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DOI:
10.1136/bmjopen-2018-025436

BMJ Open

Association between child maltreatment and central sensitivity syndromes: a systematic review protocol

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To cite: Chandan JS, Thomas T, Raza K, *et al*. Association between child maltreatment and central sensitivity syndromes: a systematic review protocol. *BMJ Open* 2019;**9**:e025436. doi:10.1136/bmjopen-2018-025436

► Prepublication history and additional material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2018-025436).

Received 14 July 2018
Revised 19 November 2018
Accepted 5 December 2018

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ABSTRACT

Introduction A growing body of evidence is identifying the link between a history of child maltreatment and a variety of adverse health outcomes ultimately leading to significant social and healthcare burden. Initial work has identified a potential association between child maltreatment and the development of a selection of somatic and visceral central sensitivity syndromes: fibromyalgia, chronic fatigue syndrome, temporomandibular joint disorder, chronic lower back pain, chronic neck pain, chronic pelvic pain, interstitial cystitis, vulvodynia, chronic prostatitis, tension-type headache, migraine, myofascial pain syndrome, irritable bowel syndrome and restless legs syndrome.

Methods and analysis Primary electronic searches will be performed in the Embase, MEDLINE, PubMed, Scopus, PyscINFO, CINAHL and Cochrane Library databases and a number of Grey Literature sources including child protection and paediatric conference proceedings. Following independent screening of studies by two review authors, the Preferred Reporting Items for Systematic Reviews and Meta-Analyses template will be used to aid extraction. A meta-analysis will be conducted on the included case-control and cohort studies. The Newcastle-Ottawa grading system will be used to assess the quality of included studies. Results will be expressed as pooled ORs for binary data and mean differences for continuous data.

Ethics and dissemination Ethics approval will not be required. The final results of the review and meta-analysis will be submitted for peer-review publication and also disseminated at relevant conference presentations.

PROSPERO registration number CRD42018089258.

Strengths and limitations of the study

- This systematic review will provide a comprehensive and systematic assessment of the risk of developing central sensitivity syndromes (CSS) after a documented history of child maltreatment.
- The results of this review will aid clinicians in early identification of those who are at risk of developing CSS which can be challenging and costly to treat.
- This review will not be able to build on any causal links between child maltreatment and CSS but only go onto describe the strength of the association in more detail. The likelihood of small cohort sizes being included may affect the risk estimate.
- A limitation of the study will relate to the fact that the definition of child maltreatment is so heterogenous, therefore it is difficult to accumulate all types of abuse into one exposure of interest.

INTRODUCTION

Defining child maltreatment

The United Nations[1] define a child as any person under 18 years old unless 'under the law applicable to the child, majority is attained earlier'. Similarly, to adults, children are entitled to living a safe and joyous life under the Human Rights Act (1998).[2]

Child maltreatment can be challenging to define, however the UK government's most recent guidance on child safeguarding states[3] that, maltreatment includes abuse (physical, sexual and emotional), neglect and child sexual exploitation, each of which signify a breach of human rights. The WHO expands on this definition[4] to suggest that exposure to intimate partner violence is also a form of child maltreatment. The WHO estimates the global prevalence of emotional, physical, sexual abuse and neglect in children at 36.3%, 22.6%, 18% (in females) and 16.3%, respectively.[5] Recent UK studies conducted by the National Society for the Prevention of Cruelty to Children (NSPCC)[6] identified up to one in four young adults have disclosed to having had experienced some form of maltreatment in their childhood. These estimates indicate the considerable burden associated with child maltreatment.

Defining central sensitivity syndromes

Central sensitivity syndromes (CSS) cover a broad range of conditions characterised by distressing and debilitating symptoms, which often have unclear clinical pathology.[7] Often there is a considerable overlap in the symptomology of these conditions, as many present with pain and fatigue.[8] Although

these conditions appear to affect multiple systems (musculoskeletal, gastrointestinal and neurological), they congruently demonstrate a hypersensitivity to pain, termed 'central sensitisation'.[9] Central sensitisation refers to an enhancement of nociceptive neuronal pathways due to reduced inhibition, increased membrane excitability, increased synaptic efficacy and somatosensory plasticity when the individual is exposed to activity, inflammation or injury.[9 10] This results in a circumstance where pain occurs but may not be associated with an acute cause.

For this review we are including a selection of CSS, defined by their individual WHO International Classification of Disease-10[11] codes: fibromyalgia (M79.7), chronic fatigue syndrome (G93.3), temporomandibular joint disorders (K07.6), chronic lower back pain (M54.5), chronic neck pain (M54.2), chronic pelvic pain (r10.2), interstitial cystitis (N30.10), vulvodynia (N94.81), chronic prostatitis (N41.1), tension-type headache (G44.209), migraine (G43.91), myofascial pain syndrome (M54.6), irritable bowel syndrome (K58) and restless legs syndrome (G25.81). The selection of conditions we are exploring in this review have pain patterns which are either somatic or visceral in nature.

These conditions also appear to be highly prevalent within the general population and often have very complex multifactorial aetiology. For example, chronic lower back pain, characteristic of pain in the lumbarsacral region often leading to physical and psychological morbidity, affects a significant proportion of the population (approximately 11% of men and 16% of women).[12] There have been over 100 possible risk factors of this type of pain identified in the literature,[13] signifying the lack in clarity of understanding the aetiology of this condition. Another example relates to fibromyalgia and chronic fatigue syndrome. Fibromyalgia is characterised by widespread pain and estimated to be present in up to 8% of the population.[14] Age of diagnosis is most often between 30 and 55 years old and it is more predominant in women than men (up to 9:1).[15] Chronic fatigue syndrome, although similar to fibromyalgia in presentation (pathological malaise that can be worse after exertion), is defined as a separate condition due to differing physiological derangements in terms of autonomic function and endocrine response.[16 17] However, chronic fatigue syndrome is also more common in women than men (2:1) and although it can affect individuals of all ages it is also more common in middle-aged women.[16] Similarly to fibromyalgia, no clear cause has been found that predisposes an individual to developing chronic fatigue syndrome however, several explanations have been tested which include a genetic predisposition, viral triggers and immune dysfunction across a wide spectrum of immune complex cell lines.[18] These examples highlight the shared presentations, similar physical and psychological burdens of CSS but demonstrate a clear difficulty we currently have in understanding their aetiology and predisposing risk factors.

The association between child maltreatment and CSS

A recent systematic review[19] indicated that there is a growing body of evidence suggesting the impact of child maltreatment on the development of negative health outcomes. There have been associations made to respiratory disease,[3] cancer,[4] cardiovascular disease,[20] liver disease,[6] mental health difficulties, including depression,[7] alcoholism[8] and suicide.[21]

Specifically, the data assessing the link between child maltreatment and CSS has been less well synthesised and understood. A previous meta-analysis[22] has explored the link between childhood abuse and chronic pain (covering several conditions under the umbrella of CSS) in adulthood, identifying 16 observational studies prior to 2001. These suggested an association between childhood abuse and chronic pain. However, since this date there have been multiple observational studies and some reviews exploring the risk of developing certain pain syndromes following child maltreatment. For example, recent work has suggested, there have been variations in the effect size examining the relationship between child maltreatment with fibromyalgia[23–25] in studies undertaken in population based or small settings. In another study, childhood trauma and maltreatment was present in 33% of individuals presenting with chronic fatigue syndrome.[26] Although unable to provide a pooled risk ratio, a narrative systematic review of 31 studies examining the relationship of chronic fatigue syndrome/fibromyalgia and child maltreatment identified strong association between the two conditions.[27] In a self-reported study childhood abuse was seen as a risk factor in the development of lower back pain[28] and another identified an association between altered pain thresholds affecting intensity of chronic back pain after exposure to child maltreatment.[29] Another frequently explored relationship is between childhood abuse and chronic pelvic pain. Recent observational studies reaffirmed a positive association with exposure to childhood abuse and subsequent developing of chronic pelvic pain, identified in previous research.[30–32]

The biological link between child maltreatment and its effects on future state of health are complex and not fully understood. Several areas theorising this link are well established[33–40]:

1. Physical changes in the developing brain due to stress.
2. Difficulties in forming and maintaining relationships.
3. Psychological related responses to stress and trauma.
4. Development of adult behaviour patterns depending on those observed at home (eg, intimate partner violence).
5. Disruption to education and social relationships.
6. Relationship between child maltreatment and unhealthy coping mechanisms (smoking, alcohol use, drug use and obesity).
7. Association with low socio-economic status.

In the case of the CSS described above it is theorised that the link with child maltreatment could relate to an increased inflammatory response and abnormal hypothalamic-pituitary-adrenal axis brought on by

childhood stress.[27] Recent work has identified an association between the presence of childhood maltreatment and raised C reactive protein levels (an inflammatory marker) further elaborating this link. A particular relationship is noticed between the high circulating levels of interleukin and tumour necrosis factors, as well blunted cortisol responses following childhood stress which appears to also be mechanistic for the development of chronic fatigue syndrome and fibromyalgia.[27]

Why it is important to do this review?

Although there are established negative physical and psycho-social outcomes following maltreatment, there has been little evidence on synthesising this data when relating to conditions which are possible to abnormalities in the processing of pain. The most recent comprehensive meta-analysis exploring the relationship between childhood abuse and all types of chronic pain which fall under the category of CSS was synthesised using data prior to 2001.[20] Following which, many observational studies have been published exploring these links further. Specifically, the most recent systematic review[27] exploring chronic fatigue syndrome and fibromyalgia was conducted in 2013, and over the past 5 years, more observational studies have been released exploring this association. There have been no attempts at synthesising the data relating to the relationship of child maltreatment with lower back pain, temporomandibular joint disorders and many other conditions which fall under the collective umbrella of CSS. Due to the significant prevalence of these abnormal pain processing syndromes, which cause a sizeable burden on the health service, it is important to understand factors affecting their aetiology. Therefore, it is crucial to understand the complex interplay between child maltreatment and the development of CSS in order to identify opportunities for early intervention, and also shed further light on the aetiology of CSS.

Objectives

This systematic review will assess the development of CSS following an exposure of child maltreatment compared with those who have not been exposed to a history of child maltreatment.

This systematic review will be conducted and reported in accordance to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[41] The review will adhere to this protocol which has been registered with PROSPERO.[42]

Methods and analysis

Types of study

Observational studies including cohort and case-control without restriction on language or publication status will be included. Where multiple publications arise from the same population, the most recent report will be included. Studies in any settings will be included.

Types of participants

The exposure group will consist of all those individuals who have experienced child maltreatment. The definition of child maltreatment will include abuse (physical, sexual and emotional), neglect and child sexual exploitation experienced by individuals under the age of 18. The control group will be individuals in the above studies who have not experienced child maltreatment.

Types of outcomes

The primary outcomes of interest will be the development of the following conditions (defined previously) after follow-up:

1. Fibromyalgia.
2. Chronic fatigue syndrome.
3. Chronic lower back pain.
4. Temporomandibular joint disorder.
5. Chronic neck pain.
6. Chronic pelvic pain.
7. Interstitial cystitis.
8. Vulvodynia.
9. Chronic prostatitis.
10. Tension-type headache.
11. Migraine.
12. Myofascial pain syndrome.
13. Irritable bowel syndrome.
14. Restless legs syndrome.

Search methods for identification of studies

Primary electronic searches will be performed in the Embase, MEDLINE, PubMed, Scopus, PyscINFO, CINAHL and Cochrane Library databases. Reference lists of all included studies will be checked and authors will be contacted if necessary, to provide reference lists. Secondary searches will be conducted in Grey Literature, Open Grey and Google Scholar for potential grey literature and relevant reviews. Abstracts, conference and symposia proceedings from relevant organisations relating to child maltreatment or paediatric health will be identified. The references will be recorded on Mendeley 1.17.10 and duplicates removed. The search strategy used for MEDLINE (via the OVID platform) is attached in online supplementary data 1. Literature will be translated to English using Google Translate software if non-English articles are identified. Studies published up to 1 November 2018 with no limit on the earliest publication will be included.

Data collection and analysis

Study selection

This will be a three-step process which will be documented by the PRISMA flow diagram method with reviewer decisions recorded:

1. After removing duplications, titles with abstracts will be initially screened by two of the reviewers independently (JSC and TT) using predefined screening criteria based on whether studies (i) included patients who have experienced child maltreatment, (ii) were

observational studies and (iii) included information about the outcomes of interest.
2. The two lists from the above screening will be discussed until consensus is reached. Discrepancies will be resolved through joint consensus.
3. Full texts of the potentially relevant articles will be obtained and inclusion-exclusion criteria applied.

Data extraction and management

Data extraction will be carried by two of the reviewers independently (JSC and TT) and data will be extracted into a template adapted from the PRISMA statement.[41] The PRISMA statement includes a template referring to the extraction of the title, abstract, methods, results, discussion and funding. Disagreements in extraction will be resolved through joint consensus and use of a third reviewer (JT) where required. JSC will then go onto input the data into the Review Manager Software V.5.3. A second reviewer TT will check the accuracy of the input of this data.

Assessment of risk of bias in included studies

The methodological quality of included studies will be assessed using the Newcastle-Ottawa Scale independently by two reviewers (JSC and TT).[43] This method uses a star system to judge three broad areas of the studies including: the selection of the study groups, the comparability of the groups, the ascertainment of the exposure and outcome of interests for observational studies. If there are difficulties in assessing the risk of bias due to unclear or insufficient data, authors of the original studies will be contacted. Any disagreements in deciding risk of bias will be resolved by discussion with a third reviewer (JT).

Measures of treatment effect

For binary data, pooled ORs with 95% CIs will be presented. For continuous data, we will use the mean difference with 95% CIs.

Dealing with missing data

Where missing data appears, we will contact the corresponding authors of the original articles to attempt to collect this data. If the data is not available, we will not use an imputation approach, instead we will omit the data from the respective analysis being conducted.

Assessment of heterogeneity

We will identify overlapping CIs presented in the forest plot. There will also be an assessment of heterogeneity (using the I^2 statistic) between studies for each outcome of interest.

Assessment of reporting bias

If at least 10 studies are included in the meta-analysis with no significant evidence of heterogeneity a funnel plot will be used to explore the existence of publication bias by visual inspection.

Data synthesis

If there are enough numerical studies to conduct a meta-analysis, then provided the studies being included are of sufficient similarity we will use Review Manager software V.5.3 to pool the data for analysis in order to identified pooled ORs.

Subgroup analysis

If sufficient data is collected, then we will conduct subgroup analysis based on participant characteristics. These will include variations posed by gender, age, socio-economic status, age at which child maltreatment occurred, age of onset of CSS and geographical variation.

Sensitivity analysis

If the analysis produces a sufficient number of studies, then we will perform a sensitivity analysis to assess the robustness of our meta-analysis findings. Sensitivity analysis will be conducted to assess the impact of quality of paper, bias, sample size.

Ethics and dissemination

The final review paper will be submitted for publication in a peer-reviewed journal and presented at relevant conferences.

Patient and public involvement

Neither patients nor the public were involved in the development of the research question or design of the review. Patients or the public will not be involved in the study selection, extraction nor synthesis stages of the review. The final review will be disseminated via publication and clinicians who support patients with exposure to childhood abuse, will be informed of the results.

DISCUSSION

It is anticipated that the results of our systematic review will be able to provide key information surrounding the magnitude of the burden of CSS associated with child maltreatment. If the link is established this could provide useful insight into pain and musculoskeletal service planning for individuals who may have experienced child maltreatment.

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Acknowledgements The authors would like to thank the medical school library services at University of Birmingham for their help in development of the search strategy for this review. The authors would also like to thank the peer-reviewers for their expertise and are extremely helpful comments throughout the process.

Contributors JSC, TT, JT, SB, KN and KR conceived the idea, planned and designed the study protocol. JSC wrote the first draft and this was corroborated with TT. All authors agreed upon the methods for study selection, extraction and also the final written manuscript of the protocol. JSC will be the guarantor of the review. KN, SB and JT are equal senior authors for this paper.

Funding This systematic review was supported by the Sandwell and West Birmingham, 'Sandwell Medication Education Centre Trustee' grant for junior doctors. Open access fees will be provided by the University of Birmingham.

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval Ethics approval is not required for this study.

Provenance and peer review Not commissioned; externally peer reviewed.

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