

## **Anxiety at 13 and its effect on pain, pain-related anxiety, and pain-related disability at**

### **17. An ALSPAC cohort longitudinal analysis**

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## **Anxiety at 13 and its effect on pain, pain-related anxiety, and pain-related disability at 17: An ALSPAC cohort longitudinal analysis**

### **Abstract**

The aim of the present study was to investigate the influence of anxiety at 13 years of age on the presence of chronic pain, pain-related anxiety, and pain-related disability at 17 years of age in a large longitudinal cohort. We hypothesized that mother-reported anxiety at 13 would be associated with the presence of chronic pain at 17 and an increase in pain-related anxiety using all available data from the longitudinal cohort. Further, we hypothesized that anxiety at 13 would predict pain-related disability in adolescents who reported chronic pain at 17 years of age. Participants were recruited from the Avon Longitudinal Study of Parents and Children based in the UK who attended a university research clinic at 17. Child anxiety (reported by the mother) was extracted at child age 13, and self-report of the presence of chronic pain, pain-related anxiety, and pain-related disability at 17. Analyses revealed that child anxiety at 13 was not significantly associated with the presence of chronic pain at 17 ( $n = 842$ ). However, anxiety at 13 was significantly associated with pain-related anxiety at 17 ( $n = 1831$ ). For the subsample of adolescents who reported chronic pain, anxiety at 13 was associated with pain-related disability at 17 ( $n = 393$ ). Further analyses revealed that pain-related anxiety at 17 mediated the association between anxiety at 13 and pain-related disability at 17, suggesting that pain-related anxiety should be a target for treatment in adolescents with chronic pain, to reduce the impact of pain in later adolescence. General anxiety at 13 was unrelated to the presence of chronic pain at 17 but should be considered a risk factor for later pain-related anxiety and disability in a subset of adolescents who develop chronic pain.

**Keywords:** Adolescents; ALSPAC; Anxiety; Chronic Pain; Disability.

## Introduction

Pain is a normal, though largely benign, complaint of childhood (Perquin et al., 2000). For some children pain persists, becoming chronically disabling and distressing (King et al., 2011). Children with chronic or recurrent pain often present anxiously: with higher levels of general anxiety compared to the population prevalence (Costello, Mustillo, Erkanli, Keerler, & Angold, 2003; Kashikar-Zuck et al., 2008; Simons, Sieberg, & Claar, 2012). Girls report higher levels of chronic pain and anxiety (Costello et al., 2003; King et al., 2011). Cross-sectional studies have shown higher levels of anxiety to be associated with poorer social and physical functioning, pain severity, and pain frequency in children with chronic pain (Cohen, Vowles & Eccleston, 2010; Kaczynski, Simons, & Claar, 2011; Simons et al., 2012). Further, children who are anxious are more likely to experience pain-related anxiety (Carleton, Abrams, Asmundson, Antony, & McCabe, 2009; Folayan, Idenhen, & Ojo, 2004; Klingberg, 1995), which is in turn associated with higher levels of disability as posited by the fear avoidance model (Simons & Kaczynski, 2012). In addition, high levels of anxiety can increase the risk of later chronic or recurrent pain (Carleton et al., 2009). However, all findings are based on cross-sectional data. No study has reported on the role of early anxiety and the presence of chronic pain, expression of pain-related anxiety, or pain-related disability in later adolescence.

In this study, we use the Avon Longitudinal Study of Parents and Children (ALSPAC) database, designed to examine child development and determinants of health and disease throughout childhood. When this study was first established in 1991, the originators did not include any child self-report measures of anxiety, so general anxiety data at 13 years of age are mother-reported. Measures taken at 17 years are self-reported.

Three hypotheses were (1) general anxiety at 13 will be associated with the presence of chronic pain at 17; (2) general anxiety at 13 will be associated with pain-related anxiety at

17; and (3) in a sub-sample of adolescents who reported chronic pain at 17 years of age, general anxiety at 13 will be associated with pain-related disability at 17.

## **Methods**

### ***Study population***

The Avon Longitudinal Study of Parents and Children (ALSPAC) includes children born between April 1991 and December 1992 (Boyd et al., 2013; Fraser et al., 2013). A total of 14,541 pregnancies from the Avon County of the UK were enrolled and 13,988 children survived to 12 months (see [www.alspac.bris.ac.uk](http://www.alspac.bris.ac.uk) for more information, see [www.bris.ac.uk/alspac/researchers/data-access/data-dictionary](http://www.bris.ac.uk/alspac/researchers/data-access/data-dictionary) for details of data available through a searchable data dictionary). This study is based on participants who were able to attend a university research clinic at 17 years of age and completed a pain-specific questionnaire ( $N = 3974$ ). Ethical approval was obtained from the ALSPAC Law and Ethics Committee, the Local Research Ethics Committee, and two University of Bath Ethics Committees.

### ***Measures***

*General anxiety (mother-report)* When the child reached 13 years of age, mothers completed parts of the validated Development and Well-Being Assessment parent version (Goodman, Ford, Richards, Gatward, & Meltzer, 2000) aimed at making DSM IV diagnoses of psychiatric disorders including generalized anxiety disorder (American Psychiatric Association, 2000). Mothers reported the extent (from ‘not at all’ = 1 to ‘often’ = 3) their child worried about various situations (e.g. school work, disasters). A sum of the seven items was calculated per child, with higher scores indicating higher general anxiety (mother

perceived). The internal consistency in our sample was moderate ( $\alpha = .58$ ). Child report of anxiety at 13 was not available.

*Chronic pain (adolescent-report)* At 17, adolescents attending the research clinic were asked two questions to determine the presence of chronic pain. First, they were asked if, over the previous month, they had any aches or pains that lasted for a day or longer. If they responded 'yes', they were asked to report whether the pain started 'less than' or 'more than' three months ago (Von Korff, Ormel, Keefe, & Dworkin, 1992). This questionnaire was composed from a previously validated questionnaire used with UK populations (Mallen, Peat, Thomas, & Croft, 2006). In this study, recent pain is defined as pain that started less than three months ago. Chronic pain is defined as pain that started more than three months ago. Although we suspect that in some cases, this may capture recurrent or intermittent pains, the International Association for the Study of Pain (IASP) classifies pain that persists for longer than three months as 'chronic' (Merskey & Bogduk, 1997). The most commonly reported pain conditions in adolescence are head and stomach pain (King et al., 2011), which often present as episodic rather than as continuous pain conditions. Consequently, the definition from IASP was adopted.

*Pain-related anxiety (Adolescent-report)* At 17, adolescents were asked to complete the Pain Specific Anxiety subscale of the Bath Adolescent Pain Questionnaire (BAPQ) (Eccleston et al., 2005). All subscales of the BAPQ have shown good internal consistency and construct validity, and have been validated within a rheumatology outpatient sample (Eccleston et al., 2005). The Pain Specific Anxiety subscale contains seven items regarding specific worries or concerns about pain. Adolescents reported how often they experienced these worries (from 'Never' = 0 to 'Always' = 4). The scores on these seven items were summed to create a total score, ranging from 0 to 28, with higher scores indicating higher anxiety. The internal consistency in our sample was good ( $\alpha = .86$ ).

*Pain-related disability (Adolescent-report)* Adolescents were asked to complete three questions of pain-related disability at 17, using a questionnaire validated in chronic pain populations (Von Korff et al., 1992). First, adolescents reported the number of days that pain prevented usual activities (0-6 days, 7-14 days, 15-30 days, 31+ days). Second, adolescents reported the level of pain interference in daily activities (1 = no interference, 10 = unable to carry on activities) and change in ability to take part in daily activities (1 = no change, 10 = extreme change). These two latter scores were combined to produce a mean score reflecting pain interference. The two disability scores (number of days pain prevented activities and pain interference) are analysed separately. The internal consistency in our sample was good ( $\alpha = .75$ ).

### ***Data analyses***

The following analyses use all available data from the sample; however, some questionnaires were not completed by all participants at each extraction point leading to different sample sizes for each analysis. A flow diagram showing the total number of participants that completed each questionnaire and are entered into each analysis is shown in Figure 1.

A logistic regression analysis was used to investigate hypothesis one: children identified by their mothers as having high levels of general anxiety at 13 were more likely to self-report chronic pain at 17. Data were available from 842 adolescents for the anxiety measure at 13 *and* the measure of the presence of recent or chronic pain at 17. Linear regression was used to investigate hypothesis two: mother-reported general anxiety at 13 was associated with self-reported pain-related anxiety at 17. Data from 1831 adolescents were entered into the regression; all available data from those completing measures of anxiety at 13 *and* pain-related anxiety at 17.

Only adolescents reporting chronic pain were included in analyses to investigate hypothesis three: that higher levels of general anxiety at 13 were associated with increased self-reported pain-related disability at 17. Data were available from 393 adolescents who completed the anxiety measure at 13, reported chronic pain, *and* completed pain-related disability measures at 17. The impact of interference due to pain and the number of days that pain prevented usual activities were investigated with linear regression. Adolescent sex was controlled for in the first step of each analysis as girls have higher levels of chronic pain and are more anxious compared to boys (Costello et al., 2003; King et al., 2011). SPSS version 21 data package was used to analyse the data.

## **Results**

### ***Descriptive Statistics***

For the whole university research clinic population who completed the pain questionnaire ( $N = 3974$ ; males = 1651, females = 2323), girls had higher level of general anxiety at 13 years of age, as reported by their mothers, compared to boys ( $t = -6.30$ ,  $p < .01$ ,  $M_{\text{Girls}} = 9.82$ ,  $SD_{\text{Girls}} = 1.96$ ,  $M_{\text{Boys}} = 9.29$ ,  $SD_{\text{Boys}} = 1.62$ ). Girls also had significantly higher levels of pain-related anxiety compared to boys ( $t = -9.41$ ,  $p < .01$ ,  $M_{\text{Girls}} = 4.06$ ,  $SD_{\text{Girls}} = 4.80$ ,  $M_{\text{Boys}} = 2.77$ ,  $SD_{\text{Boys}} = 3.73$ ). Of the total clinic sample, 1820 reported that they had experienced pain for a day or longer in the previous month. Of these 1820 adolescents, 855 (47.0%; males = 293, females = 562) reported chronic pain (pain lasting  $>3$  months). Recent pain (pain lasting  $<3$  months) was reported by the remaining 965 adolescents (53.0%; males = 396, females = 569).

### ***Association between early anxiety and later report of chronic pain***

Adolescents who had available data from the anxiety questionnaire at 13 and reported the presence of chronic or recent pain at 17 were entered into a logistic regression ( $n = 842$ ; females = 532, males = 310). The model containing sex and general anxiety at 13 predicted who would report chronic pain ( $\chi^2 = 6.60, p < .05$ ). However, general anxiety at 13 alone did not predict whether adolescents reported the presence of chronic pain at 17. Only child sex helped to explain the experience of chronic pain at 17 ( $Wald = 6.69, OR = .69, p < .05$ ). Specifically, the relative risk revealed girls to be 1.22 (95% confidence interval = 1.04 to 1.42) times more likely to report chronic pain than boys.

#### ***Association between early anxiety and later report of pain-related anxiety***

To determine whether general anxiety at 13 was associated with pain-related anxiety at 17, data were available for 1831 adolescents (females = 1109, males = 722). Children identified by mothers as being anxious at 13 were more likely to have high self-reported pain-related anxiety at 17 ( $\beta = .08, t = 3.45, 0.6\%$  explained variance,  $p < .01$ , Table 1). Further, girls were more likely than boys to have higher levels of pain-related anxiety at 17 ( $\beta = .13, t = 5.66, 1.8\%$  explained variance,  $p < .01$ ).

#### ***Association between early anxiety and later report of pain-related disability***

Adolescents who had data available from the anxiety measure at 13, reported chronic pain at 17 and completed the pain-related disability measures at 17, were entered into a linear regression to investigate associations between anxiety at 13 and pain-related disability at 17 (days pain prevented usual activities and pain interference;  $n = 393$ ; females = 265, males = 128). Linear regression revealed that higher levels of mother-reported child anxiety at 13 were associated with a higher number of days when pain prevented usual activities at 17 years ( $\beta = .14, t = 2.89, 2.1\%$  explained variance,  $p < .01$ , Table 1). Girls were more likely to



have a higher number of days where chronic pain prevented usual activities at 17 compared to boys ( $\beta = .12$ ,  $t = 2.34$ , 1.4% explained variance,  $p < .05$ ). Results also revealed that children who had greater anxiety at 13 were more likely to experience higher pain interference at 17 ( $\beta = .14$ ,  $t = 2.76$ , 3.0% explained variance,  $p < .01$ ). Finally, girls with chronic pain, compared to boys, were more likely to report pain interference at 17 ( $\beta = .18$ ,  $t = 3.66$ , 1.6% explained variance,  $p < .01$ ).

### ***Further analysis: Testing for mediation***

A mediation analysis was conducted to explore the findings. We investigated whether the association between general anxiety at 13 years and pain-related disability at 17 years was mediated by pain-related anxiety at 17 years in those adolescents who reported chronic pain.

To test for mediation, the following conditions should be met: (1) significant association between the predictor and the mediator (path A, Figure 2), (2) significant association between the mediator and the outcome variable (path B, Figure 2), and (3) significant association between the predictor and the outcome variable (path C, Figure 2). If all conditions were met, a Sobel's significance test was used to determine whether the relation between the predictor and outcome variable was significantly reduced upon introduction of a mediator (Holmbeck et al., 2002). This test is preferred with large samples (Field, 2013).

Our findings of the mediation analysis are shown in Figure 1. For pain-related disability, both scores were used in the analysis: number of days pain prevented usual activities, and pain interference. All of the conditions were met; anxiety at 13 was significantly associated with pain-related anxiety and pain-related disability at 17 and, after controlling for anxiety at 13, pain-related anxiety was significantly associated with pain-related disability. The Sobel test revealed a significant drop in the relation between anxiety at

13 and pain-related disability when adding the mediator ‘pain-related anxiety’ ( $Z = 2.81, p < .01_{\text{pain interference}}, Z = 2.77, p < .01_{\text{days pain prevented usual activities}}$ ).

## Discussion

We investigated the relationship between maternal perception of anxiety at 13 on the emergence of chronic pain and pain-related anxiety at 17 years of age using the ALSPAC population. Further, we investigated the effects of early anxiety at 13 and later pain-related disability at 17 in those adolescents reporting chronic pain. We were particularly interested in the mother’s report of the frequency of anxious thinking in early adolescence, and focused on the expression of internalizing worry, the cognitive component of anxiety most relevant to later patterns of affect regulation and disability (McLaughlin, Mennin, & Farach, 2006; Simons & Kaczynski, 2012).

Our hypotheses were partially supported. With regard to the whole population, we found no evidence for early anxiety as a risk factor for later chronic pain. However, anxiety at the age of 13 was positively related to pain-specific anxiety and disability at 17 in the whole sample. Further analyses revealed that for adolescents who reported chronic pain, general anxiety at 13 was associated with pain-related disability four years later. In addition, pain-related anxiety mediated the association between early anxiety and later pain-related disability. This highlights the important role of early anxiety in children, which increases the likelihood of having higher levels of pain-related anxiety at 17.

Sex differences were also identified. First, girls who were more anxious at 13 were more likely to report chronic pain than boys. Second, girls were found to have higher levels of pain-related anxiety. Third, girls who reported chronic pain and higher levels of pain-related anxiety are more likely to be disabled by their condition, supporting previous findings (King et al., 2011).

The finding that mother-reported higher anxiety at 13 did not predict the presence of chronic pain at 17 is contrary to previous suggestions that higher levels of general anxiety may be a risk factor for later chronic pain (Carleton et al., 2009). However, higher levels of early anxiety may be a risk factor for the way pain influences functioning when confronted with chronic pain experiences. For example, higher early anxiety was associated with a higher risk of later pain-related anxiety, which has been associated with more passive coping strategies and increased disability (Kaczynski et al., 2011).

Our findings highlight future clinical implications. Emphasis could be placed on identifying and reducing anxiety during early adolescence through psychological therapies such as cognitive behavioural therapy, which targets negative thoughts and encourages coping (Stallard, 2013). For older adolescents with chronic pain, high levels of anxiety about pain are associated with increased disability, regardless of pain intensity (Cohen et al., 2010; Simons et al., 2012). Therefore, anxiety, rather than pain may be an important target of treatment to improve functioning. These findings support the fear avoidance model (Simons & Kaczynski, 2012) and provide reason to extend the framework to include early anxiety as a predictor of later pain-related anxiety.

There are limitations to this study. First, as stated throughout, no child-reported data on anxiety or persistent pain were available at 13. We were limited to mother-reported child anxiety at this age. Typically, mother-report of anxiety underestimates self-reported child anxiety (Dirks et al., 2014). Therefore, any bias in mother-reported anxiety in this study may be towards under-identification. Further, when this longitudinal study was designed (over 20 years ago), there was little understanding of the relationship between parental anxiety about pain and child pain expression. Although the measure of general anxiety at 13 is brief, the questionnaire covers common childhood worries and is a reliable assessment of general worry (Goodman, et al., 2000). Second, the pain measures at 17 were relatively global and

no data are available on the number of pain episodes, or on the nature of the pain as persistent. In epidemiological studies of this kind, one is inevitably working with older concepts and measures. Third, reasons for attrition were not collected from participants, although we can speculate that this is due to fatigue, relocation, or lack of interest. Those attending the research clinic at 17, and therefore included in this study, were perhaps more conscientious than those who did not attend. Despite this, our sample sizes were still large and whilst replication of our findings are needed, we do not consider the attrition as a major flaw of this study. Fourth, the clinical validity of this associative analysis needs to be established. Finally, we are cautious that the associations between early anxiety and later pain-related anxiety and disability are modest. Future research should investigate predictors of early anxiety and later pain-related anxiety with a focus on pain. Parent modelling of anxious and pain behaviours are associated with child pain and anxious behaviours (Burstein & Ginsburg, 2010; Goodman & McGrath, 2003). In addition, higher levels of behavioural inhibition have been associated with anxiety in childhood (Fox & Pine, 2012). Finally, research is needed to explore whether one type of pain-specific anxiety (e.g. catastrophizing, fear of pain, anxiety sensitivity) is more reliable at predicting disability within adolescents with chronic pain.

To conclude, anxiety at 13 years of age is not associated with the development of chronic pain at 17 years of age, but is associated with later pain-related anxiety and pain-related disability. Replication, further investigation of individual differences, and effects of anxiety on treatment outcome are needed.

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