PAIN® 155 (2014) 983–993

PAIN®

www.elsevier.com/locate/pain

Sex differences in experimental pain among healthy children: A systematic review and meta-analysis

Katelynn E. Boerner [a,b,*], Kathryn A. Birnie [a,b], Line Caes [b], Meghan Schinkel [a,b], Christine T. Chambers [a,b,c]

[a] Department of Psychology and Neuroscience, Dalhousie University, Halifax, Nova Scotia, Canada
[b] Centre for Pediatric Pain Research, IWK Health Centre, Halifax, Nova Scotia, Canada
[c] Department of Pediatrics, Dalhousie University, Halifax, Nova Scotia, Canada

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

ARTICLE INFO

Article history:
Received 30 September 2013
Received in revised form 19 December 2013
Accepted 30 January 2014

Keywords:
Children
Experimental pain
Meta-analysis
Sex differences

ABSTRACT

Sex differences in response to experimental pain are commonly reported in systematic reviews in the adult literature. The objective of the present research was to conduct a systematic review and meta-analysis of sex differences in healthy children's responses to experimental pain (eg, cold pressor, heat pain, pressure pain) and, where possible, to conduct analyses separately for children and adolescents. A search was conducted of electronic databases for published papers in English of empirical research using experimental pain tasks to examine pain-related outcomes in healthy boys and girls between 0 and 18 years of age. Eighty articles were eligible for inclusion and were coded to extract information relevant to sex differences. The systematic review indicated that, across different experimental pain tasks, the majority of studies reported no significant differences between boys and girls on pain-related outcomes. However, the meta-analysis of available combined data found that girls reported significantly higher cold pressor pain intensity compared to boys in studies where the mean age of participants was greater than 12 years. Additionally, a meta-analysis of heat pain found that boys had significantly higher tolerance than girls overall, and boys had significantly higher heat pain threshold than girls in studies where the mean age of participants was 12 years or younger. These findings suggest that developmental stage may be relevant for understanding sex differences in pain.

1. Introduction

Sex differences represent a rapidly growing body of literature in the areas of biology, medicine, and neuroscience as researchers attempt to illuminate the mechanisms that underlie differences between men and women [14]. According to the World Health Organization, sex refers to the biological and physiological distinctions between women and men. This can be contrasted with gender, which is defined as a psychosocial construct that embodies the attributes, behaviours, and roles that a given society considers to be acceptable for men and women [116].

Sex differences are commonly reported in adult pain, with numerous reviews providing evidence of greater prevalence rates of acute and chronic pain among women, with women also demonstrating greater sensitivity to experimental pain tasks, though the strength of this effect differs between pain modalities, outcome measures, and time points, and is considered to be a controversial phenomena [38,74,88]. The abundance of literature on adult sex differences in pain has allowed researchers to explore mechanisms through which pain differs in men and women, including both biological and psychosocial mechanisms [28,38,57,87]. Such research has important implications with regards to the assessment and treatment of pain in adults, such as recent advances in theories of personalized pain management through research on the differential analgesic responding of men and women [81]. As a result of developmental factors it is inappropriate to generalize adult findings to pediatric populations, and the literature on sex differences in children's pain is comparatively sparse.

Epidemiological studies of chronic pain in childhood suggest that prevalence of chronic pain is greatest among adolescent girls, with the emergence of sex differences in chronic pain conditions seen around the time of pubertal development [59]. These findings are concordant with speculation from the adult literature that sex hormones are one of the mechanisms through which sex differences in pain perception and responding are explained [4,44]. Given the complexity of the numerous factors implicated in the development of chronic pain, a systematic review of research on

* Corresponding author. Address: Centre for Pediatric Pain Research, K8536 (8th floor, Children's Site), IWK Health Centre, 5850/5980 University Ave, Halifax, Nova Scotia B3K 6R8, Canada. Tel.: +1 902 470 6769; fax: +1 902 470 7118.
E-mail address: katelynn.boerner@dal.ca (K.E. Boerner).

http://dx.doi.org/10.1016/j.pain.2014.01.031
0304-3959/

sex differences in healthy children's pain is needed to fully understand and explore potential mechanisms. Experimental pain provides a starting point for such examinations, controlling for many of the confounding factors that complicate interpretations of results in studies of clinical pain. Prior reviews have only provided narrative descriptions of select studies of sex differences in experimental pain among children and adolescents [56,78]. The primary objectives of the present study were: (1) to systematically review the existing literature on sex differences in responses to experimental pain in healthy children, and (2) to perform a meta-analysis of data from published studies on experimental pain in boys and girls to provide a further investigation of sex differences beyond those statistics reported in published articles. Additionally, where possible, meta-analyses were to be conducted separately for children (participant mean age less than 12 years) and adolescents (participant mean age of 12 years or older). Finally, an additional objective was to examine the reporting practices of sex and gender in the studies included in the review.

2. Methods

2.1. Search method

A search was conducted of key electronic databases (PsycInfo, Embase, CINAHL, PubMed) from the inception of the databases through November 2012. The basic structure of the search strategy was as follows: [((pediatric) OR child) OR adolescent] AND [pain] AND [(((((((experimental pain) OR cold pressor) OR quantitative sensory test) OR water load) OR heat pain) OR thermal pain) OR pressure pain) OR exercise task], searching primarily titles and abstracts of these key databases, using truncations as appropriate for the database (eg, child*, adolescen*, quantitative sensory test*). Keywords were chosen to capture the population age range of interest, to find studies that included pain as an outcome, and to focus the search specifically on studies including an experimental pain task.

2.2. Eligibility criteria

Eligibility criteria required that included articles: (1) be an empirical investigation using an experimental pain task to examine pain-related outcomes (pain intensity, pain tolerance, pain threshold, pain affect, facial activity in response to pain, or physiological responses to pain); (2) be published in article form in English; (3) use community/healthy samples of children between 0 and 18 years of age only (or a healthy control group included in studies of clinical populations); and (4) include both boys and girls. Experimental pain tasks were defined as any task that was intended to induce pain for which a pain-related outcome was measured.

2.3. Screening for eligibility, coding, and requests for missing data

The initial search revealed 519 unique abstracts once duplicates were removed. Each abstract was reviewed by 2 coauthors (KEB and KAB) to determine eligibility. If eligibility could not be determined from the abstract, the full article was examined. A total of 440 abstracts were excluded for the following primary reasons: participants did not complete an experimental pain task (n = 33, 7.5%), the study did not measure any pain-related outcomes (n = 8, 1.8%), the abstract was not published in article form (eg, dissertations, book chapters, conference abstracts, n = 46, 10.5%), the article was not published in English (n = 8, 1.8%), the study was conducted with a clinical sample and did not include a healthy control group (n = 69, 15.7%), the study included individuals outside of the range of 0 to 18 years of age (n = 254, 57.7%), the study sample was composed of only boys or only girls (n = 8, 1.8%), and the study was conducted with animals (n = 14, 3.2%).

Therefore, from the initial search, 79 articles were identified as being eligible. Each of the 79 articles was read and data were extracted by a study author (KEB, KAB, LC, or MS) using an author-created coding form that documented sample characteristics, details of the experimental pain tasks performed, and details related to any pain-related outcomes measured (including mean and standard deviation [SD] of the pain outcome for both boys and girls, as well as the results of any statistical tests conducted to examine sex differences). During coding, 3 additional articles were identified as being eligible for inclusion, as they were referenced in the article as reporting on additional results from the same study sample [83,102,108]. These 3 articles were also coded and included in the study, resulting in a total of 82 articles coded for inclusion. Fig. 1 provides a study flow chart that uses the PRISMA model [75].

Coding sheets were examined to identify missing data. Authors were contacted and asked to supply data for any article that did not include the following: age range of participants, mean age of participants, and mean and SD for boys and girls separately for any pain outcome. When applicable, data were requested for baseline/control experimental pain tasks (ie, tasks that did not involve an intervention or experimental manipulation) and for healthy/community samples only. Two attempts were made to contact the corresponding author of each article where data were missing. On the basis of author responses, 2 articles that had originally been included in the review [11,103] were excluded, as it was revealed that the sample fell outside of the range of 0 to 18 years old. This resulted in a final total of 80 articles included, reporting on 81 separate studies, as 1 article reported on 2 studies with separate samples [109].

2.4. Overlapping samples

Every attempt was made to avoid the inclusion of overlapping samples in the review, as this would involve an overrepresentation of a subset of children. If it was unclear whether samples were overlapping, authors were e-mailed to confirm this information. Where it was known that samples were overlapping (ie, >1 study included in the review that reported on the same sample of children), the authors of the present review went back to the first published study from that sample and worked forward chronologically through multiple publications reporting on the same sample of children, making note of outcomes the first time that full data were reported (eg, means and SDs of pain outcome for boys and girls separately, and statistics regarding sex differences). If full data were not available from any of the studies involved in the overlapping sample, the authors were contacted and asked to provide data about the first chronological incidence of reporting. Where it was unclear whether samples were overlapping, the authors were contacted and asked to indicate whether multiple publications reported on the same sample of children. If authors did not respond, the studies were assumed to represent different samples of children and were treated as such in the review.

2.5. Data analytic approach

Information from data extraction coding sheets were entered into SPSS 20, and information from the systematic review was summarized using descriptive statistics. As a result of the small number of studies included in the systematic review, results were combined across different experimental pain tasks. Sufficient data were available to conduct meta-analyses separately for cold pressor pain, heat pain, and pressure pain. Data needed to be available from at least 2 studies to conduct a meta-analysis for a particular pain outcome. All data suitable for pooling was analyzed by