	.24	.01
		BRIEF2 - Shift	.15		
		BRIEF2 – Emotional control	.27		
		BRIEF2 – Working memory	.16		
Pain interference	1	Age	.20	.38*	.32*
		Pain intensity	.15		
	2	BRIEF2 -Inhibit	-.24	.36**	.63**
		BRIEF2 - Shift	.04		
		BRIEF2 – Emotional control	.42 <sup>+</sup>		
		BRIEF2 – Working memory	.52*		
Quality of Life	1	Age	.01	.64	.58***
		Pain intensity	.15		
		Pain-related interference	-.22		
	2	BRIEF2 -Inhibit	-.00	.22	.79**
		BRIEF2 - Shift	-.07		
		BRIEF2 – Emotional control	-.46*		
		BRIEF2 – Working memory	-.37 <sup>+</sup>		

Neuropsychological assessments of executive functioning					
Criterion variable	Step	Predictor	$\beta$	R2 change	Adjusted R2
Pain intensity	1	Age	.15	.03	-.02
		Number Letter Switching	-.23	.31	-.19
	2	Category switching – Total correct responses	.50		
		Category switching – Total switching accuracy	-.20		
		Inhibition	-.24		
		Inhibition switching	.73		
		Digit Span	.20		
		Letter Number Sequencing	.07		
Pain interference	1	Age	.21	.48	.41**
		Pain intensity	.81**		
	2	Number Letter Switching	.14	.24	.44
		Category switching – Total correct responses	-.11		
		Category switching – Total switching accuracy	-.26		
		Inhibition	.52		
		Inhibition switching	-.86*		
		Digit Span	-.48		
Quality of Life	1	Age	.06	.54**	.44
		Pain intensity	-.04		
		Pain-related interference	-.73**		
	2	Number Letter Switching	.19	.25	.51
		Category switching – Total correct responses	.15		
		Category switching – Total switching accuracy	.02		
		Inhibition	-.34		
		Inhibition switching	.28		
3	Digit Span	.47			
	Letter Number Sequencing	-.36			

<sup>+</sup> $p=.05$  - .10, \* $p < .05$ , \*\* $p < .01$ , \*\*\* $p < .001$

### 3.4.2 Neuropsychological assessment of executive functioning

Like the findings with self-reported executive functioning, none of the tested models for *pain intensity* were significant and none of the formally assessed executive functioning skills made a significant contribution to explaining pain intensity (see Table 4).

Only the first model (which did not include the neuropsychological assessment scores) tested for *pain-related interference* was significant, showing a significant contribution of pain intensity ( $\beta=.81$ ,  $p < .01$ ) in explaining pain-related interference (see Table 4). Despite the full model for pain-related interference not reaching significance ( $p=.09$ ), Inhibition Switching scores ( $\beta=-.86$ ,  $p < .05$ ) showed

a significant association with pain-related interference (see Table 4), indicating that adolescents with more problems in their inhibition skills could report higher levels of pain-related interference.

With respect to *HRQOL* as an outcome, only the first model (which did not include the neuropsychological assessment scores) was significant, with pain-related interference making a significant contribution ( $\beta=-.73$ ,  $p < .01$ ; see Table 4) in explaining HRQOL.

## 4. Discussion

The aim of this pilot study was to evaluate the feasibility and utility of a multi-method approach to assess and compare the associations between executive functioning, chronic pain, and

HRQOL in adolescents with and without chronic pain. The findings highlight how a multi-method approach, combining self-report and neuropsychological tasks, is feasible, acceptable (even enjoyed) by participants and allows for a comprehensive exploration of executive functioning, as well as associations with chronic pain experiences, in adolescents. Furthermore, the results reveal how all assessments of the three core components of executive functioning (i.e., inhibition, working memory and cognitive flexibility) are highly interrelated with each other. Lastly, the findings provide preliminary evidence that adolescents with chronic pain are at risk to report and show impairments across all 3 core executive functioning skills. Depending on the executive functioning skill reported on, 45-54% of adolescents with chronic pain received an elevated or problematic score. Over half (i.e., 54%) of the adolescents with chronic pain also reported elevated problems with emotional control. Furthermore, compared to the pain-free adolescents, adolescents with chronic pain reported significantly more problems in working memory. With respect to performance on neuropsychological tasks, depending on the assessed executive functioning skills, 23-62% of adolescents had a problematic performance. Across all three executive functioning skills, adolescents with chronic pain had a significantly worse performance compared to age- and sex-matched pain-free adolescents. Lastly, self-reported problems with working memory and emotional control contributed to higher levels of pain-related interference and lower levels of HRQOL. No associations were found for the neuropsychological assessments of executive functioning with pain experiences or HRQOL.

These findings align with and further extend previous findings which identified that about half of adolescents with chronic pain, who seek treatment at a tertiary pain clinic, struggle with sustained attention and working memory<sup>7,8</sup>. While findings in adults with chronic pain have demonstrated deficits across all three components of executive functioning, and associated difficulties in the completion of everyday tasks<sup>12</sup>, research in adolescents had so far mainly focused on working memory. To the best of our knowledge, this is the first study to comprehensively assess all three core components of executive functioning in adolescents with chronic pain and compare them to age- and sex-matched pain-free adolescents. In following such a systematic, comprehensive, and rigorous approach, these unique findings underscore that the difficulties extend beyond just working memory, but also impact cognitive flexibility skills to a similar level and inhibition skills to a lower extent.

Furthermore, our findings establish that these deficits are prevalent both in the objective, neuropsychological performance tests as well as adolescent's own perspective and report of their executive functioning skills.

Importantly, and like the findings from Ludwig and colleagues (2018), which were limited by only focusing on parent-reported executive functioning levels, these deficits, as reported by adolescents themselves, was also associated with the extent to which chronic pain disrupted their daily activities and HRQOL<sup>3</sup>. As there was no significant relation found with pain intensity scores, this highlights how executive functioning skills might play a unique role in how adolescents cope with the pain experience regardless of the intensity level of the pain. However, no association between the neuropsychological assessment of executive functioning skills and pain experiences, pain interference or HRQOL was found. This appears likely due to a lack of power, given the small sample size of this study and only variables with a medium to large effect sizes found to be significant. Furthermore, due to the large variety in reported pain intensity and interference, it was important to control for this in the analyses with pain interference and HRQOL, but given the small sample size, this could have inhibited finding any influence of neuropsychological assessments beyond the role of pain experiences. The main limitation of this pilot study is the small sample size, and most adolescents with chronic pain being recruited from a single outpatient clinic. Consequently, generalisability of the findings is limited, and further exploration and confirmation of these preliminary findings is needed within larger, more diverse samples.

The development of executive functioning skills is closely related and relevant to the development of efficient emotional regulation, which requires exploration of these skills in tandem rather than in isolation<sup>22</sup>. Our results indeed showed significant and strong positive (>.60) correlations between self-reports of emotional control on the one hand and working memory, inhibition and shifting on the other hand, thereby confirming their interrelation. Similar to the findings for executive functioning, about half of the adolescents with chronic pain reported problems with emotional regulation. Furthermore, self-reported problems with emotional regulations showed a contribution, beyond the impact of working memory skills, to adolescents' increased pain-related interference and reduced HRQOL. Understanding the substantial challenges many adolescents face with emotional regulation is of great clinical importance, as Connelly and colleagues (2012) identified that adaptive regulation of intense negative emotions is

an important self-management skill to reduce functional disability due to pain<sup>23</sup>. Taken together, our findings reveal a critical need to screen for and address any potential deficits in executive functioning, and associated emotional regulation, in adolescents with chronic pain. Given that optimal executive functioning and emotional regulation skills are crucial to be able to successfully engage with various components of pain self-management (e.g., remembering to take medication, engage in healthy self-management strategies including relaxation, activity management, goal setting, flexible problem solving, and controlling thoughts)<sup>3,7</sup>, addressing such deficits through dedicated interventions (e.g., cognitive training<sup>24</sup>) is key. It also has the potential to optimise adolescents' successful engagement with self-management and thereby off-set potential lifelong disability.

Beyond the clinical implications, these preliminary findings have important theoretical implications and suggest potential directions for future research. First, the observed correlation pattern between both self-reported and neuropsychological assessed executive functioning skills identified that moderate to strong correlations between the three core executive functioning skills, regardless of assessment type. Such correlation matrix is in accordance with and provides further confirmation on the contemporary view towards executive functioning that reflects unity and diversity between the various skills<sup>25,26</sup>. Indeed, both in adult<sup>26</sup> and child samples<sup>25</sup> executive functioning skills seemed to be best mapped by a three-factor model (i.e., Shifting, Updating/Working Memory, and Inhibition) in which the three components are distinguishable, but not completely independent, and hence share some underlying commonality. Consequently, systematically adopting multiple neuropsychological tasks to assess all core components is of crucial importance to gain a comprehensive understanding of the impairments in adolescents' executive functioning.

Secondly, the findings provide preliminary support for the main association proposed within the COPES model<sup>13</sup>: an interrelation between reduced capacity of executive functioning and emotional regulation on the one hand and interference in daily life activities due to chronic pain on the other hand,

in adolescents who experience chronic pain<sup>13</sup>. However, data collection was cross-sectional, preventing interpretations with respect to causality or cyclical character of the associations. Moreover, no assessment of engagement in self-management tasks or parental support took place, due to the particular focus of the pilot study on evaluating the multi-method approach towards the core concepts (i.e., executive functioning, chronic pain). Consequently, a prospective investigation, starting in early adolescence, is needed to comprehensively test the theoretical assumptions and clinical implications of a potential cyclical association between chronic pain and executive functioning, as proposed in COPES<sup>13</sup>.

## 5. Conclusion

Taken together, the pilot study findings provide support for and identify a critical need for multimethod and prospective investigations in larger samples to establish the 1) exact nature of the relation between chronic pain and executive functioning in adolescents and 2) role of reduced executive functioning capacity in understanding pain-related interference and adolescents' ability to engage in self-management. Adolescence is a crucial developmental stage to explore these associations, as it reflects a transfer phase in which young people take over responsibility for key domains of self-management from their parents. A prospective investigation will clarify the cyclical relation between executive functioning, emotional regulation, self-management and chronic pain, and thereby identify how to optimise self-management to off-set potential lifelong disability.

## Conflict of interest statement

None of authors have any conflicts of interest to declare.

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