Caregiver and Young Child Biological Attunement In Distress Contexts: A Systematic Review and Narrative Synthesis

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Abstract

The objective of the current study was to systematically review the literature on caregiver-child biological attunement within distress contexts during the first three years of life. A total of 9932 unique abstracts were identified through Medline, Embase, PsycINFO, CINAHL, and Scopus databases. Thirty-six studies provided data from caregivers and their infants or toddlers within a distress paradigm, used biological indicators of distress, and assessed the relations between caregiver and child biological indicators. Findings were synthesized based on biological indicators, type of analysis, and measurement epochs pre- and post-distress. Most articles examined cortisol. Associations between caregiver and child cortisol indicators were moderate to large, though findings varied depending on the analysis used and measurement epochs examined. Many of the findings examining relations between mother and child cardiac, sAA, and EEG indicators were weak or inconsistent, likely due to the limitations of methodological approaches used to capture the complexity of the caregiver-child attunement process. Gaps in the literature and suggestions for future research are discussed.

Key words: Caregiver-child, Biological Attunement, Infancy, Toddlerhood

1. Introduction

The first few years of life are marked by acquisition and differentiation of a set of skills implicated in the process of regulation (e.g., language development, executive attentional control, theory of mind; Thompson et al., 2008). As these skills develop, a transition occurs from relying heavily on one's caregiver, as an external regulator, to more self-directed regulation attempts (Ekas et al., 2018). Longitudinal research using a behavioural distress indicator has shown substantial variability in patterns regarding how children regulate from distress across the first years of life (i.e., from infancy to preschool; Pillai Riddell et al., 2011; Waxman et al., 2017). Thus, understanding the developmental origins of emotion regulation is crucial for determining implications of regulation deficits and the risk of long-term psychopathology. A child's immediate response and ability to recover from distress in early life is multi-determined, involving an interplay between individual (e.g., genetics, temperament) and contextual characteristics (e.g., relationship with caregiver) (Calkins & Hill, 2007). Although individual factors are important, significant developments in regulation skills early in life occur in the context of the caregiver-child relationship (Ainsworth, 1979; Bowlby, 1982). Tronick (1989) proposed a theoretical model explaining the reciprocal nature of caregiver-child interactions and the importance of these interactions for scaffolding affect regulation. According to Tronick's Mutual Regulation model (MRM; Beeghly & Tronick, 2011; Tronick, 1989), the capacity to recover from distress emerges early in life from within a dyadic mutually regulating communication system, which includes a child subsystem, a caregiver subsystem, and ongoing communication between them. Both children and caregivers use communicative signals (e.g., crying, touching, physical separation) to convey their biobehavioural regulatory states.

For decades, researchers have observed the nature of caregiver-child interactions within stressful contexts as the dyad works toward a mutually regulated state. The caregiver-child

interactions in stress contexts typically involve dynamic, contingent, and reciprocal responses between dyad members to aid in recovery from distress (i.e., each dyad member produces and responds to the other's communicative signals; Bell, 2020; DiCorcia & Tronick, 2011). However, the caregiver is primarily responsible for driving regulation in young children given the child's limited capacity early in life. If a child is distressed, ideally the caregiver will be able to understand the child's inner state of distress, regulate their own behavioural and biological responses to stress, and respond sensitively and contingently to regulate the child. Caregiver self-regulatory abilities influence how they respond to their child's distress, which in turn influences their child's ability to regulate from distress (Bridgett et al., 2015) and subsequently contributes to the caregiver's regulation of distress. As a result, the caregiver and child are able to adjust and regulate their distress together (Creavy et al., 2020; Provenzi et al., 2018). During this process, the caregiver's use of regulatory strategies within the dyadic interaction helps build the child's repertoire of cognitive, behavioural, and biological strategies (Calkins & Hill, 2007; Tronick, 2017). However, this pattern may not always occur, as caregiver-child interactions can be disrupted by the caregiver's inability to regulate their own distress (DiCorcia & Tronick, 2011; Tronick, 2017).

Many researchers have studied these caregiver-child exchanges and the degree to which biological or behavioural regulatory states of caregivers and their children are temporally coordinated. These interaction patterns have been referred to using various terms such as caregiver-child *attunement*, *synchrony*, *matching*, *co-regulation*, *concordance*, and *affect contagion* (Bernard et al., 2016). Based on our theoretical understanding of early caregiver-child dynamics, for the purpose of this review, attunement was the term used and defined as the dynamic and reciprocal influence between caregivers and their children over time as they work towards a regulated state (Atkinson et al., 2016; Beeghly & Tronick, 2011). While there are a

number of dimensions of attunement (e.g., behavioural, cognitive-emotional), the current work focused exclusively on biological attunement.

1.1. Dyadic biological attunement in stress contexts

Within the last two decades, there has been a greater focus on studying biological attunement as a critical underlying mechanism of caregiver-child distress regulation. Basic control of biological processes is necessary to support use of behavioural emotion regulation strategies (Calkins & Hill, 2007). Cycles of mutual influence and feedback are then established between biological and behavioural levels of regulation (Feldman, 2007; Feldman, 2016). The link between caregiver and child biological systems is a primitive process evidenced very early in the child's life, including prenatally (e.g. the effect of prenatal stress on a child's HPA axis and brain development; Lautarescu et al,. 2020; Oberlander et al., 2008) and during the neonatal period (e.g. skin-to-skin contact that modulates infant heart rate, sleep patterns, and temperature; Feldman et al., 2002; Moore et al., 2016). Caregiver physiology, through its effect on caregiver behaviours in response to their child's distress (e.g., sensitive or insensitive behaviours), bodily contact with the child (e.g., skin-to-skin contact), and the sensory experience of the child (e.g., the child hearing caregiver's calm heart rate during skin-to-skin contact), operates as a "hidden regulator" of young children's physiological response (Braren et al., 2019; Hofer, 2010). As such, biological attunement provides a unique window into understanding coregulatory dynamics of the caregiver-child relationship.

Common tasks used to examine the co-regulatory dynamics between caregivers and their children include parent-child interaction tasks that disrupt or threaten the attachment relationship through separation (e.g., the Strange Situation Procedure [Ainsworth et al., 1978]) or disrupted behavioural communication (e.g., the Still Face Paradigm [Tronick et al., 1978]). There are also tasks that elicit fear and frustration in the infant or toddler through exposure to novel stimuli or

situations, such as the LabTAB paradigm (Goldsmith et al., 1993). These various tasks have shown evidence of eliciting a biological stress response in young children, particularly the paradigms that interfere with the child's main source of coping and security (i.e., their caregiver) (Gunnar et al., 2009; Jones-Mason et al., 2018; Provenzi et al., 2016).

The current review is focused on examining patterns of attunement during distress across different biological indicators and statistical procedures used by researchers. Specifically, there are multiple systems that have been studied to capture the biological attunement process, including the hypothalamic pituitary adrenal axis (HPA), the autonomic nervous system (ANS), which is further subdivided into the parasympathetic nervous system (PNS) and the sympathetic nervous system (SNS), and neural systems. The HPA axis plays a central role in one's bodily response to stress, as it manages reactivity to challenging situations via a cascade of hormones released in the body and ends with the production of cortisol (Smith & Vale, 2006). When individuals are exposed to stressful stimuli, activity of the HPA axis increases and an individual's stress response is reflected in their cortisol levels. The PNS also plays an important role in the body to regulate stress-related arousal via the influence of the vagus nerve on one's heart. A commonly indexed measure of parasympathetic activity is respiratory sinus arrythmia (RSA), which reflects the rhythmic fluctuation in heart period at the respiratory frequency (Berntson, Cacioppo, & Quigley, 1993). Porges' polyvagal theory (Porges, 1995; Porges, 2011) suggests PNS activity is an important indicator of self-regulatory capacity, as it allows the dynamic regulation of one's arousal to either foster engagement or disengagement in response to situational demands. In addition to cortisol and RSA, other biomarkers used to index stress include salivary alpha amylase (sAA; SNS system), electroencephalography (EEG; neural activity) and heart period (HP; index of joint PNS and SNS arousal). The literature on these

biomarkers in the attunement literature is nascent but are summarized briefly herein to provide a comprehensive overview of the biological attunement literature to date.

Arguably, the greatest complexity in examining attunement involves the analytic approach used to capture the dyadic process. Researchers have used various analytic approaches that significantly differ in terms of their underlying assumptions about the concept under study (Bernard et al., 2017). For example, a simple correlation suggests that attunement is an association between caregiver and child responses at one point in time, whereas a cross-lagged model considers both changes in individual response patterns over time and the reciprocal influence between caregivers and their children. Thus, to draw conclusions about caregiver-child biological attunement, patterns across different measurement and analytic approaches needs to be examined to clarify and further our understanding of this phenomenon.

1.2. Current Study

The primary goal of the current review is to provide an in-depth summary of the available studies examining caregiver-child biological attunement in early life, particularly within a distress context. To our knowledge, this is the first review to focus on synthesizing research over the first few years of life. A narrative synthesis methodology was undertaken because the complexity inherent in this literature precluded a meta-analysis. This complexity related to the variety of a) biological indicators, b) types of statistical analyses, c) epoch definitions (i.e., time periods such as the immediate response [initial reactions to distressing stimulus] or recovery response [return to homeostasis]) between and within biological indicators, d) developmental ages or stages, and e) covariates and moderators used to examine caregiver-child biological attunement.

Thus, the review synthesized results according to biological indicator and analysis approach. Results are discussed separately for each biological indicator (cortisol, sAA, cardiac

indicators [RSA, HP], and EEG) and further subdivided according to three broad statistical analysis groupings: *static concurrent and non-reciprocal* (e.g., correlations or regressions), *dynamic concurrent and non-reciprocal* (e.g., multilevel modeling examining rates of change), and *dynamic concurrent and reciprocal* (e.g., cross-lagged modeling). Further details of analysis groupings are included in the methods section (see section 2.7. Data Synthesis). Results were also synthesized based on epoch type (i.e., outcomes examined separately for baseline, immediate response, and recovery periods or collapsed across time). Broad syntheses of developmental patterns (Infancy [0-11months], Early Toddlerhood [12-23 months], and Middle/Late Toddlerhood [24-47 months]) and covariates and moderators are discussed. For each indicator by analysis grouping of articles, the synthesis included a general description of the indicator and its measurement, a description of the relationship direction (positive, negative), and a general summary comment on the overall quality, magnitude, and consistency of the findings.

2. Methods

2.1. Protocol and Registration

The current study followed an *a priori* protocol using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (PRISMA; Moher et al., 2009). See Appendix A for PRISMA checklist. Our protocol was submitted for registration prior to data extraction with the International Prospective Register of Systematic Reviews (PROSPERO; registration no. CRD42019137782).

2.2. Eligibility Criteria

Prospective-observational studies were included if: 1) participants included caregivers and their infants or toddlers (0 to 3 years of age), 2) biological indicators for both caregivers and children were measured, 3) biological indicators were measured within the context of an acutely distressing stimulus or event, and 4) relationships between caregiver and child biological

indicators were estimated. Studies were excluded if 1) animal subjects were used, 2) children were older than 3 years of age, 3) methods did not include a distressing event, 4) either caregiver or child biological indicators were not measured, 5) caregiver and child biological indicators were not measured during the same period (i.e., within the same paradigm), or 6) estimates of the associations between caregiver and child biological indicators were not reported. Further, non-empirical articles (reviews, book chapters, commentaries, conference proceedings) and non-English articles were also excluded.

2.3. Systematic Search

A systematic literature search was conducted by an academic librarian from the Hospital for Sick Children in Toronto, Ontario, Canada. The original search was completed in January 2019 using Medline, Embase, PsycINFO, CINAHL, and Scopus databases. Ongoing weekly Google Scholar updates were conducted to include any relevant articles published between January 2019 and August 2020. An updated systematic search was conducted in December 2020 to find relevant articles published after the date of the original search. Database-specific subject headings and text word fields fell into three categories related to the constructs of (1) the caregiver-child relationship, (2) biological measures (cardiac indicators, cortisol, salivary alpha amylase, electroencephalography), and (3) children ages zero to three years (see Appendix B for search terms and pairings). References of all included studies were also searched. No date limits were applied to ensure the review encompassed relevant historical and current literature.

2.4. Study Selection

Two authors, with previous systematic review experience, designed the abstract selection criteria. Following removal of duplicates, all titles and abstracts from the systematic search were reviewed to determine eligibility for inclusion by three independent reviewers. Covidence online software, a systematic review management tool (www.covidence.org), was used to support and

improve the efficiency of screening abstracts for inclusion among the independent reviewers. Approximately one-third of the abstracts (33%) were double-coded, and the overall average agreement rate was 94.4%. All disagreements reached a consensus through discussion.

Articles that met inclusion criteria based on the title and abstract were flagged for full-text review (see Figure 1 for PRISMA flowchart). Of note, studies with either distress or non-distress contexts were originally considered for inclusion (PROSPERO; registration no. CRD42019137782). However, given the substantial amount of literature found in the distress context, which is our primary interest, we narrowed our focus to the current analyses. Articles that were confirmed to meet the inclusion criteria during full-text review were included in the narrative review.

2.5. Data Collection Process

The following data were obtained from the final sample of 36 studies, including research group, demographic and study characteristics (country, study type [cross-sectional, longitudinal], age of child), methodology (biological indices, distress paradigm, the number and timing of pre- and post-distress epochs, type of analyses), study results, and additional variables (i.e., covariates, moderators) that were included when examining the relation between caregiver and child biological indicators. It is important to consider covariates and moderators because there are many procedural and individual factors that can affect biological systems (Clements, 2013; Provenzi et al., 2016; Waxman et al., 2016). Effect sizes were prioritized for data extraction, particularly standardized effects (i.e., correlations, standardized path coefficients), as they can be effectively interpreted and compared across studies with different biological indicators and measurement approaches (Flora, 2020). When data were not provided (e.g., Pearson *r*s not reported for null associations, baseline data collected but not reported), authors were contacted via email on two occasions. Of twelve authors contacted, six responded to the email request for

data. Three authors provided missing data, and three authors were unable to provide data requested, as the data were inaccessible. Three authors extracted data from included studies, with the lead author double extracting all studies to ensure consistency in the process. Discrepancies were minimal and resolved through discussion.

2.6. Risk of Bias Assessment

To examine the validity of results of the included studies, a 15-item checklist was developed based on the National Heart, Blood, and Lungs Institute Quality Assessment (National Heart, Lungs and Blood Institute, 2017), Downs and Black (1998), and Crombie (2007) checklists. The full list of items is in Appendix C. For each item, scores reflected whether the quality index was present (1), absent (0), or not applicable. Quality assessments for each study were double-coded by the lead author and one of the co-authors. There were minimal disgagreements (inter-rater agreement was 93.8%) which were resolved through discussion.

An overall quality score was caculated for each article by summing the quality indices. The summed scores were converted to a percentage, excluding non-applicable ratings. Higher percentages reflect higher quality study methodology that was also well reported. Quality scores are reported for each study in Table 1 and discussed in the results section to inform the validity of results reviewed.

2.7. Data Synthesis

The extracted data were stratified by biological indicator (cortisol, sAA, cardiac indicators, and EEG) and type of analytic approach. Although researchers may be trying to measure the same concept of attunement, many of the analysis approaches used have different underlying assumptions about the phenomenon under study (Bernard et al., 2017). The type of analyses used to study attunement differed based on whether they considered the dynamic nature of the process (i.e., changes over time) or the reciprocal influence (i.e., who is responding to

whom) between dyad members. Analyses were organized based on the following broad groupings: (1) *static concurrent and non-reciprocal analyses*—includes bivariate correlations, regressions, and multilevel analyses that assume attunement is an association between caregiver and child biological indicators at individual time points (i.e., "match of phase"; Feldman, 2007) and does not account for bidirectional reciprocal influences (i.e., current biological responses of each dyad member influences their partner's subsequent biological response), (2) *dynamic concurrent and non-reciprocal analyses*—includes correlations or regressions of change scores (i.e., change from pre-to-post stressor) and multilevel growth models, suggesting attunement occurs when caregivers and children "match in the direction of change" (Feldman, 2007) but does not consider the reciprocal influences, and (3) *dynamic concurrent and reciprocal analyses*—includes cross-lagged analyses that assume attunement involves concurrent changes in caregiver and child biological indicators over time and reciprocal influence between dyad members. The Actor-Partner-Independence Model (APIM; Kenny 1996) describes the theoretical basis of using a cross-lagged model to examine the interdependence within dyadic interactions, as dyadic data are not independent. There are three important components of the model, including (1) stability of responses within the same individual (i.e., actor effects) for children and their caregivers, (2) the prediction of child responses from caregiver responses at an earlier time point and vice versa (i.e., partner effects), and (3) the concurrent relations between caregiver and child responses at any one time point (Bader et al., 2021). Lastly, broad syntheses of data according to developmental patterns, covariates (i.e., variables examined to have additive effects on outcomes), and moderators (i.e., variable that interacts with another predictor to have multiplicative effect on outcome) are also reported. The narrative synthesis includes a description of consistency, magnitude (standardized effect sizes were reported if quantitative results were provided), and general direction (positive, negative) of findings, as well as a general comment on

quality of studies. If quantitative results were not reported, often due to lack of statistical significance, results were summarized accordingly.

3. Results

3.1. Study Description

3.1.1. Study Selection

After removing duplicate records, the electronic searches identified 9,932 unique abstracts, including five additional records found from Google Scholar updates. Using the *a priori* selection criteria, a total of 218 articles were selected for full-text review. Of these, 36 articles fulfilled the inclusion criteria for the narrative synthesis. See Figure 1 for the PRISMA flow chart outlining the stages of article selection.

3.1.2. Study Characteristics

The key characteristics of the studies included in this review are outlined in Table 1. The studies are organized by research group or sample. There are 26 unique samples and most of the research was conducted in the United States (69%). The remaining studies were completed in Canada, Brazil, Scotland, Israel, Sweden, and the Netherlands. Most studies were cross-sectional (83%). Of the five articles that included longitudinal data, two examined data separately at each age using the same distress context (Braren et al., 2019; Davis & Granger, 2009) and three collapsed across ages in the main analyses (Atkinson et al., 2013; Hibel et al., 2015; Laurent et al., 2020). All articles reported data on children between 0 and 3 years of age, with most being within the first year of life (Infancy [0-11 months] = 20 articles, Early Toddlerhood [12-23 months] = 12 articles, Mid-Late Toddlerhood [24-47 months] = 8 articles). Sixteen articles, most using cortisol as a biological indicator, included a clinical or high-risk sample. All studies included mothers as the primary caregiver except for one study that included a very small

subsample of fathers (2 out of 83 parents; van Bakel & Riksen-Walraven, 2008). Thus, results are summarized according to mother and child outcomes.

Regarding study methodology, a variety of biological indicators (Cortisol = 24 articles, sAA = 5, RSA = 10, HP = 2, EEG = 2; 8 articles measured two biological indicators) were used to measure mother and child stress responses and recovery, though most articles used cortisol. Many different distress paradigms were used, with the most common being the Still-Face Paradigm (Tronick et al., 1978), the Strange Situation Procedure (Ainsworth et al., 1978), and the Lab-TAB paradigm (Goldsmith & Rothbart, 1993). All studies measured mother and child stress responses either before (i.e., baseline), after the stressor (i.e., immediate response or recovery), or both. The number of post-stress epochs ranged from one to four. Timing of post-stressor epochs varied widely across studies, both for studies that used different biological indicators across epochs and those that used the same indicator. The *baseline* epoch was considered a measurement taken while the mother and child were at rest before the distress paradigm. The *immediate response* epoch was defined as a measurement during (cardiac indicators) or subsequently after (cortisol and sAA) the stressor. The *recovery response* epoch included a measurement taken after the stressor during which time the mother and child are working to return to baseline. A variety of variables were controlled across studies (see Table 5), including various maternal, child, and procedural factors, as well as moderators, which were often either individual (e.g., age), risk (e.g., maternal mental health), or protective factors (e.g., caregiver sensitivity).

3.1.3. Handling Multiple Effects

Several studies included multiple results as evidence of attunement for one or more of the following reasons: 1) participants underwent two different distress tasks; 2) there was more than one cortisol or sAA sample taken to capture the immediate response or recovery response; 3) two different groups were examined (e.g. very preterm and preterm infants); 4) the data were

examined using more than one biological indicator (e.g. cortisol and sAA) or analysis (e.g. correlations and growth curve modeling); and 5) children participated at multiple ages. If participants underwent two different distress tasks within a particular age grouping (e.g., early toddlerhood [12-23 months of age]), the results from the more distressing task (as indicated by the paper or author consensus) were summarized. Biological samples taken post-stressor that closely resembled the methodologies for other included studies were summarized to minimize heterogeneity. For example, the cortisol sample taken closest to 20 minutes post-stressor was considered the immediate response and the sample taken closest to 40 minutes post-stressor was considered the recovery response. However, for studies that used multivariate analyses and collapsed across epochs, all samples were included. Data from all participants examined, regardless of sample group, were reported. If data were examined using multiple analyses within the same analysis grouping (e.g., static concurrent, non-reciprocal analyses: correlation and regression), results that could be reported as a standardized effect size, most often correlations, were included. Articles that examined data with different biological indicators or analysis groupings were included in the summary, as the findings could be differentiated. Finally, because broad developmental patterns were summarized according to three age groups (infancy, early toddlerhood, and middle to late toddlerhood), articles that presented results within different age groupings were included for the narrative synthesis.

3.1.4. Quality Assessment

Quality percentage scores ranged from 53% to 87%, with a median score of 73%. The distributions of articles that received credit for each quality item are illustrated in Figure 2. The following are items that commonly reduced an article's quality score (i.e., the items for which at least 50% of articles did not receive credit): study population was not clearly defined (i.e., type of sample, the range of dates when participants were recruited), recruitment rate of 50% or more of

eligible participants was not reported or was not reached, blinding of outcome assessors was not detailed, and exact *p*-values were not reported (e.g., $p < .05$ instead of $p = .03$).

3.2. Synthesis of Results: Relations between caregiver and child biological indicators

Below is a narrative summary of existing evidence on the relation between caregiver and child biological indicators in distress contexts. Tables 2 (a, b and c), 3, 4, and 5 summarize findings for each study in the narrative synthesis, according to biological indicator and further organized by analysis groupings. Results within each table also summarize results by epoch (baseline, immediate response, recovery response). Broad patterns of findings related to age and covariates or moderators across all articles are also discussed.

3.2.1. Salivary Cortisol

Cortisol is the final glucocorticoid released and is the primary biomarker of HPA activity (Clements, 2013). For this review, all articles used saliva samples of cortisol. For sampling, there are theoretical rationales and empirical evidence to suggest that cortisol peak responses (i.e., reactivity) occurs around 20 minutes post-stressor, and a recovery response is to be expected around 30 to 40 minutes post-stressor, though timing tends to vary widely among studies (Provenzi et al., 2016), which is evident in the current review.

The current review included 25 studies, representing 18 distinct samples, that examined relations between mother and child cortisol in a distress context (see Table 1). Five articles (Atkinson et al., 2013; Braren et al., 2019; Davis & Granger, 2009; Hibel et al., 2015; Laurent et al., 2020) included longitudinal data. The samples in 16 studies (64%) were identified as clinical or high-risk. Timing of cortisol samples varied across studies from during the stressor to 50 minutes post-stressor. Samples ranging from 5 to 20 minutes post-stressor were considered the immediate distress response and samples taken between 35- and 50-minutes post-stressor were considered to capture the recovery response. Articles reporting cortisol outcomes were of higher

quality on average (mean quality score = 76.16%, range = 67 – 87%). Results are summarized in Tables 2a–c according to analysis groupings.

3.2.1.1. Static Concurrent and Non-Reciprocal (Cortisol): As summarized in Table 2a, 23 articles examined the association between mother and child cortisol using static concurrent, non-reciprocal analyses, including correlations, regressions, and multilevel modeling (concurrent model). Only one study did not use a validated lab paradigm (Hendrix et al., 2018) and three studies used a routine vaccine or heel lance as the stress-inducing stimulus (Castral et al., 2015; Davis & Granger, 2009; Spratt et al., 2016). Partial standardized effect sizes are reported for five studies that controlled for various procedural or individual characteristics that commonly affect cortisol outcomes (see Table 6 for list of covariates; Hibel et al., 2015; Kalomiris & Kiel, 2018; Kivlighan, 2009; Laurent et al., 2012; Laurent et al., 2020).

Seventeen studies examined relations between mother and child cortisol according to baseline or post-distress epochs. Most studies that examined the relation between mother and child cortisol at baseline (14 of 16 articles) reported a positive association, with effects ranging from small to large (r = .14 to .71; partial b^* = 0.47). Most of the reported effects (12/14) are moderate to large, positive relations between mother and child baseline cortisol (r > .23). Associations during the immediate response period were variable (r = -.09 to .49, partial b^* = 0.23, or non-significant and unreported). However, most studies (10/15) that examined the immediate response period found evidence of moderate, positive associations between mother and child cortisol (r = .22 to .49; partial b^* = 0.23). The relations between mother and child cortisol during the recovery period ranged from weak to moderate (r = -.07 to .54, partial b^* = 0.05, or non-significant and unreported). Evidence of covariation between mother and child cortisol during the recovery response remains unclear, as half of the studies (6/12) found

moderate, positive effects and the other half found weak or non-significant effects. Most articles (8/10) that reported weak (< .20) or non-significant effects across the different epochs had sample sizes of fewer than 100 dyads.

Six studies in this section collapsed across epochs (baseline, immediate response, and recovery). Evidence of covariation between mother and child cortisol using this approach is unclear, as half of the articles (3/6) reported moderate, positive effects (r =.32, r = .58, and partial *b = 0.49), and the other half reported weak (partial b* = -0.05 to 0.09) or non-significant relations. Again, the articles that reported weak or non-significant effects had sample sizes of fewer than 100 dyads.

3.2.1.2. Dynamic Concurrent and Non-Reciprocal (Cortisol): Nine studies from six distinct samples reported on the covariation between mother and child cortisol over time (see Table 2b). The different analyses used included correlations between mother and child slopes (correlated growth curve modeling), correlations between the change in child's cortisol from baseline with the change in mother's cortisol from baseline (difference score/dynamic correlation), and correlations and regressions using area under the cure increase (AUC_I), which captures cortisol change over time without accounting for baseline. Eight studies used a validated lab paradigm and one study used a heel stick procedure (Spratt et al., 2016).

Four studies examined changes in cortisol from baseline to the immediate response or recovery periods. Three out of four studies evidenced weak associations between mother and child cortisol (r = -.14 to .15). Five studies in this section collapsed across epochs, most of which (4/5) provided evidence of moderate to large, positive relations (r = .21 to .60) between changes in mother and child cortisol over time. Sample sizes of studies that collapsed across epochs and found stronger effects were much larger (N > 200 dyads) compared to the studies that evidenced weaker effects and analyzed epochs separately.

3.2.1.3. Dynamic Concurrent and Reciprocal (Cortisol): Three studies (Bernard et al., 2017; Hendrix et al., 2018; Nofech-Mozes et al., 2020) used a cross-lagged model to examine stability in cortisol levels over time (e.g. child's previous cortisol levels predict their subsequent cortisol levels) and reciprocity between mother and child cortisol (e.g. mother's cortisol levels predict child's subsequent cortisol levels, and vice-versa; see Table 2c). Two of the three studies used a validated lab distress paradigm (Bernard et al., 2017; Nofech-Mozes et al., 2020).

Only one study examined results for epochs separately (Hendrix et al., 2018). All three studies provided evidence of moderate to large, positive relations (partial $b^* = 0.55$ to 0.83) between prior and subsequent cortisol levels for individual dyad members (i.e., stability of cortisol levels over time). Further, all three articles provided evidence of positive, albeit weak to moderate reciprocal relations (partial $b^* = 0.04$ to 0.23) between mother and child cortisol. All three articles in this section had large samples ($N > 150$ dyads).

3.2.2. Salivary Alpha Amylase

Salivary alpha amylase (sAA) is an enzyme in saliva that reflects activity of the SNS. sAA levels can be measured from 2 months of age onwards, though levels remain lower than among adults until 24 months of age (Davis et al., 2007). Further, reactivity to stress has not been demonstrated until 6 months of age. Compared to salivary cortisol, sAA demonstrates a quicker response to stress, peaking within 5 to 10 minutes post-stressor (Davis & Granger, 2009). Recovery is typically measured within 15 minutes, as return to baseline occurs by 20 minutes post-stressor. While both salivary cortisol and sAA have shown to be valid indicators of stress, they respond differently to stressors. For example, Mize and colleagues (2005) found that more children showed greater increases in sAA compared to cortisol on the same battery of tasks. Researchers have suggested that the HPA axis may be more responsive to stressors that evoke

higher distress, whereas the SNS is more sensitive to a wider range of stressors (Hill-Soderlund et al., 2008).

A total of five studies from four distinct samples examined associations between mother and child sAA. One article (Davis & Granger, 2009) provided longitudinal data across infancy, early, and mid-late toddlerhood. Timing of sAA samples ranged from 5 to 20 minutes post-stressor for the immediate response and 20 to 45 minutes for the recovery response. The quality scores for articles in this section were generally high (mean quality score = 76.4%, range = 67 – 87%). Three studies included a clinical or high-risk sample. Results are discussed below and are summarized in Table 3.

3.2.2.1. Static Concurrent and Non-Reciprocal (sAA): All sAA studies included in the current review examined the association between mother and child cortisol using static concurrent, non-reciprocal analyses, including correlations, regressions, and multilevel modeling. Four studies used a validated lab paradigm and one study used a vaccine as the stress-inducing stimulus (Davis & Granger, 2009). Partial standardized effect sizes are reported for three studies, as procedural, child, or maternal characteristics were adjusted for in the main analyses (see Table 6 for list of covariates; Davis & Granger, 2009; Kivlighan, 2009; Laurent et al., 2012).

Most studies (4/5) analyzed results separately for baseline, immediate response, and recovery response epochs. Three of four studies that analyzed baseline evidenced positive associations between mother and child sAA, ranging from small to large effects (r = .12 to .65). The strongest associations (r = .47 to .65) were reported by a study with small sample sizes across ages ($N \leq 22$; Davis & Granger, 2009). Three studies examined post-stressor epochs and consistently found non-significant associations between mother and child sAA during the immediate response and recovery phases. Effect sizes were not reported for these epochs. Only one study (Laurent et al., 2011) examined relations between mother and child sAA collapsed

across epochs. A small, positive partial effect ($b^* = 0.23$) was found, whereby increases in mother's sAA predicted higher levels of infant sAA across the duration of the stress task.

3.2.3. Cardiac Indicators (Respiratory Sinus Arrythmia and Heart Period)

There is also a small but growing literature on caregiver and child attunement using cardiac indicators. Respiratory sinus arrythmia (RSA), which is one of the most common indices of heart rate variability, reflects the variability in heart rate that occurs at the frequency of spontaneous breathing (Hastings & Miller, 2014). In the absence of a perceived stressor, the parasympathetic nervous system acts as a "brake" on the heart via the vagus nerve (Porges, 2007). This adaptive resting state is indexed by high RSA (i.e., steady and low heart rate), suggesting homeostasis is being maintained. In stress contexts, the vagal brake is withdrawn which facilitates mobilization of the SNS and allows for emotional and behavioural responses. Vagal withdrawal, indexed by decreasing RSA (i.e., RSA suppression), allows individuals to orient, respond, and engage in active coping (Hastings & Miller, 2014; Porges, 2007).

Another cardiac biomarker that has been examined in the attunement literature is heart period. However, research using this biological indicator is very limited. Heart period refers to the timed interval between heartbeats (Bazhenova et al., 2001). It reflects a combination of parasympathetic and sympathetic activity and is inversely related to heart rate (i.e., low heart period corresponds to high heart rate). Heart period and RSA are typically highly interrelated in both theory and practice; however, they can behave differently since HP also integrates sympathetic activity (Stevenson-Hinde & Marshall, 1999).

A total of ten studies, representing seven distinct samples, examined the relation between mother and child cardiac indicators. Across all studies, 15 or 30 second epochs were analyzed and averaged across the duration of the stressor to capture the immediate response or the recovery response. All studies examined RSA in mothers and their children, and two of the ten studies also

captured heart period (Busuito et al., 2019; Moore et al., 2009). Compared to the articles in other sections, the quality scores for articles reporting on cardiac indicators were lower (mean quality score = 64.6%, range = 53 – 80%). Furthermore, these articles often did not report on the reliability of cardiac editing procedures. One study (Ostlund et al., 2017) included a clinical or high-risk sample. Results are summarized in Table 4.

3.2.3.1 Static Concurrent and Non-Reciprocal (Cardiac Indicators): All ten studies that examined the relations between mother and child cardiac indicators used static concurrent and non-reciprocal analyses, including correlation, regression, or multilevel modeling. Nine of the ten studies used a validated stress paradigm. Only half of the studies (5/10) reported correlations or standardized partial slopes. The one study that reported standardized partial coefficients adjusted for within-individual variability in RSA, overall mean RSA for mother's or infants, and mother's baseline RSA (Skoranski et al., 2017).

All studies examined cardiac indicators for separate baseline, immediate response, and recovery epochs. Generally, there was a consistent pattern of weak (r = .07 to .17; partial b^* = 0.11 to 0.19) or non-significant relations between mother and child RSA across epochs. Results for mother and child heart period at baseline were either small or moderate positive associations (r = .13 and r = .32). There were weak (r = .01 and .09) or non-significant relations between mother and child heart period during the immediate response and recovery period. Studies examining cardiac may not have had sample sizes large enough to detect small effects, as nine out of ten studies had a sample size of fewer than 100 dyads.

3.2.4. Electroencephalography (EEG)

The newest line of research examining caregiver-child attunement uses measures of brain activity, commonly with electroencephalography (EEG), and specifically, frontal asymmetric activity within the alpha band (8-13 Hz for adults and 6-9 Hz for infants and young children).

Frontal EEG asymmetry is an indicator of the balance of brain activation in left and right frontal areas of the brain and serves as a biomarker of emotional reactivity and regulation (Fox, 1991). Positive emotions and approach-related behaviours are thought to be organized and processed within the left frontal hemisphere, whereas negative emotions and avoidance behaviours are organized and processes within the right frontal hemisphere (Davidson, 2000; Fox, 1991). Thus, during a distress task that elicits negative affect, greater right frontal asymmetry would be expected.

Two studies examined associations between mother and child frontal asymmetry patterns using EEG (Atzaba-Poria et al., 2017; Krzeczkowski et al., 2020). EEG data were acquired from both mothers and children during a baseline period and a distress task. One of the studies used a validated paradigm, a musical piece shown to elicit fear or negative affect in adults and infants (Krzeczkowski et al., 2020). Atzaba-Poria et al., (2017) used a challenging puzzle task as their distress paradigm. The quality of studies in this section were 67% (Krzeczkowski et al., 2020) and 73% (Atzaba-Poria et al., 2017). Both studies collected data from normative populations. Results are summarized below and presented in Table 5.

3.2.4.1. Static Concurrent and Non-reciprocal (EEG): Both studies examined mother and child frontal asymmetry patterns using static, concurrent, and non-reciprocal analyses, specifically correlations. Baseline associations between mother and child frontal asymmetry were consistently weak (r = -.09 and r = .002). During the tasks (i.e., the immediate reactivity period), relations between mother and child frontal asymmetry differed across studies, as one study reported a weak association (r = -.01; Krzeczkowski et al., 2020) and the other reported a moderate, positive association (r = .25; Atzaba-Poria et al., 2017). Both studies had small sample sizes (Ns < 35).

3.2.4.3. Dynamic Concurrent and Reciprocal (EEG): One of the studies in this section also examined associations between mother and child frontal asymmetry patterns using a cross-lagged model (Krzeczkowski et al., 2020); that is, stability of frontal asymmetry within individuals and reciprocity between mother and child outcomes over time. Both mothers and their infants evidenced positive, moderate stability in frontal asymmetry activity during baseline and the stress task (b^* = 0.35 and b^* = 0.41). However, similar to the correlation results reported by this study, there were very weak reciprocal relations (b^* = 0.03 and b^* = -0.01) between mother and infant frontal asymmetry from baseline to the distress task.

3.2.5. Summary of Covariates/Moderators

Patterns of findings according to the different age groupings were examined. Developmental patterns were not discernable according to the age groupings. The majority of studies examined children during the infancy period (25/36), highlighting the need for more examinations of caregiver-child attunement during the second and third years of life.

Broad covariate or moderator patterns were examined across all studies included in the current review. A summary of covariates and moderators across studies is in Table 6. Most studies (30/36) examined potential covariates (e.g., common variables that are known to affect different biological measures but were not associated with outcomes) or included covariates in main analyses. Generally, there was lack of consistency in covariates examined across studies, as well as for studies using the same biomarker which precluded synthesis. Generally, covariates examined included infant variables (e.g., time of last feed), maternal (e.g., maternal body mass), and procedural factors (e.g., time of day).

Similar to covariates, a variety of moderators was examined including those hypothesized to negatively impact (i.e., risk factors) and those expected to augment (i.e., protective factors) mother-child attunement. The most common moderator examined across biological indicators

was maternal mental health. Two studies demonstrated that higher maternal depressive symptoms were associated with greater concordance between mother and child cortisol (Khoury et al., 2016; Laurent et al., 2011) and three studies reported that maternal depression did not significantly interact with maternal biological indicators to predict infant responses (Hendrix et al., 2018; Lunkenheimer et al., 2018; Ostlund et al., 2017). Other moderators examined in more than one study had inconsistent results; these included: intimate partner violence (Bernard et al., 2017; Hibel et al., 2009), negative parenting behaviours (Hibel et al., 2009; Lunkenheimer et al., 2018; Skoranski et al., 2017), and attachment status (Hill-Soderlund et al., 2008; Nofech-Mozes et al., 2020). Parent sensitivity was the only moderator that evidenced consistent results across two studies, as higher parent sensitivity was related to more concordance between parent and child cortisol (Atkinson et al., 2013; van Bakel & Riksen-Walraven, 2008).

4. Discussion

The current study is the first known to systematically review evidence of caregiver-child biological attunement within distress contexts and during the first few years of life. The main goal of this review was to qualitatively summarize and synthesize the literature based on methodological characteristics, including biological indicators used to measure distress, type of analyses used to examine attunement, and measurement epochs examined pre- and post-distress. Further, a broad summary of covariates and moderators was provided. Findings varied across methodological approaches used to study attunement. The variability in findings is likely due, in part, to the lack of consensus regarding a conceptualization of attunement which typically informs the methodology researchers use to study the dyadic process (Bernard et al., 2017; Nofech-Mozes et al., 2020). The heterogeneity of definitions and methods used poses an issue for the attunement literature, as studies cannot be compared, or consistent result patterns cannot be

easily discerned. There were some patterns gleaned from the literature that are discussed below, along with limitations of the extant literature and important avenues for future research.

4.1. Associations between caregiver and child biological indicators

4.1.1. Cortisol

Cortisol studies provide the bulk of evidence that can be summarized across different types of analyses. Findings suggest moderate to large, positive relations between mother and child cortisol responses during baseline, as well as moderate, positive associations between mother and child cortisol during the immediate response period. Evidence of covariation between mother and child cortisol during the recovery period and when outcomes were collapsed across epochs is unclear, as weak to moderate effects were equally prevalent. There was consistent evidence of moderate to large, positive relations between changes in mother and child cortisol over time and collapsed across epochs. These static and dynamic (non-reciprocal) results should be carefully contextualized, as examining static individual phases, one-way predictions (mother cortisol predicting infant cortisol), and collapsing across epochs over time oversimplifies the complex interaction between caregivers and their children.

There was also evidence of prospective associations between dyad members' cortisol during infancy and early toddlerhood (6 to 17 months of age), with weak to small, positive reciprocal relations between mother and child cortisol from baseline to post-distress epochs. There were no studies that examined dynamic and reciprocal relations during mid to late toddlerhood. Considering the significant growth and differentiation of infant emotion and skills required for regulation within the first year to two years of life (Feldman, 2007; Izard et al., 2011), concurrent coordination of distress with mothers may be less stable during this time. The process of attunement is undergoing transformation from *external regulation* (i.e., infants rely on caregivers to facilitate their regulation from distress) to *mutual regulation* (i.e., greater

contingency and reciprocity as both partners attempt to regulate together) as the infant gains more skills (e.g. cognitive, motor, etc.) to interact with their primary caregiver in an attuned manner (Feldman, 2007). Thus, it is important to examine the dynamic and reciprocal components of biological attunement, with more research including mid to late toddlerhood, to capture how the attunement process initially develops as being primarily constructed by the caregiver and transforms into a process of mutual regulation (Feldman, 2007).

Weak effects or non-significant results were often reported by studies with samples sizes that were smaller than 100 dyads. Thus, future studies should aim to have at least 100 dyads in order to obtain precise estimates of small effects. Challenges in measuring cortisol may have also weakened findings in the current review. Capturing cortisol early in life is particularly challenging because infants and toddlers sometimes have very little or no response to stressors (Clements, 2013). Further, research has demonstrated considerable variability in timing of peak distress for infants (Ramsay & Lewis, 1994). It is also important to consider that dyad reciprocal interactions are very dynamic which should be reflected in the biological measure (Nofech-Mozes et al., 2020). Three or four cortisol measurements may not accurately capture dynamic changes. An attempt to decrease measurement error would require increasing the frequency of cortisol samples taken, with smaller time increments between samples to increase the likelihood of observing peak distress and dynamic changes during recovery. It is also important to note that a wide variety of variables can affect cortisol levels (e.g. biological sex, medications, time of day, oral contraceptives, etc.; Clements, 2013; Provenzi et al., 2016). However, a portion of studies (5/25 cortisol articles) in this review did not report controlling for known sources of cortisol variation. Thus, if researchers are using cortisol as a measure, careful consideration of which variables should be controlled is necessary to reduce measurement error. Researchers are

encouraged to think about their measurement procedure (e.g., frequency of measure, controlling for factors, etc.) and whether the indicator accurately captures caregiver-child attunement.

4.1.2. Salivary Alpha Amylase (sAA)

Consistent with cortisol findings, results indicate caregiver and child sAA positively covary during baseline, with effect sizes ranging from small to large. There were consistent non-significant associations between dyad sAA during the immediate response and recovery periods. No studies examined sAA using dynamic concurrent and non-reciprocal or dynamic concurrent and reciprocal analyses. More research is needed to determine whether sAA is a sensitive and reliable biological indicator of attunement. Since sAA is a measure of SNS activity, it reflects immediate arousal or responsivity to an environmental stressor (Augustine & Leerkes, 2019). If measured on its own, it may not adequately represent the attunement process which largely involves the recovery process, which is a dynamic and transactional process that unfolds between caregivers and their children to reach a regulated state. As such, inconsistent findings may have occurred because sAA as a biomarker is not aligned theoretically with attunement as a co-regulatory process. If researchers use it as an biological indicator of stress, it should be coupled with another indicator that measures regulatory processes (e.g. RSA; Augustine & Leerkes, 2019).

Further, there is a lack of stability in sAA levels for the first two years of life, with substantial variability in overall sAA levels (Bright et al., 2014; Davis et al., 2007). Given that it is not a very stable indicator early in life, it may be difficult for sAA to capture reliable patterns of attunement between caregivers and their children during this time period. All of the studies that examined attunement using sAA in the current review included children 24 months age or younger. sAA also has a similar limitation as cortisol related to variability in peak distress (Hill-

Soderlund et al., 2008) and is influenced by numerous contextual factors (e.g., teeth development, diet) that may contribute to sources of variation in the data (Davis & Granger, 2009).

4.1.3. Cardiac Indicators (RSA and HP)

Similar to analysis limitations of sAA, the relation between mother and child cardiac indicators was examined using only static concurrent and non-reciprocal analyses. Relations between mother and child RSA and heart period during baseline and post-stressor epochs were generally weak. Overall, these data suggest that dyadic regulatory processes are not captured by cardiac indicators. These findings may be partly due to how the studies were designed. All studies either averaged 15 or 30 second epochs over the duration of a task or used static analysis approaches that do not capture the temporal dynamics of the attunement process. Researchers should analyze smaller epoch intervals that have been used to detect dynamic changes in RSA (e.g., 30-second epoch; Hastings & Kahle, 2019). In addition, nine of ten studies that examined cardiac indicators had a sample size of fewer than 100 dyads. These samples may not have been large enough to estimate the population effect precisely.

Another important consideration is the rapid developmental changes that occur in the PNS, similar to the SNS and HPA axis, which may affect biological attunement. More research is needed to determine whether RSA is a stable indicator of distress within the first few years of life (also see Waxman et al., 2020). The cardiac studies included in the current review had the lowest quality scores on average, as most studies did not estimate or report reliability coefficients for cardiac editing procedures. Despite these limitations, RSA holds promise as an indicator to uniquely capture the attunement process, as the PNS is suited to support interpersonal interactions due to its ability to rapidly modulate arousal through neural innervation of the heart (Porges, 2007). Thus, the measurement of RSA can capture rapid and dynamic changes. Researchers are encouraged to continue developing this area of research with consideration of

methodological limitations discussed. Heart period is an understudied biological indicator and its ability to capture attunement process is currently unknown.

4.1.4. Electroencephalography (EEG)

The summary of relations between mother and child EEG (more specifically frontal asymmetry) in the current review is limited, as only two studies with small sample sizes were available for synthesis. This finding is not unexpected given that brain measures have only recently been used to capture caregiver-child dynamics. Both articles included in the current review examined the data using static concurrent and non-reciprocal approaches. The evidence available indicated weak baseline associations between mother and child frontal asymmetry. Further, weak and small, positive associations between mother and child frontal asymmetry were found during distressing tasks. One article also examined the dynamic concurrent and reciprocal relations between mother and child frontal asymmetry, but only weak reciprocal associations were found.

Many different approaches can be used (functional magnetic resonance imaging [fMRI], magnetoencephalography [MEG], EEG, or functional near-infrared spectroscopy [fNIRS]) to index brain activity. These measures have been used to monitor activity patterns during a variety of tasks, though typically social interactions (Mayo & Gordon, 2020). There is great potential in assessing attunement via EEG given the high temporal resolution of the measure which allows for the capture of real-time dynamic changes in dyadic interactions. Previous research in a non-distress context has shown that EEG changes are evident when there are subtle shifts in an adult-infant dyadic interaction (Leong et al., 2017; Wass et al., 2018). For example, Leong and colleagues (2017) demonstrated that brief aversions of adult eye gaze produced a significant change in EEG synchronicity between adult-infant pairs. More research is needed examining

attunement using brain measures to determine their contributions as biomarkers in capturing early dyadic processes that support distress regulation.

4.2. Additional conceptual and methodological challenges

One of the most widespread inconsistencies in the attunement literature regards how the dyadic process is conceptualized, which ends up informing the methods researchers use, particularly analyses approaches. Some researchers have defined attunement as an 'empathic psychophysiological response' or 'matching of states' which is reflected by the static analyses (i.e., time-specific correlations and regressions) used to examine this concept (Thompson & Trevathan, 2009; van Bakel & Riksen-Walraven, 2008). More recently, researchers have started to probe the complexity of the attunement process by examining dynamic changes in interactions over time and the interactive reciprocity between dyad members (Bernard et al., 2017; Nofech-Mozes et al., 2020). These features that are intrinsic to attunement have been observed behaviourally, as caregivers and infants engage, respond, and adjust to one another, as they regulate from distress over time (Tronick & Beeghly, 2011).

Static concurrent and non-reciprocal analyses are the most common approaches used to study attunement to date. However, this analysis approach is unable to map the complexity of the attunement process (Calkins & Hill, 2007), as it represents an association at one time point and does not consider reciprocal influences unfolding between dyad members. Another limitation of using correlations or ordinary linear regression is the inability to account for repeated measures, which is often needed when examining biomarkers of distress (Kivlighan, 2008). Further, some researchers using regression techniques only examined a one-way prediction (i.e., mothers predicting infants, or infants predicting mothers), overlooking the bidirectional nature of the attunement process.

Compared to static approaches, dynamic concurrent and non-reciprocal analyses (e.g., correlated growth models) capture the temporal aspect of attunement. Specifically, the dynamic and concurrent aspect of these analyses is consistent with a conceptualization of attunement as a concurrent process between caregivers and their children that unfolds across time. It is limiting as an analysis approach because it does not account for the 'lead-and-lag' or 'back-and-forth' structure of the attunement process. Further, researchers that have used growth models within the attunement literature often do not distinguish the patterns of growth that occur over time, despite the availability of this information (Nofech-Mozes et al., 2020). This makes it difficult to distinguish what positive or negative covariation means. For example, caregivers and children could have positive correlations between their cortisol trajectory slopes, but both members are either regulating from distress together (i.e., adaptive attunement), or demonstrating correlated increases in biological reactivity that may look attuned, though each member of the dyad is reacting to the same challenging circumstance separately and unable to mutually regulate (i.e., lack of attunement) (Nofech-Mozes et al., 2020). Dyadic response profiles should be mapped to visualize how each partner is reacting to the same challenging circumstance. Further, consideration of the psychosocial factors impacting the dyad is necessary to further elucidate whether dyads may be regulating together or reacting to their own stressors (Nofech-Mozes et al., 2020). For example, a caregiver experiencing intimate partner violence (e.g., Hibel et al., 2009) may process a challenging situation as threatening to themselves rather than responding to their infant's distress. Furthermore, as highlighted by Bernard and colleagues (2017), researchers' statistical analysis should ultimately reflect the definition of dyadic attunement which involves two important components, including time and reciprocity.

It is possible to specify and estimate models (e.g., autoregressive cross-lagged models also known as APIM models; Kenny, 1996) that can assess both the concurrent temporal and

reciprocal nature of the attunement process. APIM is a modelling strategy that captures the interdependence of a dyadic interactions, including the stability of caregiver and child responses across time (actor effects) and concurrent relations between caregiver and child responses at any time point. Most importantly, the APIM model can capture the 'lead-and-lag' structure of attunement (partner effects) that is thought to emerge within the first few years of life when caregivers serve primarily as the external regulator for the infant and thus drive the dyadic regulatory response. Similar to other analyses discussed, positive and negative coefficients provided through cross-lagged analysis do not provide information about the distinct pattens of the distress response and recovery over time. Thus, although cross-lagged models capture important aspects of attunement, additional analyses should be explored to map the trajectory patterns of attunement (Nofech-Mozes et al., 2020).

Moving forward, researchers need to better capture trajectory patterns of positive, negative, and weak (i.e., close to 0) covariation. The dominant tone in the literature is 'the more in sync, the better' (Mayo & Gordon, 2020). However, caregivers and children who appear to have correlated biological responses at one time or correlated changes over time may be experiencing attunement or lack of attunement. In addition, patterns of mismatch, manifesting as weak and/or negative associations in distress contexts, can be adaptive. Tronick and colleagues have suggested a lack of harmony in biobehavioural states between caregivers and their children is not only typical but also crucial for a child's development (DiCorcia & Tronick, 2011; Tronick & Gold, 2020). In typical interactions, dyads oscillate between mismatched and matched biobehavioural states (Beeghly & Tronick, 2011; DiCorcia & Tronick, 2011). Mismatches can occur due to many different factors, including rapidly changing regulatory demands of a child, response time of caregivers to their child's distress signals, and the likelihood of missed distress cues (DiCorcia & Tronick, 2011). Despite these times of interactive disorganization, missteps

within the interaction can be corrected and the dyad can repair into a more organized, regulated state, as caregiver regulatory input begins to match infant regulatory needs. This process of repairing mismatches and working towards a regulated state is known as *reparation* (Beeghly et al., 2016; DiCorcia & Tronick, 2011). Challenges with the reparation process (also known as *interactive ruptures*; Montirosso & McGlone, 2020) may reflect lack of attunement (i.e., when a caregiver is unable to regulate themselves or and has little regard for infant's emotional state or attempts to communicate). The process of reparation allows caregivers to serve as an external regulator but also scaffold skills in their children by providing them with moments to self-regulate. As such, the form and quality of the reparatory process is crucial for developing a young child's adaptive regulatory capacity.

Considering this notion, it is possible that many of the weak static associations evidenced in this review reflect the typical mismatches and subsequent reparations that occur between caregivers and their children. Analyses that map trajectory patterns, such as parallel-process growth modeling, are necessary to elucidate characteristic patterns of attunement and lack of attunement, as it is unlikely all dyads display similar attunement patterns. Further, as researchers are encouraged to move beyond simple conceptualizations of positive, negative, or weak covariation, interactions patterns should not just be considered as attuned or not attuned, as attunement is not an all-or-none condition (Harrist & Waugh, 2002). With more research and evidence to support this notion, the definition of attunement should include consideration of how quickly dyads can repair interactive errors and successfully move back and forth between discordant and attuned states.

4.2.3. Timing of outcome measurement

Another important methodological consideration is the timing of measurement. Baseline, immediate reactivity, and regulation have been clearly distinguished in research examining

biological indicators (Leerkes & Parade, 2015; Rothbart & Bates, 2006). Researchers have suggested that distress outcomes should be measured with temporally sensitive approaches due to dynamic changes of biology. Dynamic changes are expected to occur as part of the attunement process, as caregivers and children respond to a distressing stimulus and subsequently regulate from distress together. However, most studies in the current review either collapsed across epochs when analyzing data or only examined certain epochs (e.g., only baseline). These studies likely did not truly capture the concept of attunement that changes with time (i.e., reparation process), as the demands of the environment change. More research is needed to distinguish differences in attunement across these epochs, with more complex analyses (e.g., cross-lagged and trajectory models) than can capture dynamic changes and reciprocity across time.

4.2.4. Developmental Patterns and Moderators

Caregiver-child attunement was examined according to different developmental stages, including infancy (0-11 months), early toddlerhood (12-23 months), and mid to late toddlerhood (24-47) months). However, patterns of findings were not apparent across these different age groups. Developmental patterns may not have emerged, as the bulk of the studies (70%) examined attunement during infancy. More studies are needed that examine attunement in caregivers and their children during toddlerhood, as attunement is purported to be an early life process that changes over time as a child develops (Feldman, 2007).

A variety of moderators was examined including those hypothesized to hinder (i.e., risk factors) or augment (i.e., protective factors) adaptive attunement. Results were variable for common moderators examined, including maternal mental health, intimate partner violence, attachment status, and negative parenting behaviour. These inconsistent findings further highlight the need to examine the data with more complex analyses to map patterns of attunement according to different levels of the moderator (e.g., high vs. low depressive symptoms). Parent

sensitivity was the only moderator to evidence consistent results across studies, with higher parent sensitivity associated with greater concordance of distress outcomes between children and their parents. This finding is consistent with theory and research that demonstrate sensitive caregivers structure their interactions in a manner that is contingent and appropriate to the child's distress responses (Bowlby, 1982; Leerkes et al., 2016; Spanglar et al., 1994).

4.3 Limitations

We carried out a narrative synthesis due to the wide variety of methodology used to study attunement. Until there is greater consistency in moderator tracking, experimental controls, epoch timing, and statistical technique, our ability to gather a nuanced understanding of the conditions under which adaptive or maladaptive biological attunement exists is limited. The current review has discussed the improvements in methodology needed to better capture the biological process of attunement. The synthesis of literature was also limited by the number of unique samples available. Some studies were from an affiliated group of researchers that used the same sample which should be considered when interpreting results. Additionally, there are a lack of studies within the mid to late toddlerhood age range which may result in important developmental patterns being missed. Almost all studies used a cross-sectional design which highlights the need for longitudinal investigations. Further, most studies examined North American samples which limits the generalizability of findings. A handful of studies did not report an estimate of the relation between caregiver and child biological indicators if the effect was non-significant, which interfered with consistent reporting of the size of effects. Finally, there is a need for more complex analyses to examine the dynamic and reciprocal patterns of attunement, as a majority of the studies in the current review used oversimplified approaches.

4.4 Conclusions and Future Directions

The present study aimed to contribute a better understanding of the emergence and patterns of caregiver-child biological attunement during the first few years of life. Overall, we assert that the types and variability of methodological approaches have hampered the ability to optimally capture the early caregiver-child attunement process and move the field forward. Despite these limitations, there were some patterns of results gleaned from the synthesis including: (1) consistent evidence of positive covariation at rest (i.e., baseline) between maternal and child cortisol (moderate to large effects) and sAA (small to large effects); (2) moderate, positive covariation between maternal and child cortisol during the immediate reactivity period (i.e., response to stressor); (3) emergence of moderate to large positive associations between changes in maternal and child cortisol occurring from baseline through to the recovery period; (4) weak to small, positive reciprocal relations were found between mother and child cortisol within infancy and early toddlerhood (less than 17 months old); (5) weak associations or limited evidence of associations between caregiver and child cardiac and EEG indicators were found; and (6) higher parent sensitivity (protective factor) was associated with positive covariation between caregiver and child cortisol levels. Significant gaps in the literature were highlighted, including the need for better measurement procedures of biological indicators, the use of more nuanced analyses that better capture the concept of attunement as a dynamic and reciprocal process and patterns of change that occur over time, more research examining mid to late toddlerhood, consistent covariates used across studies, and more examinations of key risk and protective factors that influence attunement.

It is possible that inconsistent findings were due to the limitations of methodological practices used to study attunement. Based on our review of the literature, we recommend the following for future work examining caregiver-child biological attunement:

1. Choose biomarkers that theoretically align with the concept under study (i.e., attunement as a co-regulatory process).
2. Consider limitations of biomarkers being used and address them when possible (e.g., control for variables that impact biomarkers, use more frequent measurement to capture variability in distress responses).
3. Use multiple biomarkers to better determine unique contributions of different systems (e.g., PNS, SNS and HPA axis) in measuring attunement.
4. Improve measurement approaches (e.g., distinguishing between pre- and post-stimuli responses, utilizing frequent and consecutive epochs to capture peak distress and dynamic changes) and reporting practices (e.g., calculate reliability of data editing, determine recruitment rates, detail study characteristics, and report blinding procedures).
5. Use analysis approaches that better capture the process of attunement, including cross-lagged models that can capture the dynamic and reciprocal nature of the dyadic process, and parallel-process growth models that can capture distinct patterns of attunement.

There are additional areas to highlight for future research. There was only one study (van Bakel & Riksen-Walraven, 2008) in the current review that included two fathers in their sample. This underrepresentation originates from traditional gender-based roles which may not widely reflect current caregiving practices (Davison et al., 2017). This is an important area for future research, as research has demonstrated greater affect attunement between same-gender parent-infant dyads (Feldman, 2003). Relatedly, sex differences have been overlooked in the biological attunement literature. Parents may have different expectations for children's emotion experiences

depending on the sex of the child, which may result in differences in how they respond to children's distress responses (Creavy et al., 2020).

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Figure 1

Study inclusion flow chart based on PRISMA guidelines.

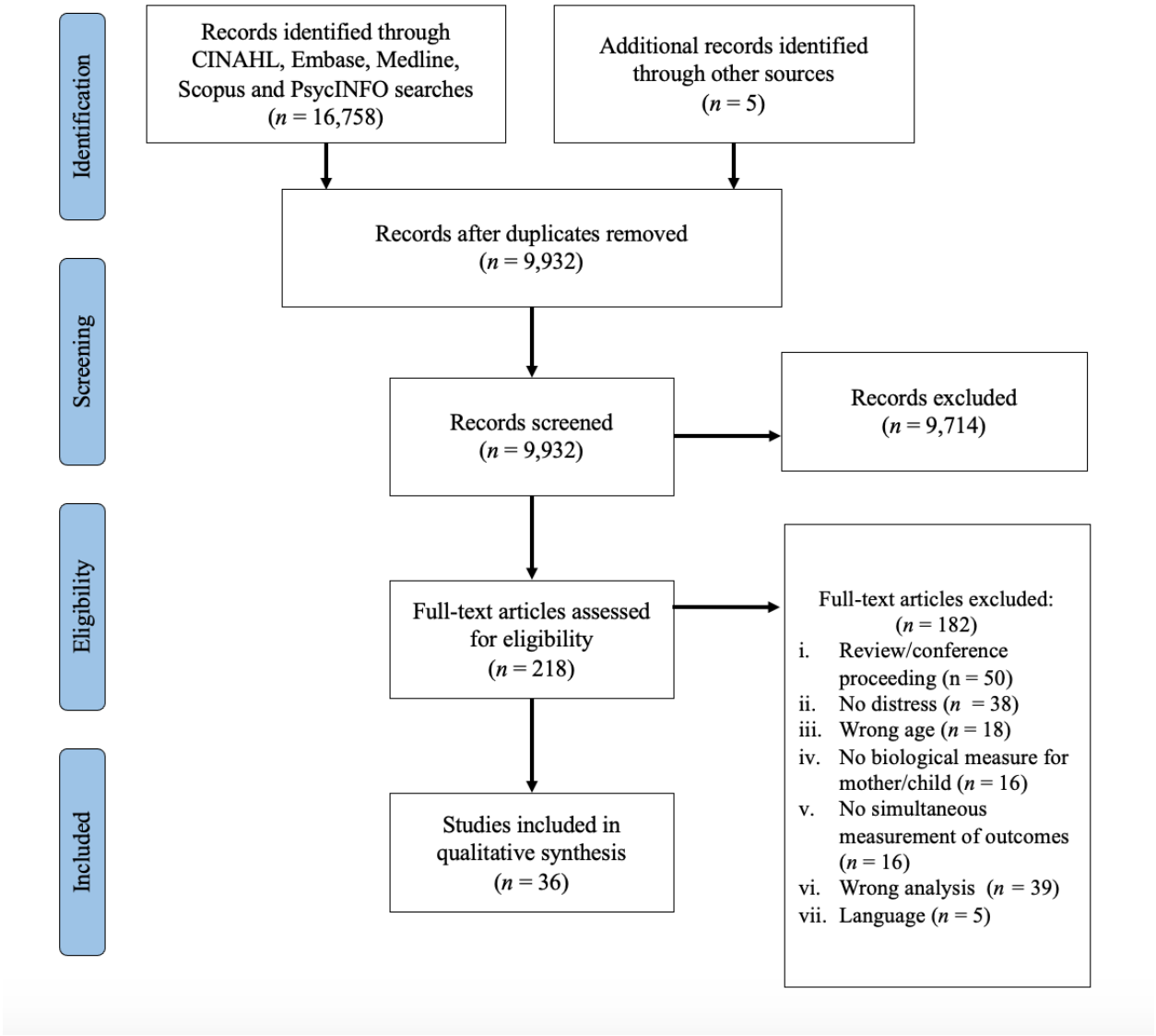

Figure 2

Distribution of studies meeting each quality assessment item.

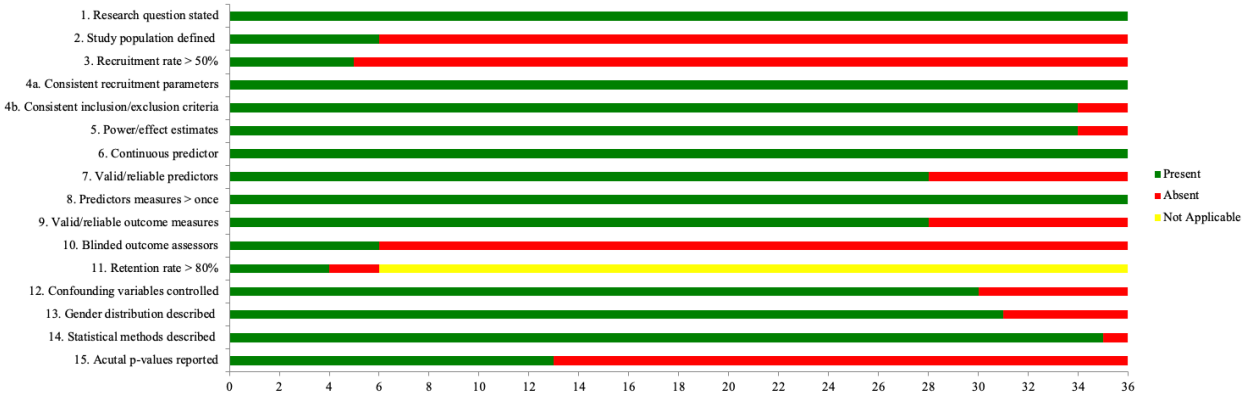

Table 1

Study Characteristics

Research Group/ Sample	Study	Biological Measure[a]	Country	Type of Study[b]	Sample Type	Child Age[c]	Distress Paradigm[d]	Epochs[e]	Overall Quality (%)
Atkinson 1	Atkinson 2013	Cortisol	Canada	B	Normative	Infant	*16 months:* Toy Frustration Procedure *17 months:* Strange Situation Procedure	Pre-task (B) +20 (IR) +40 (RR)	81
Atkinson 2	Khoury 2016	Cortisol	Canada	CS	Normative	Infant	Strange Situation Procedure	Pre-task (B) +20 (IR) +40 (RR)	75
Atkinson 3	Nofech-Mozes 2019	Cortisol	Canada	CS	Normative	Infant	Strange Situation Procedure	Pre-task (B) +20 (IR) +40 (RR)	80
Family Life Project 1	Braren 2019	Cortisol	USA	B	Clinical/Risk	Infant, Early Toddler, Mid-Late Toddler	Lab-TAB paradigm: *Infant*: masks, barrier, arm restraint *Toddler*: masks, toy removal	Pre-task (B)	75
Family Life Project 2	Granger 2006	Cortisol, sAA	USA	CS	Clinical/Risk	Infant	Lab-TAB paradigm: reach, masks, barrier and arm restraint	*Cortisol & sAA:* Pre-task (B) +20 (IR) +40 (RR)	67
Family Life Project 3	Hibel 2009	Cortisol	USA	CS	Clinical/Risk	Infant	Lab-TAB paradigm: masks, barrier, arm restraint	Pre-task (B) +20 (IR) +40 (RR)	80
Family Life Project 4	Hibel 2015	Cortisol	USA	B	Clinical/Risk	Infant, Early Toddler,	Lab-TAB paradigm: *Infant*: masks, barrier, arm restraint	Pre-task (B) +20 (IR) +40 (RR)	75

						Mid-Late Toddler	*Toddler*: masks, toy removal		
Family Life Project 5	Kivlighan 2009	Cortisol, sAA	USA	CS	Clinical/Risk	Infant	Lab-TAB paradigm: mask, barrier and arm restraint	*Cortisol & sAA:* Pre-task (B) +20 (IR) +40 (RR)	87
Laurent 1	Laurent 2011	Cortisol	USA	CS	Clinical/Risk	Early Toddler	Strange Situation Procedure	Pre-task (B) +5 (IR) +20 (IR) +50 (RR)	80
Laurent 2	Laurent 2012	Cortisol, sAA	USA	CS	Clinical/Risk	Early Toddler	1. Clean-up task 2. Lab-TAB paradigm (fear, frustration, and joy tasks)	*Cortisol:* Pre-task (B) +5 (IR) +20 (IR) +40 (RR) *sAA:* Pre-task (B) +5 (IR) +20 (RR)	80
Lunkenheimer 1	Lunkenheimer 2015	RSA	USA	CS	Normative	Mid-Late Toddler	1. Free play 2. Clean up Task 3. Parent-Child Challenge Task	30s epochs averaged within Challenge Task (IR)	60
Lunkenheimer 2	Lunkenheimer 2018	RSA	USA	CS	Normative	Mid-Late Toddler	1. Free play 2. Clean up Task 3. Parent-Child Challenge Task	30s epochs averaged within Challenge Task (IR)	60
Lunkenheimer 3	Skoranski 2017	RSA	USA	CS	Normative	Mid-Late Toddler	1. Free play 2. Clean up Task 3. Parent-Child Challenge Task	Thirty-six 30s epochs analyzed across tasks (B & IR)	60
Moore 1	Moore 2009	RSA	USA	CS	Normative	Infant	Still-Face Paradigm	15/30s epochs averaged within episode: Pre-task (B) Normal Play	53

								Still-Face (IR) Reunion (RR)	
Moore 2	Moore, Hill-Soderlund 2009	RSA, HP	USA	CS	Normative	Infant	Still-Face Paradigm	15s epochs averaged within episode: Pre-task (B) Normal Play Still-Face (IR) Reunion (RR	60
Unique	Atzaba-Poria 2017	EEG	USA	CS	Normative	Mid-Late Toddler	Puzzle Interaction Task	Pre-task (B) Puzzle Task (IR)	73
Unique	Bernard 2017	Cortisol	USA	CS	Clinical/Risk	Early Toddler	Modified Lab-TAB arm restraint task	Pre-task (B) +20 (IR) +40 (RR)	73
Unique	Busuito 2019	RSA, HP	USA	CS	Normative	Infant	Still-Face Paradigm	30s epochs averaged within episode: Pre-task (B) Normal Play Still-Face (IR) Reunion (RR)	73
Unique	Castral 2015	Cortisol	Brazil	CS	Clinical/Risk	Infant	Heel lance	Pre-task (B) +20 (IR)	87
Unique	Crockett 2013	Cortisol	Scotland	CS	Clinical/Risk	Infant	Still-Face Paradigm	Pre-task (B) +18 (IR) +38 (RR)	80
Unique	Davis 2009	Cortisol, sAA	USA	B	Normative	Infant, Early Toddler, Mid-Late Toddler	Vaccine	Pre-task (B)	75
Unique	Feldman 2009	Cortisol	Israel	CS	Clinical/Risk & Normative	Infant	Lab-TAB paradigm: masks	Pre-task (B) +20 (IR) +35 (RR)	80

Unique	Feldman 2010	Cortisol, RSA	Israel	CS	Normative	Infant	Still-Face Paradigm	*Cortisol:* Pre-task (B) +20 (IR) +35 (RR) *RSA:* 15s epochs averaged within episode: Free play (B) Still-Face (IR) Reunion (RR)	67
Unique	Hendrix 2018	Cortisol	USA	CS	Clinical/Risk	Infant	1. Infant-Mother Separation 2. Arm Restraint 3. Noise Burst	Pre-task (B) *After Separation:* +20 *After Arm Restrain & Noise Burst:* +15-20 (IR) +30-40 (RR)	73
Unique	Hill-Soderlund 2008	RSA, sAA	USA	CS	Normative	Early Toddler	Strange Situation Procedure	*sAA:* Pre-task (B) +15 (IR) +45 (RR) *RSA:* 15/30s epochs averaged within episode: Mother-Infant Interaction (B) Separations (IR) Reunions (RR)	73
Unique	Kalomiris 2018	Cortisol	USA	CS	Normative	Mid-Late Toddler	Risk Room and Spider Procedure	Pre-task (B) +20 (IR)	67
Unique	Krzeczkowski 2020	EEG	Canada	CS	Normative	Infant	Emotion-Eliciting Music Fear Condition	Pre-task (B) Fear condition (IR)	67

Unique	Laurent 2020	Cortisol	USA	B	Clinical/Risk	Infant, Early Toddler	*Infant*: Still-Face Procedure *Early Toddler*: Strange Situation Procedure (12 months), Lab-TAB maternal separation and stranger approach	Pre-tasks (B) +0 (IR) +20 (IR) +30 (RR)	69
Unique	Luecken 2019	Cortisol	USA	CS	Clinical/Risk	Infant	1. Free play 2. Lab-TAB Arm Restraint 3. Teaching task (skill 1-2 months beyond capacity) 4. Peek-a-boo	Pre-Task (B) *After peek-a-boo:* +0 (IR) +20 (IR) +40 (RR)	73
Unique	Morelius 2015	Cortisol	Sweden	CS	Clinical/Risk & Normative	Infant	Still-Face Procedure	Pre-task (B), +30 (IR)	87
Unique	Ostlund 2017	RSA	USA	CS	Clinical/ Risk	Infant	Still-Face Procedure	5s epochs averaged within Reunion Episode (RR)	80
Unique	Provenzi 2019	Cortisol	Italy	CS	Clinical/Risk & Normative	Infant	Double Still-Face Paradigm	Pre-task (B) +10 +20 (IR) +30 (RR)	73
Unique	Spratt 2016	Cortisol	USA	CS	Normative	Infant	Heel Stick	Pre-task (B) +20 (IR)	67
Unique	Tronick 2020	Cortisol	USA	CS	Normative	Infant	1. Caregiver Acute Stress Paradigm 2. Still-Face Procedure	Pre-task (B) *After SFP:* +10 +20 (IR) +40 (RR)	73
Unique	van Bakel 2008	Cortisol	Netherlands	CS	Normative	Early Toddler	Stranger-Robot Procedure	Pre-task (B) +21 (IR)	80

Unique	Waters 2017	RSA	USA	CS	Normative	Early Toddler	1. Trier Social Stress Test 2. Dyad reunion 3. Child Interaction with Adult Stranger 4. Free play	30s epochs averaged within episode: Dyad Reunion (RR) Stranger Interaction with child (IR) Free play	60

Note. [a]Biological Measure: sAA = Salivary Alpha Amylase, RSA = Respiratory Sinus Arrythmia, EEG = Electroencephalogram.

[b]Type of Study: Cross-sectional (CS), Both (B) = Longitudinal and Cross-Sectional.

[c]Child Age: Infant = 0-11 months, Early Toddler = 12-23 months, Mid-Late Toddler = 23-47 months.

[d]Distress Paradigms: Caregiver Acute Stress Paradigm (Tronick et al., 2020), Double Still Face Paradigm (DiCorcia et al., 2015), Lab-TAB (LT; Goldsmith & Rothbart, 1988; Goldsmith & Rothbart, 1993), Modified Lab-TAB Arm Restraint task (Goldsmith & Rothbart, 1996), Parent-Child Challenge Task (PCCT; Lunkenheimer et al., 2017), Puzzle Interaction Task (Atzaba-Poria et al., 2017), Risk Room and Spider procedure (Buss and Goldsmith, 2000), Still Face Paradigm (SFP; Tronick et al., 1978), Stranger-Robot Procedure (SRP; adapted from Mullen, Snidman, and Kagnan, 1993), Strange Situation Procedure (SSP; Ainsworth et al., 1978), Toy Frustration Procedure (TFP; Braungart-Rieker & Stifter, 1996); Trier Social Stress Test (TSST; Kirschbaum & Hellhammer, 1994).

[e]Epochs**:** B = Baseline, IR = Immediate response, RR = Recovery response.

Table 2a

Studies examining static concurrent and non-reciprocal relationships between mother and child cortisol outcomes

Study	Age	N (Dyads)	Analysis	Baseline	Immediate Response	Recovery
Bernard 2017	Infant	Mothers: 174 Infants: 163	Correlations	*r* = .29	*r* = .22	*r* = .40
Braren 2019	Infant	1133	Correlations	*r* = .29		
	Early Toddler	1070	Correlations	*r* = .26		
	Mid-Late Toddler	1014	Correlations	*r* = .30		
Castral 2015	Infant	42	Correlations		*r* = .25	
Crockett 2013	Infant	62	Correlations	*r* = .16	*r* = -.09	*r* = -.07
Davis 2009	Infant	19	Correlations	∅		
	Early Toddler	22		∅		
	Mid-Late Toddler	22		∅		
Feldman 2009	Infant	100	Correlations	*r* = .71	*r* = .42	∅
Feldman 2010	Infant	53	Correlations	*r* = .27	∅	∅
Granger 2006	Infant	86	Correlations	*r* = .31	∅	∅
Hendrix 2018	Early Toddler	233	Correlations	*r* = .51	*r* = .35	*r* = .33

Hibel 2015	Infant, Early & Mid-Late Toddler	Infant: 1141 Early Toddler: 1058 Mid-Late Toddler: 1036	MLM Concurrent	Mother → Child: *b** = .47	Mother → Child: *b** = .23	Mother → Child: *b** = .05
Hibel 2009	Infant	702	Correlations	*r* = .27	*r* = .26	*r* = .25
Kivlighan 2009	Infant	284	Correlations (partial)	*r* = .23	∅	∅
Morelius 2015	Infant	19 (standard care group)	Correlations	*r* = .14	*r* = .49	
Nofech-Mozes 2019	Early Toddler	256	Correlations	*r* = .34	*r* = .39	*r* = .38
Provenzi 2019	Infant	49 (full-term group)	Correlations	*r* = .31	*r* = .42	*r* = .31
Spratt 2016	Infant	42	Correlations	*r* = .68	∅	
Tronick 2020	Infant	52	Correlations	∅	*r* = .27	*r* = .54
Collapsed across epochs:						
Kalomiris 2018	Mid-Late Toddler	70	Regressions (AUC_G)	Mother → Child: *b** = .49		
Khoury 2016	Early Toddler	256	Correlations (AUC_G)	*r* = .58		
Luecken 2019	Infant	204	Correlations (AUC_G)	*r* = .32		
Laurent 2011	Early Toddler	86	MLM Concurrent	Mother → Child: ∅		
Laurent 2012	Early Toddler	86	MLM Concurrent	Mother → Child: *b** = .09		
Laurent 2020	Infant & Early Toddler	63	MLM Concurrent	Mother → Child *b** = -.05 Child → Mother *b** = .01		

Note. Infant = 0-11 months of age, Early Toddler = 12-23 months of age, Mid-Late Toddler = 24-47 months of age. MLM = Multilevel Model. N reflects number of participants with full data used in analyses. → = direction of prediction, *r* = correlation coefficient, *b** = standardized slope, ∅ = coefficients not provided due to non-significant results. Where no data is available, grey shading is used.

Table 2b

Studies examining dynamic concurrent and non-reciprocal relationships between mother and child cortisol outcomes

Study	Age	N (Dyads)	Analysis	Baseline	Immediate Response	Recovery
Bernard 2017	Infant	Mothers: 174 Infants: 163	Difference Score Correlations		*r* = -.08	*r* = .06
Kalomiris 2018	Mid-Late Toddler	70	Regressions (AUC_I)		Mother → Child: *b** = .12	
Spratt 2016	Infant	42	Difference Score Correlations		r = -.14	
van Bakel 2008	Early Toddler	83	Difference Score Regressions		Child → Parent: *High parent sensitivity b** = .29 *Low parent sensitivity b** = -.24	
Collapsed across epochs:						
Atkinson 2013	Early Toddler	297	MLM Correlated Growth Model	*r (slopes)* = .60		
Hibel 2009	Infant	702	MLM Correlated Growth Model	*r (slopes)* = .01		
Khoury 2016	Early Toddler	256	Correlations (AUC_I)		*r* = .25	
Luecken 2019	Infant	204	Correlations (AUC_I)		*r* = .21	
Nofech-Mozes 2019	Early Toddler	256	MLM Correlated Growth Model	*r (slopes)* = .39		

Note. Infant = 0-11 months of age, Early Toddler = 12-23 months of age, Mid-Late Toddler = 24-47 months of age. MLM = Multilevel Model. N reflects number of participants with full data used in analyses. → = direction of prediction, *r* = correlation coefficient, *b** = standardized slope, ∅ = coefficients not provided due to non-significant results. Where no data is available, grey shading is used.

Table 2c

Studies examining dynamic concurrent and reciprocal relationships between mother and child cortisol outcomes

Study	**Age**	**N (Dyads)**	**Analysis**	**Baseline**	**Immediate Response**	**Recovery**
Hendrix 2018	Infant	233	Cross-lagged Model	*Stability over time:* Mother B→ Mother IR1: *b**= .83 Infant B → Infant IR1: *b**= .72 *Concurrent relationships*: Not reported *Reciprocal influence:* Mother B → Infant IR1: *b**= .02 Infant B→ Mother IR1: *b**= .04	*Stability over time:* Mother IR1→ Mother IR2: *b**= .83 Infant IR1 → Infant IR2: *b**= .55 *Concurrent relationships*: Not reported *Reciprocal influence:* Mother IR1 → Infant IR2: *b**= .16 Infant IR1→ Mother IR2: *b**= .12	*Stability over time:* Mother IR2→ Mother RR: *b**= .81 Infant IR2 → Infant RR: *b**= .61 *Concurrent relationships*: Not reported *Reciprocal influence:* Mother IR2 → Infant RR: *b**= .12 Infant IR2→ Mother RR: *b**= .04
Collapsed across epochs:						
Bernard 2017	Infant	Mothers: 174 Infants: 163	Cross-lagged Model	*Stability over time:* Mother → Mother: *b** = .74 Infant → Infant: *b** = .59 *Concurrent relationships*: Not reported *Reciprocal influence:* Mother → Infant: *b** = .23 Infant → Mother: *b** = .04		

Nofech-Mozes 2019	Early Toddler	256	Cross-lagged Model	*Stability over time:* Mother → Mother: $b^* = .75$ Infant → Infant: $b^* = .60$ *Concurrent relationships*: Not reported *Reciprocal influence:* Mother → Infant: $b^* = .11$ Infant → Mother: $b^* = .09$

Note. Infant = 0-11 months of age, Early Toddler = 12-23 months of age. MLM = Multilevel Model. N reflects number of participants with full data used in analyses. → = direction of prediction, r = correlation coefficient, b^* = standardized slope, ∅ = coefficients not provided due to non-significant results. Where no data is available, grey shading is used.

Table 3

Studies examining static concurrent and non-reciprocal relations between mother and child salivary alpha amylase (sAA) outcomes

Study	**Age**	**N (Dyads)**	**Analysis**	**Baseline**	**Immediate Response**	**Recovery Response**
Davis 2009	Infant	19	Correlations (partial)	r = .65		
	Early Toddler	22	Correlations (partial)	r = .58		
	Mid-Late Toddler	22	Correlations (partial)	r = .47		
Granger 2006	Infant	86	Correlations	r = .29	∅	∅
Kivlighan 2009	Infant	284	Correlations (partial)	r = .12	∅	∅
Hill-Soderlund 2008	Early Toddler	Mothers: 98 Infants: 96	Regressions	Mother → Child: ∅	Mother → Child: ∅	Mother → Child: ∅
Collapsed across epochs:						
Laurent 2012	Early Toddler	86	MLM Concurrent	Mother → Child b^* = .23		

Note. Infant = 0-11 months of age, Early Toddler = 12-23 months of age, Mid-Late Toddler = 24-47 months of age. MLM = Multilevel Model. N reflects number of participants with full data used in analyses. → = direction of prediction. r = correlation coefficient. b^* = standardized slope. ∅ = coefficients not provided due to non-significant results. Where no data is available, grey shading is used.

Table 4

Studies examining static concurrent and non-reciprocal relations between mother and child cardiac (RSA and heart period) outcomes

Study	Age	N (Dyads)	Analysis	Baseline	Immediate Response (IR)	Recovery (RR)
Busuito 2019	Infant	140	Correlations	RSA: r = .12 HP: r = .13	RSA: r = .02 HP: r = .01	RSA: r = .10 HP: r = .09
Feldman 2010	Infant	53	Correlations	∅	∅	∅
Hill-Soderlund 2008	Early Toddler	Mothers: 95 Infants: 87	Regressions	Mother → Child: ∅	Mother → Child: ∅	Mother → Child: ∅
Lunkenheimer 2015	Mid-Late Toddler	47	Correlations		r = .17	
Lunkenheimer 2018	Mid-Late Toddler	47	Correlations		*Same results as Lunkenheimer 2015*	
Moore 2009	Infant	47	Correlations	∅	∅	∅
Moore, Hill-Soderlund 2009	Infant	Baseline: 66 IR: 86 RR: 83	Correlations	RSA: ∅ HP: r = .32	RSA: ∅ HP: ∅	RSA: ∅ HP: ∅
Ostlund 2017	Infant	95	Correlations			r = .07
Skoranski 2017	Mid-Late Toddler	47	MLM Concurrent		Mother → Child: *b = .19 Child → Mother: *b = .11	
Waters 2017	Early Toddler	98	Regressions		Child → Mother: ∅	Child → Mother: ∅

Note. Infant = 0-11 months of age, Early Toddler = 12-23 months of age, Mid-Late Toddler = 24-47 months of age. MLM = Multilevel Model. N reflects number of participants with full data used in analyses. r = correlation coefficient. *b = standardized slope. ∅ = coefficients not provided due to non-significant results. Where no data is available, grey shading is used.

Table 5

Studies examining relations between mother and child EEG (frontal asymmetry) outcomes

Study	Age	N (Dyads)	Analysis	Baseline	Immediate Response (IR)	Recovery (RR)
Static Concurrent and Non-reciprocal:						
Atzaba-Poria 2017	Mid-Late Toddler	34	Correlations	*r* = -.09	*r* = .25	
Krzeczkowski 2020	Infant	29	Correlations	*r* = .002	*r* = -.006	
Dynamic Concurrent and Reciprocal:						
Krzeczkowski 2020	Infant	29	Cross-lagged Model	*Stability over time:* Mother → Mother: *b** = .35 Infant → Infant: *b** = .41 *Concurrent relationships*: Not reported *Reciprocal influence:* Mother → Infant: *b** = .03 Infant → Mother: *b** = -.01		

Note. Infant = 0-11 months of age, Early Toddler = 12-23 months of age, Mid-Late Toddler = 24-47 months of age. MLM = Multilevel Model. N reflects number of participants with full data used in analyses. *r* = correlation coefficient. *b** = standardized slope. ∅ = coefficients not provided due to non-significant results. Where no data is available, grey shading is used.

Table 6

Summary of study covariates and moderators

Research Group/ Sample	Study	Biological Measure	Covariates	Moderator Effect (Y/N)	Summary of Moderator Effect
Atkinson 1	Atkinson 2013	Cortisol	Child wake time, mother and child average cortisol levels, change in cortisol across challenges, samples across epochs, maternal sensitivity	Maternal sensitivity (Y)	↑ Maternal sensitivity → ↑ Mother-child concordance
Atkinson 2	Khoury 2016	Cortisol	Maternal sensitivity, child breakfast time, ethnicity	Maternal depressive symptoms (Y)	↑ Maternal depressive symptoms → ↑ Mother-child concordance
Atkinson 3	Nofech-Mozes 2019	Cortisol	Family income, maternal education, maternal relationship status, maternal age, maternal and Child feeding times, wake times, medication status, sleep disruptions the previous night, maternal smoking, menstrual stage, breastfeeding status, and insomnia status	Attachment disorganization (Y)	Attachment disorganization → ↓ Mother-child concordance *Moderation emerged when using growth curve modeling but not cross-lagged modeling
Family Life Project 1	Braren 2019	Cortisol	Child race, child gender, child age, mother age, pregnancy status, medication use, tobacco use, parity	Socioeconomic risk (N) Age (N)	

			status, breastfeeding duration and status, child and mother body mass index, child and mother body temperature, parenting, time of day at visit, time between each saliva collection, SES risk, maternal depression, intimate partner violence, child emotional reactivity		
Family Life Project 2	Granger 2006	Cortisol sAA			
Family Life Project 3	Hibel 2009	Cortisol	Time of day at visit	Maternal experience of intimate partner violence (Y) Restrictive and punitive parenting behaviours (Y)	Maternal experience of intimate partner violence → ↑ Mother-Child Concordance Restrictive and punitive parenting behaviours → ↑ Mother-Child Concordance
Family Life Project 4	Hibel 2015	Cortisol	Time of day, race, income-to-needs ratio, child emotional reactivity, positive parenting	Child emotional reactivity (Y) Positive maternal behaviours (Y) Negative maternal behaviours (N)	↑ Child emotional reactivity → ↓ Mother-child concordance ↓ Positive maternal behaviour → ↓ Mother-child concordance
Family Life Project 5	Kivlighan 2009	Cortisol	Maternal: Time of day at visit, hours since eating, hormonal contraceptives, age, race, marital status *Child:* Time of day at visit, hours since eating, total hours of sleep, age, race, weight		

		sAA	Maternal: Hours since eating, time of day at visit, hours since sleeping, body temperature, cigarettes per day, hormonal contraceptives, NSAIDs, age, years of education, marital status *Child:* Hours since eating, cough-cold over the counter medications, race		
Laurent 1	Laurent 2011	Cortisol	Medications, recent eating/drinking or brushing teeth, dental work, illness, sleep time/duration, body mass index, age, arrival time to lab, infant birth outcomes and attachment status	Maternal depressive symptoms (Y)	↑ Maternal depressive symptoms from prenatal to 18 months postnatal → ↑ Mother-child concordance
Laurent 2	Laurent 2012	Cortisol	Maternal body mass index, maternal age		
		sAA	Maternal dental work		
Lunkenheimer 1	Lunkenheimer 2015	RSA	SES, maternal education, child sex, child age, stability of within person RSA, individual differences in overall mean RSA	Child externalizing (Y) *Interaction with RSA outcomes collapsed across tasks	↑ Child externalizing → ↓ Mother-child concordance
Lunkenheimer 2	Lunkenheimer 2018	RSA	SES, maternal education, child sex, child age, stability of within person RSA, individual	Child externalizing (N) Child internalizing (N) Maternal depression (N)	

			differences in overall mean RSA	Maternal aggression (N) *Interactions with RSA outcomes during challenge task	
Lunkenheimer 3	Skoranski 2017	RSA	SES, maternal education, child age, stability of within person RSA, individual differences in overall mean RSA	Maternal baseline RSA (Y) Maternal teaching (i.e., time spent teaching during task) (Y) Maternal disengagement (Y)	↑ Maternal Baseline RSA → ↓ Mother-child concordance ↑ Maternal teaching → ↑ Mother-child concordance ↑ Maternal disengagement → ↓ Mother-child concordance
Moore 1	Moore 2009	RSA	Ethnicity, income, maternal age, child age, child sex		
Moore 2	Moore, Hill-Soderlund 2009	RSA HP	Ethnicity, income, Child sex, Child negative affect		
Unique	Atzaba-Poria 2017	EEG	Child age, maternal age, child negativity, maternal negativity		
Unique	Bernard 2017	Cortisol	Time of afternoon, time from child's last feeding, time from when child last slept	Maternal experience of intimate partner violence (Y)	↓ Maternal experience of intimate partner violence → ↑ Mother-Child Concordance
Unique	Busuito 2019	RSA HP	Child age, time from Child's last feeding, Child sex, whether Child was fed during lab visit, feeding method, parity, race, maternal age, maternal education		
Unique	Castral 2015	Cortisol	Child sex, gestational age, post-natal age, painful experiences prior to 24h, sleep-		

			wake state at baseline, previous experience with kangaroo care, number of heel punctures, duration of blood collection, and maternal use of corticosteroids		
Unique	Crockett 2013	Cortisol	Maternal age, maternal education, household income, food and dairy consumption, maternal anxiety and depression, and time of day cortisol was assessed	Maternal Disrupted Communication (Y)	Severely disrupted communication → ↓ Mother-Child Concordance
Unique	Davis 2009	Cortisol sAA	Time of day at visit		
Unique	Feldman 2009	Cortisol			
Unique	Feldman 2010	Cortisol RSA			
Unique	Hendrix 2018	Cortisol	Child sex, child age, birth weight, feeding time, number of siblings, number of hours away from mother per week, maternal age, tobacco use, current menstruation, aerobic activity before lab visit, hours slept night before, medication use, stress, breastfeeding, number of pregnancy complications	Maternal depressive symptoms (N) Time spent gazing at Child (N) Maternal positive affect (Y)	↑ Maternal positive affect → ↑ Mother-child Concordance
Unique	Hill-Soderlund 2008	RSA		Avoidant vs. secure attachment (N)	

		sAA	Income, Child race, Child sex, Child age, attachment group		
Unique	Kalomiris 2017	Cortisol	Time of day at visit, # hours toddler was awake		
Unique	Krzeczkowski 2020	EEG		Maternal social approach (Y) Maternal social avoidance (Y)	↑ Maternal social avoidance → ↑ Mother-child Concordance ↓ Maternal social approach → ↑ Mother-child Concordance
Unique	Laurent 2020	Cortisol	Use of medications or other substances, sleep/wake times, sickness, body mass index, and infant feeding during the session	Social Support Satisfaction (Y) Family Resources (Y) Parental Stress (N)	↑ Social support satisfaction → ↓ Mother-child Concordance ↑ Family resources → ↓ Mother-child Concordance
Unique	Luecken 2019	Cortisol	Maternal age, country of birth, number of children, marital status, time of day, child birthweight, gestational age, child sex and breastfeeding status		
Unique	Morelius 2015	Cortisol	Hospital site, maternal sensitivity		
Unique	Ostlund 2017	RSA	Maternal and Child baseline RSA, maternal postpartum anxiety and depressive symptoms	Maternal anxiety symptoms (N) Maternal depressive symptoms (N)	
Unique	Provenzi 2019	Cortisol			

Unique	Spratt 2016	Cortisol	Child age, maternal age, child sex, race, feeding type, mother present for blood draw		
Unique	Tronick 2020	Cortisol			
Unique	van Bakel 2008	Cortisol	Child sex, home vs. daycare, time since morning feeding, parental time since morning awakening, maternal reported pregnancy	Parent sensitivity (Y)	↑ Parent sensitivity → ↑ Parent-child concordance
Unique	Waters 2017	RSA	Maternal body mass index	Touch manipulation (N) Episode type (N)	

Note. Results displayed as direction of association (↑ = higher, ↓ = lower, → = moderation effect).

Appendix A

PRISMA Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	Abstract submitted as separate file
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5-6
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5-6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	7
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	7-8
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	8
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix B
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	8
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	9-10
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	9-10

Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	10
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	10-11
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	10-11
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	10
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	12
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	12-13, Table 1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Table 1
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Tables 2a-c, 3, 4, and 5
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	15-24
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	14-15, Figure 2
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	25-30
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	35
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	36-37
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	38

Appendix B

PsycINFO Search Terms and Pairings

#	Searches	Results
1	Parent Child Relations/ or Father Child Relations/ or Mother Child Relations/ or Parenting/	57622
2	("child mother relation*" or "child parent relation*" or "child parent spatial pattern*" or "father child relation*" or "father infant relation*" or "father-child relation*" or "maternal fetal relation*" or "maternal patterns of care" or "maternal-fetal relation*" or "mother child interaction*" or "mother child relation*" or "mother fetus relation*" or "mother infant interaction*" or "mother infant relation*" or "mother-child interaction*" or "mother-child relation*" or "mother-fetus relation*" or "mother-infant interaction*" or "mother-infant relation*" or "parent child correlation" or "parent child relation*" or "parent infant bonding" or "parent infant relation*" or "parental role*" or "parent-child relation*" or "parenting").tw.	54099
3	Mothers/ or Fathers/	41822
4	(father or fathers or mother or mothers).tw.	135908
5	or/1-4	182521
6	Hypothalamic Pituitary Adrenal Axis/ or ("adrenal hypophyseal axis" or "adrenohypophyseal axis" or "diencephalon adrenal axis" or "hypophyseal adrenal axis" or "hypophyseal adrenal system" or "hypophyseal adrenocortical system" or "hypophyseoadrenocortical system" or "hypophysis adrenal axis" or "hypophysis adrenal cortex system" or "hypophysis adrenal function" or "hypophysis adrenal gland" or "hypophysis adrenal system" or "hypophysoadrenal axis" or "pituitary adrenal axis" or "pituitary adrenal function" or "pituitary adrenal system" or "pituitary adrenocortical function" or "pituitary adrenocortical regulation" or "pituitary adrenocortical system" or "pituitary gland adrenal gland axis" or "pituitary-adrenal system").tw.	6986
7	Parasympathetic Nervous System/ or ("acetyl cholinergic system" or "cholinergic mechanism" or "cholinergic nerve system" or "cholinergic nervous system" or "cholinergic pathway" or "cholinergic receptor system" or "parasympathetic nerve plexus" or "parasympathetic nerve system" or "parasympathetic nervous system" or "parasympathetic nervous systems" or "parasympathetic system" or "parasymphatic nervous system").tw.	1033
8	Heart Rate/ or ("cardiac chronotropism" or "cardiac chronotropy" or "cardiac frequency" or "cardiac rate" or "cardiac rates" or "heart frequency" or "heart rate" or "heart rates" or "pulse rate" or "pulse rates" or "ventricle rate" or "ventricle rates").tw.	23875
9	Sympathetic Nervous System/ or ("adrenergic mechanism" or "adrenergic nerve system" or "adrenergic nervous system" or "adrenergic regulatory mechanism" or "adrenergic system" or "beta adrenergic system" or "ortho sympathetic nervous system" or "orthosympathetic nervous system" or	3452

	"sympathetic nerve system" or "sympathetic nervous system" or "sympathetic system" or "sympathic nervous system" or "sympathicoadrenal system" or "sympathoadrenal system" or "vasomotor system" or "vasomotor systems").tw.	
10	Hydrocortisone/ or ("11 epicortisol" or 11-epicortisol or acticort or "aeroseb hc" or "aeroseb-hc" or ala-cort or ala-scalp or alfacort or algicortis or "alpha derm" or alphaderm or anucort-hc or anumed-hc or anutone-hc or aquanil hc or balneol-hc or barseb hc or beta-hc or biacort or cetacort or cobadex or colocort or "compound f" or "cordicare lotion" or coripen or "cort dome" or cort-dome or cortef or "cortef cream" or cortenema or cortibel or corticorenol or cortifair or cortifan or cortiphate or cortisol or cortisole or cortispray or cortoderm or cortril or cotacort or covocort or cremicort-h or cutaderm or "dermacrin hc lotion" or dermaid or "derm-aid cream" or dermocare or dermocortal or dermolate or dioderm or eczacort or "ef cortelan" or efcortelan or egocort or eksalb or eldecort or emo-cort or epicort or epicortisol or ficortril or filocot or flexicort or glycort or gly-cort or "hc no. 1" or "hc no. 4" or h-cort or hebcort or "hemorrhoidal hc" or hemril-30 or "hemril-hc uniserts" or hi-cor or hidrotisona or hycor or hycort or hydracort or hydrasson or "hydro ricortex" or hydrocort or hydrocorticosteroid or hydrocortisate or hydrocortison or hydrocortisone or hydrocortisonum or hydrocortisyl or hydrocortone or hydrogalen or hydrokort or hydrokortison or hydro-rx or hydrotopic or hysone or hytisone or hytone or "incortin h" or "instacort 10" or kyypakkaus or "lacticare hc" or lacticare-hc or "lemnis fatty cream hc" or lenirit or "medihaler cort" or "medihaler duo" or medrocil or mildison or "mildison fet krem" or "mildison lipocream" or mildison-fatty or "mitocortyl demangeaisons" or munitren or "nogenic hc" or novohydrocort or nutracort or optef or "otosone f" or penecort or plenadren or prepcort or "prevex hc" or "pro cort" or procort or proctocort or "procto-kit 1%" or "procto-kit 2.5%" or "proctosert hc" or proctosol-hc or proctosone or procutan or rectasol-hc or rectocort or rederm or sanatison or scalp-aid or schericur or "schericur 0.25%" or "scherosone f" or "sistral hydrocort" or skincalm or stie-cort or "substance m" or synacort or texacort or triburon-hc or unicort or vasocort).tw.	15181
11	("SA nodal arrhythmia" or "SA node arrhythmia" or "sinoatrial arrhythmia" or "sinoatrial arrhythmias" or "sinoatrial node arrhythmia" or "sino-atrial node arrhythmia" or "sinus arrhythmia" or "sinus arrhythmias" or "sinus arrhythmica" or "sinus node arrhythmia" or "sinus node syndrome").tw.	1079
12	Autonomic Nervous System/ or ("automatic nervous system" or "autonomic nerve system" or "autonomic nervous system" or "autonomic nervous systems" or "autonomic system" or "autonomous nervous system" or "involuntary nervous system" or "neuroautonomic system" or "neurovegetative system" or "organic nervous system" or "splanchnic nervous system" or "systema nervosum autonomicum" or "vegetative nervous system" or "vegetative nervous systems" or "vegetative system" or "visceral nervous system" or "visceral nervous systems").tw.	6129
13	Galvanic Skin Response/ or ("cutaneous galvanic response" or "electric skin response" or "electrodermal response" or "electrodermal responses" or "galvanic skin reflex" or "galvanic skin response" or "galvanic skin responses" or "GSR" or "psychogalvanic reflex" or "psychogalvanic skin reflex" or "skin conductance response" or "skin electric conductance" or "skin galvanic response" or "skin potential response").tw.	5174

14	("adrenal cortex" or "adrenal cortical activity" or "adrenal cortical activities" or "adrenal cortical system" or "adrenal cortical systems" or "adrenal gland cortex" or "adreno cortical activity" or "adreno cortical activities" or "adrenocortical activity" or "adrenocortical activities" or "adrenocortical system" or "adrenocortical systems" or "adrenocortical tissue" or "cortex glandulae suprarenalis").tw.	964
15	Saliva/ or (spittle or saliva or salivas).tw.	4312
16	("parotid amylase" or "parotid amylases" or "saliva alpha amylase" or "saliva alpha amylases" or "saliva amylase" or "saliva amylases" or "salivary alpha amylase" or "salivary alpha amylases" or "salivary alpha amylase" or "salivary alpha amylases" or "salivary alpha-amylase" or "salivary alpha-amylases" or "salivary amylase" or "salivary amylases" or "salivary gland amylase" or "salivary gland amylases").tw.	374
17	("diencephalohypophyseal system" or "diencephalohypophyseal systems" or "diencephalohypophysis system" or "diencephalohypophysis systems" or "hypophyseal hypothalamic system" or "hypophyseal hypothalamic systems" or "hypophyseal portal system" or "hypophyseal portal systems" or "hypophysis hypothalamus system" or "hypophysis hypothalamus systems" or "hypothalamic hypophyseal axis" or "hypothalamic hypophyseal system" or "hypothalamic hypophyseal systems" or "hypothalamic neurohypophyseal system" or "hypothalamic neurohypophyseal systems" or "hypothalamic neuropituitary system" or "hypothalamic neuropituitary systems" or "hypothalamic pituitary axis" or "hypothalamic pituitary system" or "hypothalamic pituitary systems" or "hypothalamic pituitary unit" or "hypothalamic-pituitary unit" or "hypothalamo hypophysary axis" or "hypothalamo hypophyseal connection" or "hypothalamo hypophyseal system" or "hypothalamo hypophyseal systems" or "hypothalamo hypophyseal tract" or "hypothalamo neuropituitary system" or "hypothalamo neuropituitary systems" or "hypothalamo pituitary axis" or "hypothalamo pituitary system" or "hypothalamo pituitary systems" or "hypothalamohypophyseal axis" or "hypothalamohypophyseal neurosecretory system" or "hypothalamohypophyseal neurosecretory systems" or "hypothalamohypophyseal system" or "hypothalamohypophyseal systems" or "hypothalamo-hypophyseal system" or "hypothalamo-hypophyseal systems" or "hypothalamohypophysis axis" or "hypothalamohypophysis system" or "hypothalamohypophysis systems" or "hypothalamoneurohypophyseal system" or "hypothalamoneurohypophyseal systems" or "hypothalamopituitary axis" or "hypothalamopituitary function" or "hypothalamopituitary system" or "hypothalamopituitary systems" or "hypothalamus hypophyseal axis" or "hypothalamus hypophyseal system" or "hypothalamus hypophyseal systems" or "hypothalamus hypophysis" or "hypothalamus neurohypophysis system" or "hypothalamus neurohypophysis systems" or "hypothalamus neuropituitary system" or "hypothalamus neuropituitary systems" or "hypothalamus pituitary gland axis" or "hypothalamus pituitary system" or "hypothalamus pituitary systems").tw.	304
18	"respiratory sinus arrhythmia".tw.	1033
19	Human Biological Rhythms/ or ("circadian clock" or "circadian clocks" or "circadian cycle" or "circadian fluctuation" or "circadian periodicity" or "circadian rhythmicity" or "circadian variation" or "day night rhythm" or "diurnal cycle" or "diurnal fluctuation" or "diurnal pattern" or "diurnal rhythm" or "diurnal rhythmicity" or "diurnal variation" or "diurnal variations" or "nychtohemeral" or "circadian rhythm" or "circadian rhythms" or "diurnal	13403

	rhythm" or "diurnal rhythms" or "nycthemeral rhythm" or "nycthemeral rhythms" or "nyctohemeral rhythm" or "nyctohemeral rhythms" or "twenty four hour rhythm" or "twenty-four hour rhythm" or "twenty-four hour rhythms" or "biological rhythm" or "biological rhythms").tw.	
20	vagus nerve/ or ("cranial nerve x" or "nerve x" or "nerve xs" or "pneumogastric nerve" or "pneumogastric nerves" or "tenth cranial nerve" or "tenth cranial nerves" or "regeneration nervi vagi" or "tenth cranial nerve" or "vagal nerve" or "vagal receptor" or "vagosympathetic trunk" or vagus).tw.	2469
21	homeostasis/ or (autoregulation or homeostasis or "homeostatic equilibrium" or "homeostatic mechanism" or homoeostasis or homoiostasis).tw.	10212
22	("adrenal hypophyseal axis" or "adrenohypophyseal axis" or "diencephalon adrenal axis" or "hypophyseal adrenal axis" or "hypophyseal adrenal system" or "hypophyseal adrenal systems" or "hypophyseal adrenocortical system" or "hypophyseal adrenocortical systems" or "hypophyseoadrenocortical system" or "hypophyseoadrenocortical systems" or "hypophysis adrenal axis" or "hypophysis adrenal cortex system" or "hypophysis adrenal cortex systems" or "hypophysis adrenal function" or "hypophysis adrenal gland" or "hypophysis adrenal gland system" or "hypophysis adrenal gland systems" or "hypophysoadrenal axis" or "pituitary adrenal axis" or "pituitary adrenal function" or "pituitary adrenal system" or "pituitary adrenal systems" or "pituitary adrenocortical function" or "pituitary adrenocortical regulation" or "pituitary adrenocortical system" or "pituitary adrenocortical systems" or "pituitary gland adrenal gland axis" or "pituitary-adrenal system" or "pituitary-adrenal systems").tw.	5259
23	exp electroencephalography/ or ("alpha activit*" or "alpha rhythm" or "alpha rhythms" or "alpha wave" or "alpha waves" or "beta activit*" or "beta rhythm" or "beta rhythms" or "beta wave" or "beta waves" or "brain activity" or "brain electric activit*" or "brain electrical activit*" or "brain wave" or "brain waves" or "brainwave" or "brainwaves" or "delta activit*" or "delta rhythm" or "delta rhythms" or "delta wave" or "delta waves" or "e.e.g." or EEG or electroencephalogram or electroencephalograms or electroencephalography or "electric encephalography" or "electrical encephalography" or "electro encephalography" or "electric encephalogram" or "electrical encephalogram" or "electro encephalogram" or "gamma activit*" or "gamma rhythm" or "gamma rhythms" or "gemma wave" or "gemma waves" or "theta activit*" or "theta rhythm" or "theta rhythms" or "theta wave" or "theta waves").tw.	54864
24	("cortical synchronisation" or "cortical synchronization").tw.	73
25	or/7-24	129729
26	5 and 25	2899
27	(infan* or newborn* or "new born*" or baby* or babies or toddler* or minors* or "under* age*" or pediatric* or paediatric* or peadiatric* or prematur* or pre-term or preterm*).mp. or (child* or pediat*or paediat*).jn.	212440
28	26 and 27	1423

Appendix C

Quality Assessment Checklist

1. **Was the research question or objective in this paper clearly stated?**
    - Usually in the last paragraphs of the Introduction, you will notice that the author will describe the study and what their research questions/aims/objectives are for the current study.
    - For example, "The objective of this study was to…"
    - Possible responses: yes/no

2. **Was the study population clearly specified and defined?**
    - All three criteria are important to consider:
        - Did the authors specify whether it was a normative / clinical / abused / SES at risk sample?
        - Did the authors specify what country or city participants were recruited from?
        - Did the authors specify when the participants were recruited (i.e., between what time points)
    - For example:
        - Participants included a normative sample of mother-child dyads recruited between January and December of 1990, from the USA.
    - This information is usually found within the "Participants" section.
    - Possible responses: yes/no

3. **Was the participation rate of eligible persons at least 50%?**
    - Does the study describe the number of eligible people?
    - If fewer than 50% of eligible persons participated in the study, then there is concern that the study population does not adequately represent the target population. This increases the risk of bias.
    - You are comparing the number of people who were approached with the number of people who agreed to participate in the study. If this information is not provided at all, the answer should be "no".

    Note: If the required information is not included in the current article, but another paper is cited that has more detailed information about the study sample, please include the reference for the linked article and MD will look up the required information.
    - Even if the paper is analyzing one wave of a longitudinal study, it's still important to know that the initial recruited sample was representative of the population it's supposed to be representing. If this information is not mentioned, or if another paper with more details is not cited, the answer is "no".
    - Possible responses: yes/no

4A. Were all the subjects selected or recruited from the same or similar populations (including the same time period)?

- If two groups of participants are being compared (e.g., children of depressed mothers vs. children of non-depressed mothers), were both participant groups recruited from the same population?
- If all participants in the study were recruited using the same means (for example, a community mail-out), and if you have no reason to believe that participants were recruited from different samples, then the answer to this question would be "yes".
- If the authors did not specify the time period during which participants were recruited,

the answer to this question would be “no”.

- Please note: this needs to be discussing the population that was used for our specific analyses.
- Possible responses: yes/no

4B. Were inclusion and exclusion criteria for being in the study pre-specified and applied uniformly to all participants?

- There are two criteria that must be met in order to answer “yes” to this question:
  1. Were the inclusion/exclusion criteria determined ahead of time and used to screen participants during recruitment, or were they determined *after* recruitment and used to exclude participants who had been recruited already?
  2. Were the same inclusion/exclusion criteria used for all participants in the study?
- Note: this question *is not* asking whether or not inclusion/exclusion criteria were used. It is ensuring that, if inclusion/exclusion criteria were used, they were used planned in advance and used consistently across subjects.
- Possible responses: yes/no/NA
- Note: If no inclusion/exclusion criteria are described, the answer to this question should be “NA”.

5. **Was a sample size justification, power description, variance accounted for or effect estimates provided?**
   - Did the authors present their reasons for selecting or recruiting the number of people included or analyzed? Do they note or discuss the statistical power, variance accounted for or effect estimates of the study?
   - A paragraph in the methods section of the article may explain the sample size needed to detect a hypothesized difference in outcomes. You may also find a discussion of power in the discussion section (e.g., the study had 85 percent power to detect a 20 percent increase in the rate of an outcome of interest, with a 2-sided alpha of 0.05).
   - Sometimes estimates of variance accounted for and/or estimates of effect size are given, instead of sample size calculations. In any of these cases, the answer would be "yes."

- This information may be found in the "Participants" or "Results" section.
- Possible answers: yes/no

6. **For predictor variables (e.g., caregiver/child neurobiological outcome) that can vary in amount or level, did the study examine different levels of the predictor/examine as a continuous variable as related to the outcome?**
   - Is it possible to investigate a dose-response relationship for the child level factors? And if yes, was a dose-response relationship investigated? For example, this would involve comparing the relationship between caregiver and child neurobiological outcomes as continuous variables. If the authors used a dichotomous variable they would receive a "No".
   - Possible answers: yes/no/NA

7. **Were the predictor variables clearly defined, valid, reliable, and implemented consistently across all study participants?**
   - For studies where the neurobiological outcomes are clearly described, the question should be answered "yes". For studies which refer to previous research supporting this claim, or that demonstrate the outcome measures are reliable within their own sample (i.e., reporting interrater reliability), the question should be answered "yes."
   - Our criteria for inter-rater reliability include:
     - Minimum 75% agreement between coders *or*
     - Kappa equal to or greater than 0.5.
   - As long as the study's coder training criteria or actual agreement/ Kappa values meet **at least one** of our criteria, the study receives credit for this item.
   - If inter-rater reliability was not reported on, or if it did not meet our criteria, the answer to this question is "no".
   - Possible answers: yes/no

8. **Was the predictor variable assessed more than once over time?**
   - Multiple measurements with the same result increase our confidence that the predictor variable was correctly classified.
   - Possible answers: yes/no

9. **Were measures of the outcome variable clearly defined, valid, reliable, and implemented consistently across all study participants?**
   - Same criteria as #7.
   - Possible answers: yes/no

10. **Were the outcome assessors (e.g. heart rate editors) blinded to the study hypotheses?**
    - Is it likely that the person collecting data or coding would know or would be able to figure out the study hypotheses?
    - Look for a line, usually in the Methods section, that states that coders/editors were blind to study hypotheses. If this isn't stated, answer should be "no".
    - Possible answers: yes/no

11. Was loss to follow-up after baseline 20% or less?

- Note: This study is specific to longitudinal studies. If the study is not longitudinal, it automatically receives "NA" for this item.
- Typically, an acceptable overall follow-up rate is considered to be 80% or more.
- The information you are looking for is whether the authors have included a participation rate that represents how many participants were recruited vs. how many participated in all study procedures.
- If there isn't a rate calculated, but the authors give the number of non-participants, participants lost to follow up, or participants with missing data who were excluded from analyses, you can calculate it using a simple calculation.
- For example: 64 mother-child dyads participated at Time 1 and 55 participated at Time 2. 55/64 = 85% therefore, they would get a "yes" since only 15% (or 100-85) was lost to follow-up.
- Possible answers: yes/no/NA

12. Were key potential confounding variables measured? Was the relationship adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?

- For the purposes of this research, key potential confounding variables may include:
  - Age, sex, baseline characteristics, feeding time, sleep time, time of day
  - **Note:** as long as ***one*** of the above mentioned variables is included then they get a point
- Was the relationship between these variables and outcomes investigated? If significantly associated with outcomes, were the variables statistically adjusted for?
- Note: we want to know whether authors *considered* the influence of these variables on outcomes. If they investigated the relationship between gender and outcomes, found that there was no relationship, and thus did not control for gender, they still receive credit here (and the answer here should be "yes").
- Possible answers: yes/no

13. Is the distribution of the overall study population by gender described?

- Have the authors included how many male and female children are in the sample.
- The information may be found in the demographics/participant characteristics table; however, some studies will include it in the "Participants" or "Results" section.
- Possible answers: yes/no

14. Are the statistical methods described?

- The information you need is whether they have described what type(s) of analyses (e.g., correlations, regression) were conducted.
- This information can be found in the "Statistical Analysis" or "Results" section.
- Possible answers: yes/no

15. Have actual probability values been reported (e.g., 0.035 rather than < 0.05) for the main outcomes except where the probability value is less than 0.001?*

- This information can be found in the "Results" section or results tables.
- We are only focusing on the statistics for the analyses that we are interested in for the purposes of this review paper (i.e., those relating caregiver and child neurbiological outcomes). For these analyses, we expected to see p values reported regardless of whether or not the analysis was significant.
- If probability values are all less than 0.001, then mark as a "yes"
- Possible answers: yes/no

QUALITY SYNTHESIS

- The National Heart, Lung and Blood institute (2014) stated that the checklist is not intended to create a list that you simply tally up to arrive at a summary judgment of quality. The creators suggest that the best approach is to think about the questions in the tool and how each one tells you something about the potential for bias in a study.
- As such, we are critically examining the items endorsed on the checklist for each study.
- Please make a judgement (i.e., Higher/Lower Quality) based on the studies endorsement of certain items:
    - Was a sample size justification, power description, variance accounted for or effect estimates provided? (Question 5)
    - Were the predictor variables clearly defined, valid, reliable, and implemented consistently across all study participants? (Question 7)
    - Were the outcome variables clearly defined, valid, reliable, and implemented consistently across all study participants? (Question 9)
    - Were the outcome assessors blinded to the study hypotheses? (Question 10)
    - Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)? (Question 12)