RUNNING HEAD: Child maltreatment, ANS responsivity, and psychopathology

Child maltreatment, autonomic nervous system responsivity, and psychopathology: Current state of the literature and future directions

Abstract

Child maltreatment may affect autonomic nervous system (ANS) responsivity, and ANS responsivity may influence the impact of child maltreatment on later outcomes, including long-term mental/physical health. This review systematically evaluated the evidence regarding effects of maltreatment on ANS responsivity in children and examined how ANS responsivity may influence the association between maltreatment and psychopathology, with attention to relevant developmental issues. We searched the literature for relevant studies using PRISMA guidelines. We searched five electronic databases, performed keyword searches in relevant journals, hand searched reference sections of relevant articles, and contacted experts in the field. Articles were extracted according to inclusion criteria and their quality assessed. The search produced 1,388 articles; 22 met inclusion criteria. Most of the studies suggested blunted cardiovascular responsivity generally and sympathetic activation specifically in response to stress in maltreated children compared to non-maltreated children. Findings around vagal responsivity and skin conductance were mixed. Limited evidence was found for ANS responsivity as a moderator or mediator of psychopathology risk among maltreated children. Maltreatment may be associated with blunted sympathetic activation in stressful situations. Differences in ANS responsivity may influence psychopathology risk among maltreated children. Further research is needed to confirm the nature and magnitude of such effects.

Keywords: Psychopathology; maltreatment; children; stress; autonomic nervous system

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Background

Child maltreatment (physical abuse or neglect, sexual abuse, emotional abuse or neglect, witnessing domestic violence) is associated with numerous negative outcomes throughout the lifespan (Nemeroff, 2016), including dysregulation of the human stress response (Alink, Cicchetti & Kim, 2012). A normal response to stress involves activation of the autonomic nervous system (ANS), followed by activation of the hypothalamic-pituitary-adrenal (HPA) axis, which produces cortisol in humans, and subsequent deactivation of the ANS. Timely activation and deactivation of the stress response allows an individual to manage threat and return to normal functioning following threat cessation. Conversely, abnormal stress responses include a prolonged ("hyper-responsivity") or a diminished ("hypo-responsivity") response. Both hyper- and hypo-responsivity of stress systems may result in an inability to respond adaptively to a stressor (Hunter, Minnis & Wilson, 2011). Such stress responses may have long-term negative consequences for emotional and cognitive functioning and contribute to the development and maintenance of psychopathology (de Kloet, Joels & Holsboer, 2005). Much of the relevant literature to date has focused on associations between child maltreatment and dysregulation of the HPA axis, with less attention to the ANS. The goal of the current review is to summarize and synthesize findings from the extant literature regarding ANS responsivity among children who have experienced maltreatment. A secondary goal is to explore the role of ANS responsivity in the known pathway between child maltreatment and psychopathology.

ANS indicators and functioning

The stress response system functions to coordinate an organism's response to threats and encode information about the safety of the environment (Del Giuduce, Ellis & Shirtcliff, 2011). The ANS comprises two reciprocal branches, the sympathetic nervous system (SNS)

and the parasympathetic nervous system (PNS) (Figure 1). The SNS coordinates the "fight or flight" response, mobilizing an individual's resources to respond to environmental demands (Porges, 2004). The PNS functions to reduce physiological arousal and to promote homeostasis, thereby supporting self-regulation, sustained attention, and social engagement (Del Giudice et al., 2011) and inhibiting sympathetic arousal (Porges, 2004). Under stress, PNS activity may be reduced, thus facilitating SNS activation to increase arousal. Following threat cessation, the PNS reasserts its influence over the SNS to reduce arousal and promote recovery.

When the SNS is activated, heart rate becomes faster and more regular. Pre-ejection period (PEP), the period between contraction of the ventricles of the heart and the ejection of blood into the aorta, is considered a "pure" measure of SNS activation, as it has been found to precisely mirror activation of heart contraction by the SNS (Schachinger, Weinbacher, Kiss, Ritz & Langewitz, 2001). Indirect measures of SNS activation include heart rate, systolic blood pressure (maximum pressure during one heart beat), and diastolic blood pressure (minimum pressure in between two heart beats). SNS activation can also be measured through indices of skin conductance, which reflects arousal through SNS-controlled changes in the activity of the eccrine sweat gland (Dawson, Schell & Filion, 2000). This arousal can be measured as tonic (skin conductance level [SCL]) or rapid, phasic changes (e.g., skin conductance response [SCR], galvanic skin response [GSR]). Thus, SNS activation may be indicated by measures of shortened PEP, accelerated heart rate, increased blood pressure, and/or increased SCL/SCR/GSR.

PNS activation both reduces heart rate and allows heart rate to become irregular, with heart rate increasing with inhalation and decreasing with exhalation. This respiratory system modulation of autonomic outflow to the heart and blood vessels—respiratory sinus arrhythmia (RSA)—is often used as an index of cardiac vagal activity. RSA under non-stress

conditions ("baseline RSA") is an index of vagal tone. "Vagal tone" indicates the degree to which the vagus nerve, which regulates homeostasis in the body, can cause the body to relax. "Vagal responsivity" reflects a change from baseline RSA to RSA under conditions of challenge, with vagal suppression or withdrawal reflecting decreased RSA from baseline to challenge. Thus, vagal withdrawal (i.e., decreased RSA) indicates reduced parasympathetic control over sympathetic activation to facilitate the mounting of a stress response to cope with challenge (Figure 1). Additionally, decreased heart rate and blood pressure may indirectly reflect parasympathetic activation.

Child maltreatment and ANS functioning

Systematic reviews and meta-analyses have demonstrated that individuals who have experienced child maltreatment have an increased risk throughout the life course for various forms of psychopathology, including post-traumatic stress disorder (PTSD), anxiety disorders, depressive disorders, disruptive behaviour disorders, eating disorders, sleep disorders, substance misuse, and suicidality (e.g., Brown, 2003; Chen et al., 2010; Kendall-Tackett, Williams & Finkelhor, 1993; Mulvihill, 2005; Paolucci, Genius & Violato, 2001). However, not all maltreated children develop psychopathology (e.g., Cicchetti, 2010). While literature in this area is developing (e.g., see Afifi & MacMillan (2011) for a review), more research is needed to determine why some children are resilient to these negative outcomes and others are not.

The extant literature suggests that differences in stress responsivity, including functioning of the ANS, may contribute to risk for psychopathology following maltreatment (McLaughlin, Sheridan, Alves & Berry Mendes, 2014b). First, children exposed to adversity are at increased likelihood for experiencing ANS dysregulation (e.g., Ellis, Essex & Boyce, 2005; Miscovic, Schmidt, Georgiades, Boyle & MacMillan, 2009). Second, ANS dysregulation is

associated with psychopathology. For example, a meta-analysis conducted by Graziano and Derefinko (2013) demonstrated negative associations between vagal responsivity and internalising and externalising psychopathology in children. Less is known about the potential link between SNS activity and psychopathology, but patterns of low ANS responsivity have been found in children with externalising problems (e.g., Crowell et al., 2006; Snoek, Van Goozen, Matthys & Buitelaar, 2004; Van Goozen, Matthys, Cohen-Kettenis, Buitelaar & Van Engeland, 2000). These findings are suggestive, but by no means conclusive, that disruptions to ANS functioning may mediate associations between child maltreatment and psychopathology. Additionally, El Sheikh (2005) found that marital conflict was associated with greater externalising problems in girls who showed high sympathetic responsivity measured via skin conductance, suggesting that ANS responsivity may moderate associations between adversity exposure and psychopathology risk. Thus, there is limited evidence that ANS disruptions may serve as both a mediator and moderator of links between child maltreatment and psychopathology. Work is needed to explicate the exact nature of these associations.

Theoretical constructs

At least two theoretical models may be relevant for considering the potential role of ANS functioning in the association between child maltreatment history and psychopathology risk. The Differential Susceptibility Theory (DST; Belsky, Bakermans-Kranenburg & van IJzendoorn, 2007) postulates that children vary in susceptibility to environmental influences (e.g., parental behaviours). Those most susceptible suffer the worst outcomes when exposed to poor/harmful parenting behaviours but the most optimal outcomes in response to positive parenting. These differences in susceptibility may be the result of genetic or other biologically-based factors, including differences in the responsivity of stress systems (e.g., Belsky et al., 2007). Thus, pre-existing individual differences in ANS responsivity may

influence children's susceptibility to the negative effects of maltreatment. Following from this theory, ANS functioning moderates risk for psychopathology from maltreatment exposure.

The Adaptive Calibration Model (ACM; Del Giudice et al., 2011) builds on the theory of biological sensitivity to context (e.g., Boyce & Ellis, 2005) to argue that individual differences in stress responsivity are the result of an individual's adaptation to their environment. In this way, children adaptively respond to both unsupportive and protective family environments by modifying biologically and evolutionarily based stress response systems. The specific nature of a child's calibration of the stress response depends in part on the quality of the child's environment, particularly in early life when stress response systems are more plastic. Thus, in this model, early life experiences influence future susceptibility to environmental influences. Under highly stressful conditions, such as in the context of maltreatment, a very reactive stress response system ("hyper-responsivity") may be most adaptive to allow the child to detect threat and act appropriately. Conversely, low responsivity of the stress response system ("hypo-responsivity") may be adaptive to promote insensitivity to threat for children experiencing persistent, severe stress. Data suggest that the nature of maltreatment (i.e., whether maltreatment involves emotional, physical, and/or sexual abuse, and/or neglect) and the age at which the child experiences maltreatment influence whether stress systems become hypo-or hyper-responsive (Gunnar & Quevedo, 2007). Although potentially adaptive in the immediate context, both hypo-and hyper-responsive patterns may have long-term negative consequences (Gunnar & Quevedo., 2007; Parker, Buckmaster, Sundlass, Schatzberg & Lyons, 2006). Hyper-responsivity may result in exposure to excessive levels of stress hormones, which may contribute to psychopathology (e.g., Staufenbiel, Penninx, Spijker, Elzinga & van Rossum, 2013). Hypo-responsivity may also increase risk for poor health outcomes (Phillips, Ginty & Hughes, 2013), including

psychopathology (de Rooij, 2013). Following this theory, ANS reactivity may both be affected by the experience of maltreatment (i.e., mediate) and influence (i.e., moderate) the impact of later maltreatment on psychopathology risk.

The current review

The overall goal of this review was to systematically evaluate the evidence regarding ANS responsivity in maltreated children. All types of child maltreatment – physical, emotional, and sexual abuse and physical and emotional neglect – were considered, as the current literature is not developed well enough to indicate how different types of maltreatment may influence ANS outcomes (Gunnar & Quevedo, 2007). Furthermore, co-occurrence of different kinds of maltreatment is common (Cicchetti & Toth, 1995). Studies that included domestic violence (i.e., child witnessing or being a victim of domestic violence) occurring alongside other forms of abuse or neglect were also considered. Studies that assessed marital violence but not child maltreatment were excluded, as this was considered a distinct construct (i.e., not involving neglect or violence directed toward the child) from other forms of maltreatment (e.g., Saltzman, Holden & Holahan, 2005). This review aimed to address the following question: Is a history of maltreatment associated with abnormalities of ANS responsivity in children? A secondary objective was to explore the role of ANS responsivity in the pathway to psychopathology among children who have experienced maltreatment. Studies were reviewed with attention to important developmental issues, such as age at exposure and assessment.

Methods

Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed. Electronic searches of the following databases were conducted: Embase (Ovid; 1947-2019), Medline (Ovid; 1946 – 2019), ASSIA (1987 – 2019), PsycINFO (1887 –

2019), and CINAHL (1981 – 2019). The final search was conducted in March 2019. Key word searches utilising the following terms were performed:

1. Child abuse OR abuse OR domestic violence OR child neglect OR child sexual abuse OR interpersonal violence OR maltreatment

2. Cardiovascular response OR cardiovascular reactivity OR autonomic nervous system OR heart rate variability OR sinus arrhythmia OR pre-ejection period OR heart rate OR stress reactions OR vagal OR sympathetic OR parasympathetic

3. Skin conductance OR galvanic skin response OR GSR OR skin conductance level OR SCL OR skin conductance response OR SCR

Key word searches were also performed in relevant journals (Journal of Clinical Child and Adolescent Psychology, Journal of Biological Psychiatry, Journal of Biological Psychology, Child Abuse and Neglect, Child Maltreatment), and several authors with expertise in the area were contacted to enquire about any missed studies or studies in press. Reference sections of articles were hand-searched to ensure that no relevant articles had been missed.

Articles were selected on the basis of meeting the following inclusion criteria:

1. Participants were children (0 – 19 years).

2. Childhood maltreatment was assessed via self- or parent/caregiver-report or outside agencies (e.g., Child Protection Agencies).

3. Cardiovascular or skin conductance measures of ANS (PEP, RSA, heart rate, blood pressure, SCL, SCR, and/or GSR) were taken during a stressful task.

4. Where mediation and/or moderation was examined, associations between ANS responsivity and symptoms of psychopathology, including

internalising/externalising symptoms and specific diagnoses e.g. PTSD, were assessed.

Data were extracted from the selected studies. The quality of selected studies was assessed independently by two of the authors using the Crowe Critical Appraisal Tool (CCAT). This tool includes scoring of items covering preliminaries, introduction, design, sampling, data collection, ethical matters, results, and discussion, resulting in a total score out of 40 that indicates the assessed quality overall. According to the tool's guidelines, a score of <20 is considered low quality, a score of 20-29 moderate quality, and a score of 30-40 high quality.

Results

The search produced a total of 1,388 articles (Figure 2). Articles were removed/excluded if they were duplicates (n=204), conference proceedings or masters theses (n=10), or not about ANS responsivity or child maltreatment (n=1,119). Abstracts for 55 articles were read, and those that clearly did not meet the inclusion criteria were excluded (n=19), leaving 36 articles that were read in full. Twenty-one articles met the inclusion criteria. Additional hand searches and contacting experts yielded one additional article that met inclusion criteria, resulting in a total of 22 articles for inclusion. All included articles were assessed as being of high or moderate quality via the CCAT tool (i.e., received a score ≥ 20). There was good agreement between two independent ratings of the articles. Where there were differences in agreement, an agreed score was settled upon through conference.

Heterogeneity of studies

Table 1 provides a summary of each study. Of the 22 studies, one tested moderation effects of ANS responsivity on the association between child maltreatment and psychopathology, and six tested whether ANS responsivity mediated the association between child maltreatment

and psychopathology. One tested a moderated-mediation model for the association between ANS responsivity and psychopathology. Ten utilised generic cardiovascular responsivity measurements (heart rate or blood pressure), 10 utilised specific measures of SNS activity (PEP, SCR or SCL), and 11 utilised specific measures of PNS activity (RSA) (Figure 1).

The age of participants in the included studies ranged from 2 years to 19 years. Seventeen studies investigated physical abuse; five studies examined physical neglect; 17 studies examined sexual abuse; six studies examined emotional abuse; and three studies examined emotional abuse or neglect. Four studies included witnessing domestic violence, and one study did not specify the type of maltreatment experienced by participants. Two studies drew samples from institutionalised children, where neglect was presumed to have occurred. Nineteen studies included a non-maltreated comparison group, and three studies compared ANS responsivity within maltreated samples.

Reflective of the wide age range of participants in the included studies, the type of stimuli used to assess participants' stress responses also varied, including physical, emotional, and cognitive challenges. One study used a clinical venepuncture; two a fear conditioning paradigm; one images that were positive, negative, or sexually allusive; one an interview asking participants to describe a stressful event or a free association task; one used the Video Apperception Test (during which participants watched video clips of scenes depicting everyday situations or conflict between a child and an adult and answered questions about them); one used a modified Strange Situation Procedure; one presented children with relaxation and test conditions (e.g., math calculations) via slide projections; two used an affect recognition task and video clips depicting conflict; one used a background conversation including periods of active and unresolved anger; one used mother-child joint tasks and individual tasks representing cognitive and emotional challenges; one used mother-child joint puzzle tasks; one used a timed mental rotation task (during which participants determined

whether two rotated stimuli were the same objects or one was an inverted image of the other); and eight used a version of the Trier Social Stress Test (TSST; a structured set of tasks that includes making a speech).

As the goal of this review was to take first steps to evaluate the state of the literature, a meta-analysis was outside the scope of this review. A narrative synthesis of findings is therefore presented in the following section.

Studies examining cardiovascular responsivity and maltreatment

The majority of the studies examining cardiovascular responsivity demonstrated that maltreated children exhibited a blunted response in the form of diminished SNS activity compared to non-maltreated children. Carrey, Butter, Persinger and Bialik (1995) compared physiological responses to relaxation and test conditions among children aged 7–13 years who had been physically or sexually abused and a non-abused control group. Compared to non-abused children, abused children exhibited significantly lower pulse height at baseline and smaller changes in pulse height from baseline to test conditions. Hill, Blechfield, Brunstetter, Herbert and Steckler (1989) measured heart rate in 7- to 15-year-old physically abused and non-abused children during the Video Apperception Test and found that physically abused children showed slower heart rate compared to baseline in response to video scenes depicting conflict or fearful situations. Leitzke, Hilt and Pollak (2015) measured ANS activity while children aged 9-14 years participated in a surprise speech task. Compared to non-maltreated children, maltreated children exhibited lower systolic blood pressure after the stressor and lower diastolic blood pressure at both baseline and post-stressor. Pollak, Vardi, PutzerBechner and Curtin (2005) gave physically abused and non-abused children aged 4-5 years a task to complete while a conflict conversation that included periods of active and unresolved anger played in the background. During the conflict and resolution, physically

abused children showed slower heart rate compared to baseline, which the authors interpreted as indicating attentional arousal in response to the active anger, unresolved anger, and resolution periods. These findings suggest maintenance of a state of anticipatory monitoring throughout the conversation. This contrasts to the response of non-abused children, who showed initial slowed heart rate compared to baseline in response to anger but then recovered to baseline when the conflict was resolved. Finally, Ford, Fraleigh, Albert and Conor (2010) exposed paediatric psychiatric inpatients aged 13 years to a clinical venepuncture. Those who exhibited slower heart rate relative to baseline following the stressor were more likely to have a history of physical abuse, as opposed to sexual abuse or no abuse, than those who showed no change or an increase in heart rate.

In contrast to these findings, two studies demonstrated either heightened cardiovascular responsivity among maltreated children or no differences between maltreated and non-maltreated children. Koopman and colleagues (2004) exposed maltreated children aged 11-16 years from a juvenile probation centre to stressful and non-stressful interviews and found that heart rate during these interviews varied with magnitude of maltreatment exposure: mean heart rate during both interviews was faster among those who had higher scores on the Childhood Trauma Interview, which assessed physical, sexual, and emotional abuse and physical and emotional neglect. In addition, in a longitudinal study of female children aged 12-16 years, MacMillan and colleagues (2009) found no differences in baseline or responsivity levels of heart rate following a social stress task between those who had experienced maltreatment (physical, sexual, or emotional abuse, emotional neglect, or witnessing domestic violence) and those who had not. Both groups demonstrated faster heart rate compared to baseline following the task and then a gradual decrease over time.

Studies utilising specific measures of sympathetic nervous system (SNS) activity in association with maltreatment

Six studies examined PEP in association with maltreatment. Five of these studies demonstrated that maltreated children exhibited blunted sympathetic activation during stressors compared to non-maltreated children. Busso, McLaughlin and Sheridan (2017) administered a social stress task to adolescents and found that those who were exposed to interpersonal violence (emotional abuse, physical abuse, and/or sexual abuse) exhibited blunted SNS responsivity during the speech and math components of the test compared to those who were not exposed to interpersonal violence. Gunnar, Frenn, Wewerka and Van Ryzin (2009) demonstrated that children aged 10-12 years who had been cared for predominantly in orphanages had lower overall PEP scores compared to children who had been adopted early in life and children who lived with their birth families and were therefore presumed to not have experienced maltreatment. No change in PEP relative to baseline occurred during a social stress task for any group of children. Heleniak, McLaughlien, Ormel and Riese (2016) measured PEP in adolescents while they completed a social stress task. Greater exposure to trauma, including sexual abuse, physical abuse, or another traumatic event (e.g., natural disasters, being held captive) was associated with blunted decreases in PEP responsivity during the speech component of the task. McLaughlin and colleagues (2014b) measured cardiac output during a stress task in 13- to 17-year-old adolescents who had experienced physical, sexual, and/or emotional abuse and in non-maltreated controls. Exposure to maltreatment was associated with less PEP responsivity (i.e., smaller decrease compared to baseline) during the math component of the task. McLaughlin and colleagues (2015) found that 12-year-old children in lifetime institutional care in Romania showed blunted SNS activation, including heart rate, diastolic blood pressure, and PEP, in response to a social stress task compared to children in foster care. The sixth study examined severity of maltreatment in relation to SNS activation. Oosterman, De Schipper, Fisher, Dozier and Schuengel (2010) exposed children aged 2-7 years who had experienced physical or sexual

abuse or witnessed domestic violence to an adaptation of the Strange Situation Procedure with their foster carers. Children with higher risk scores, indicating more severe maltreatment, demonstrated less PEP responsivity during the first separation from their foster carer than did those with lower risk scores.

Studies examining skin conductance and maltreatment

Five studies examined skin conductance in association with maltreatment. Among these studies, three measured SCL, two measured SCR, and one measured GSR. Reported associations between skin conductance and maltreatment were mixed, with three studies reporting blunted response among maltreated children compared to controls, and one study reporting no differences between maltreated and control children. McLaughlin and colleagues (2016) exposed maltreated children and non-maltreated controls aged 6-18 years to a fear conditioning paradigm. During the conditioning phase, maltreated children showed a blunted SCR to the conditioned stimulus. Carrey and colleagues (1995) found that maltreated children showed lower GSR than a community sample of children across relaxation and challenge stimulus conditions. Additionally, maltreated children demonstrated smaller changes in GSR from baseline than controls. Pollak and colleagues (2005) reported that when 4- to 5-year-old children were exposed to a periphery argument while completing a task, abused children showed blunted SCL, while non-abused controls demonstrated increased SCL. Jenness, Bryant Miller, Rosen and McLaughlin (2018) exposed abused and non-abused children to a fear conditioning paradigm, finding that abused children who demonstrated high levels of resting RSA showed lower SCR during extinction learning, while the non-abused group of children showed lower SCR during extinction learning among children with low resting RSA. One study did not find any associations between maltreatment and skin conductance. Ben-Amitay, Kimchi, Wolmer and Toren (2016) found no differences in SCR

between maltreated and non-maltreated children viewing video stimuli (e.g., negative, sexually allusive).

Studies utilising specific measures of parasympathetic nervous system (PNS) activity in association with maltreatment

Three studies examined RSA in association with maltreatment, with mixed findings. Oosterman and colleagues (2010) exposed children aged 2-7 years who had experienced physical or sexual abuse or witnessed domestic violence to an adaptation of the Strange Situation procedure with their foster carers. Children who had experienced sexual abuse showed decreased vagal withdrawal (i.e. smaller decreases in RSA from baseline to challenge) on separation and increased vagal withdrawal on reunion compared to children without a history of sexual abuse. Shenk, Noll, Putnam and Trickett (2010) examined physiological responses to a timed mental rotation task in sexually abused and non-abused 18-year-old females. Those who had experienced sexual abuse exhibited an asymmetric physiological response to the task, characterised by vagal withdrawal and a blunted cortisol response. Lunkenheimer, Busuito, Brown, Panlilio and Skowron (2019) examined covariation of mother-child individual and joint RSA with interactive repair during dyadic puzzle tasks in maltreating and non-maltreating dyads. Low levels of mother repair were associated with increases in child RSA in maltreating dyads, compared to decreases in child RSA in non-maltreating dyads.

ANS responsivity as a potential mediator of psychopathology following maltreatment

Six studies assessed ANS responsivity as a potential mediator of the association between maltreatment and psychopathology, including externalising/internalising problems, emotional adjustment, and PTSD. Findings regarding the role of sympathetic responsivity in mediating child maltreatment and psychopathology were varied. In a cross-sectional sample of

adolescents who completed a social stress task, Busso and colleagues (2017) did not find evidence for a mediating role of sympathetic responsivity between child violence exposure, including child maltreatment, and internalizing and externalizing symptoms. In contrast, in a cross-sectional study, Heleniak and colleagues (2016) found that blunted sympathetic responsivity among adolescents who completed a social stress task mediated the link between exposure to trauma in childhood (including sexual or physical abuse) and externalizing symptoms. Additionally, in a cross-sectional study, McLaughlin and colleagues (2016) found that, when exposed to a fear conditioning paradigm, maltreated children, relative to non-maltreated controls, showed blunted SCL responsivity to threat cues during fear conditioning and a lack of differential SCL responsivity to threat and safety cues during early conditioning. This altered fear conditioning pattern mediated the relationship between maltreatment and externalising psychopathology.

A seventh cross-sectional study conducted by Jenness and colleagues (2019) tested a moderated-mediation model. The authors exposed abused and non-abused children to a fear conditioning paradigm and found that among abused children, low SCR during early extinction learning mediated the association between high vagal tone and low levels of PTSD.

No studies demonstrated that vagal withdrawal during stress mediated the relationship between child maltreatment and psychopathology. Cipriano, Skowron and Gatze-Kopp (2011) gave a cross-sectional sample of preschool children individual or joint challenge tasks to complete with their mothers. Among children living in violent contexts, vagal withdrawal during challenging tasks was unrelated to emotional adjustment. Shenk, Putnam and Noll (2012) and Shenk, Putnam, Rausch, Peugh and Noll (2014) administered a stressor paradigm to adolescent females who had experienced physical or sexual abuse or physical neglect to investigate mediators of the relationship between child maltreatment and PTSD one year

later. Vagal responsivity alone did not significantly mediate this relationship. Rather, experiential avoidance – defined as an unwillingness to experience aversive private events, such as unwanted memories, and attempts to control or suppress such events (Hayes, Wilson, Gifford, Follette & Strosahl, 1996) – was the only significant mediator of the relationship between child maltreatment and the development of PTSD symptoms.

ANS responsivity as a potential moderator of the effects of maltreatment on psychopathology

One study found evidence that ANS responsivity moderates the association between child maltreatment and internalising symptoms. In a sample of adolescents who had or had not experienced physical, sexual, or emotional abuse, McLaughlin, Alves and Sheridan (2014a) assessed vagal tone at rest and vagal withdrawal in response to a social stress task. A positive association was found between child abuse exposure and internalising problems for adolescents with low vagal tone and low vagal withdrawal during the stressor.

Discussion

The purposes of this review were to evaluate the evidence for disruptions in ANS functioning in maltreated children and to explore the role of ANS responsivity in the pathway from maltreatment to psychopathology. The majority of studies reported a similar pattern of ANS responsivity in maltreated children in the form of blunted cardiovascular/SNS responsivity during a stress-related/challenging task. Mixed findings were demonstrated for PNS activity, with one study finding that maltreated children showed less vagal withdrawal during separation from their caregivers but increased vagal withdrawal on reunion (Oosterman et al., 2010) and another finding a more typical vagal withdrawal response to a challenging task in maltreated children (Shenk et al., 2010).

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Evidence for ANS functioning as a mediator or moderator of child maltreatment effects on psychopathology risk were mixed and limited. One study found ANS responsivity to be a potential moderator of the effects of child maltreatment on the risk for internalising problems (McLaughlin et al., 2014a). Studies investigating ANS responsivity as a mediator of child maltreatment on psychopathology reported inconsistent findings. Two studies (Heleniak et al., 2016; McLaughlin et al. 2016) found evidence that blunted SNS responsivity may mediate the association between childhood trauma, including maltreatment, and psychopathology, while four studies found no mediating role for ANS responsivity (Busso et al., 2017; Cipriano et al., 2011; Shenk et al., 2012, 2014). Interestingly, the two studies finding support for mediation effects specifically linked blunted SNS responsivity to externalizing symptoms, suggesting specificity in the associations between direction of ANS dysfunction and type of psychopathological symptoms. Notably, Heleniak and colleagues (2016) grouped a range of traumatic experiences (e.g., being involved in a natural disaster, being held captive) alongside exposure to child maltreatment. Thus, caution must be used when interpreting these results regarding the role of ANS responsivity in mediating child maltreatment effects. One study (Jenness et al., 2019) found evidence for a moderated-mediation model in which extinction learning (indexed via SCR) mediated the association between abuse and PTSD symptoms only among children with high resting RSA, suggesting that extinction learning may be a mechanism underlying the protective effects of high vagal tone in this population. Importantly, six of the seven studies testing mediation were cross-sectional (Table 1), a serious limitation. The findings from these studies should therefore be approached with caution and demonstrate a need for research that utilises longitudinal data to properly test mediation effects of ANS responsivity in maltreatment–psychopathology associations.

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Although some support was found for both the DST and ACM theories, the support is limited by inconsistencies in the findings and the study designs. DST hypothesizes that individual differences in ANS functioning may buffer or exaggerate the impact of child maltreatment effects on psychological functioning, such that the same maltreatment exposure may lead to varying levels of psychopathology depending on the individual's pre-exposure ANS responsivity tendencies. ACM posits that children's ANS functioning is influenced by their early experiences of child maltreatment and their resultant ANS functioning may influence the impact of later maltreatment exposures on psychopathology risk; thus, ACM may explain both mediation and moderation findings. Appropriate application of these models requires the study of very young children, beginning prior to maltreatment exposure, and longitudinal tracking to determine if maltreatment exposure is independent of or increases risk of ANS dysregulation and if ANS dysregulation modifies the impact of child maltreatment on psychopathology risk. As some of the study samples included in this review were adolescents, application of these models must be tempered, and further research with younger samples is required to understand how the ACM can explicate the nature of the relationship between child maltreatment, ANS responsivity, and psychopathology. Such research would need to undertake complex statistical approaches, given that the ACM predicts both hyper- and hypo-stress responsivity in contexts of stress, and these contrasting physiological responses might 'cancel out' in traditional analyses that assume linear relationships. Moreover, the ACM assumes both mediation and moderation effects, with the nature of effects varying by time and nature of maltreatment exposure (e.g., early versus later childhood; initial versus repeated maltreatment exposure). Finally, other theoretical models not discussed here may contribute to our understanding of the associations among child maltreatment, ANS functioning, and psychopathology and may deserve consideration.

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Findings from this review can be compared to others assessing constructs closely linked to maltreatment. For example, El Sheikh and Erath (2011) reviewed the literature on child ANS functioning in the context of family conflict and found that higher vagal tone and increased vagal withdrawal are protective factors among exposed children. For children living in such contexts, greater reactivity of the PNS may be adaptive given that the PNS plays a role in supporting emotion regulation and social engagement (Porges, 2007). However, the studies reviewed here found greater evidence for blunting in reactivity of both SNS and PNS among maltreated children, with maltreatment associated with blunted cardiovascular/sympathetic responsivity and lower vagal withdrawal in response to challenge. Indeed, Cipriano and colleagues (2011) suggested that extreme family violence, such as maltreatment, may overpower the ability of children's ANS to adapt flexibly to their environment. Given the state of the extant literature, the current review suggests that the role of ANS responsivity in the path from child maltreatment to psychopathology cannot yet be determined and requires further exploration.

Also relevant to consider is the different psychological/behavioral functions that may be served by different indices of ANS reactivity. For example, measures of SCL have been hypothesized to be particularly relevant to punishment sensitivity/valuation (e.g. Matthys, van Goozen, Snoek & van Engeland, 2004), whereas measures of PEP may be particularly sensitive to reward valuation (Richter & Gendolla, 2009). Consideration of these differences in function may be particularly important when studying the role of ANS functioning in the association between child maltreatment and psychopathology risk. Future studies should thus consider the constructs hypothesized to be most relevant for the particular associations of interest to be examined (e.g., punishment avoidance in relation to externalizing symptom risk) and choose ANS indices that most closely tap into those constructs.

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The inconsistencies in findings across studies are likely attributable in part to differences in study samples, methods, and statistical analyses. Consideration of different theoretical models, such as DST and ACM, may be helpful in informing future study designs. For example, DST may be more applicable to understanding how genetic differences in ANS responsivity may influence psychopathology risk in the context of maltreatment exposure, whereas ACM may be better suited for explaining the complex roles of chronic stressful experiences in both shaping ANS responsivity profiles and affecting psychopathology risk across childhood. Relevant here may be the discordant findings on the effects of child maltreatment on HPA axis functioning noted in the literature. Nemeroff (2016) suggested participant characteristics that may explain inconsistencies, including the type of maltreatment experienced, the presence/absence of psychosocial support, family history of psychiatric disorders, and genetic/epigenetic factors. The age at which the child was first exposed to maltreatment and the severity and chronicity of maltreatment exposure are also critical factors to consider. All these factors likely influence associations between child maltreatment history and ANS responsivity but have yet to be considered sufficiently in study designs. For example, not all of the reviewed studies clarified the nature of maltreatment experienced by participants or verified the occurrence of child maltreatment with child protection agencies (Table 1). The ages of participants at assessment varied across studies, from 2 to 19 years, without consideration of age at exposure. Studies are needed that examine the impact of age at exposure throughout childhood and adolescence given that there may be multiple sensitive periods for exposure effects on ANS functioning. Notably, research has identified age and gender differences in children's cardiac physiology (Fabes, Eisenberg, Karbon, Troyer & Switzer, 1994; Quas, Hong, Alkon & Boyce, 2000). Thus, normative developmental changes in ANS structure and functioning may influence the nature and magnitude of child maltreatment impact. In the reviewed studies, 19 controlled for age in

analyses (Table 1), and, of the 17 studies that included both male and female participants, 12 controlled for gender (Table 1). Future study designs should consider potential moderating effects of age and gender in their models to determine if the impact of maltreatment exposure on ANS functioning and psychopathology differ by child age and/or by gender.

A significant limitation of the study findings is the lack of gold standards for assessing ANS responsivity, including the ideal design for stress tasks. The utilization of varied measures and methods for assessing ANS responsivity hinders efforts to summarise findings across studies and to define "abnormalities" in ANS functioning. Indeed, the varying nature of the stress tasks undertaken by participants across studies may have contributed to discrepancies in the results. As child maltreatment is often interpersonal in nature, interpersonal stress tasks like the TSST may be more likely to evidence differences in maltreated children's stress responsivity. While the majority of studies (n = 16) made use of tasks that were at least in part interpersonal in nature, six did not (Table 1). In addition, Cacioppo and colleagues (1994) have highlighted the difficulty in teasing apart measurement of SNS from PNS activity, particularly when relying on heart rate and blood pressure. These measures are often used as indices of sympathetic activity despite also being influenced by the PNS (Figure 1). As such, it is important to consider that the blunted SNS response demonstrated in some of the described studies may in actuality reflect higher PNS activity, or both. In addition, baseline levels of autonomic arousal may be elevated in maltreated children, complicating analysis of changes in ANS activity in response to stress. Although the majority of studies assessed both baseline ANS functioning and stress responsivity, four studies did not (Table 1). Thus, it is difficult to establish a benchmark level of ANS responsivity that indicates that a task has been experienced as stressful for participants. A lack of change in ANS indices from baseline to stressor may indicate that the participant did not experience the task as stressful. If a task is stressful, a blunted ANS response may reflect an inability to mobilize resources to

cope with threat. Exaggerated ANS responsivity could reflect hyper-sensitivity to threat in the environment. Resolution of methodological differences may help limit discrepancies in findings across studies. Additionally, standardising methodologies and providing access to raw data within data repositories would facilitate the conduction of meta-analyses to further advance the field.

Recommendations for future work

As noted above, there is no consensus regarding the optimal task(s) to use for testing ANS responsivity, particularly with maltreated samples. The most common stress task used in the studies reviewed was the TSST, but this task cannot be used with young children due to the demands of the task. More research is needed to determine the best stress protocol(s) to use to measure ANS responsivity in maltreated children across different developmental stages. Protocols should be relevant for the populations of study and may vary, depending on the type of maltreatment as well as developmental stage. Importantly, the protocols must be ethical in light of the children's prior maltreatment experience.

The extant literature is very limited regarding the role of ANS responsivity in the association between child maltreatment and psychopathology. More research is required to assess how ANS responsivity may mediate and/or moderate associations between child maltreatment and psychopathology. Study designs should be well-informed by the developmental literature, taking into account factors the literature suggests may influence the magnitude and nature of these associations (e.g., child gender, age at exposure, type of psychopathology). Research that better characterizes samples for potential confounders is particularly needed. Careful measurement of factors that often co-vary with maltreatment and that may also contribute to ANS disruptions (e.g., socioeconomic status; other stress exposures, such as family conflict, El Sheikh & Erath, 2011) should be considered in future research. Also, the cross-sectional

design of most studies hampers efforts to determine mechanisms of effect of child maltreatment on ANS responsivity across the lifespan and prevents the drawing of conclusions regarding directions of effects. Rigorous longitudinal research is needed to address these issues. By evaluating the current state of the literature this review provided a first step toward understanding the impact of child maltreatment on ANS functioning and the role of ANS dysregulation in the association between child maltreatment and psychopathology. A suggested next step would be to determine if the disparate methodologies across studies allow for a meta-analysis to determine effect sizes and to spur additional research to address existing gaps.

Conclusion

This review suggests that ANS responsivity may be disrupted among maltreated children. Further, disruptions to ANS functioning may influence risk for psychopathology among maltreated children. As such, ANS responsivity may have important implications for intervention and treatment. As this review only examined cardiovascular and skin conductance measures of ANS responsivity, there are other issues that must be considered to develop an accurate and complete picture of stress responsivity and psychopathology in maltreated children. The current literature is far from conclusive, and much more work is needed to inform our understanding of these issues.

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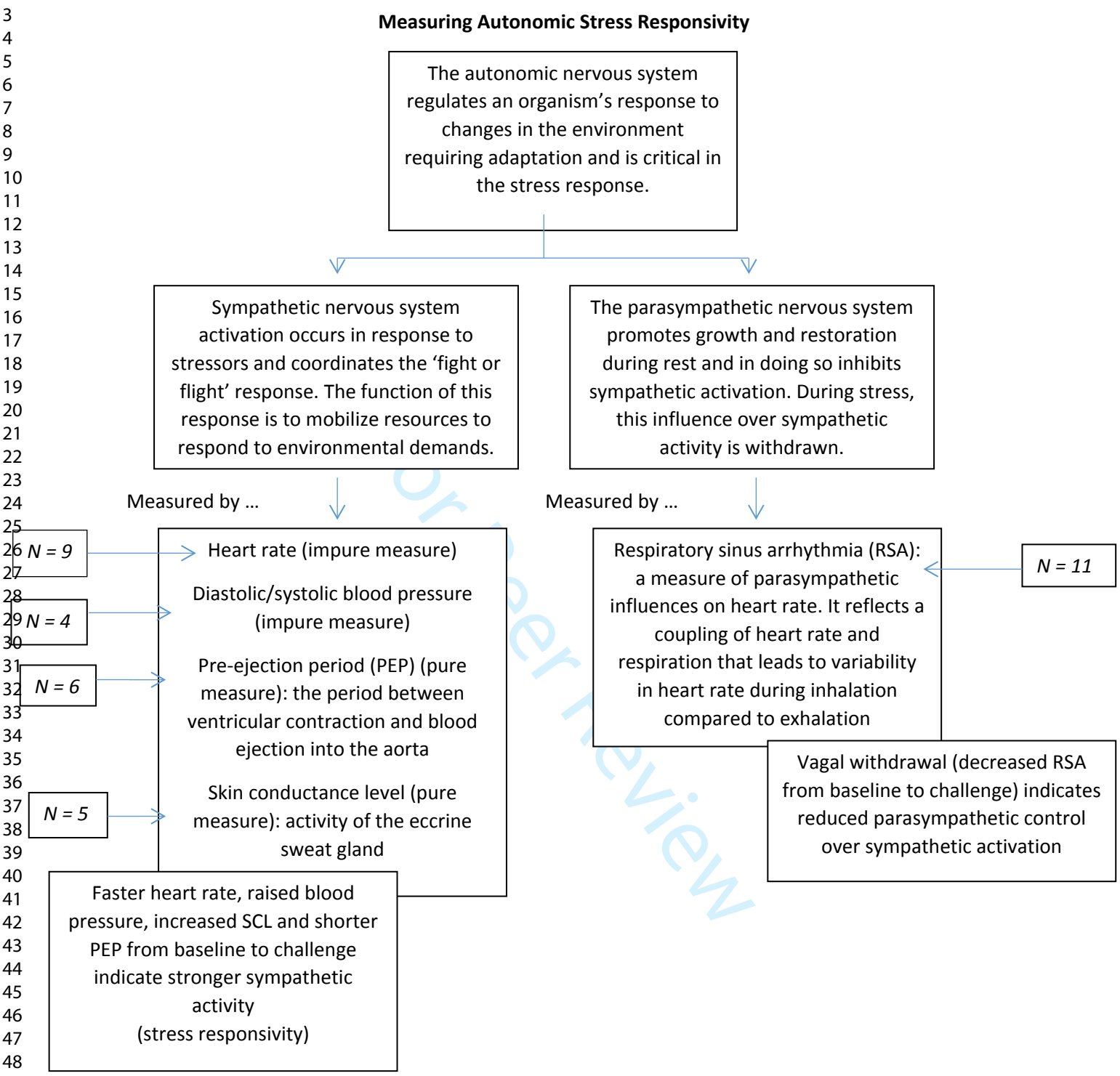

Figure 1: Description of the human autonomic nervous system stress response and measures of autonomic nervous system responsivity. N refers to the number of studies included in the systematic review utilising each measure.

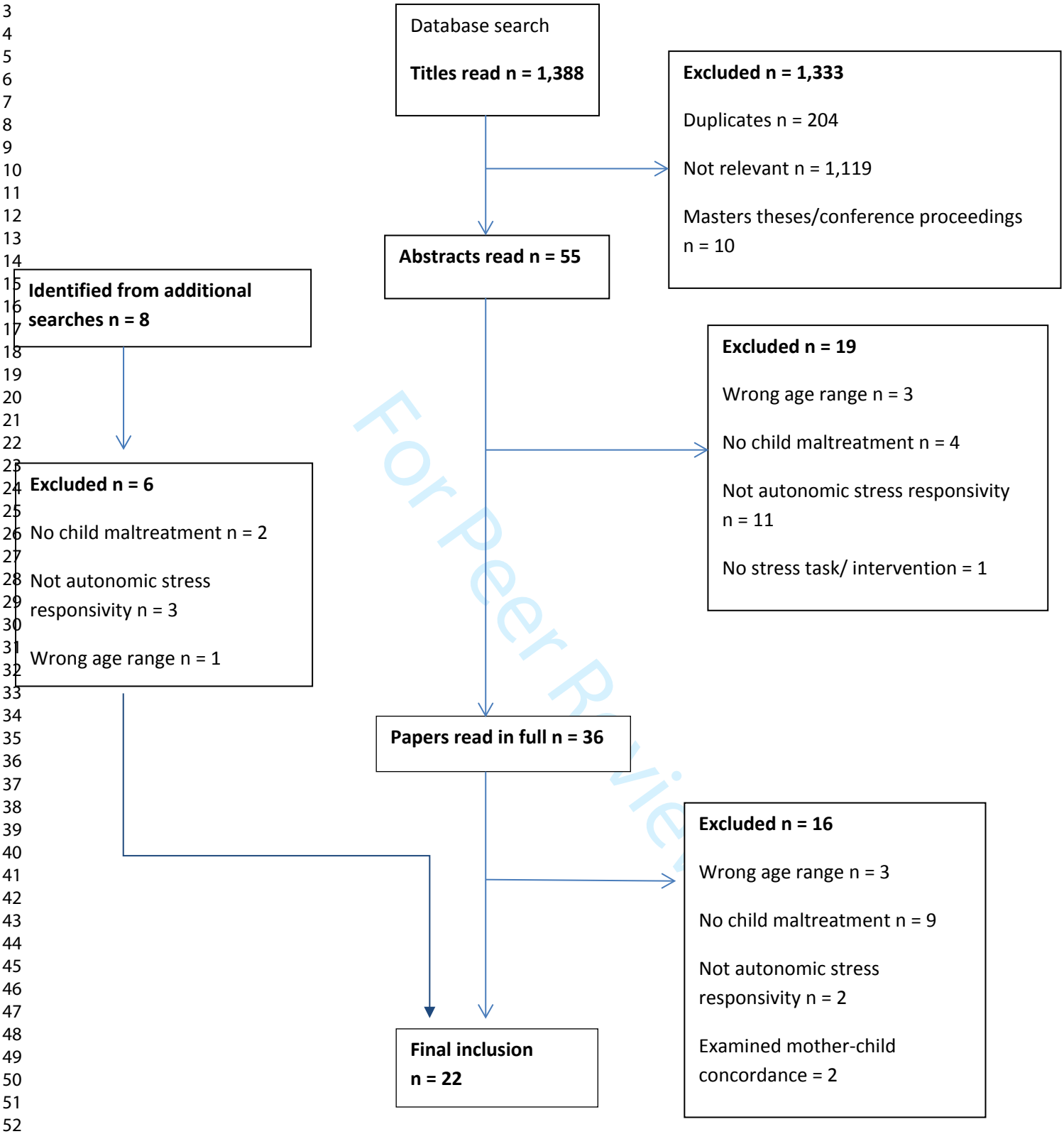

Figure 2: Inclusion and exclusion of articles

Authors/date	Study design	Outcomes	Participants (n, age, recruitment)	Type of maltreatment	Stimuli	Autonomic measures	Type of ANS measures	Confounders included in analysis	Results	CCAT Score
Ben-Amitay et al. 2016	Cross-sectional	Physiological responses to neutral and trauma-related stimuli among girls and women who experienced childhood sexual abuse	Sexually abused girls and women (n = 35) aged 7-51 years recruited from child abuse services and rape crisis centres and volunteer controls (n = 25).	Sexual abuse assessed via CTQ and interview with psychiatrist.	Images that were positive, negative, neutral, or sexually allusive	HR SCL	Responsivity	Age	Heart rate and SCL were higher when viewing a sexually allusive image among abused girls and women compared to controls.	28 Moderate
Busso et al. 2017	Cross-sectional	Associations between threat (adjusting for deprivation) and deprivation (adjusting for threat) with autonomic and neuroendocrine stress responses. Mediation of effects of childhood adversity on internalising and externalising symptoms by physiological responsivity.	Adolescents (n = 169) mean age = 14.9 years recruited from schools, after-school clubs, medical clinics at Boston Children's Hospital and the wider community.	Emotional abuse, physical abuse or sexual abuse assessed via CTQ. Exposure to violence assessed via Screen for Adolescent Violence Exposure.	TSST	RSA PEP	Baseline Responsivity	Age Gender Poverty	Interpersonal violence, adjusting for poverty, was associated with blunted sympathetic responsivity. Sympathetic responsivity did not mediate between violence exposure and psychopathology.	34 High
Carrey et al. 1995	Cross-sectional	Physiological responses of abused children to different stimuli compared to responses of a comparison group.	Abused children (n = 18) age 7 – 13 years recruited from a Children's Aid Society and a children's hospital. Comparison group recruited from schools.	Physical or sexual abuse that had been investigated legally and confirmed by medical/ psychiatric evaluations.	8 stimulus conditions (including relaxation and test conditions) presented on slides in front of child.	Pulse height SCL	Baseline Responsivity	Gender	Abused children showed significantly lower pulse height at baseline, and smaller changes in pulse height from baseline to stressful stimuli (no signal and maths conditions), as well as significantly lower SCL compared to non-abused children.	20 Moderate

Cipriano et al. 2011	Cross-sectional	Relations between cardiac responsivity, family violence exposure and preschool children's emotional adjustment.	Mother-preschooler dyads (maltreated n = 41; non-maltreated n = 33) children age 3-5 years recruited from Department of Public Welfare agencies and a database of birth announcements.	Physical abuse or neglect or emotional maltreatment identified through CYS records.	Mother-child joint Duplo task. Individual Transparent Box task. Individual Shape and Day/Night tasks.	RSA	Baseline Responsivity	Age Gender	Among children living in violent contexts (index for child maltreatment) vagal withdrawal during challenge was unrelated to their emotional adjustment.	30 High
Ford et al. 2010	Cross-sectional	Association of stress-related changes in ANS responsivity among children with a history of physical/sexual abuse.	Paediatric psychiatric inpatients (abused n = 224; non-abused n = 38) mean age = 13 years recruited from a residential treatment centre for high risk and emotionally disturbed children/adolescents.	Physical or sexual abuse documented by CPS.	Clinical venepuncture	HR DBP SBP	Baseline Responsivity	Age Gender BMI Verbal IQ Performance IQ	Participants who exhibited slower HR compared to baseline following stressor were more likely to have a history of physical abuse than those who showed no change or faster HR.	32 High
Gunnar et al. 2009	Cross-sectional	Impacts of moderate and severe early life stress on the HPA axis.	Early adopted/foster care children (n = 44) and later adopted/post-institutionalised children (n = 42) recruited from the Minnesota International Adoption Project. Non-adopted children (n = 38) recruited from the Institute of Child Development Participant Pool. Age 10-12 years.	Likely neglect as a result of institutional care; Child Life Events scale completed by carers.	TSST	PEP RSA	Baseline Responsivity	Age BMI Family income Parent/carer's education	Later adopted/post-institutionalised children (but not early adopted/foster care children) had lower overall PEP compared to non-adopted children.	30 High

Heleniak et al. 2016	Cross-sectional	Impact of childhood trauma on cardiovascular stress reactivity.	Adolescents (n = 488) participating in the TRacking Adolescents' Individual Lives Survey (TRAILS) mean age = 16.17 years.	Sexual abuse or other traumatic experience including natural disasters, life-threatening accidents, witnessing severe injury/death of another person, or being held captive/abducted assess via self-report questionnaire. Family violence/physical abuse assessed via the CTS.	GSST	PEP	Baseline Responsivity Recovery	Gender Age Maternal education	Exposure to trauma was associated with internalising and externalising symptoms. Adolescents who had been exposed to trauma exhibited blunted cardiac reactivity during the stress task. Blunted cardiac reactivity was positively associated with externalising symptoms and mediated the link between trauma and externalising psychopathology.	33 High
Hill et al. 1989	Cross-sectional	Comparison of abused and non-abused children in their perception of everyday events and their physiological response to everyday events.	Hospitalised abused (n = 29) and non-abused (n = 20) children age 7-15 years recruited from a psychiatric hospital. Non-hospitalised children (n = 50) age 7-12 years recruited from parents at the University of New Orleans.	Physical abuse that had been documented and resulted in children being removed from parents.	Video Apperception Test	HR	Baseline Responsivity	Age Gender	Abused children showed slower HR compared to baseline in response to scenes of conflict/fearful situations.	25 Moderate
Jennes et al. (2018)	Cross-sectional	Fear extinction learning as a mechanism underlying protective effect of vagal tone on PTSD symptoms among abused children.	Abused (n = 38) and non-abused (n = 56) children age 6-18 years recruited from schools, after-school clubs, medical clinics and the general community.	Physical abuse, sexual abuse, and witnessing domestic violence assessed via CECA and CTQ.	Fear conditioning task validated for children.	RSA SCR	Baseline Responsivity	Age Gender Socioeconomic status	High RSA associated with lower PTSD symptoms among abused children. This association was mediated by enhanced fear extinction learning (lower SCR during early extinction learning).	35 High
Koopman et al. 2004	Cross-sectional	Relationship of dissociative symptoms, abuse and neglect, and	Children (n = 41) age 11-16 years recruited from a juvenile probation	Physical abuse, sexual abuse, emotional abuse, physical neglect	Stressful event interview or free association interview.	HR	Responsivity	Age Gender	Mean HR was faster among those who reported more abuse or neglect. Faster mean HR was	30 High

		gender to heart rate in stressful and non-stressful interviews.	department.	and emotional neglect, assessed through the CTI.					associated with participation in the free association interview.	
Leitzke et al. 2015	Cross-sectional	ANS responsivity to a laboratory-based performance/peer rejection stressor in maltreated and non-maltreated children.	Children (maltreated n = 34; non-maltreated n = 77) age 9-14 years recruited via advertisements in the community.	Type not identified, maltreatment verified through score of >20 on the Parent-Child Conflict Tactics Scale or reports of abuse recorded with Dane County Department of Human Services.	Surprise speech task followed by negative peer feedback via computer.	HR SBP DBP	Baseline Responsivity	Age	SBP was lower for maltreated children post-stressor than for non-maltreated children. DBP was lower for maltreated children at baseline and post-stressor than for non-maltreated children.	35 High
Lunkenheimer et al. (2019)	Cross-sectional	Covarying mother and child individual and dyadic RSA with interactive repair in maltreating and non-maltreating dyads.	Maltreating (n = 59) and non-maltreating (n = 42) mother-children dyads. Children age 3-5 years. Recruited from a study on parent-child interaction and child maltreatment.	Physical abuse or neglect assessed via CPS records.	Two dyadic puzzle tasks, including a puzzle of a train, and constructing a replica of a 3-dimensional figure out of Duplo Lego.	RSA	Baseline Responsivity	Total utterances made Maternal age Maternal income	Lower levels of mother repair associated with decreases in children's RSA in non-maltreating dyads but increases in children's RSA in maltreating dyads.	33 High
Macmillan et al. 2009	Longitudinal	Differences in heart rate and cortisol resting and responsivity levels in response to a psychosocial stressor between maltreated and non-maltreated adolescents.	Maltreated female children (n = 67) age 12-16 years recruited from child protection agencies. Age-matched control group (n = 25) recruited from an existing research database.	Physical abuse, sexual abuse, emotional abuse, emotional neglect, witnessing domestic violence, identified through case review of files from Child Protection Agencies.	TSST	HR	Baseline Responsivity Recovery	Time of day	Both maltreated and non-maltreated girls showed faster HR compared to baseline following the TSST and a gradual decrease over time.	33 High
McLaughlin et al. 2014a	Cross-sectional	Vagal tone and vagal responsivity following psychosocial stressors and their influence on	Adolescents (maltreated n = 60; non-maltreated n = 97) age 13-17 years recruited from	Physical abuse, emotional abuse, sexual abuse, assessed through CTQ and SAVE.	TSST	RSA	Baseline Responsivity	Age Gender Respiration rate	Significant positive association between child abuse and internalising problems for adolescents with low baseline vagal tone. Adolescents who had	32 High

		psychopathology among adolescents exposed to childhood adversity.	schools, after school programs, medical clinics and the general community.						experienced child abuse and had low RSA withdrawal (vagal withdrawal) during the TSST were more likely to have internalising problems.	
McLaughlin et al. 2014b	Cross-sectional	Stress responsivity following child maltreatment.	Adolescents (n = 60; non-maltreated n = 97) age 13-17 years recruited from schools, after school programs, medical clinics and the general community.	Physical abuse, sexual abuse, emotional abuse, assessed through the CTQ and CECA.	TSST	BP PEP	Baseline Responsivity	Age Gender Single-parent household Poverty	During the maths component of the TSST, maltreated adolescents exhibited significantly less PEP responsivity (less decreases compared to baseline) than non-maltreated adolescents.	35 High
McLaughlin et al. 2015	Longitudinal	Development of the ANS and HPA axis in children exposed to early-life deprivation associated with institutional care.	Part of the Bucharest Early Intervention Project. Children from Romanian institutions randomized to a high-quality foster care intervention (n = 48) and children remaining in Romanian institutions (n = 43). Typically developing Romanian children (n = 47). Mean age = 12 years.	Likely neglect as a result of institutional care.	TSST Frustration task	HR SBP DBP PEP RSA	Baseline Responsivity	Pubertal development	Children remaining in institutional care showed blunted HR, DBP and PEP during the speech component of the TSST, and blunted DBP and PEP during the maths component.	37 High
McLaughlin et al. 2016	Cross-sectional	Relation of trauma and neural structure to fear conditioning in children.	Maltreated children aged 6-18 years (n = 38) and controls (n = 56) recruited from schools, after school and prevention programmes, and medical clinics.	Physical abuse, sexual abuse, or domestic violence assessed via the CECA and CTQ.	Fear conditioning paradigm using bells as the conditioned stimulus and an aversive alarm noise as the unconditioned stimulus.	SCL	Responsivity	Age Gender IQ Poverty Non-maltreatment trauma exposure Symptoms of anxiety and depression PTSD symptoms PTSD diagnosis Externalising problems	Maltreated children exhibited blunted SCL to conditioned stimulus compared to controls and failed to show differential SCL to threat cues compared to safety cues during conditioning. This altered pattern of conditioning mediated the relationship between maltreatment and externalising psychopathology.	36 High

Oosterman et al. 2010	Cross-sectional	ANS activity of children during separation and reunion with foster carers.	Foster children (n = 60) age 2-7 years and their primary foster parent.	Neglect, physical abuse, sexual abuse, witnessing domestic violence, identified through questionnaires completed by child welfare case workers.	Strange Situation (modified for older children).	PEP RSA	Responsivity	Age Time in placement Previous placements	Children with higher maltreatment scores showed less PEP responsivity (less decreases compared to baseline) during first separation. Sexually abused children showed decreased RSA (vagal withdrawal) on separation and increased RSA on reunion compared to children without a background of sexual abuse.	28 Moderate
Pollak et al. 2005	Cross-sectional	Attentional regulation in response to interpersonal anger among physically abused children.	Abused (n = 11) and non-abused (n = 22) children age 4-5 years recruited through Department of Human Services and flyers posted locally.	Physical abuse, cases substantiated by Dane County Department of Human Services.	Background conversation including baseline period, active anger period, unresolved anger period and resolution period.	HR SCL	Baseline Responsivity Recovery	Age Gender	Abused children showed slower HR compared to baseline in response to the anger period and maintained this state and showed a steady decline in SCL across the anger period. Non-abused children were initially aroused (slower HR compared to baseline and increase in SCL) in response to anger but showed recovery to baseline when the conflict was resolved.	36 High
Shenk et al. 2010	Longitudinal (assessed at six time points over 13 years)	Stress response in maltreated children and levels of psychopathology over time.	Abused females (n = 52) age 6-16 years recruited from CPS agencies. Comparison group recruited from community advertisements (n = 77). Assessments providing this data took place at age 18 and 24 years.	Sexual abuse, substantiated by CPS agencies in Washington, DC.	Timed mental rotation task; incorrect responses followed by an aversive noise.	RSA	Baseline Responsivity	Age Minority status Previous levels of internalising and externalising behaviours	Sexual abuse in childhood significantly predicted an asymmetrical physiological response (blunted cortisol response and vagal withdrawal) to stressor at late adolescence (18 years).	37 High
Shenk et al. 2012	Cross-sectional	Relationship between RSA and cortisol responsivity, experiential	Adolescent females (maltreated n = 51; non-maltreated n = 59) age 14-19 years	Physical neglect, physical abuse or sexual abuse determined by CPS agency	Performance (timed affect recognition task) and interpersonal (video clips of	RSA	Baseline Responsivity	Age Cigarette use Steroid use	Vagal responsivity alone did not significantly mediate the relationship between child maltreatment and PTSD.	36 High

		avoidance, PTSD and child maltreatment.	recruited from CPS agencies and teen health centres.	investigation.	parent-adolescent conflict) tasks.					
Shenk et al. 2014	Longitudinal (1 year follow up)	See above	See above	See above	See above	RSA	Baseline Responsivity	See above	See above	33 High

Table 1: Included articles, organised alphabetically

Abbreviations: ANS – Autonomic nervous system; BP – Blood pressure; BMI – Body mass index; CCAT – Crowe Critical Appraisal Tool; CECA – Childhood experiences of care and abuse; CPS – Child Protection Service; CTI – Comprehensive trauma interview; CTQ – Childhood trauma questionnaire; CTS – Conflict tactics scale; CYS – Children and youth services; DBP – Diastolic blood pressure; GSST – Groningen social stress task; HR – Heart rate; PEP – Pre-ejection period; PTSD – Post traumatic stress disorder; RSA – Respiratory sinus arrhythmia; SAVE – Screen for adolescent violence exposure; SBP – Systolic blood pressure; SCL – Skin conductance level; SCR – Skin conductance response; TSST – Trier social stress test