Psychophysiological activity and reactivity in children and adolescents with conduct problems

Highlights

- Meta-analysis on conduct problems and Autonomic Nervous System activity at baseline or reactivity during tasks
- Case-control studies suggest co-inhibition of parasympathetic and sympathetic reactivity to emotional tasks among those with high levels of CP
- Correlational studies point to reduced baseline heart rate and heart rate activity in relation to CP

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The aim of this study was to conduct a systematic review of the literature and meta-analysis to estimate the association between psychophysiological activity and reactivity at baseline or after a psychological task with CP among children and adolescents. We systematically reviewed published studies reporting autonomic nervous system activity in youth with CP and meta-analyzed the relationship between CP and autonomic baseline as well as task-related reactivity in 66 studies (N=10,227). Across 34 included case-control studies that were based on CP cut-off scores, we found a significant pooled effect for task related Skin-Conductance, Respiratory Sinus Arrhythmia, and cardiac Pre-Ejection Period, but no significant group differences for Heart Rate nor for any baseline measures. Findings suggested reduced parasympathetic and sympathetic reactivity to emotional tasks, pointing to co-inhibition of the two systems. However, across 32 studies with correlational design we only found a significant negative correlation of baseline and task-related heart rate with CP. The present meta-analysis derived several conclusions that have the potential to inform biological vulnerability models and biologically driven interventions.

RUNNING HEAD: PSYCHOPHYSIOLOGICAL REACTIVITY

Psychophysiological activity and reactivity in children and adolescents with conduct problems: A systematic review and meta-analysis

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Abstract

The aim of this study was to conduct a systematic review of the literature and meta-analysis to estimate the association between psychophysiological activity and reactivity at baseline or after a psychological task with CP among children and adolescents. We systematically reviewed published studies reporting autonomic nervous system activity in youth with CP and meta-analyzed the relationship between CP and autonomic baseline as well as task-related reactivity in 66 studies (N=10,227). Across 34 included case-control studies that were based on CP cut-off scores, we found a significant pooled effect for task related Skin-Conductance, Respiratory Sinus Arrhythmia, and cardiac Pre-Ejection Period, but no significant group differences for Heart Rate nor for any baseline measures. Findings suggested reduced parasympathetic and sympathetic reactivity to emotional tasks, pointing to co-inhibition of the two systems. However, across 32 studies with correlational design we only found a significant negative correlation of baseline and task-related heart rate with CP. The present meta-analysis derived several conclusions that have the potential to inform biological vulnerability models and biologically driven interventions.

Keywords: Conduct problems; Skin conductance; Heart rate; Respiratory Sinus Arrhythmia; cardiac Pre-Ejection Period.

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- Meta-analysis on conduct problems and Autonomic Nervous System activity at baseline or reactivity during tasks
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1. Introduction

Youth with conduct problems (CP; i.e., symptoms of conduct disorder and oppositional defiant disorder) engage in multiple antisocial behaviors such as bullying others, vandalism, lying, stealing, and excessive arguing with adults (American Psychiatric Association, 2013; Frick & Morris, 2004; Moffitt et al., 2008). CP behaviors place youth on a developmental pathway of low academic achievement, poor peer and parent relations, and delinquent and criminal behavior (Coie & Dodge, 1998; Keiley, Lofthouse, Bates, Dodge, & Pettit, 2003), resulting in high personal and societal costs. Thus, from a public health standpoint, it is imperative to understand the etiology and characteristics of CP, in order to inform evidence-based interventions. In the last three decades, several studies investigated the link between abnormal autonomic activity and CP in children and adolescents. This evidence has the potential to shed light on the developmental mechanisms leading to antisocial behavior as well as the identification of individuals at risk for CP (e.g., Beauchaine, 2012; Blair, 2001; Fanti, 2018; Raine, 1993). Findings from physiological studies might also inform current efforts toward research domain criteria based on biomarkers of psychological disorders (Insel et al., 2010). However, existing findings and theories regarding the physiological activity of children and adolescents with CP are contradictory, pointing to either lower or higher autonomic activity among children and adolescents with CP compared to controls. Therefore, there is a need of a quantitative evidence synthesis via a systematic review and meta-analysis that compares distinct measures of autonomic activity as well as baseline and task-related activity. This is of great importance since the last related meta-analysis was published more than a decade ago (Lorber 2004). Additionally, due to pathophysiological heterogeneity in CP (Fanti, 2018), it is important to establish to which extent differences in personality traits and comorbid psychopathology modify the association between CP and abnormal autonomic responses.

1.1 Physiological measures associated with CP

Youth with CP show deficits in physiological activity in response to emotional stimuli, known to be associated with the Autonomic Nervous System (ANS) (Fanti, 2018; Matthys, Vanderschuren, & Schutter, 2013). Measures of heart rate (HR) and electrodermal activity or skin conductance (SC) have been used in both correlational and case-control studies of CP to explain these deficits. HR and SC activity are important for understanding antisocial behavior because they are both associated with motivational systems involved in the control of behavioral responses to external stimuli (Lorber, 2004). Further, HR and SC are stress regulating mechanisms that prepare the body for fight or flight responses, and as such are important for understanding unique behaviors related to CP and aggressive behavior (Fanti, 2018; Raine & Jones, 1987). Although both measures are associated with general emotional arousal, SC is primarily controlled by the Sympathetic Nervous System (SNS), while HR is influenced by both the SNS and the Parasympathetic Nervous System (PNS) (Janig & McLachlan, 1992; Norman, Berntson, & Cacioppo, 2014). Heart Rate Variability (HRV; i.e., the variation of the period between consecutive heartbeats) is an additional index of ANS activity and relates to emotion regulation (Fanti, 2018). Increased SNS or decreased PNS activity result in heartbeat acceleration and reduced HRV, while a low SNS activity or a high PNS activity can lead to heart beat deceleration (Acharyaet al., 2006; Hansen et al., 2007; Thayer & Lane, 2000).

Low baseline HR and SC as well as low HR and SC reactivity in response to negative emotional cues, which are indicators of hypo-arousal, have been identified among youth with CP as well as in adolescents later convicted for crimes (Raine, Venables, & Mednick, 1997; Raine, Venables, & Williams, 1990; van Bokhoven, Matthys, van Goozen, & van Engeland, 2005; van Goozen, Matthys, Cohen-Kettenis, Buitelaar, & van Engeland, 2000). However, according to a recent review of the literature (Fanti, 2018) some studies did not reveal any

significant associations between HR and SC measures with CP, while additional work indicated that youth with CP show physiological hyper-reactivity and high levels of HR and SC both at rest and in response to negative and fearful emotional stimuli. These contradicting findings point to two distinct possibilities, suggesting that youth at risk for CP might either score on the low (i.e., hypo-arousal) or high (e.g., hyper-arousal) extremes in terms of their HR and SC responses to emotional stimuli. Such mixed findings are problematic and can be clarified in the context of a meta-analysis. Indeed, a meta-analysis conducted more than a decade ago (Lorber, 2004) suggested that greater HR activity is associated with CP, although there was considerable heterogeneity in effect sizes ranging from –1.24 to 0.49 across studies. On the other hand, the narrative review by Fanti (2018) suggested that the majority of studies point to low SC activity during emotional tasks among youth with CP; however, associations with HR were not as consistent. Additionally, although reduced HRV is associated with emotional dysregulation, which place youth at higher risk for CP, prior work resulted in inconsistent findings when comparing antisocial and non-antisocial youth, identifying either no differences, lower or higher HRV when comparing these groups (see Fanti, 2018 for a review). Taken together, these findings suggest differential associations of CP with HR and SC measures, and the need for additional work to clarify the direction of these differences in order to better understand the mechanisms that contribute not only to ANS related measures but also to their developmental pathways.

Because HR is influenced by both autonomic branches, it is important to investigate both sympathetic and parasympathetic systems associated with cardiac activity. Respiratory sinus arrhythmia (RSA; i.e., the variation of HR occurring during the respiratory cycle) is an index of parasympathetic cardiac control, and reflects a vagally mediated modulation of HR such that it increases during inspiration and decreases during expiration. Further, RSA responds to two different regulatory systems. During normal conditions, a coordinated

respiratory rhythm in heart rate activity facilitates oxygen diffusion, whereas during threatening or stressful conditions respiratory rhythm and RSA are suppressed (Porges, 2001). Moreover, RSA relates to the ability to regulate emotions (Beauchaine, Katkin, Strassberg, & Snarr, 2001; Grossman & Wientjes, 1986; Porges & Byrne, 1992). Low resting RSA (i.e., low vagal tone) and greater RSA withdrawal, reflected in reduced RSA reactivity to a stressor, is associated with maladaptive parasympathetic activity, poor emotion regulation, and increased risk of fight or flight responding (Beauchaine et al., 2001; Beauchaine, 2015). Indeed, children and adolescents high on CP exhibit low baseline RSA and reduced RSA reactivity (i.e., greater RSA withdrawal and parasympathetic inhibition) in response to emotional stimuli, pointing to emotion dysregulation, loss of regulatory control and increased risk of fight or flight responses (Beauchaine, Hong, & Marsh, 2008; Beauchaine et al., 2001; de Wied, van Boxtel, Zaalberg, & Goudena, 2006; El-Sheikh & Hinnant, 2011; Gatzke-Kopp et al., 2015; Mezzacappa et al., 1997; Pang & Beauchaine, 2013).

In contrast, the cardiac pre-ejection period (PEP; the systolic time interval) is an index of sympathetic cardiac activity and reflects the time between depolarization of the left ventricle and opening of the aortic valve (Brenner & Beauchaine, 2011). A shorter PEP suggests higher contractility and greater sympathetic tone and has been associated with the start of a stress reaction (Berntson et al., 1994) as well as with reward sensitivity (Tenenbaum et al., 2018). Beauchaine et al. (2001) provided evidence that adolescents with comorbid CD and ADHD symptoms exhibited longer PEP at baseline and less or decreased PEP reactivity to reward than those in ADHD-only or control groups. Both longer PEP at baseline and low PEP reactivity point to less sympathetic cardiac activity among those at risk for CD. This finding has been replicated among preschool children with Oppositional Defiant Disorder (Crowell et al., 2006) and children high on aggression and CP (Beauchaine et al., 2008).

Thus, differential effects in SC, RSA and PEP reactivity denote both sympathetic and parasympathetic functional deficits, and indicate that it is important to investigate the co-activation of both nervous systems. For example, even though parasympathetic and sympathetic systems serve opposing physiological functions, it was suggested that co-inhibition, which refers to decreased sympathetic and parasympathetic activity, or co-activation, which refers to increased activity of both branches, characterize child externalizing problems (El-Sheikh et al., 2009). We expect findings from the meta-analysis to inform this line of work and point to multisystemic physiological vulnerability factors.

1.2 Accounting for CP heterogeneity and individual differences

Studies assessing HR and SC at rest or in response to emotional stimuli among children with CP point to contradicting evidence supporting either physiological hypo-arousal or hyper-arousal. Based on these findings we can argue for the existence of heterogeneous CP groups, scoring on opposite extremes on physiological measures of arousal. Indeed, according to Fanti (2018), heterogeneity in CP can explain inconsistencies in physiological reactivity. Prior theoretical and empirical work suggests that the combination of conduct problems with either callous-unemotional (CU; i.e., lack of empathy, absence of guilt, shallow or deficient emotions) traits, internalizing symptoms such as anxiety, or symptoms of Attention-Deficit/Hyperactivity Disorder (ADHD) can result in more severe behavioral profiles (Fanti & Henrich, 2010; Frick, Ray, Thornton, & Kahn, 2014a; Lynam, 1996). As a result, examining co-occurrence between CP with CU traits, internalizing problems, and ADHD symptoms in relation to physiological measures can enhance our understanding of these higher risk subgroups of youth and inform CP heterogeneity.

Studies taking co-occurring ADHD symptoms into account suggested that boys with CP irrespective of comorbid ADHD symptoms show lower SC and HR responses to negative

emotional stimuli compared to healthy controls (Herpertz et al., 2005; Herpertz et al., 2003; Herpertz et al., 2001; Northover, Thapar, Langley, Fairchild, & van Goozen, 2016; Zahn & Kruesi, 1993). Furthermore, Beauchaine et al. (2001) found that children with a combination of CP and ADHD symptoms show lower baseline SC compared with controls, although the association between low baseline HR with CP was independent of the effects of ADHD symptoms (Scarpa & Raine, 1997). Additional work suggested that low HR and SC activity during emotional stimuli is associated with CP but not ADHD symptoms (McBurnett et al., 1993; Posthumus, Bocker, Raaijmakers, Van Engeland, & Matthys, 2009; Raine & Jones, 1987). In contrast, Waschbusch et al. (2002) found that children high on both CP and ADHD showed greater HR reactivity to emotional provocation compared to antisocial children with no ADHD symptoms. Thus, the majority of prior research suggests that children with comorbid CP and ADHD symptoms show similar physiological dysfunctions as CP youth without ADHD symptoms or that ADHD symptoms do not account for the association between CP and physiological measures. Thus, a sub-group meta-analytical approach to investigate the influence of this potential moderator seems an obvious way to integrate those contradictory findings.

Regarding internalizing problems, findings suggest that youth scoring high only on CP differ from those with comorbid CP and internalizing symptoms by being less reactive to negative situations with lower emotional arousal (Garralda, Connell, & Taylor, 1991; McBurnett et al., 1993). Indeed, non-anxious antisocial youth exhibiting lower SC and HR at rest and reactivity when compared to children and adolescents with either internalizing problems alone or with comorbid externalizing and internalizing problems (Beauchaine, Gartner, & Hagen, 2000; Garralda et al., 1991; Rogeness, Cepeda, Macedo, Fisher, & Harris, 1990; Schoorl, Van Rijn, De Wied, Van Goozen, & Swaab, 2015). It was suggested that

levels of anxiety and stress reactivity might explain the distinct physiological reactions to emotional stimuli identified in prior work (Fanti, 2018).

Findings from studies taking CU heterogeneity into account suggest that children scoring high on CP and low on CU traits exhibit higher baseline HR and low HR and SC activity in response to negative emotional stimuli compared to those high on both CP and CU traits (Anastassiou-Hadjicharalambous & Warden, 2008; de Wied, van Boxtel, Matthys, & Meeus, 2012; Kimonis, Frick, Muñoz, & Aucoin, 2008; Muñoz, Frick, Kimonis, & Aucoin, 2008; Muñoz, Kerr, & Besic, 2008; Northover et al., 2016). In addition, children and adolescents scoring high on CP and CU score lower on baseline RSA compared to youth high only on CP (de Wied et al., 2012; Mills-Koonce et al., 2015; Wagner et al., 2017). As a result, the co-occurrence between CP and CU traits may explain prior inconsistencies pointing to distinct CP groups differentiated on emotion regulation or showing either hypo- or hyper-arousal. The importance of CU traits in identifying a unique subgroup of children at risk for severe CP has led to their inclusion as a Limited Prosocial Emotions (LPE) specifier for the diagnosis of Conduct Disorder (CD) in the Diagnostic and Statistical Manual of Mental Disorders-5 (DSM-5; American Psychiatric Association, 2013). In general, evidence for the co-occurrence between CP with ADHD, CU traits, and internalizing psychopathologies suggest that by taking into account these individual differences, especially in the context of a meta-analysis, we might be able to explain prior contradicting findings.

1.3 Current study

The overarching aim of this study is to conduct a systematic review of the literature and meta-analysis to estimate the association between different measures of psycho-physiological activity and reactivity, on the one hand, and CP, on the other hand, among children and adolescents. Building on and extending a previous meta-analysis (Lorber, 2004)

as well as a systematic review (Fanti, 2018), we further aimed to explore possible moderators of the association between CP and physiological measures by means of subgroup meta-analyses. Specifically, co-occurring psychopathology (i.e., ADHD and internalizing symptoms) and CU traits were considered. This might uncover differential relations between physiological measures based on different subtypes of CP. Finally, as studies investigating sex differences found that girls exhibit greater autonomic activity than boys (Beauchaine et al., 2008), which might be another factor influencing the findings of studies using samples of boys and girls, we also tested for sex differences in the subgroup meta-analyses.

The present meta-analysis is concerned specifically with the association between physiological cardiac systems of arousal and regulation, including HR, HRV, PEP and RSA, with CP among youth. We also included studies that assess tonic (skin conductance level: SCL) or phasic components (Skin Conductance Responses: SCRs) of SC, which are indices of sympathetic nervous system activity. Because studies assess these physiological measures during both baseline (autonomic activity in the absence of external stimuli) and as a response to experimental stimuli (Lorber, 2004), we included both baseline measures or measures assessed in the context of a task (e.g. picture viewing, startle paradigm, attention-based tasks). According to a recent review of the literature, we expect deficits among youth high on CP to be more evident in measures of SC than HR or HRV (Fanti, 2018). Further, we expect to identify reduced sympathetic and parasympathetic cardiac activity among those at risk for CP, suggesting under-arousal and co-inhibition of both nervous systems. Since there was no meta-analysis testing these associations in the last decade, findings are expected to advance existing work aiming to understand the association between CP with physiological baseline activity and task-related reactivity.

2. Method

We followed the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Liberati et al., 2009). The protocol of this systematic review was registered in PROSPERO (CRD42018092305) (Fanti, Eisenbarth, Goble, Demetriou, & Cortese, 2018). Data were extracted from the published reports (journal article) of the studies or obtained from study authors. The PRISMA checklist is reported in the Supplemental Material 1.

2.1 Types of studies

Two types of studies were included: 1) Case-control studies comparing any of the outcomes of interest in subjects with conduct disorder/oppositional defiant disorder problems and healthy comparisons without conduct disorder/conduct problems; 2) Correlational studies assessing the correlation between severity of CP and any of the outcomes of interest.

2.2 Types of participants

We included studies assessing children and/or adolescents (aged ≤18 years): 1) with conduct disorder, defined based on the DSM (any version) criteria; or 2) in which conduct problems was measured by means of a validated scale, completed by parents, teachers, or self-reported by the child/adolescent, as listed in the INSERM collective report on Conduct Disorder in children and adolescents (INSERM Collective Expertise Centre, 2005): Broad-spectrum interviews: K-SADS (Orvaschel & Puig-Antich, 1987), ISC (Kovacs, 1985), DISC-IV (Shaffer, Fisher, Lucas, Dulcan, & Schwab-Stone, 2000), CSI (Gadow & Sprafkin, 2002); Behaviour scales: CBCL (Achenbach & Edelbrock, 1983), CTRS (Conners, 1969), CPRS (Conners, 1997), ECBI (Eyberg, Boggs, & Reynolds, 1980), HSQ/SSQ (Barkley, 1981), SESBI-R (Eyberg & Pincus, 1999), SBQ (Clark, 1995); Aggression scales: OAS (Silver &

Yudofsky, 1991), BDHI (Boone & Flint, 1988), DIAS (Björkqvist, Lagerspetz, & Österman, 1992), CSBS/CSBT (Crick, 1996; Crick & Grotpeter, 1995).

2.3. Outcomes

Primary outcomes included: 1) any measure of heart activity/reactivity, including heart rate (HR), heart rate variability (HRV), pre-ejection period (PEP) or Respiratory Sinus Arrythmia (RSA); 2) any measure of skin conductance, including galvanic skin reactivity parameters such as skin conductance level (SCL) or skin conductance response (SCR). Both parameters measured in the context of performing a task (e.g., picture viewing, startle paradigm, attention-based tasks) or taken as baseline measures were included (rest, activity and reactivity outcomes).

2.4 Search strategy/syntax

The following electronic databases were searched until February 13th, 2018, with no language/date/type of document restrictions: Pubmed (Medline), Ovid databases (PsycInfo, Embase+Embase classic, Ovid Medline), and Web of Knowledge databases [Web of science (Science Citation Index Expanded), Biological abstracts, Biosis, Food science and technology abstracts]. Additional details on the search strategy/syntax, including search terms for each database, are reported in the Supplemental Material 2. References of included studies were hand-searched to find additional pertinent studies not detected with the electronic search.

2.5 Study selection

Retrieved references were independently screened and blindly double-coded for eligibility by two study authors. Any disagreement was resolved by a senior author. If

needed, study authors were contacted to gather missing/additional information to clarify study inclusion.

2.6 Data extraction and statistical analysis

Data extraction was performed blindly by two of the authors, and any discrepancy between the two was resolved by consensus with a third senior author. We contacted study authors when necessary. Data extracted from each study included: 1) Publication details: year and language of publication; 2). Design: type of study (cross-sectional, case-control, cohort, correlational, etc.); study temporality (prospective, retrospective); patient enrolment (consecutive, non- consecutive); setting (clinical, general population vs epidemiological population study); 3) Study participant details: number, mean age (SD), sex distribution, Socioeconomic status (SES) and ethnicity of participants with and without CP or conduct disorder; characteristics of participants without conduct problems/disorder (healthy comparisons, other); psychiatric comorbidities of individuals with and without conduct problems/disorder (type and prevalence); method to establish the diagnosis of conduct problems/disorder (self-reported symptoms/diagnosis, diagnosis recorded in medical files/registry, structured or semi-structured interview according to clinical criteria); 4) Outcome measures: method used to define conduct problems/disorder (self-reported diagnosis, diagnosis in medical file/registry); prevalence (unadjusted and, if reported, adjusted) of conduct problems/disorder; method used to measure psychophysiological parameters; data reduction methods; tasks or paradigms used in the study. Age of onset was dropped as a variable of interest based on the low number of studies differentiating or reporting age of onset.

We included measures of baseline heart activity (HR, RSA, PEP, HRV) as well as measures of heart reactivity. In addition, we included baseline and reactivity measures of skin

conductance (SCL and SCR). Contrary to the pre-registered methods and in response to reviewer suggestions, we decided to include all available physiological data from each study, without prioritizing specific physiological outcome measures in order to be more inclusive. However, we still followed the following hierarchy in extracting and analyzing data when several options for given outcome measures were available:

Changes between baseline and activity during tasks were preferred to reactivity during task data, which in turn were preferred to baseline only data. Although we were interested in both baseline and task-related measures, we prioritize task related over baseline data because prior work provided evidence that task related measures have a greater influence on CP (see Fanti, 2018 for a review). If different types of emotional stimuli were available, preference was given to aversive tasks (e.g., fearful faces, baby crying) due to their relevance to the stress and threat system that relates to antisocial behaviors.

For mixed sample reports we included mixed sample data, and for studies reporting sex differences, we meta-analytically combined data on the two samples divided by sex. If only female or only male data were reported, we used the ones that were available.

In case of several measurement points, we used the one for which both, physiological and behavior/CP data, were reported. If both were reported for several assessment points, we used the earliest time point.

We extracted means and standard deviations for group-based results as well as zero-order correlations for correlational results. Furthermore, we extracted reactivity measures based on which types were provided. If delta scores were provided, those were included; if baseline and task data were provided, we use the measures during the task that were provided.

Random-effect models were used to compute pooled effect size for each outcome. For case-control studies, we calculated the standardized mean difference (SMD), with 95%

confidence interval (CI), with the correction of Hedges (Hedges, 1981) to avoid bias due to sample size. The pooled SMD, and related 95% CI, or correlation coefficients were calculated through the inverse variance method, and its statistical significance was assessed by the Z statistic. I^2 (Higgins & Thompson, 2002) was calculated to compare heterogeneity among studies. Finally, Egger's test (Egger, Davey Smith, Schneider, & Minder, 1997) and funnel plots were used to evaluate publication bias. Analyses were performed using Comprehensive Meta-Analysis (https://www.meta-analysis.com/) software.

3. Results

3.1 Study selection process and study characteristics

The process of the study selection can be seen in Figure 1. Details about the search can be found in Supplementary materials 2, and the reasons for excluding each study are listed in Supplementary materials 3. From an initial pool of 2016 potentially relevant references, 66 studies were retained for the quantitative analyses. Supplemental Tables 1 and 2 show the 34 case-control and 32 correlational studies, respectively, included in the meta-analyses. Of those 34 case-control studies, five reported Baseline HR data, 18 task-related HR change data, two task-related HRV, six task-related RSA data and five task-related PEP data. Regarding skin conductance outcome measures, four reported Baseline outcomes (2 SCR and 2 SCL) and 19 reported task-related outcomes (nine SCR, 10 SCL). The 32 studies with correlational design included 14 studies with Baseline (eight HR, four RSA and 2 PEP) and 19 studies with task-related (6 HR, 10 RSA and 3 PEP) cardiovascular outcome measures, as well as eight studies with SCL outcome data, of which three with Baseline data and five with task-related data. Single studies could contribute to more than one outcome to the different meta-analyses.

3.2 Meta-analyses

Table 1 summarizes the results of the meta-analyses in relation to the planned outcomes (HR, RSA, HRV, PEP, SCL and SCR) and on baseline versus task reactivity. For the **case-control studies** we found a significant effect for task-related SCL (pooled *OR* = -0.862, 95% CI [-1.725; -0.227]), indicating significantly lower SCL reactivity in tasks in the CP groups compared to control groups. However, I^2 was rather high, indicating that 66% of the variance was due to true variation among studies, rather than sampling error, and the Egger's test indicated the possibility of publication bias (p = .012). Excluding one study with a substantially large effect size (OR = -5.962; Mangina, Beuzeron-Mangina, & Grizenko, 2000) from the meta-analysis lead to a low I^2 (5.100), while the pooled effect size remained significant (pooled *OR* = -0.427, 95% CI [-0.679;-0.175]). The meta-analysis of case-control studies with SCR outcome measure in response to tasks also showed a significant effect (pooled *OR* = -0.364, 95% CI [-0.501; -0.227]), indicating a significantly lower SCR response to tasks in the CP groups compared to control groups. In this case, I^2 was low, indicating that variance was unlikely to be accounted for by study heterogeneity, but, rather, to sampling error, and Egger's test indicated low possibility of publication bias (p = .416). Furthermore, we found a significant effect for task-related RSA (pooled *OR* = -0.206, 95% CI [-0.398; -0.014]) with a low I^2, indicating low probability for a heterogeneity-based effect. The meta-analysis for task-related PEP showed a significant effect (pooled *OR* = 0.597, 95% CI [0.245; 0.948]), which could be based on heterogeneity, as I^2 was rather high. However, this might be due to the large effect of one study (Crowell et sl., 2006) with a standard difference of the means of 1.328 (95% CI [0.625;2.031]). Given that PEP reactivity is represented by shorter intervals (i.e., negative numbers), the identified positive effect indicate less PEP reactivity among those in the CP group (Brenner & Beauchaine, 2011). Meta

analyses comparing CP and control groups for baseline or task related HR or HRV and for baseline SCR or SCL did not find any significant differences (see Table 1).

For the **correlational studies**, we found a significant effect for studies with HR baseline outcome measures (pooled correlation*:* -0.139, 95% CI [-0.227; -0.048]), indicating a lower baseline HR for individuals with higher CP symptom scores. Study heterogeneity was high in this meta-analysis (79%); Egger's test indicated low possibility of publication bias (p = .099). We also found a significant effect for task-related HR (pooled correlation*:* -0.165, 95% CI [-0.265; -0.061]), pointing to lower task related HR among those high on CP. Again, high study heterogeneity (65%), and a low probability for publication bias (p = .476) was identified. Studies including baseline and task-related RSA or PEP as well as baseline and task-related SCL did not provide any significant pooled correlations (see Table 1).

3.3 Subgroup meta-analyses

For studies including subgroups, we ran additional meta-analyses independently for each subgroup if there was more than one study per outcome measure. From studies with correlational design, two reported subgroups data regarding sex. A meta-analysis restricted to boys across those two studies showed a significant effect (pooled correlation: 0.159, CI [0.055; 0.259]), indicating a positive correlation between CP measures and task-related HR increase, with a low heterogeneity score (<0.001%). As this includes only two studies, no Egger's test could be calculated. The analysis restricted to girls however did not find a significant effect. From studies with case-control design, three reported task-related HR changes for participants with CP and ADHD: there was no significant pooled OR for either groups with ADHD (ADHD+: pooled OR = -0.037, CI [-.268; 0.194]), nor groups without ADHD (ADHD-: pooled OR = 0.080, CI [-0.420; 0.580]). For three studies reporting task-related SCR, both sub-group meta-analyses for ADHD+ and ADHD- groups found

significant effects with lower task-related SCR for those with CP compared to control groups (ADHD+: pooled OR = -0.538; ADHD-: pooled OR = -0.375) For the ADHD+ subgroup, analysis study heterogeneity was rather high (65%), whereas for the ADHD- subgroup study heterogeneity was low (28%). Two studies reported data for CP groups with and without CU traits for task-related HR. Both meta-analyses for CU+ and CU- did not reveal any significant effect for groups (CU+: pooled OR = -0.109; CU-: pooled OR = -0.136).

Finally, we ran sub-group analyses for case-control (CC) studies, for clinical versus non-clinical sample studies, where we categorized clinical sample studies by group definitions using diagnostic thresholds for conduct disorder versus other measures. We computed these for all outcome measures with more than one study in each sub-group: CC HR Task: (12 clinical versus 6 non-clinical studies), CC RSA Task (2 clinical versus 2 non-clinical studies) and CC SCR Task (5 clinical versus 4 non-clinical studies). Results for each of the three outcomes did not differ between the subgroups. A meta-regression testing the difference between clinical and non-clinical samples confirmed this finding (pooled correlation*:* -0.065, 95% CI [-0.680; 0.551]; $Q(1) = 0.04$; $p = 0.837$) (see Supplementary material Figures 17-31).

3.4 Study quality

Regarding case-control studies, the average score at the Newcastle Ottawa Scale (NOS) was 6.16 (SD= 1.33). As for correlational studies, the average score was 3.1 (SD= 5.3). Details for each study are reported in Supplemental Tables 3 and 4.

4. Discussion

We systematically reviewed published studies reporting autonomic nervous system activity (cardiovascular and skin conductance) in youth with CP and meta-analyzed the

relationship between CP and autonomic baseline as well as task-related reactivity across 66 studies, including a total of 10,227 participants. Across 34 included case-control studies that were based on CP cut-off scores, we found a significant pooled effect for task related skin conductance level (SCL) and reactivity (SCR), indicating lower galvanic skin activity in response to tasks, but no significant group differences for HR or HRV nor for any baseline measures. We also identified reduced task-related RSA and PEP reactivity, pointing to co-inhibition of parasympathetic and sympathetic systems and under-arousal as a potential mechanism explaining engagement in CP behaviors. However, across 32 studies with correlational design we found only significant negative correlations between baseline and task-related HR with CP, but no significant relationship of any other physiological measures assessed during tasks nor baseline.

The identified association between baseline HR and CP agrees with a prior meta-analysis suggesting that low baseline HR assessed during childhood and adolescence is a biological marker of aggressive and antisocial behavior (Ortiz & Raine, 2004). In addition, emotion reactivity studies found a relationship with task-based HR, indicating that CP are associated with low autonomic arousal both at baseline and as a response to emotional cues. However, these findings were only identified for correlational studies and with a rather large heterogeneity score, but a low chance for publication bias. Although there was a trend towards similar relationships in the case-control studies, these were not significant and were also based on rather heterogeneous studies. The non-significant effects in the difference between baseline and task-related HR identified in case control studies could be related to the law of initial values, which has been reported to impact specifically baseline to task changes of cardiac parameters (Berntson, Uchino & Cacioppo, 1994). The inconsistency in findings regarding baseline HR for correlational versus case-control studies was also reported in a recent review of the literature, with studies showing no association or that CP are associated

with low or high baseline and HR reactivity (Fanti, 2018). Thus, despite potential relevance of the study design, based on our meta-analysis and prior review of the literature, we cannot confirm a reduced HR activity for youth with CP. In addition, baseline levels of SC were not associated with CP, suggesting that if anything, baseline levels of HR might be a better predictor of CP compared to SC. However, only seven of the identified studies included baseline SC.

An important finding in case control studies assessing cardiac measures was that individuals high on CP exhibited reduced PEP and RSA reactivity. As a result, both correlational and case-control studies suggest that CP relate to autonomic hypo-arousal and hypo-reactivity towards challenging stressors. Findings are in line with previous suggestions of greater RSA withdrawal, associated with lower RSA reactivity, and lengthening of the PEP, associated with reduced sympathetic nervous system activity, as indicators of physiological under-arousal (Murray-Close et al., 2018). Although the HR effects identified in correlational studies cannot be attributed to a specific autonomic system, RSA and PEP findings point to co-inhibition of sympathetic and parasympathetic systems that relates to low stress responsivity and fearlessness (Thomson et al., 2018). Low stress sensitivity and lack of fear might increase the likelihood to engage in high risk antisocial and CP behaviors.

Furthermore, the lower SC reactivity identified in case-control studies also suggest reduced sympathetic reactivity among those high on CP. These results have to be interpreted carefully. Across the different studies assessing SCL there was a very large heterogeneity and a higher potential for a publication bias, while the effect for the SCR based studies can be considered more substantial due to a very low heterogeneity and low possibility of publication bias. However, after excluding one study with a very large effect size that used a working memory task (Mangina et al., 2000) heterogeneity was reduced substantially, while the overall effect of lower SCL during tasks for those with CP remained. Interestingly, the

task-based SC levels were not related to dimensional approaches of measuring CP in the correlational studies and there were no studies included in the analyses that reported skin conductance reactivity. In contrast to correlational studies that mainly used social stress tasks, the case-control studies relied on a variety of different tasks including physical, social performance, stress or fear conditioning. However, there was no task related pattern in the case-control studies that could explain the null finding identified in correlational studies.

Nevertheless, the findings provide greater support for SC compared to HR reactivity in understanding CP at the level of group comparison, which might involve more clinical populations. Indeed, the majority of prior work suggests that SC reactivity during emotional tasks is lower among youth high on CP compared to controls, which was not true for HR reactivity (Fanti, 2018; Lorber, 2004). A direct comparison of clinical versus non-clinical samples within the group comparison studies did not reveal any differences though, pointing potentially to differences based on extreme group rather than clinical versus non-clinical types of samples. Similar to a prior meta-analysis (Lorber, 2004), heterogeneity in effect sizes for HR reactivity ranged from negative to positive, suggesting considerable heterogeneity in effect sizes. The heterogeneity of effect sizes across studies might also be related to high inter-individual differences in HR and heart rate reactivity, especially in children, which has been discussed in the fitness assessment literature as well (Oliveira et al, 2017; Brooke et al., 2014).

Regarding the analyses taking individual differences and co-occurring psychopathology into account, we were only able to run subgroup analyses for comorbid ADHD, CU traits and sex. No studies met inclusion criteria to test differences in relation to internalizing co-occurrence. This is unfortunate, since it has been suggested that co-occurring internalizing symptomatology can explain heterogeneity in CP (Fanti & Kimonis, 2017). As a result, subgroup meta-analyses were not possible to the extent intended.

Our results for comorbid ADHD subgroups could be affected by the selection criteria: we excluded four correlational studies because they were using ADHD as main diagnostic criterion for CP (El-Sheikh & Hinnant, 2011; Keller & El-Sheikh, 2009; Prätzlich et al., 2018), while no case-control studies had to be excluded for this reason. At the same time, across the different correlational studies, the majority of them did not report ever screening for ADHD, so it was not possible to determine any subgroup analyses, while the majority of case-control studies screened for ADHD criteria. Still, we found that comorbid ADHD did not change the main findings regarding the relationship between task-related SCR and SCL being reduced in youth with CP in case-control-design studies. Similarly, no effect for task-related HR was identified after taking ADHD symptoms into account. Based on these findings, we can conclude that co-occurrence with ADHD symptoms does not influence the low SC reactivity identified among CP youth. Thus, the core physiological underpinnings associated with antisocial behavior might be similar in the two CP subgroups. Several studies reported that children with CP irrespective of ADHD symptoms show lower autonomic SC responses to aversive emotional stimuli, and interestingly both CP subgroups differed from healthy controls or youth with ADHD symptoms alone (Herpertz et al., 2003; Herpertz et al., 2001; Northover et al., 2016; Zahn & Kruesi, 1993). This finding is noteworthy and suggests heterogeneity within ADHD symptoms when it comes to autonomic functioning, but not within CP.

Similarly, we found no difference for groups with or without comorbid CU traits for task-related HR and conduct problems. This is not in line with suggestions from the literature (see Frick, Ray, Thornton, & Kahn, 2014b for a review), but only two studies met inclusion criteria in the present meta-analyses pointing to contradicting evidence (Anastassiou-Hadjicharalambous & Warden, 2008; de Wied et al., 2012): Anastassiou-Hadjicharalambous and Warden (2008) found that children with combined CP and CU traits showed less HR

change in response to an emotion evoking film (i.e., associated with fear) compared to both CP-only and control groups. In contrast, de Wied et al. (2012) found no group differences in response to angry films. Based on our data extraction decision, we did not include a finding from the latter study, which suggested that sad film stimulation provoked significantly lower reactivity in the CD+CU group compared to the CD-only and control groups. However, exploratory analysis that used the data from the sad movie condition did not change the overall results. As a result, no clear conclusions can be drawn based on existing findings. Additional work comparing CP-only with CP+CU groups is therefore needed, especially since this distinction has clinical importance due to the inclusion of a CU specifier to the DSM-5 diagnosis of conduct disorder (American Psychiatric Association, 2013).

The only two studies (Crozier et al., 2008; Eisenberg et al., 1996) that reported results separately for boys and girls suggested that higher task-related HR reaction was related to boys CP, but not girls. Unfortunately, no other studies reported related data, which would be important in order to investigate sex differences in physiological reactivity (see e.g. Prätzlich et al., 2018). This finding contradicts prior work suggesting that girls exhibit greater autonomic activity than boys (Beauchaine et al., 2008). In the case of the latter publication, our inclusion criteria did not allow to accommodate studies that created groups of youth based on latent class analyses. However, all studies reporting HR monitored during a task, included mixed samples of boys and girls and showed a trend for reduced HR reaction to tasks, although the pooled effect was not significant. Interestingly, Crozier et al. (2008) and Eisenberg et al. (1996) are the only studies that show a positive correlation in the main analysis. In these two studies, boys seem to drive the effect in terms of higher heart rate reactivity during task for those higher on CP, while there was no significant correlation for girls. The resulting high diversity of the studies in the main analysis reflects the differences between studies, which could be based on the diversity in the tasks, with a Trier Social Stress

Test, Social Performance Paradigm or Social Stress Task on the side of the studies identifying negative correlations (Choy et al., 2015; Hastings et al., 2011; Hastings, Zahn-Waxler, & Usher, 2007; Portnoy et al., 2014) and an imagination task or watching crying babies films task on the side of the studies identifying positive correlations (Crozier et al., 2008; Eisenberg et al., 2012). This could point to a differentiation between (social) stress inducing situations compared to empathy evoking tasks. Eisenberg et al. (2012) argue that their finding might be due to the lower baseline in their data, while Crozier et al. (2008) argue that they found an increase in HR directly after the provocation was presented, but a decrease immediately prior to the provocation and therefore there might be different processes involved in each condition. Considering empathy provoking (other-related) situations to be significantly different from the more stress inducing tasks, they seem to lead to higher heart rate reactions in boys with conduct problems, while stress provoking (self-related) situations provoke less heart rate reactions with increased conduct problems.

4.1 Limitations

This systematic review and meta-analysis has some limitations: despite a large amount of studies reporting psychophysiological data in relationship to conduct problems (n = 75), only a smaller subset of 66 studies could be included due to non-reported data and difficulties obtaining respective data from authors. This points to an urgent need for a more complete and open reporting in the field. Furthermore, we had to exclude several studies based on them reporting types of outcome measures that were unique in our reviewed studies sample (e.g., blood pressure or SCR for a correlational design) and therefore could not be pooled with other similar measures from any other study retained in our meta-analysis. These are limitations that come with reviewing psychophysiological data, which can be very diverse in terms of specific outcome measures and reported data type. In addition, as we had to create a

set of hierarchies for the inclusion criteria for measurement types and for task type (if there were several ones), we could have introduced a selection bias. Although heterogeneity in experimental stimuli might contribute to the contradicting findings identified in physiological studies, Lorber (2004) suggested that taking the valence of the experimental stimuli into account might resolve some of these inconsistencies. In the present meta-analysis, we mostly focused on negative valenced stimuli following this suggestion, and, as discussed above, our descriptive comparison of tasks and stimuli used in the included studies showed no pattern based on the type of stimuli or tasks, but rather consistent effects across different types of stimuli and tasks. Finally, the assessment with the NOS suggested that most of the items were correctly addressed in the majority of the studies; however, there is no consensus on how to define evidence at high or low risk of bias based on the NOS.

4.2 Future Directions and Conclusions

There are several important conclusions derived from this meta-analysis that can inform future work. First, SC reactivity might be an important biomarker for identifying youth high on CP, irrespective of ADHD comorbidity. Thus, the sympathetic nervous system, which is responsible for the "fight or flight" response, is a good candidate for explaining youth antisocial behavior. Lower responsiveness and stress reactivity to threatening stimuli, as indicated by the identified lower SC response, among children with CP might drive their engagement in antisocial behaviors, without considering the negative consequences associated with these behaviors (Fanti, 2018; Fanti et al., 2018). Thus, the assessment of SC reactivity should be a research priority among studies interested in physiological measures that tap into stress or emotions. Based on evidence that baseline and task-related HR were identified as predictors of CP in correlational studies, we might be able to conclude that these physiological measures should also be used in empirical studies interested in the prediction of

CP. HR was found to be an important measure for the identification of at risk children and the prediction of developmental stability in antisocial behavior (Fanti, 2019; Raine, 2015; Raine et al., 1997). Future longitudinal work might consider assessing baseline and task-related HR as well as SC reactivity as part of an etiological model to explain the development of stable and severe CP.

Interestingly, although we did not identify an effect of HRV, co-inhibition of sympathetic (PEP) and parasympathetic (RSA) systems, was associated with CP. The majority of prior work fail to assess both sympathetic and parasympathetic autonomic activity, which might result in an incomplete picture of physiological deficits, especially since physiological systems work dynamically (Fanti, 2019; Porges, 2001; Thomoson et al., 2019). Investigating the interaction between parasympathetic and sympathetic activity in response to emotional stimuli can provide a more complete picture of emotion dysregulation deficits (see Thomson et al., 2019 for an example). Moreover, there is a need to move beyond the single biomarker approach to better understand the impact of physiological stress response systems on antisocial behavior (Buss, Jaffee, Wadsworth, & Kliewer, 2018; Fanti, Kyranides, Petridou, Demetriou, & Georgiou, 2018). Emotional experiences involve coordinated changes in the activity of various physiological systems, and variations in distinct physiological systems might provide evidence to explain prior contradicting findings. Current findings provide support for co-inhibition of sympathetic, as indicated by both SC and PEP measures, and parasympathetic, in accordance with RSA, systems pointing to decreased sympathetic and parasympathetic activity. This finding agrees with work suggesting that co-inhibition puts children at risk for conduct problems by making them more vulnerable to stressful environmental experiences (El-Sheikh et al., 2009). Thus, it is important for future work to investigate multisystem physiological responses to aversive

stimuli to identify vulnerability factors associated with the expression of CP or other forms of psychopathology.

Another important message derived from the present meta-analyses is that correlational and case-control studies can result in different findings, and future empirical work should consider this information during study design. Furthermore, there is great variability in the experimental tasks used in physiological research. The use of standardized tasks to understand physiological reactivity might help to advance this line of work. Importantly, experimental tasks used in physiological work might not represent ecologically valid assessments, and future work might consider incorporating novel techniques, such as virtual reality tasks.

Finally, despite the complexity of existing work, the present meta-analysis was able to derive several conclusions that have the potential to inform biological vulnerability models. In fact, current findings can inform efforts towards research domain criteria and can be used as a basis for the design of novel biologically driven interventions. Based on the findings, the effectiveness of interventions designed for children and adolescents high on CP might increase if they focus on stress reactivity deficits as indicated by the co-inhibition in both sympathetic and parasympathetic autonomic systems. The assessment of both clinical and physiological outcomes can inform the mechanisms underlying treatment effects, and can advance the current state of the art.

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Figure Captions

Figure 1. Prisma chart for the study selection process

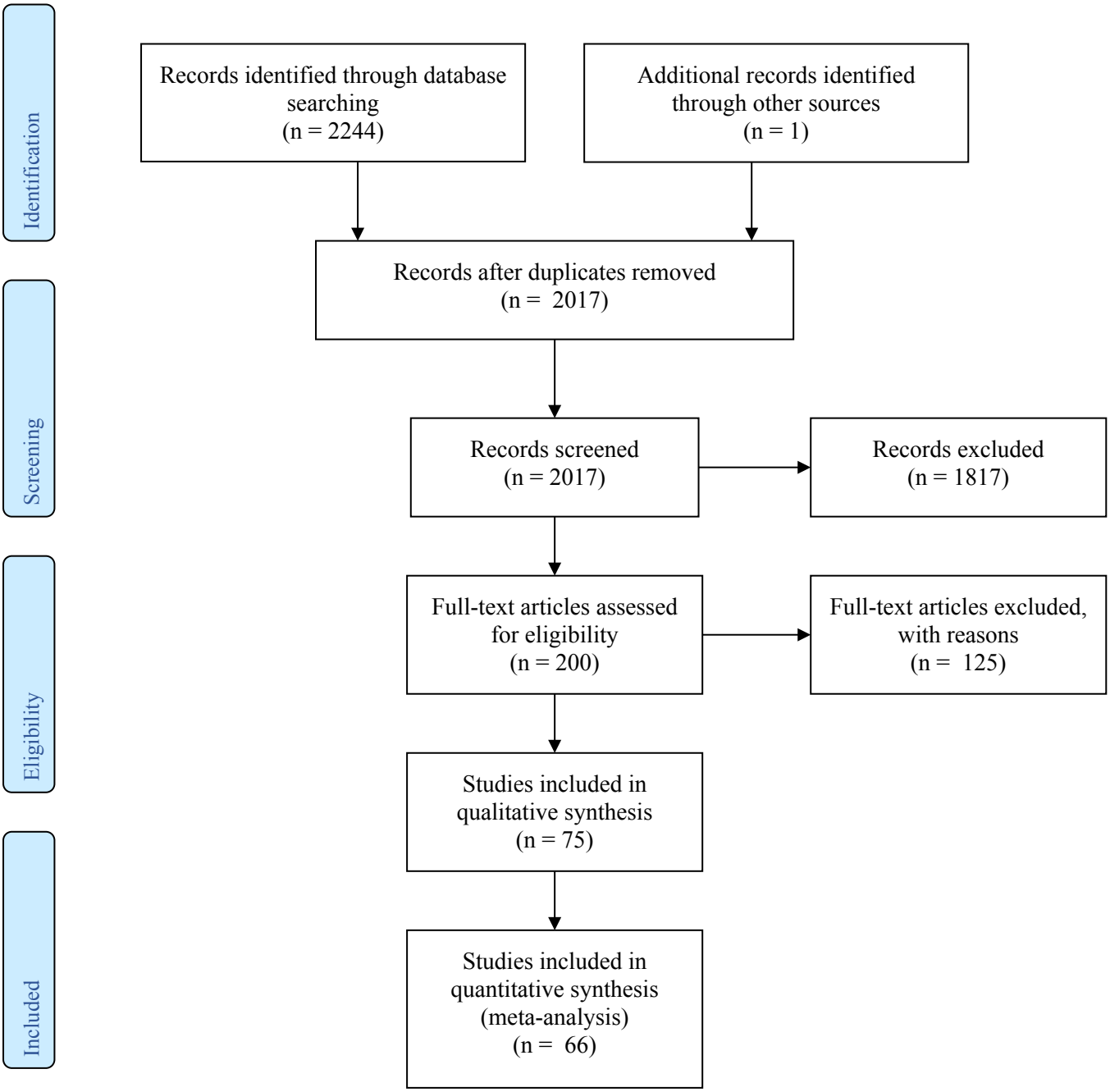

Identification
Screening
Eligibility
Included
Records identified through database searching (n = 2244)
Additional records identified through other sources (n = 1)
Records after duplicates removed (n = 2017)
Records screened (n = 2017)
Records excluded (n = 1817)
Full-text articles assessed for eligibility (n = 200)
Full-text articles excluded, with reasons (n = 125)
Studies included in qualitative synthesis (n = 75)
Studies included in quantitative synthesis (meta-analysis) (n = 66)

Figure 1

Table 1

Meta-analytic results overview.

Design	Outcome variable	Number of studies	Meta analytic effect	CI	I^2
Case-Control	Baseline HR	5	-0.326	[-0.784; 0.132]	65.337
	Task-related HR	18	-0.155	[-0.415; 0.105]	80.055
	Task-related HRV	2	-0.300	[-0.654; 0.053]	0.000
	Baseline RSA	0			
	Task-related RSA	6	-0.206*	[-0.398; -0.014]	0.000
	Task-related PEP	5	0.597*	[0.245; 0.948]	55.245
	Baseline SCL	2	-0.188	[-0.763; 0.387]	57.479
	Task-related SCL	10	-0.862*	[-1.450; -0.274]	90.946
	Baseline SCR	2	-0.478	[-1.397;0.441]	76.690
	Task-related SCR	9	-0.364*	[-0.501; -0.227]	0.000
Correlational	Baseline HR	8	-0.139*	[-0.227; -0.048]	79.714
	Task-related HR	7	-0.165*	[-0.265; -0.061]	64.805
	Baseline RSA	4	-0.060	[-0.132; 0.013]	0.000
	Task related RSA	11	0.004	[-0.044; 0.051]	0.000
	Baseline PEP	2	-0.020	[-0.115; 0.077]	0.000
	Task PEP	3	-0.056	[-0.270; 0.164]	67.675
	Baseline SCL	3	0.049	[-0.058; 0.154]	40.452
	Task-related SCL	7	0.023	[-0.122; 0.167]	74.255
	Baseline SCR	0			

Task-related SCR	0

*Note: * = significant meta analytic effect, I^2 = Information criterion*

Table 2

Subgroup Meta-analyses overview

Design	Outcome variable	Number of studies	Subgroup	Meta analytic effect	CI	I^2
Correlational	Task-related HR	2	Boys	0.159*	[0.055; 0.259]	0.000
			Girls	-0.004	[-0.135; 0.127]	0.000
Case-control	Task-related HR	3	ADHD+	-0.037	[-0.268; 0.194]	0.000
			ADHD-	0.080	[-0.420; 0.580]	73.887
	Task-related SCR	3	ADHD+	-0.538*	[-0.937; -0.138]	64.773
			ADHD-	-0.375*	[-0.697; -0.053]	27.666
	Task-related HR	2	CU+	-0.109	[-0.492; 0.274]	0.000
			CU-	-0.136	[-0.609; 0.336]	33.514

SUPPLEMENTAL MATERIAL

Index of Supplementary materials:

Supplemental Material 1. 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.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3-9
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	8-9
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.	9
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.	9-10

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.	10-11
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Suppl. 2
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).	11
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.	11-12
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	11-13
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.	11-12
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	11-13
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.	11-13

Supplemental Material 2. Search strategy and results from each database (Last search February 13th, 2018)

SEARCH STRATEGY AND RESULTS FROM EACH DATABASE

SEARCH 1

PUBMED (MEDLINE)

Search terms:

(conduct disorder OR conduct problem*) AND (heart rate OR beats per minute OR blood pressure OR heart rate variability OR pre-ejection period OR respiratory sinus arrythmia OR electrodermal activity OR galvanic skin response OR electrodermal response OR psychogalvanic reflex OR skin conductance response OR sympathetic skin response OR skin conductance level) AND (child* OR adolesc* OR youth* OR pediatric* OR paediatric*)

Limits: **none**

Results: **79 hits**

OVID databases

PsycInfo, EMBASE+EMBASE classic, OVID Medline

Search terms:

(conduct disorder OR conduct problem*) AND (heart rate OR beats per minute OR blood pressure OR heart rate variability OR pre-ejection period OR respiratory sinus arrythmia OR electrodermal activity OR galvanic skin response OR electrodermal response OR psychogalvanic reflex OR skin conductance response OR sympathetic skin response OR skin conductance level) AND (child* OR adolesc* OR youth* OR pediatric* OR paediatric*)

Limits: **none**

Results: **321 hits**

WEB OF KNOWLEDGE

(Web of science (science citation index expanded), Biological abstracts, Biosis, Food science and technology abstracts)

Search terms:

conduct disorder OR conduct problem*

heart rate OR beats per minute OR blood pressure OR heart rate variability OR pre-ejection period OR respiratory sinus arrythmia OR electrodermal activity OR galvanic skin response OR electrodermal response OR psychogalvanic reflex OR skin conductance response OR sympathetic skin response OR skin conductance level

child* OR adolesc* OR youth* OR pediatric* OR paediatric*

Limits: **none**

Results: **1844 hits**

AFTER MERGING AND partially REMOVING DUPLICATES: 2016 POTENTIAL REFERENCES TO SCREEN

Supplemental Material 3. References discarded after reading the full text, with reasons for exclusion.

Paper reference	Reasons for exclusion
Aman, M. G., Buican, B., & Arnold, L. E. (2003). Methylphenidate treatment in children with borderline IQ and mental retardation: analysis of three aggregated studies. *Journal of Child and Adolescent Psychopharmacology*, *13*(1), 29-40.	Drug Trial
Aman, M. G., Hollway, J. A., Leone, S., Masty, J., Lindsay, R., Nash, P., & Arnold, L. E. (2009). Effects of risperidone on cognitive-motor performance and motor movements in chronically medicated children. *Research in developmental disabilities*, *30*(2), 386-396.	Drug Trial
Aman, M. G., Kern, R. A., Mc Ghee, D. E., & Arnold, L. E. (1993). Fenfluramine and methylphenidate in children with mental retardation and ADHD: Clinical and side effects. *Journal of the American Academy of Child & Adolescent Psychiatry*, *32*(4), 851-859.	Duplicate
Ardizzi, M., Martini, F., Umiltà, M. A., Sestito, M., Ravera, R., & Gallese, V. (2013). When early experiences build a wall to others' emotions: an electrophysiological and autonomic study. *PloS one*, *8*(4), e61004.	Not specific enough to CD
Babel, K. A., Jambroes, T., Oostermeijer, S., van de Ven, P. M., Pompa, A., Vermeiren, R. R. J. M., Doreleijers, T. A. H., & Jansen, L. M. C. (2016). Do post-trauma symptoms mediate the relation between neurobiological stress parameters and conduct problems in girls? *Child and Adolescent Psychiatry and Mental Health, 10,* 42-52.	No relevant outcomes
Barboza, M., Sepúlveda, S., & Montalvo, D. (2007). Frontal neurocysticercosis and attention deficit. *Colombia Medica* , *38*(1), 21-27.	Not specific enough to CD

Beauchaine, T. P. (2000). Disinhibitory psychopathology in male adolescents: Discriminating Conduct Disorder from ADHD through Concurrent Assessment of Multiple Autonomic States	Thesis / Dissertation
Beauchaine, T. P. (2001). Vagal tone, development, and Gray's motivational theory: Toward an integrated model of autonomic nervous system functioning in psychopathology. *Development and psychopathology*, *13*(2), 183-214.	Review
Beauchaine, T. A. (2002). Autonomic substrates of heart rate reactivity in adolescent males with conduct disorder and/or attention-deficit/hyperactivity disorder. *Advances in Psychology Research, 18*(18), 83-95.	Conference Proceedings
Beauchaine, T. P. (2015). Respiratory sinus arrhythmia: A transdiagnostic biomarker of emotion dysregulation and psychopathology. *Current opinion in psychology*, *3*, 43-47.	Review
Beauchaine, T. P., Gartner, J., & Hagen, B. (2000). Comorbid Depression and heart rate variability as predictors of aggressive and hyperactive symptom responsiveness during inpatient treatment of Conduct-Disordered, ADHD boys. *Aggressive Behavior, 26,* 425-441.	Physiological and behavioral data not from same time point
Beauchaine, T. P., & Gatzke-Kopp, L. M. (2012). Instantiating the multiple levels of analysis perspective in a program of study on externalizing behavior. *Development and psychopathology*, *24*(3), 1003-1018.	Review
Beauchaine, T. P., & Gatzke-Kopp, L. M., Mead, J. K. (2007). Polyvagal Theory and developmental psychopathology: Emotion dysregulation and conduct problems from preschool to adolescence. *Biological Psychology, 74,* 174-184.	Review

Beauchaine, T. P., Katkin, E. S., Strassberg, Z., & Snarr, J. (2001). Disinhibitory psychopathology in male adolescents: Discriminating conduct disorder from attention-deficit/hyperactivity disorder through concurrent assessment of multiple autonomic states. *Journal of abnormal psychology*, *110*(4), 610.	Thesis / Dissertation
Brammer, W. A., Jezior, K. L., & Lee, S. S. (2016). Psychopathic traits mediate the association of serotonin transporter genotype and child externalizing behavior. *Aggressive Behavior, 42*(5), 455-470.	No relevant outcomes
Bushman, B. J., Newman, K., Calvert, S. L., Downey, G., Dredze, M., Gottfredson, M., Jablonski, N. G., Masten, A. S., Morrill, C., Neill, D. B., Romer, D., & Webster, D. W. (2016). Youth violence: What we know and what we need to know. *American Psychologist, 71*(1), 17-39.	Review
Buitelaar, J. K., Cohen-Kettenis, P., & Melman, C. T. (2001). A randomized controlled trial of risperidone in the treatment of aggression in hospitalized adolescents with subaverage cognitive abilities. *The Journal of clinical psychiatry*, *62*(4), 239-248.	Drug Trial
Bymaster, F., & McKinney, A. A. (2014). Treatment of attention deficit-hyperactivity disorder or related behavioral disorder or substance abuse disorder by administering pharmaceutical composition comprising (1R,5S)-(plus)-1-(naphthalen-2-yl)-3-azabicyclo(3.1.0)hexane.	Drug Trial
Calkins, S. D. & Dedmon, S.E. (2000). Physiological and Behavioral Regulation in Two-Year-Old Children with Aggressive/Destructive Behavior Problems. *Journal of Abnormal Child Psychology, 28*(2), 103–118.	Missing data

Calkins, S. D., Graziano, P. A. & Keane, S. P. (2007). Cardiac vagal regulation differentiates among children at risk for behavior problems. *Biological Psychology, 74,* 144–153.	Missing data
Cao, Y., Chen, A., Radcliffe, J., Dietrich, K. N., Jones, R. L., Caldwell, K., & Rogan, W. J. (2009). Postnatal cadmium exposure, neurodevelopment, and blood pressure in children at 2, 5, and 7 years of age. *Environmental health perspectives*, *117*(10), 1580-1586.	Not specific enough to CD
Cappadocia, M. C., Desrocher, M., Pepler, D., & Schroeder, J. H. (2009). Contextualizing the neurobiology of conduct disorder in an emotion dysregulation framework. *Clinical psychology review*, *29*(6), 506-518.	Review
Childress, A. C., & Berry, S. A. (2012). Pharmacotherapy of attention-deficit hyperactivity disorder in adolescents. *Drugs*, *72*(3), 309-325.	Drug Trial
Chen, F. R., Raine, A., Glenn, A. L., & Granger, D. A. (2016). Hypothalamic pituitart adrenal activity and autonomic nervous system arousal predict developmental trajectories of children's comorbid behavior problems. *Developmental Psychobiology, 58*(3), 393-405.	No relevant outcomes
Clerpka, M., Lück, M., Strüber, D., & Roth, G. (2007). Zur ontogenese aggressiven verhaltens. *Übersichten, 52,* 87-101.	Review
Cohn, M. D., Pompa, A., van den Brink, W., Pape, L. E., Kindt, M., van Domburgh, L., Doreleijers, T. A. H., & Veltman, D. J. (2013). Fear conditioning, persistence of disruptive behavior and psychopathic traits: An Fmri study. *Translational Psychiatry*, e319. doi: 10.1038/tp.2013.89.	No baseline data

Cole, P. M., Zahn-Waxler, C., Fox, N. A., Usher, B. A., & Welsh, J. D. (1996). Individual differences in emotion regulation and behavior problems in preschool children. *Journal of Abnormal Psychology, 105*(4), 518-529.	Only correlation with expressive type
Compas, B. E., Jaser, S. S., Bettis, A. H., Watson, K. H., Gruhn, M. A., Dunbar, J. P., Williams, E., & Thigpen, J. C. (2017). Coping, emotion regulation, and psychopathology in childhood and adolescence: A meta-analysis and narrative review. *Psychological Bulletin, 143*(9), 939-991.	Review
Connor, D. F., & Rubin, J. (2010). Guanfacine extended release in the treatment of attention deficit hyperactivity disorder in children and adolescents. *Drugs of today (Barcelona, Spain: 1998)*, *46*(5), 299-314.	Drug Trial
Connor, D. F., & Spencer, T. J. (2005). Short-term cardiovascular effects of mixed amphetamine salts extended release in children and adolescents with oppositional defiant disorder. *Cns Spectrums, 10*(10), 31-38.	Drug Trial
Connor, D. F., Barkley, R. A., & Davis, H. T. (2000). A pilot study of methyiphenidate, clonidine, or the combination in ADHD comorbid with aggressive oppositional defiant or conduct disorder. *Clinical Pediatrics*, *39*(1), 15-25.	Design not appropriate
Connor, D. F., Findling, R. L., Kollins, S. H., Sallee, F., López, F. A., Lyne, A., & Tremblay, G. (2010). Effects of guanfacine extended release on oppositional symptoms in children aged 6–12 years with attention-deficit hyperactivity disorder and oppositional symptoms. *CNS drugs*, *24*(9), 755-768.	Drug Trial
Conradt, E., Degarmo, D., Fisher, P., Abar, B., Lester, B. M., Lagasse, L. L., Shankaran, S., Bada, H., Bauer, C. R., Whitaker, T. M., & Hammond, J. A. (2014). The contributions of early adverse experiences and trajectories of respiratory sinus arrhythmia on the development of neurobehavioral	parental alcohol use focus

disinhibition among children with prenatal substance exposure. *Development and Psychopathology, 26,* 901-916.	
Cornet, L. J., de Kogel, C. H., Nijman, H. L., Raine, A., & van der Laan, P. H. (2014). Neurobiological factors as predictors of cognitive–behavioral therapy outcome in individuals with antisocial behavior: a review of the literature. *International journal of offender therapy and comparative criminology*, *58*(11), 1279-1296.	Review
Dadds, M. R. & Salmon, K. (2003). Punishment Insensitivity and Parenting: Temperament and Learning as Interacting Risks for Antisocial Behavior. *Clinical Child and Family Psychology Review*, 6(2), 69-86.	Review
Delamater, A. M. & Lahey, B. B. (1983). Physiological Correlates of Conduct Problems and Anxiety in Hyperactive and Learning-Disabled Children. *Journal of Abnormal Child Psychology, 11*(1), 85-100.	Missing SD data
Deshmukh, P., Kulkarni, G., & Barzman, D. (2010). Recommendations for pharmacological management of inpatient aggression in children and adolescents. *Psychiatry (Edgmont)*, *7*(2), 32.	Review
De Vries-Bouw, M., Popma, A., Vermeiren, R., Doreleijers, T. A. H., van de Ven, P. M., & Jansen, L. M. C. (2011). The predicitive value of low heart rate and heart rate variability during stress for reoffending in delinquent male adolescents. *Psychophysiology, 48,* 1596-1603.	Offending, not CD
De Wied, M., van Boxtel, A., Posthumus, J. A., Goudena, P. P., & Matthys, W. (2009). Facial EMG and heart rate responses to emotion-inducing film clips in boys with disruptive behavior disorders. *Psychophysiology 46,* 996-1004.	Replication of the data

Diamond, L. M., & Cribbet, M. R. (2013). Links between adolescent sympathetic and parasympathetic nervous system functioning and interpersonal behavior over time. *International Journal of Psychophysiology*, *88*(3), 339-348.	Not specific enough to CD
Dierckx, B., Tulen, J. H. M., Tharner, A., Jaddoe, V. W., Hofman, A., Verhulst, F. C., & Tiemeier, H. (2011). Low autonomic arousal as vulnerability to externalising behaviour in infants with hostile mothers. *Psychiatry Research, 185,* 171-175.	Physiological and behavioral data not from same time point
El-Sheikh, M., Ballard, M., & Cummings, E. M. (1994). Individual differences in preschoolers' physiological and verbal responses to videotaped angry interactions. *Journal of Abnormal Child Psychology, 22*(3), 303-320.	Only correlation with situational anger
Finger, B., Schuetze, P., & Eiden, R. D. (2014). Behavior problems among cocaine exposed children: Role of physiological regulation and parenting. *Neurotoxicology and Teratology, 42*, 51-59.	No relevant outcomes
Gao, Y., Raine, A., Venables, P. H., Dawson, M. E., & Mednick, S. A. (2010). Reduced electrodermal fear conditioning from ages 3 to 8 years is associated with aggressive behavior at age 8 years. *Journal of Child Psychology and Psychiatry, 51*(5), 550-558.	Only task related physio
Garralda, M. E., Connell, J., & Taylor, D. C. (1990). Peripheral psychophysiological reactivity to mental tasks in children with psychiatric disorders. *European archives of psychiatry and clinical neuroscience*, *240*(1), 44-47.	No normal control group
Glenn, A. L., & Raine, A. (2014). Neurocriminology: implications for the punishment, prediction and prevention of criminal behaviour. *Nature Reviews Neuroscience*, *15*(1), 54.	Review

Griffiths, K. R., Quintana, D. S., Hermens, D. F., Spooner, C., Tsang, T. W., Clarke, S., & Kohn, M. R. (2017). Sustained attention and heart rate variability in children and adolescent with ADHD. *Biological Psychology, 124,* 11-20.	No assesment of children having CD
Harden, P. W., Pihl, R. O., Vitaro, F., Gendreau, P. L., & Tremblay, R. E. (1995). Stress response in anxious and nonanxious disruptive boys. *Journal of Emotional and Behavioral Disorders*, *3*(3), 183-190.	Duplicate
Hassan, S. I., Kazmi, K., Jahan, F., Badruddin, S. H., & Ahmed, S. (2008). An assessment of cardiovascular disease risk factors and behavior in Pakistani adolescents. *Circulation, 118*(12), E440-E441.	Conference Proceedings
Hazell, P. L., & Stuart, J. E. (2003). A Randomized Controlled Trial of Clonidine Added to Psychostimulant Medication for Hyperactive and Aggressive Children. *Year Book of Psychiatry & Applied Mental Health*, *2005*, 70-71.	Drug Trial
Hill, J. (2001). Biosocial influences on antisocial behaviours in childhood and adolescence.	Thesis/ Dissertation
Hinnant, J. B., Elmore-Staton, L., & El-Sheikh, M. (2011). Developmental trajectories of respiratory sinus arrhythmia and preejection period in middle childhood. *Developmental psychobiology*, *53*(1), 59-68.	No assessment of children having CD
Hinnant, J. B., Forman-Alberti, A. B., Freedman, A., Byrnes, L., & Degnan, K. A. (2016). Approach behavior and sympathetic nervous system reactivity predict substance use in young adults. *International Journal of Psychophysiology, 105*, 35-38.	Not relevant for CD
Holzman, J. B., & Bridgett, D. J. (2017). Heart rate variability indices as bio-markers of top-down self-regulatory mechanisms: A meta-analytic review. *Neuroscience and Biobehavioral Reviews, 74,* 233-255.	Review

Iacono, W. G., Carlson, S. R., Taylor, J., Elkins, I. J., & McGue, M. (1999). Behavioral disinhibition and the development of substance-use disorders: Findings from the Minnesota Twin Family Study. *Development and Psychopathology, 11,* 869-900.	No correlation and no group comparison
Isen, J. D., Iacono, W. G., Malone, S. M., & Mc Gue, M. (2012). Examining electrodermal hyporeactivity as a marker of externalizing psychopathology: A twin study. *Psychophysiology*, *49*(8), 1039-1048.	Not specific enough to CD
Isen, J., Raine, A., Baker, L., Dawson, M., Bezdjian, S., & Isabel Lozano, D. (2010). Sex-Specific Association Between Psychopathic Traits and Electrodermal Reactivity in Children. *J Abnorm Psychol, 119*(1), 216-225.	Only study with correlation SCR data
Ivarsson, M., Anderson, M., Åkerstedt, T., & Lindblad, F. (2009). Playing a violent television game affects heart rate variability. *Acta paediatrica*, *98*(1), 166-172.	No assessment of children having CD
Jansen, L. M. C., Gispen-de Wied, C. C., Jansen, M. A., van der Gaag, R. J., Matthys, W., & van Engeland, H. (1999). Pituiitary-adrenal reactivity in a child psychiatric population: Salivary cortisol response to stressors. *European Neuropsychopharmacology, 9,* 67-75.	No HR or SCR data per group
Jennings, J. R., Pardini, D. A., & Matthews, K. A. (2017). Heart rate, health, and hurtful behavior. *Psychophysiology , 54*, 399-408.	No assesment of children having CD
Johnson, A. C. (2015). Developmental pathways to attention-deficit/hyperactivity disorder and disruptive behavior disorders: Investigating the impact of the stress response on executive functioning. *Clinical psychology review*, *36*, 1-12.	Review

Juujarvi, P., Kaartinen, J., Laitinen, T., Vanninen, E., & Pulkkinen, L. (2006). Effects of physical provocations on heart rate reactivity and reactive aggression in children. *Aggressive Behavior, 32*(2), 99-109.	Sample too old
Kara, K., Karaman, D., Erdem, U., Congologlu, M. A., Durukan, I., & Ilhan, A. (2013). Investigation of Autonomic Nervous System Functions by Pupillometry in Children with Attention Deficit Hyperactivity Disorder. *Klinik Psikofarmakoloji Bülteni-Bulletin of Clinical Psychopharmacology*, *23*(1), 49-56.	No relevant outcomes
Karpuz, D., Hallioglu, O., Toros, F., & Tasdelem, B. (2017). The effect of metilpheniydate, risperidone, and combination therapy on ECG in children with attention-deficit hyperactivity disorder. *Journal of Electrocardiology, 50,* 410-415.	Review
Katz, L. F. (2007). Domestic violence and vagal reactivity to peer provocation. *Biological Psychology, 74*(2), 154-164.	Only study that reported vagal tone as outcome measure
Keynan, J. N., Meir-Hasson, Y., Gilam, G., Cohen, A., Jackont, G., Kinreich, S., Ikar, L., Or-Borichev, A., Etkin, A., Gyurak, A., Klovatch, I., Intrator, N., & Hendler, T. (2016). Limbic activity modulation guided by functional magnetic resonance imaging–inspired electroencephalography improves implicit emotion regulation. *Biological Psychiatry*, *80*(6), 490-496.	No relevant outcomes
Knyazev, G. G., Slobodskaya, H. R., & Wilson, G. D. (2002). Psychophysiological correlates of behavioural inhibition and activation. *Personality and Individual Differences*, *33*(4), 647-660.	Sample too old

Kragel, P. A., & LaBar, K. S. (2013). Multivariate pattern classification reveals autonomic and experiential representations of discrete emotions. *Emotion*, *13*(4), 681.	Sample too old
Kruesi, M. J. P., Hibbs, E. D., Zahn, T. P., Keysor, C. S., Hamburger, S. D., Barko, J. J., & Rapoport, J. L. (1992). A 2-year prospective follow-up study of children and adolescents with Disruptive Behavior Disorders. *Archives of General Psychiatry, 49*(6), 429-435.	Complete sample fulfills CD criteria
Kuschnir, M. C., & Mendonca, G. (2008). Common mental disorders and hypertension in adolescents - Rio de Janeiro, Brazil. *Circulation, 118*(12), E270-E270.	Conference Proceedings
Kyranides, M. N., Fanti, K. A., & Panayiotou, G. (2016). The disruptive adolescent as a grown-up: Predicting adult startle responses to violent and erotic films from adolescent conduct problems and callous-unemotional traits. *Journal of Psychopathology and Behavioral Assessment*, *38*(2), 183-194.	Sample too old at relevant outcome measurement timepoint
Lahey, B. B., Krueger, R. F., Rathouz, P. J., Waldman, I. D., & Zald, D. H. (2017). A hierarchical causal taxonomy of psychopathology across the life span. *Psychological Bulletin, 143*(2), 142-186.	Review
Liu, J., & Wuerker, A. (2005). Biosocial bases of aggressive and violent behavior—implications for nursing studies. *International Journal of Nursing Studies*, *42*(2), 229-241.	Review
Loeber, R., Pardini, D. A., Stouthamer-Loeber, M., & Raine, A. (2007). Do cognitive, physiological, and psychosocial risk and promotive factors predict desistance from delinquency in males? *Development and Psychopathology, 19,* 867-887.	No correlations or group means

Lorber, M. F. (2004). Psychophysiology of aggression, psychopathy, and conduct problems: a meta-analysis. *Psychological bulletin*, *130*(4), 531.	Review
Lovallo, W. R. (2013). Early life adversity reduces stress reactivity and enhances impulsive behavior: Implications for health behaviors. *International journal of psychophysiology*, *90*(1), 8-16.	Review
Lynch, M., Manly, J. T., & Cicchetti, D. (2015). A multilevel prediction of physiological response to challenge: Interactions among child maltreatment, neighborhood crime, endothelial nitric oxide synthase gene (eNOS), and GABA (A) receptor subunit alpha-6 gene (GABRA6). *Development and psychopathology*, *27*(4pt2), 1471-1487.	No assessment of children having CD
Mangina, C. A., Beuzeron-Mangina, H. J., & Grizenko, N. (2000). Event-related brain potentials, bilateral electrodermal activity and Mangina-Test performance in learning disabled / ADHD pre-asolescents with severe behavioral disorders as compared to age-matched normal controls. *International Journal of Psychophysiology, 37,* 71-85.	No baseline data included
Marchel, J. R. (1993). *Effects of incentives and nonreward on heart rate and skin conductance in conduct disordered adolescents* (Doctoral dissertation, ProQuest Information & Learning).	Thesis / Dissertation
Masi, G., Manfredi, A., Nieri, G., Muratori, P., Pfanner, C., & Milone, A. (2017). A naturalistic comparison of methylphenidate and risperidone monotherapy in drug-naïve youth with Attetion-Deficit/Hyperactivity Diorder comorbid with Oppositional Defiant Disorder and Aggression. Journal of Clinical Psychopharmacology, 37(5), 590-594.	No relevant design

Matthys, W., Vanderschuren, L. J., & Schutter, D. J. (2013). The neurobiology of oppositional defiant disorder and conduct disorder: altered functioning in three mental domains. *Development and psychopathology*, *25*(1), 193-207.	Review
Mawson, A. R. (2009). On the association between low resting heart rate and chronic aggression: Retinoid toxicity hypothesis. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, *33*(2), 205-213.	Review
McBurnett, K., & Lahey, B. B. (1994). Psychophysiological and neuroendocrine correlates of conduct disorder and antisocial behavior in children and adolescents. *Progress in experimental personality & psychopathology research*, 199-231.	Review
McBurnett, R. K. (1991). *Adrenal and gonadal hormone correlates of child psychopathology.* (Doctoral Dissertation, University of Georgia).	Thesis / Dissertation
McLaughlin, K. A., Sheridan, M. A., Gold, A. L., Duys, A., Lambert, H. K., Peverill, M., Heleniak, C., Shechner, T., Wojcieszak, Z., & Pine, D. S. (2016). Maltreatment Exposure, Brain Structure, and Fear Conditioning in Children and Adolescents. *Neuropsychopharmacology, 41,* 1956-1964.	No relevant outcomes
McNulty, T. M., Zisner, A. R., Howard, A., Gatzke-Kopp, L. M., & Beauchaine, T. P. (2014). Baseline pep, baseline RSA, and RSA reactivity to incentives prospectively predict longitudinal changes in internalizing and externalizing symptoms among children with conduct disorder and/or depression. *Psychophysiology, 51*, S55-S55.	Conference abstract

Mead, H. K., Beauchaine, T. P., Brenner, S. L., Crowell, S., Kopp, L. M., & Marsh, P. (2004). Autonomic response patterns to reward and negative mood induction among children with conduct disorder, depression, and both psychiatric conditions. *Psychophysiology, 41*, S52-S52.	Conference Proceedings
Mezzacappa, E., Kindlon, D., & Earls, F. (1996). Methodologic issues in the use of heart rate and heart-rate variability in the study of disruptive behavior disorders. In D. M. Stoff & R. B. Cairns (Eds.), *Aggression and violence: Genetic, neurobiological, and biosocial perspectives* (pp. 125-143). Mahwah, NJ, US: Lawrence Erlbaum Associates Publishers.	Chapter
Mills-Koonce, W. R., Wagner, N. J., Willoughby, M. T., Stifter, C., Blair, C., Granger, D. A., & The Family Life Project Key Investigators (2015). Greater fear reactivity and psychophysiological hyperactivity among infants with later conduct problems and callous-unemotional traits. *Journal of Child Psychology and Psychiatry, 56*(2), 147-154.	RSA / HR baseline measures were taken at another time point then the CD/CU traits measures
Murray, J., Hallal, P. C., Mielke, G. I., Raine, A., Wehrmeister, F. C., Anselmi, L., & Barros, F. C. (2016). Low resting heart rate is associated with violence in late adolescence: a prospective birth cohort study in Brazil. *International Journal of Epidemiology*, *45*(2), 491-500.	Not focusing on CD problems
Murray-Close, D. (2013) Psychophysiology of Adolescent Peer Relations I: Theory and Research Findings. *Journal of Research on Adolescence*, *23*(2), 236-259.	Review
Neuhaus, E., Beauchaine, T. P., Reid, M. J., & Webster-Stratton, C. (2009). Coercive processes and child vagal tone in families of preschoolers with Attention-Deficit/Hyperactivity Disorder. In S. M. Gordon, & A. E. Mitchell (Eds), Attention Deficit Hyperactivity Disorder. Nova Science.	Chapter

Nevels, R. M., Dehon, E. E., Alexander, K., & Gontkovsky, S. T. (2010). Psychopharmacology of aggression in children and adolescents with primary neuropsychiatric disorders: a review of current and potentially promising treatment options. *Experimental and clinical psychopharmacology*, *18*(2), 184.	Review
Newcorn, J. H., & Ivanov, I. (2007). Psychopharmacologic treatment of attention-deficit/hyperactivity disorder and disruptive behavior disorders. *Pediatr Ann, 36*(9), 564-574.	Review
Newton, J. E. O., Dykman, R. A., Oglesby, D. M., Ackerman, P. A., & McPherson, B. Heart rates in abused children with high and low Conduct Disorder scores.	Abstract
Nijman, H., Bowers, L., Oud, N., & Jansen, G. (2005). Psychiatric nurses' experiences with inpatient aggression. *Aggressive Behavior, 31,* 217-227.	Adult population
Northover, C., Thapar, A., Langley, K., & van Goozen, S. H. M. (2015). Pain Sensitivity in Adolescent Males with Attention-Deficit/Hyperactivity Disorder: Testing for Associations with Conduct Disorder and Callous and Unemotional Traits. *PLoS ONE, 10*(7): e0134417.	Focus on pain sensitivity
Oldenhoff, H., Nauta-Jansen, L., & Popma, A. (2015). Physiological parameters in relation to conduct disorder in girls: Preliminary results from the FemNAT-CD study. *European Child and Adolescent Psychiatry, 1*, S83-S84.	Conference proceedings
Ortiz, J., & Raine, A. (2004). Heart rate level and antisocial behavior in children and adolescents: A meta-analysis. *Journal of the American Academy of Child & Adolescent Psychiatry*, *43*(2), 154-162.	Review

Paysnick, A. A. (2015). *Moderating effects of coping on associations between stress reactivity and internalizing and externalizing problems* (Doctoral dissertation, The University of Vermont and State Agricultural College).	Thesis/ Dissertation
Popma, A., Nauta-Jansen, L., & Oldenhof, H. (2017). Developmental aspects of HPA-axis activity and Automomic Nervous System activity in relation to juvenile antisocial behavior. *Psychoneuroendocrinology, 83,* 50.	Conference abstract only
Portnoy, J., & Farrington, D. P. (2015). Resting heart rate and antisocial behavior: An updated systematic review and meta-analysis. *Aggression and violent behavior*, *22*, 33-45.	Review
Quay, H. C. (1993). The psychobiology of undersocialized aggressive conduct disorder: A theoretical perspective. *Development and psychopathology*, *5*(1-2), 165-180.	Review
Raine, A. (2002). Annotation: The role of prefrontal deficits, low autonomic arousal, and early health factors in the development of antisocial and aggressive behavior in children. *Journal of Child Psychology and Psychiatry*, *43*(4), 417-434.	Review
Reynaud-Roepke, S. (1995). *Social and psychophysiological correlates of undersocialized-aggressive conduct disorder and socialized-aggressive conduct disorder in institutionalized male youth and adolescents: a biosocial approach* (Doctoral dissertation, University of Southern California).	Thesis/ Dissertation
Rogeness, G. A., Cepeda, C., Macedo, C. A., Fischer, C., & Harris, W. R. (1990). Differences in heart rate and blood pressure in children with conduct disorder, major depression, and separation anxiety. *Psychiatry Research, 33*(2), 199-206.	Only study with only blood pressure outcome

Scarpa, A., & Raine, A. (2004). The psychophysiology of child misconduct. *Pediatric annals*, *33*(5), 296-304.	Review
Scheepers, F. E., Buitelaar, J. K., & Matthys, W. (2011). Conduct disorder and the specifier callous and unemotional traits in the DSM-5. *European child & adolescent psychiatry*, *20*(2), 89-93.	Review
Schmidt, K., Solant, M. V., & Bridger, W. H. (1985). Electrodermal activity of undersocialized aggressive children: A pilot study. *Journal of Child Psychology and Psychiatry*, *26*(4), 653-660.	Duplicate
Schoorl, J., Van Rijn, S., De Wied, M., Van Goozen, S. H., & Swaab, H. (2016). Variability in emotional/behavioral problems in boys with oppositional defiant disorder or conduct disorder: the role of arousal. *European child & adolescent psychiatry*, *25*(8), 821-830.	Duplicate
Schoorl, J., Van Rijn, S., De Wied, M., Van Goozen, S. H., & Swaab, H. (2017). Neurobiological stress responses predict aggression in boys with oppositional defiant disorder/conduct disorder: a 1-year follow-up intervention study. *European Journal of Child and Adolescent Psychiatry, 26,* 805-813.	No healthy control sample
Schvehla, T. J., Mandoki, M. W., & Sumner, G. S. (1994). Clonidine therapy for comorbid attention deficit hyperactivity disorder and conduct disorder: preliminary findings in a children's inpatient unit. *Southern medical journal*, *87*(7), 692-695.	Drug Trial
Schwenck, C., Ciaramidaro, A., Selivanova, M., Tournay, J., Freitag, C. M., & Siniatchkin, M. (2017). Neural correlates of affective empathy and reinforcement learning in boys with conduct problems: fMRI evidence from a gambling task. *Behavioral Brain Research, 320,* 75-84.	No relevant outcomes

Shahrestani, S., Stewart, E. M., Quintana, D. S., Hickie, I. B., & Guastella, A. J. (2014). Heart rate variability during social interactions in children with and without psychopathology: A meta-analysis. *Journal of Child Psychology and Psychiatry*, *55*(9), 981-989.	Review
Shea, S., Turgay, A., Carroll, A., Schulz, M., Orlik, H., Smith, I., & Dunbar, F. (2004). Risperidone in the treatment of disruptive behavioral symptoms in children with autistic and other pervasive developmental disorders. *Pediatrics*, *114*(5), e634-e641.	Drug Trial
Silberg, J. L., & Eaves, L. J. (2004). Analysing the contributions of genes and parent–child interaction to childhood behavioural and emotional problems: A model for the children of twins. *Psychological Medicine*, *34*(2), 347-356.	Not specific enough to CD
Stadler, C., Grasmann, D., Fegert, J. M., Holtmann, M., Poustka, F., & Schmeck, K. (2008). Heart rate and treatment effect in children with disruptive behavior disorders. *Child Psychiatry Hum Dev, 39*(3), 299-309.	No control group data
Stankovic, A., Fairchild, G., Aitken, M. R., & Clark, L. (2014). Effects of psychosocial stress on psychophysiological activity during risky decision-making in male adolescents. *International journal of psychophysiology*, *93*(1), 22-29.	No assessment of children having CD
Sulik, M. J., Eisenberg, N., Silva, K. M., Spinrad, T. L., & Kupfer, A. (2013). Respiratory sinus arrhythmia, shyness, and effortful control in preschool-age children. *Biological Psychology, 92,* 241-248.	Not specific enough for CD
Taskiran, C., Karaismailoglu, S., Cak Esen, H. T., Tuzun, Z., Erdem, A., Dicle Balkanci, Z., Barak Dolgun, A., & Cengel Kultur, S. E. (2017). Clinical features and subjective/physiological responses to emotional stimuli in the	No relevant sample type

presence of emotion dysregulation in attention-deficit hyperactivity disorder. *Journal of Clinical and Experimental Neuropsychology, 40*(4), 389-404.	
Tucker, T. L. (1992). Psychophysiological correlates in children with conduct disorders. *Dissertation Abstracts International, 53*(2-A), 450.	Dissertation
Turpyn, C. C., Chaplin, T. M., Cook, E. C., & Martelli, A. M. (2015). A person-centered approach to adolescent emotion regulation: Associations with psychopathology and parenting. *Journal of experimental child psychology, 136,* 1-16.	Latent profile analysis based groups
Tuvblad, C., & Beaver, K. M. (2013). Genetic and environmental influences on antisocial behavior. *Journal of criminal justice*, *41*(5), 273.	Review
Van Bokhoven, I., Matthys, W., Van Goozen, S. H., & Van Engeland, H. (2005). Prediction of adolescent outcome in children with disruptive behaviour disorders. *European Child & Adolescent Psychiatry*, *14*(3), 153-163.	Unclear subsample with or without ADHD criteria
Van Goozen, S. H. (2015). The role of early emotion impairments in the development of persistent antisocial behavior. *Child Development Perspectives*, *9*(4), 206-210.	Review
Van Goozen, S. H., Langley, K., Northover, C., Hubble, K., Rubia, K., Schepman, K., O'Donovan, M. C., & Thapar, A. (2016). Identifying mechanisms that underlie links between COMT genotype and aggression in male adolescents with ADHD. *Journal of Child Psychology & Psychiatry, 57*(4), 472-480.	Number of participants per group not available
Van Hulle, C., Zahn-Waxler, C., Robinson, J. L., Hyun Rhee, S., Hastings, P. D., & Knafo, A. (2013). Autonomic correlates of children's concern and disregard for others. *Social Neuroscience, 8*(4), 275-290.	Only situational measure for emotion

Van Lang, N. D. J., Tulen, J. H. M., Kallen, V. L., Rosbergen, B., Dieleman, G., & Ferdinand, R. F. (2007). Autonomic reactivity in clinically referred children attention-deficit/hyperactivity disorder versus anxiety disorder. *European Journal of Child and Adolescent Psychiatry, 16,* 71-78.	No healthy control, focus on ADHD
Vasilev, C. A., Crowell, S. E., Beauchaine, T. P., Mead, H. K., & Gatzke-Kopp, L. M. (2009). Correspondence between physiological and self-report measures of emotion dysregulation: A longitudinal investigation of youth with and without psychopathology. *Journal of Child Psychology and Psychiatry, 50*(11), 1357-1364.	Only delta RSA data
Vloet, T. D., Herpertz-Dahlmann, B., & Herpertz, S. (2006). Predictors of dissocial behavior. *The Nerve Doctor, 77* (7), 782-790.	Review
Vries-Bouw, D., Popma, A., Vermeiren, R., Doreleijers, T. A., Van De Ven, P. M., & Jansen, L. (2011). The predictive value of low heart rate and heart rate variability during stress for reoffending in delinquent male adolescents. *Psychophysiology*, *48*(11), 1597-1604.	Not specific enough to CD
Wee, C. Y., Tuan, T. A., Broekman, B. F. P., Ong, M. Y., Chong, Y. S., Kwek, K., Shek, L., Saw, S. M., Gluckman, P. D., Fortier, M. V., Meaney, M. J., Qiu, A. (2017). Neonatal Neural Networks Predict Children Behavioral Profiles Later in Life. *Human Brain Mapping, 38,* 1362-1373.	No relevant outcomes
Wilkes, T. C., & Nixon, M. K. (2015). Pharmacological treatment of child and adolescent disruptive behaviour disorders: between the scylla and charybdis, what do the data say? *The Canadian Journal of Psychiatry*, *60*(2), 39-41.	Review

Yamashiro, D., Aihara, M., Ono, C., Kanemura, H., Aoyagi, K., Goto, Y., Iwadare, Y., & Nakazawa, S. (2004). Evaluation of Sympathetic Skin Response in Patients with Attention Deficit/Hyperactivity Disorder Presenting with Comorbid Disorders. [Japanese]. *No To Hattatsu, 36*(1), 49-54.	Duplicate
Zahn-Waxler, C., Cole, P. M., Welsh, J. D. & Fox, N. A. (1995). Psychophysiological correlates of empathy and prosocial behaviors in preschool children with behavior problems. *Development and Psychopathology, 7*, 27-48.	Missing data

Supplemental Table 1: Study characteristics of case-control studies included in the quantitative analyses .

First author and year	Outcome measure	Task	Baseline	Group definition	CD				Control group		Comments
					N (f/m)	Age: M (SD) or range	Subgroups (N, f/m)	Age: M (SD) or range	N (f/m)	Age: M (SD) or range	
Anastassiou-Hadjicharala-mbous, 2008	HR	Watching an emotion evoking film		CDRTS for School-age Children	29 (27/2)	9.29 (0.92)	CD/CU+ 75% on CU and 50% on CD: 33 (1/32); CD/CU- <50% on CU and 50% on CD: (0/29); 9.4 (1.17)	CD/CU+ 9.4 (1.17), CD/CU- 9.29 (0.92)	33 (2/31)	9.31 (0.77)	Task data extracted
Beauchaine, 2001	RSA / PEP	Repetitive response task involving reward and loss	5 min baseline period	ASI / CBCL	20 (0/20)	14.0 (1.6)	ADHD only 17 (0/17)	13.1 (1.2)	22 (0/22)	13.2 (1.3)	RSA task data extracted

Beauchaine, 2003	HR / RSA / PEP	Learning task with reward trials and extinction trials	Last 2 min of a 5 min baseline	Adolescent Symptom Inventory / CBCL (Aggression, Hyperactivity, Delinquent Behaviour and Anxious/Depressed Subscales)	20 (0/20)	14.0 (1.6)	ADHD only 17 (0/17)	13.1 (1.2)	22 (0/22)	13.2 (1.3)	HR during reward incentive task extracted
Beauchaine, 2008	SCR / RSA / PEP	Repetitive response task with blocks of reward		CSI / CBCL (CLINICAL)	86 (33/53)	M 9.8 (1.5), F 9.4 (1.5)	CSI ADHD symptom met	M 16.4 (6.6) F 17.4 (9.7)	89 (32/57)	M 9.8 (1.5), F 9.3 (1.5)	SCR baseline extracted due to missing task data, RSA reward change data from baseline to task extracted Pre-meta-analysis computing SMD and SE across males and females

Crowell, 2006	SCR / HR / RSA / PEP	Reward task (perfection game)	5 mins	CBCL/ CSI (CLINICAL)	18 (7/11)	4-6			20 (9/11)	4-6	Baseline SCR and HR extracted
Da Silva, 2014	SC	Sequence of 10 very mild electric stimuli		YSR	38 (18/20)	13.84 (1.46)					Pre-meta-analysis computing SMD and SE across stimuli
De Vries-Bouw, 2012	HR / HRV (power analysis of component frequencies)	Psychosocial stress task		YSR / CBCL / DISC (CLINICAL)	48 (0/48)	18.4 (0.9)	DP- no DBD diagnosis (33) DP+ with DBD diagnosis (15)	DP- 18.42 (0.83) DP+ 18.09 (0.93)	16 (0/16)	18.42 (0.91)	Task data extracted
De Wied, 2006	HR	Emotional film clip		DSM-IV (CLINICAL)	22 (0/22)	10.18 (1.22)	ADHD 8 (0/8)		22 (0/22)	10.09 (1.27)	Task data extracted
De Wied, 2012	HR / RSA	6 emotional film clips		DISC / APSD (CLINICAL)	31 (0/31)	13.29 (0.85) 13.93 (1.07)	DBD/CU- 17 (0/17) DBD/CU+ 14 (0/14), ADHD diagnosis met: (21/0)		32 (0/32)	13.75 (0.76)	HR during task (anger condition) extracted
Fairchild,	HR	Stress	5 min at	K-SADS-PL	42	15.79	Adolescen	15.61	95 (0/95)	15.69	Task data

2008a		induction task (competition)	rest	(CLINICAL)	(0/42)	(0.81)	t onset CD 28 (0/28), ADHD criteria met: EO-CD 11 (0/11), AO-CD 5 (0/5)	(0.86)		(0.85)	extracted
Fairchild, 2008b	SCR / SCL	Fear conditioning		Kiddie-SADS-PL (CLINICAL)	71 (0/71)	15.62 (0.86) 15.88 (0.87)	Early Onset (43), Adolescent Onset (28), ADHD criteria met: EO-CD (10), AO-CD (4)		54 (0/54)	15.84 (0.89)	SCR task data extracted
Fairchild, 2010	SCL	Fear conditioning paradigm (noise)		K-SADS- PL (CLINICAL)	25 (25/0)	15.6 (1.00)			30 (30/0)	15.3 (0.7)	Acquisition phase 1 data extracted

Fung, 2005	SCR	Unsignaled white noise in countdown stressor task	3 min sitting still	Child Psychopathy Scale	65 (0/65)	16.02 (0.93)	ADHD criteria met: 28 (0/28)		65(0/65)	15.93 (0.67)	Task data extracted
Garralda, 1991	SCL / HR	Imagination task with pleasant and unpleasant situations, Alerting task, Listening to music, Challenging Arithmetic task	2 min	ICD-9 (CLINICAL)	25 (21/4)	10.04 (1.99)	Emotional Disorders 25 (12/13)	9.72 (1.76)	25 (10/15)	9.48 (1.78)	Baseline data extracted due to missing task data
Gatzke-Kopp, 2015	SCR / HR	Go/no-go task	2 minutes	SDQ	105 (35/70)	5.64 (0.37)			135 (53/82)	5.65 (0.32)	Task reactivity extracted
Grimes, 2004	SCL	Violent movie clips	During questionnaire filling before task	DICA-IV / CBCL (CLINICAL)	59 (0/59)	10.5 (1.5)	ADHD 53 (0/53)		44 (0/44)	10.6 (1.6)	Task data extracted

Harden, 1995	SCR / HR	Arithmetic Stress task		Social Behaviour Questionnaire NS	18 (0/18)	10.35 (0.32)	Disruptive : > 70th percentile for disruptive scale 18 (0/18), Anxious Disruptive : anxiety > 65th percentile and disruptive > 70th percentile 18 (0/18)		15 (0/15)	10.35 (0.32)	Data related to loses only extracted
Herpertz, 2001	SCL / SCR / HR	Orienting paradigm, tones of 1000hz		Kinder-DIPS (CLINICAL)	26 (0/26)	10.35 (1.89)	ADHD 21 (0/21)	10.29 (1.92)	21 (0/21)	9.83 (1.55)	SCR during task extracted, Baseline HR extracted
Herpertz, 2003	SCR / SCL / HR	Orienting paradigm (ten1000-Hz tones)		The Diagnostic DISYPS (CLINICAL)	20 (0/20)	11.55 (1.67)	ADHD 28 (0/28) ADHD + CD 50 (0/50)	10.5 (2.28), 10.41 (2.00)	25 (0/25)	9.66 (1.63)	Total SCR amplitude for Orienting response extracted, Baseline

											HR extracted due to missing task data
Herpertz, 2005	SCR / HR change	Presentation of pleasant, unpleasant and neutral pictures from IAPS set		Diagnostic Interview for Psychiatric Disorders in Childhood and Adolescence (CLINICAL)	21 (0/21)	11.57 (1.63)	ADHD + CD 54 (0/54) ADHD only (43/0)	10.31 (2.01) 10.19 (1.91)	43 (0/43)	10.37 (1.82)	Reactions to unpleasant stimuli extracted
Maliphant, 1990	HR	Stress induction by Sets D and E of Standard Ravens matrices		Teacher rating for disruptive behavior	12 (12/0)	(12-13)	Moderately well behaved 12 (12/0)	(12-13)	20 (20/0)	(12-13)	Task data extracted
Mangina, 2000	SCL / SCR	Mangina test (stimulus discrimination)		DSM-IV (CLINICAL)	10 (2/8)	10.9			10 (3/7)	10.6	Pre-meta analysis computing SMD and SE across sessions, only left hand SCR included

Marsh, 2008	SC / RSA / PEP	Monetary incentive and extinction task (Sad emotion induction)	3 min baseline	CBCL / CSI	31 (0/31)	9.8 (1.4)	CSI ADHD symptom count: DBD: , ADHD criteria met: DBD 13 (0/13)	11.8 (4.4)	23 (0/23)	10.5 (1.5)	SC and RSA task data extracted
Mattys, 2004	SCL / HR	Door opening task (reward)		DSM-IV / CBCL (CLINICAL)	19 (0/19)	9.8 (1.2)	ADHD criteria met 12 (0/12)		20 (0/20)	9.7 (1.6)	Task data extracted

Muñoz, 2008	SCR	Competitive Reaction Time Task (CRTT)		Peer Conflict Scale, NS	85 (0/85)	15.53 (1.28)	RA+ high RA and low PA (0/29), RA CU+ high RA and CU (0/19), RA CU- high RA and low CU (0/10), High RA and PA (0/16), CU+ High RA and PA (0/11), CU- High RA and high PA (0/5)		Low PA and low RA 40 (0/40) Low PA and low RA CU+ 13 (0/13) Low PA and low RA CU- 27 (0/27)		Task minus baseline extracted
Pang, 2013	RSA	Emotional film clips		CSI / CBCL (CLINICAL)	30 (0/30)	9.9 (1.52)	Depression 28, CD + Depression 80	9.9 (1.52)	69 (0/69)	9.9 (1.52)	T1 RSA reactivity extracted

Popma, 2006	SC / HR	Psycho-social stress test		DISC-IV (CLINICAL)	71 (0/71)	(12-14)	DP- no DBD diagnosis 49 (0/49) DP+ DBD diagnosis 22 (0/22), ADHD criteria met: DP- 5 (0/5) DP+ 9(0/9)	DP- 13.93 (0.78), DP+ 13.63 (0.69)	30 (0/30)	13.30 (0.70)	Task data for HR and SC data extracted
Posthumus, 2009	SCL / SCR / HR	one-minute window following the exciting moment		CBCL / (DISC-IV-P) (CLINICAL)	ODD/CD 43 (16/27)	4.3 (0.3)	ODD/CD + ADHD 45 (14/31), High aggressive 124 (45/ 79)	ODD/CD + ADHD 4.2 (0.3), High aggressive 4.3 (0.3)	101 (36/65)	4.3 (0.2)	Task data extracted
Schmidt, 1985	SCL	Presentation of eight 75Db tones	5 min	DSM-III / NS (CLINICAL)	11(4/7)	9.7			11 (4/7)	10.35	SCL task data extracted
Schoorl, 2016	SCL / HR / HRV (square root of the squared	Stress induction (performance task)		DISC-IV (CLINICAL)	66 (0/66)	10.3 (1.28)	ADHD 46 (0/46); Anxiety 39 (0/39); Depressio		36 (0/36)	10 (1.25)	Task data extracted

	means differences of N-N intervals)						n 9 (0/9); ASD 43 (0/43); Eating disorders 18 (0/18)				
Snoek, 2004	HR	Provocation phase of response perseveration task		Diagnostic Interview Schedule for Children version 2.3 (CLINICAL)	15 (3/12)	10.4 (0.9)	OD/AD 31 (4/27); ADHD 23 (4/19)	10 (1.6); 9.8 (1.4)	26 (6/20)	10.3 (1.3)	Baseline data extracted as control task data were missing
Van Goozen, 2000	HR / SCL	Stress induction (competition) for 30 mins		DSM-IV (CLINICAL)	26 (6/20)	10.1	ADHD 12; Dysthymic 2; Posttraumatic 1; Encopresis 2		26	10	Only task data extracted
Waschbusch, 2002	HR	Modified lab provocation task		K-SADS / Disruptive Behaviour Disorders Rating Scale (CLINICAL)	23 (0/23)	11.1 (1.0)	ADHD 17 (0/17), ADHD/ODD/CD 20 (0/20)	ADHD 11 (0.9), ADHD/ODD/CD 10.8 (0.8)	115 (0/115)	11 (0.9)	Loss message with high provocation (‘middle 2’) extracted

Zahn, 1993	SCL / SCR / HR	Reaction time task		DICA / DIPCA (CLINICAL)	29 (0/29)	11.1 (3.3)	ADHD 25 (0/25)		33 (0/33)	12.3 (2.8)	Task 3 data extracted

Note: CDRT = Conduct Difficulties Rutter Teacher Scales for School-age Children; CD = ; DBD= ; RA = reactive aggression; PA = proactive aggression, DISC-P = Diagnostic Interview Schedule for Children IV—Parent version; Kinder-DIPS = Diagnostic Interview for Psychiatric Disorders in Childhood and Adolescence; BP = blood pressure; HRV = heart rate variability; DICA = Diagnostic Interview for Children and Adolescents; DIPCA = Diagnostic Interview for the Parents of Children and Adolescents; DISC = Diagnostic Interview Schedule for Children; ASPD = Antisocial Process Screening Device; DISYPS= System for Psychiatric Disorders in Childhood and Adolescence; DABWA = Development and Well Being Assessment; ASI-4R = Adolescent Symptom Inventory; ICU = Inventory of Callous-Unemotional Traits; K-SADS-PL = Kiddie Schedule for Affective Disorders and Schizophrenia Present and Lifetime; (CLINICAL) refers to inclusion into clinical sample sub-group analysis

Supplemental Table 2: Study characteristics of correlational design studies included in the quantitative analyses

First author and year	outcome measure	Task comments	Baseline comments	Group definition	N (f/m)	Mean age (SD) or range	Comorbidities	Mean age (SD) or range	Comments
Beauchaine, 2013	RSA / PEP	Behavioural challenge with parents	PEP and RSA averaged across 30-s epochs	CBCL	99 (No information about M/F)	Ages 4-6	ECBI problem behavior / SCS emotion regulation, All children met criteria for ADHD		RSA Baseline data extracted
Bubier, 2008	RSA / PEP	Social, cognitive, physical and emotional challenging tasks to evoke stress		Child Symptom Inventory-4	63 (34/29)	7.79 (1.08)	ADHD symptoms met: M ADHD-I, M ADHD-H, F ADHD-I, F ADHD-H	ADHD symptoms met: M ADHD-I (10.7), M ADHD-H (9.7), F ADHD-I (5.9), F ADHD-H (7.0)	RSA change from baseline extracted Pre meta-analysis conducted computing r and SE across boys and girls
Bubier, 2009	RSA / PEP	Social, cognitive, physical and emotional challenging tasks to evoke stress		Child Symptom Inventory-4	57 (28/29)	7.77 (1.08)	N/A	N/A	RSA task reactivity extracted

Choy, 2015	HR	Trier Social Stress Test	Rest	DSM-IV-TR based questionnaire for CD and ODD	388 (198/190)	(11–12)	General antisocial / Delinquency / Aggressive vs. Non-aggressive / Child Psychopathy		Task data extracted
Colasante, 2017	HR	Watching moral transgression video		CBCL physical aggression scale	110 (51/59)	5.23 (.52), 8.02 (.29), 12.08 (.29)			Zero order correlation data extracted
Crozier, 2008	HR	Imagination task (being victimized in hypothetical provocation situation)	173-s baseline period	ABQ / YSR / CBCL	386 (131/ 255)				Pre meta-analysis conducted computing r and SE across males and females
Eisenberg, 1996	HR	Distressing film		Child Problem Behavior Checklist	199 (97/102)	90 months (14)			Task data extracted Pre meta-analysis conducted computing r and SE across males and females
Eisenberg,	RSA	Crying babies	Neutral	Infant Toddler	213	17.76			Residual

2012		film	smiling babies film	Social and Emotional Assessment	(94/119)	months (0.48)			change scores for task data and Mother-reported aggression/ defiance data extracted
El-Sheikh, 2011	RSA	Audio stimulus with an argument between 2 adults		Personality Inventory for Children II (Externalizing)	413 (194/219) (222/0)	8.13 (0.33), 8.98 (0.28), 10.05 (0.31), 11.03 (0.45)	N/A	N/A	Task reactivity extracted
Fagan, 2017	HR / HRV (power analysis of component frequencies) / PEP	Emotion learning task, Emotion regulation task, Reward Paradigm		DISC-IV / CBCL	339 (176/163)	9.06 (0.6)	ASPD - narcissism and Impulsivity scales / ICU		HR data extracted, Pre meta-analysis conducted computing r and SE across males and females
Fortunato, 2013	RSA	12 min Emotion induction paradigm (film, Fear / Sadness / Happiness / Anger)		SDQ Externalizing scale	(273/0)				Fear related data extracted

Galan, 2017	HR	No task (resting)	Averaged five 60s epochs	SRD	160 (0/160)	Age 12			
Glenn, 2018	SCL / RSA	Watching neutral video	last 60 s of the video	RPQ / BASC-II	250 (88/162)	9.72 (0.62)			SCL and RSA data and T1 reactive aggression data and Parent ratings of RA extracted
Gray, 2017	RSA	Trier Social Stress Test for Children (TSST-C)		CBCL Externalizing	92 (52/40)	(5-16)	Preschool Age Psychiatric Assessment (PAPA) / Potentially traumatic events		Task data extracted
Hastings, 2011	HR / Mean Arterial Pressure	Social Performance Paradigm		CBCL / YSR	215 (106/109)	13.67 (1.80)			T1 HR data extracted
Hastings, 2007	HR / BP	Social Performance Paradigm		CBCL / TRF / YSR	86 (34/52)	54.85 months (3.35)	Mother report / Youth report		Speech task data extracted
Hinnant, 2009	RSA	Argument task (audiotaped argument)		Personality Inventory for Children – II	176 (98/ 78)	8.68 (0.36)			Argument task reactivity and Externalizing problems at T1

									extracted
Hinnant, 2015	RSA	Star tracing task	3 min	Personality Inventory for Children II / Delinquency	251 (122/129)	8.23 (0.72)	N/A	N/A	Age 8 RSA task data extracted
Hinnant, 2016	SCL	Star tracing	3 min	YSR Externalizing scale	252 (134/118)	15.79 (0.81)	Permissive Parenting / Affiliation with deviant peers / Substance Use		Baseline SCL and RSA extracted
Jimenez-Camargo, 2017	SCL / PEP	Iowa gambling Task as stress induction		BASC-II Aggression subscale	360 (125/235)				Task data extracted
Keller, 2009	RSA	Audio stimulus with an argument between 2 adults		Personality Inventory for Children II (Externalizing)	54 (36/28)	8.72 (5.6 months)	N/A	N/A	T1 task reactivity extracted
Kochanska, 2017	SCL	composite across all episodes of social stress		Composite score based on CSI-4 / ASI-4R / ICU	81 (37/ 44)	Age 8			Task data extracted
Kochanska, 2015	SCL	3 min Rest, 2 min Deep breathing, 3 min Startle task, 3 min Rest, 2 min		Child Symptoms Inventory-4 (CSI-4)	81 (37/ 44)	Age 8			Parent rated behavior data extracted

		Gift anticipation							
Murray-Close, 2014	SCL / BP	Social Competence Interview(SCI)		Children's Social Behaviour Scale – Teacher Report	(161/0)	(8.53 - 12.44)	Relational A 157, Physical aggression 157		SCL and Systolic BP and Physical aggression extracted
Paysnick, 2015	SCL / RSA	Social Competence Interview (revealing stressful experience)	4 min	CBCL Externalizing scale	66 (40/26)	16.6 (0.5)	YSR Externalizing scale		Task related SCL and RSA data and CBCL Externalizing extracted
Portnoy, 2014	HR	Social stressor task (2 mins thinking about the worst or most stressful event)		Self-reported Delinquency Scale (SRD)	335 (0/335)	16.15 (0.89)	RA / PA / Violent behavior / Non-violent behavior / Psychopathy	N/A	Stress task data extracted and violent behavior subscale
Prätzlich, 2018	HR	No task		K-SADS-PL	1010 (659/351)	14.2 (2.4)			HR baseline extracted
Raine, 1987	HR	Average across examination time (including continuous performance task)	Overall baseline of three sampling periods	RBPC	40 (40/0)	11.5			Overall HR baseline extracted
Sijtsema, 2013	HR	No task	4 min	ASB	809 (454/355)	11.09 (0.56)			T1 ASB extracted

Van Goozen, 1998	HR	Frustration and aggression provocation task (competition)		CBCL / TRF	52 (0/52)	10.2	CBCL (Delinquent, Aggressive, Externalizing) / TRF (Delinquent, Aggressive, Externalizing), ADHD diagnosis met: (9/0)		CBCL Externalizing extracted
Xu, 2014	HR	No task	4 mins in a quiet room	Teachers ratings of PA and RA	189 (91/98)	7.64	PA / RA		T1 RA extracted
Zhang, 2017	RSA	Emotion regulation task	Average of two 2min resting periods	CBCL Externalizing scale	253 (132/121)	9.05 (0.60)	CBCL Internalizing		T1 task data extracted, Pre meta-analysis conducted computing r and SE across males and females

Note: CDRT = Conduct Difficulties Rutter Teacher Scales for School-age Children; CD = ; DBD= ; RA = reactive aggression; PA = proactive aggression, DISC-P = Diagnostic Interview Schedule for Children IV—Parent version; Kinder-DIPS = Diagnostic Interview for Psychiatric Disorders in Childhood and Adolescence; BP = blood pressure; HRV = heart rate variability; DICA = Diagnostic Interview for Children and Adolescents; DIPCA = Diagnostic Interview for the Parents of Children and Adolescents; DISC = Diagnostic Interview Schedule for Children; ASPD = Antisocial Process Screening Device; DISYPS= System for Psychiatric Disorders in Childhood and Adolescence; DABWA = Development and Well Being Assessment; ASI-4R = Adolescent Symptom Inventory; ICU = Inventory of Callous-Unemotional Traits; K-SADS-PL = Kiddie Schedule for Affective Disorders and Schizophrenia Present and Lifetime

Supplemental Table 3. Scores on the Newcastle Ottawa Scale (NOS), case-control studies.

Study first author (year)	Selection				Comparability	Exposure			Total score
	Is the case definition adequate?	Representativeness of cases	Selection of controls	Definition of controls	Comparability of cases and controls	Ascertainment	Same method for cases and controls	Non-response rate	
Anastassiou-Hadjicharalambous, 2008	*		*	*	*				4
Beauchaine, 2001	*	*	*	*	*	*	*		7
Beauchaine, 2003	*	*			**		*		5
Beauchaine, 2008	*	*	*	*	**	*	*		8
Crowell, 2006	*		*	*	*	*	*		6
Da Silva, 2014	*	*	*	*	*		*		6
De Vries-Bouw, 2012	*	*		*	*		*		5
De Wied, 2006	*	*	*	*	**	*	*	*	9
De Wied, 2012	*		*	*	**	*	*		7
Fairchild, 2008a	*	*	*	*	*		*		6
Fairchild, 2008b	*	*	*	*	*	*	*		7
Fairchild, 2010	*	*	*	*	*		*		6
Fung, 2005	*	*	*	*	**	*	*		8
Garralda, 1991	*	*	*	*	*		*		6
Gatzke-	*		*	*	*		*		5

Kopp, 2015									
Grimes, 2004	*		*	*	*	*	*		6
Harden, 1995	*	*	*	*	*	*	*		7
Herpertz, 2001	*		*		**				4
Herpertz, 2003	*	*	*	*	*		*		6
Herpertz, 2005	*		*	*	*	*	*		6
Maliphant, 1990		*			*				2
Mangina, 2000	*		*	*	*	*	*		6
Marsh, 2008	*	*	*	*	**		*		7
Mattys, 2004	*	*	*	*	*		*		6
Muñoz, 2008	*	*			*	*	*		5
Pang, 2013	*	*	*	*	**		*		7
Popma, 2006	*	*	*	*	*		*		6
Posthumus, 2009	*	*	*	*		*	*		6
Schmidt, 1985	*		*	*	**	*	*		7
Schoorl, 2016	*	*	*	*	*	*			6
Snoek, 2004	*	*	*	*	**	*	*		8
Van Goozen, 2000	*	*	*	*	*		*		6
Waschbusch, 2002	*	*		*	**	*	*		7
Zahn, 1993	*	*		*	**				5

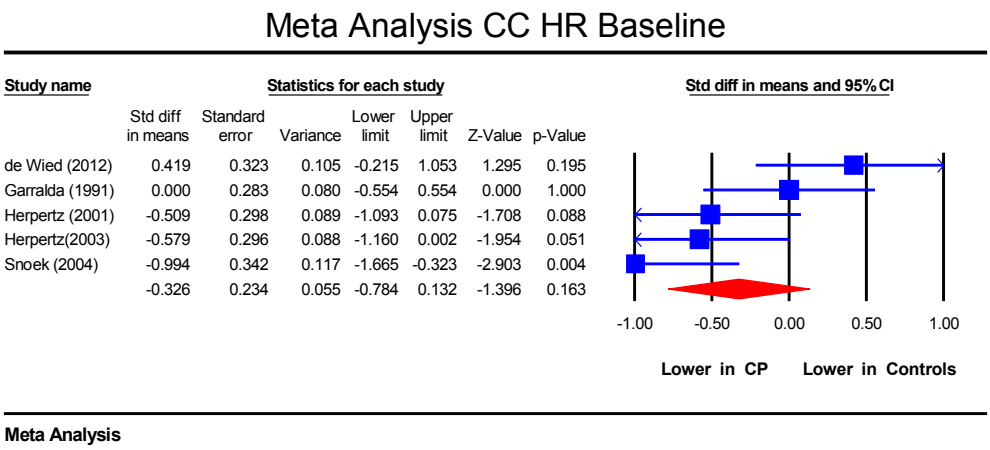
Supplemental Table 4. Scores on the Newcastle Ottawa Scale (NOS), correlational studies.

Study first author (year)	**Selection**		**Exposure**		
	Is the case definition adequate?	Representativeness of cases	Ascertainment	Non-response rate	
Beauchaine, 2013	*	*			2
Bublier 2008	*	*	*	*	4
Bubier, 2009	*		*		2
Choy, 2015	*	*	*	*	4
Colasante, 2017	*	*	*	*	4
Crozier, 2008	*	*			2
Eisenberg, 1996	*				1
Eisenberg, 2012	*				1
El-Sheikh, 2011	*	*			2
Fagan, 2017	*	*	*		3
Fortunato, 2013	*				1
Galan, 2017					0
Glenn, 2018	*	*			2
Gray, 2017	*	*	*		3
Hastings, 2011					0
Hastings, 2007	*	*	*		3
Hinnant, 2009			*		1
Hinnant, 2015	*			*	2
Hinnant, 2016	*	*	*		3
Jimenez-Camargo, 2017	*	*	*	*	1
Keller, 2009	*	*			2
Kochanska, 2017	*		*		2
Kochanska, 2015			*		1
Murray-Close, 2014	*				1
Paysnick, 2015	*	*	*		3
Portnoy,	*	*	*	*	4

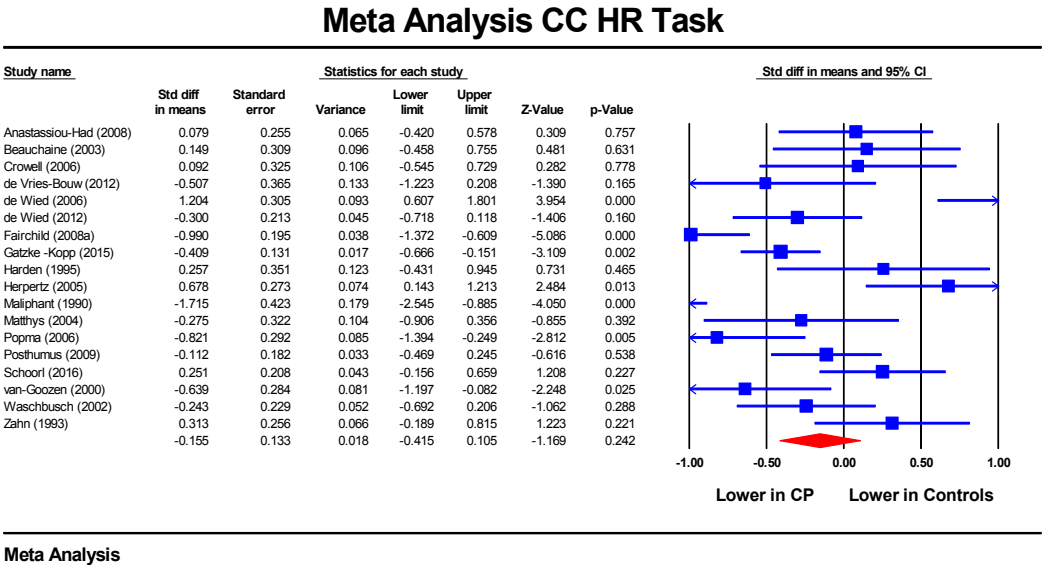
2014					
Prätzlich, 2018	*	*	*		3
Raine, 1987			*		1
Sijtsema, 2013	*	*		*	3
Van Goozen, 1998			*	*	2
Xu, 2014	*	*	*	*	4
Zhang, 2017	*	*	*		3

Supplementary figures 1-29: Forest plots for each outcome.

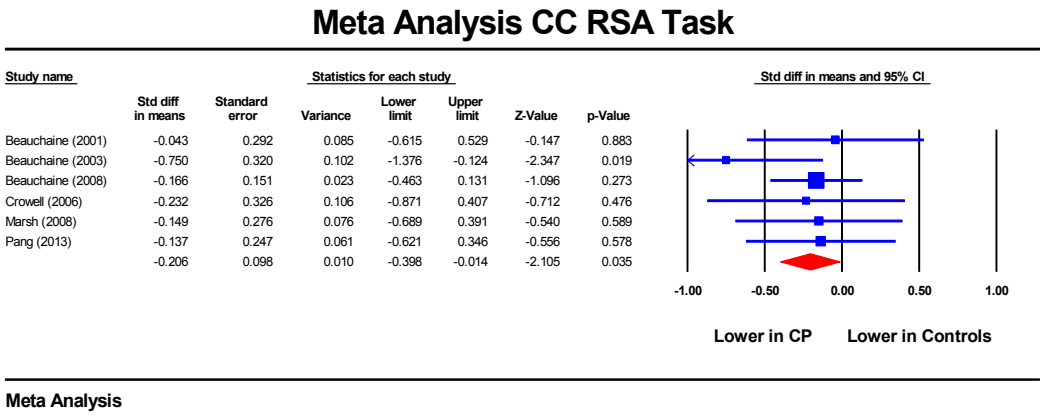
Forest plots for each outcome.



Suppl. Figure 1: Case-Control HR Baseline, SMD: -0.326, CI [-0.784; 0.132], I^2: 65.337, Egger: p=.335

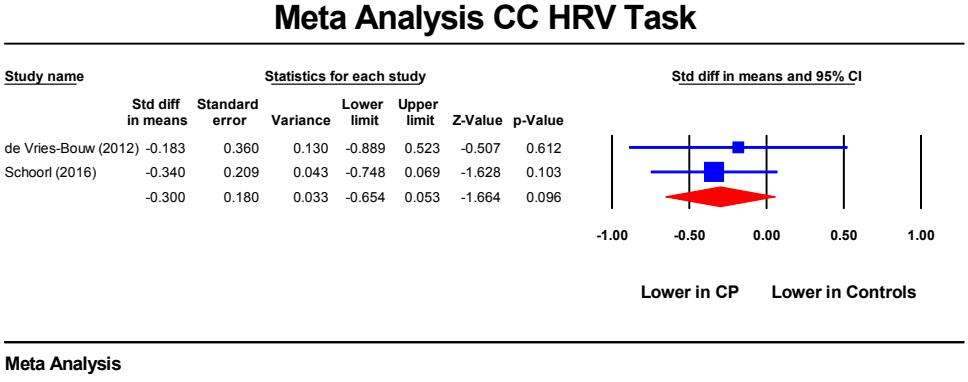


Suppl. Figure 2: Case-Control HR During Task, SMD: -0.155, CI [-0.415; 0.105], I^2: 80.055 Egger: p=.539

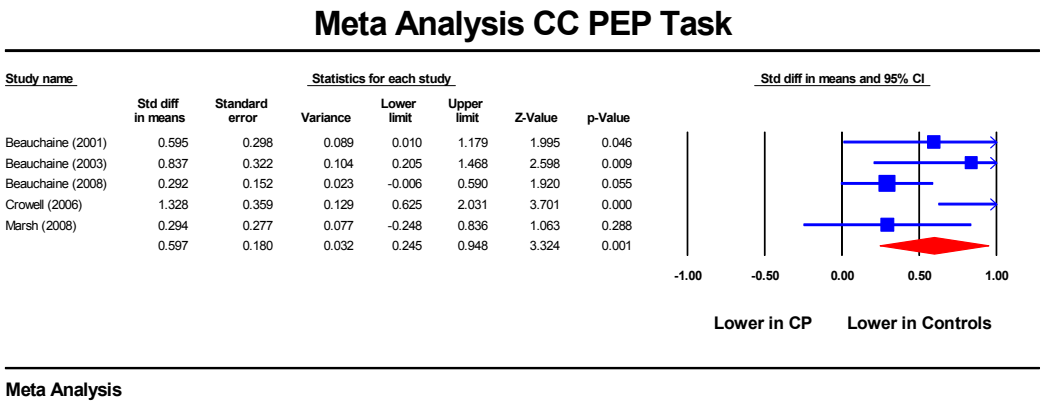


Suppl. Figure 3: Case-Control RSA During Task, SMD: -0.206, CI [-0.398; -0.014], I^2: 0.000

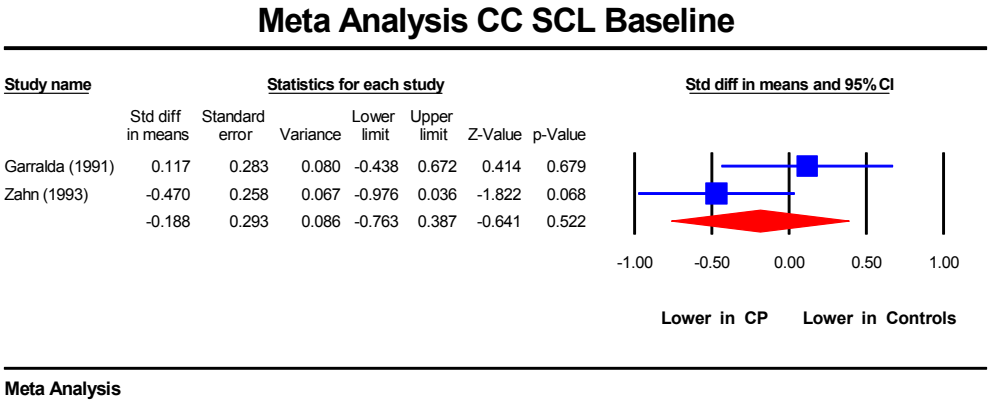
Egger: p=.492



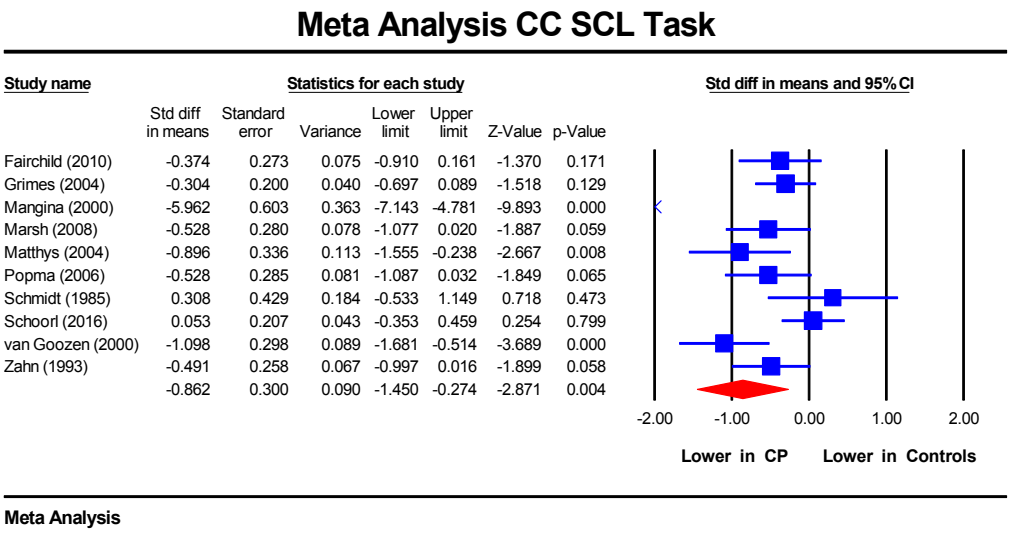
Suppl. Figure 4: Case-Control HRV During Task, SMD: -0.300, CI [-0.654; 0.053], I^2: 0.000



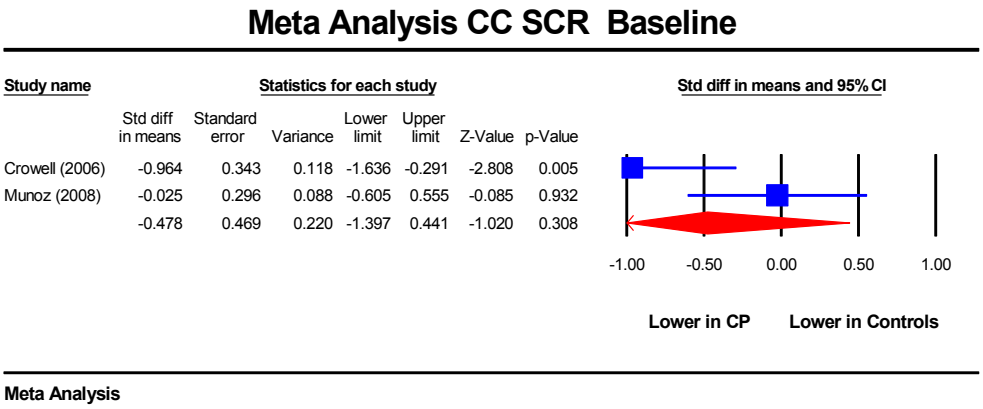
Suppl. Figure 5: Case-Control PEP During Task, SMD: 0.597, CI [0.245; 0.948], I²: 55.245 Egger: p=.105



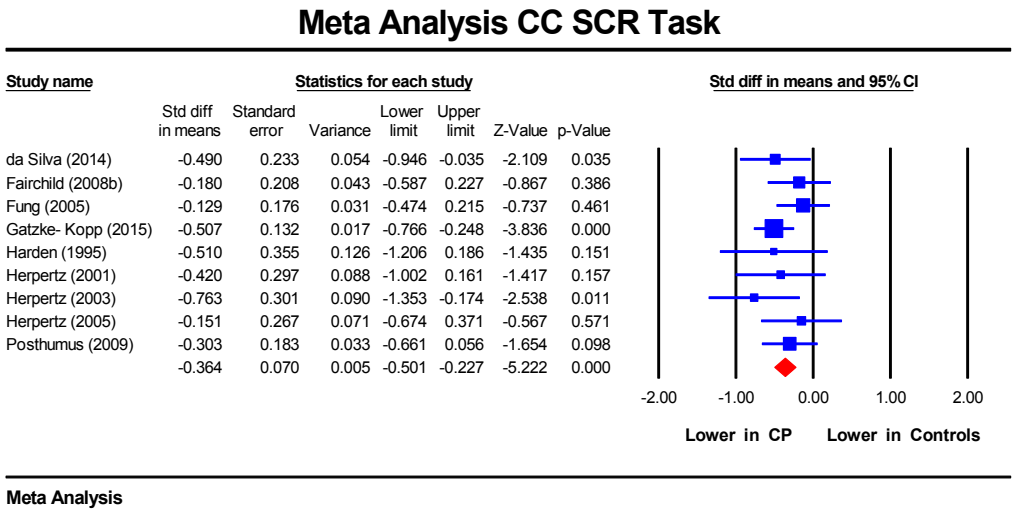
Suppl. Figure 6: Case-Control SCL Baseline, SMD: -0.188, CI [-0.763; 0.387], I²: 57.479



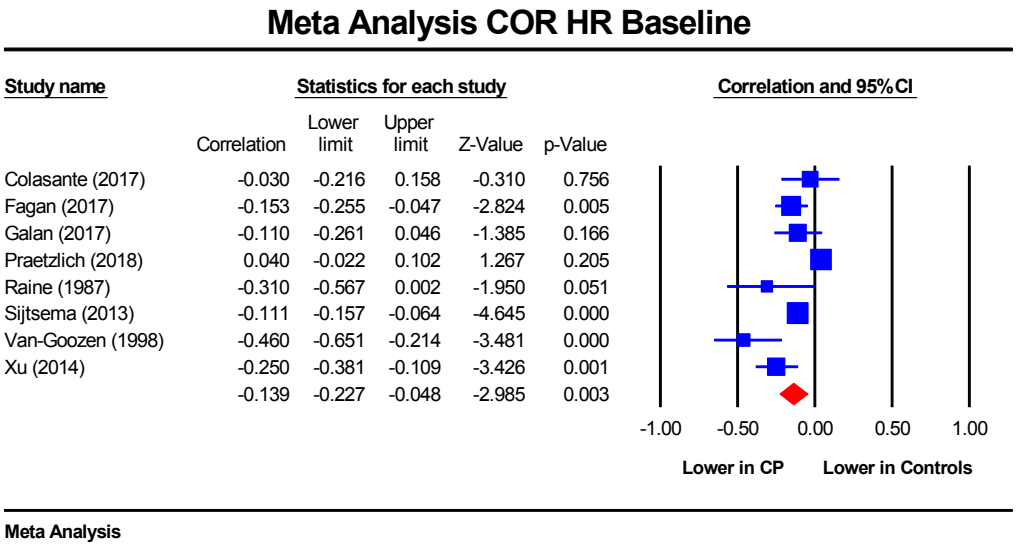
Suppl. Figure 7: Case-Control SCL During Task, SMD: -0.862, CI [-1.450; -0.274], I^2: 90.946, Egger: p=.012



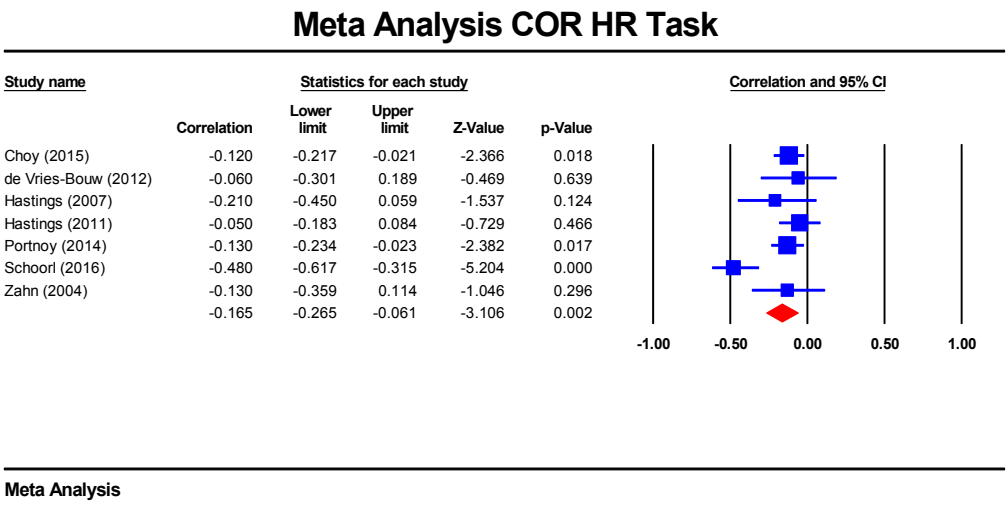
Suppl. Figure 8: Case-Control SCR Baseline, SMD: -0.478, CI [-1.397;0.441], I^2: 76.690



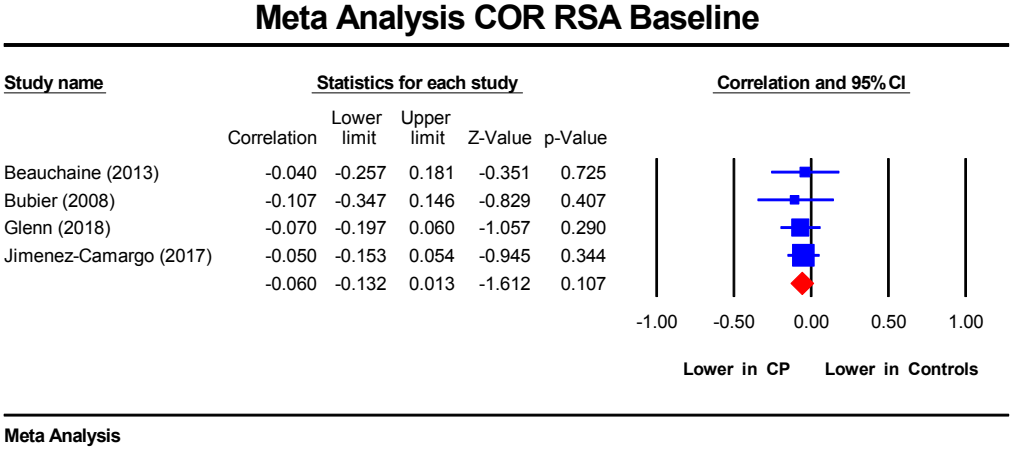
Suppl. Figure 9: Case-Control SCR During Task SMD: -0.364, CI [-0.501; -0.227], I^2: 0.000, Egger: p = .416



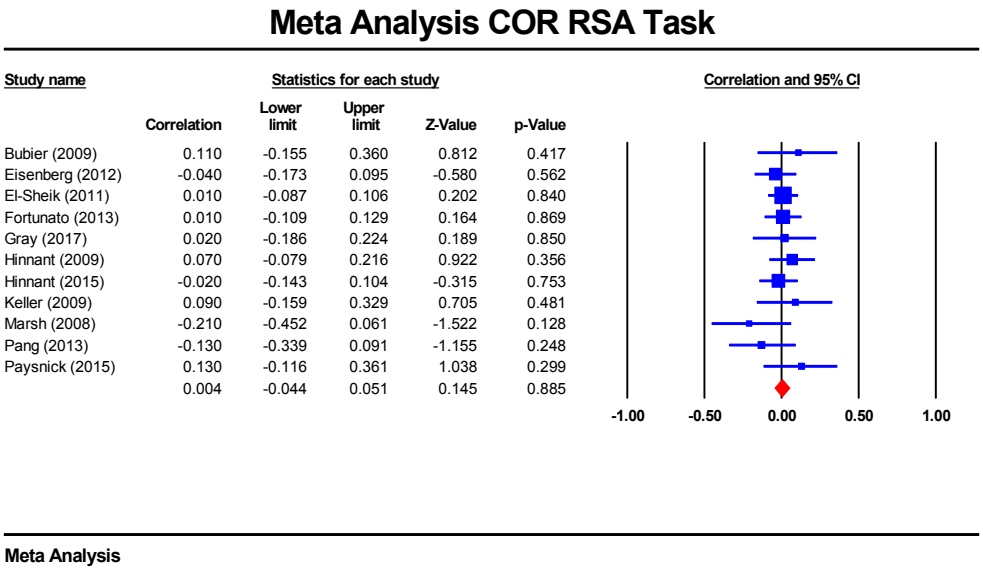
Suppl. Figure 10: Correlational HR Baseline, *r* = -0.139, CI [-0.227; -0.048], I^2: 79.714, Egger: p= .099



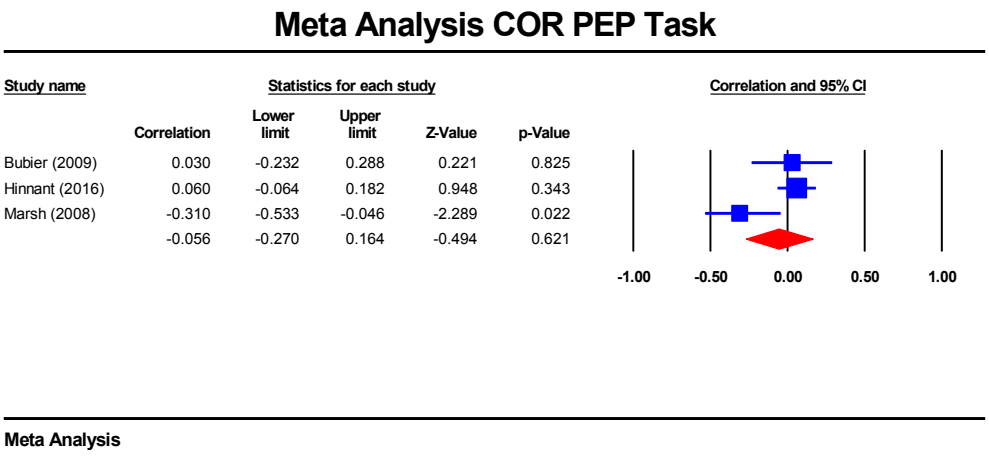
Suppl. Figure 11: Correlational HR During Task: *r* = -0.165, CI [-0.265; -0.061], I^2:64.805, Egger: p= .476



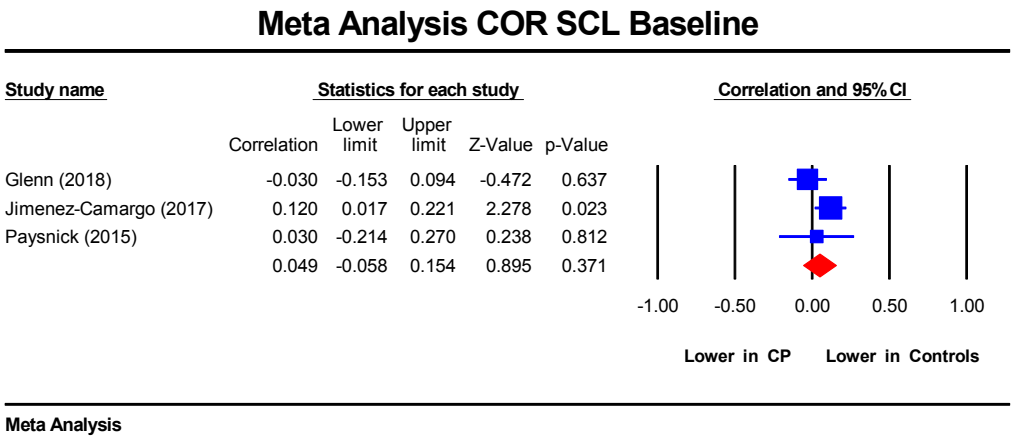
Suppl. Figure 12: Correlational RSA Baseline, *r* = -0.060, CI [-0.132; 0.013], I^2: 0.000, Egger: p=.263



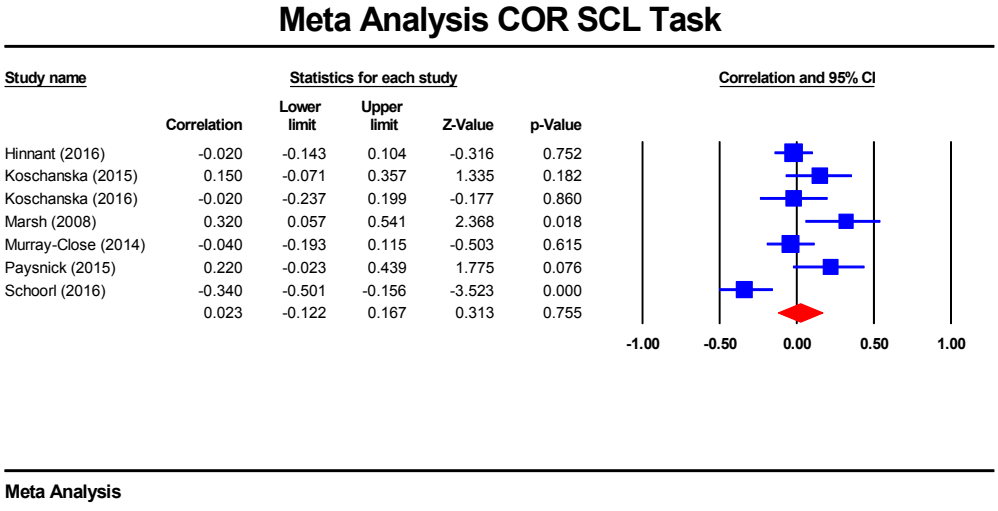
Suppl. Figure 13: Correlational RSA During Task, *r* = 0.004, CI [-0.044; 0.051], I²:0.000, Egger: p= .992



Suppl. Figure14: Correlational PEP During Task, *r* = -0.056, CI [-0.270; 0.164], I²:67.675, Egger: p= .493

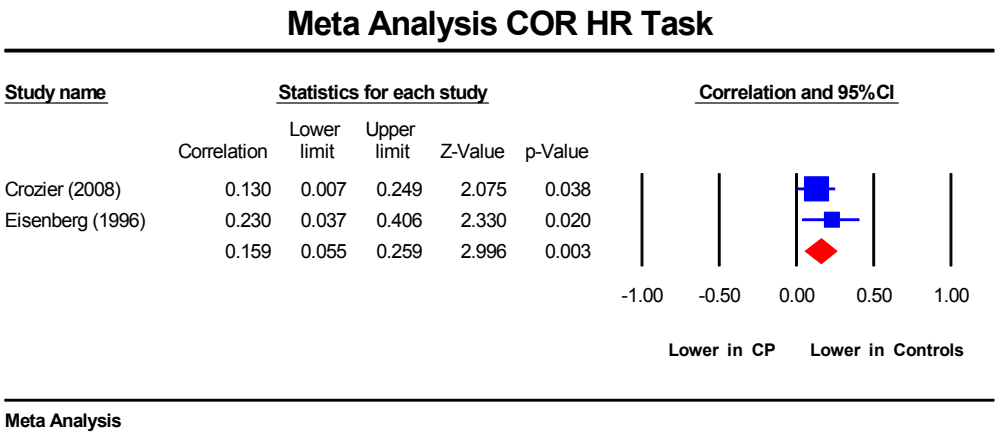


Suppl. Figure 15: Correlational SCL Baseline, *r* = 0.049, CI [-0.058; 0.154], I²: 40.452, Egger: p = .384

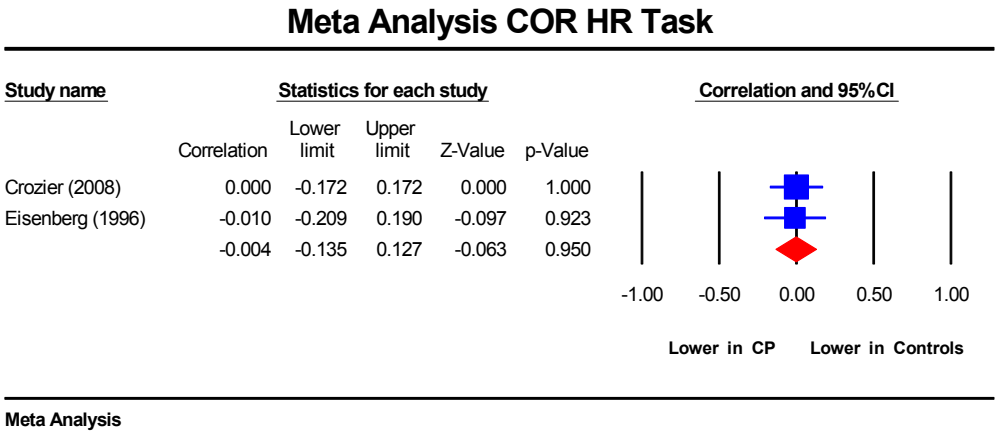


Suppl. Figure 16: Correlational SCL During Task, *r* = 0.023, CI [-0.122; 0.167], I²:74.255, Egger: p= .347

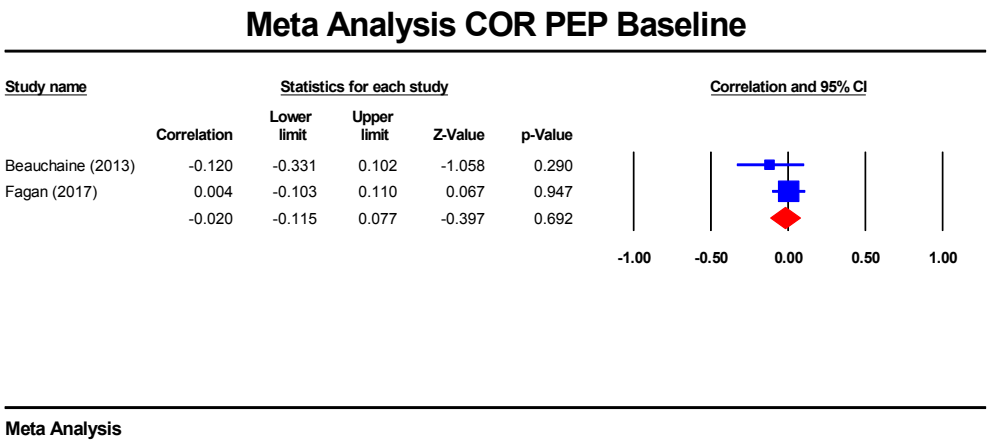
Subgroup Meta Analyses: Gender



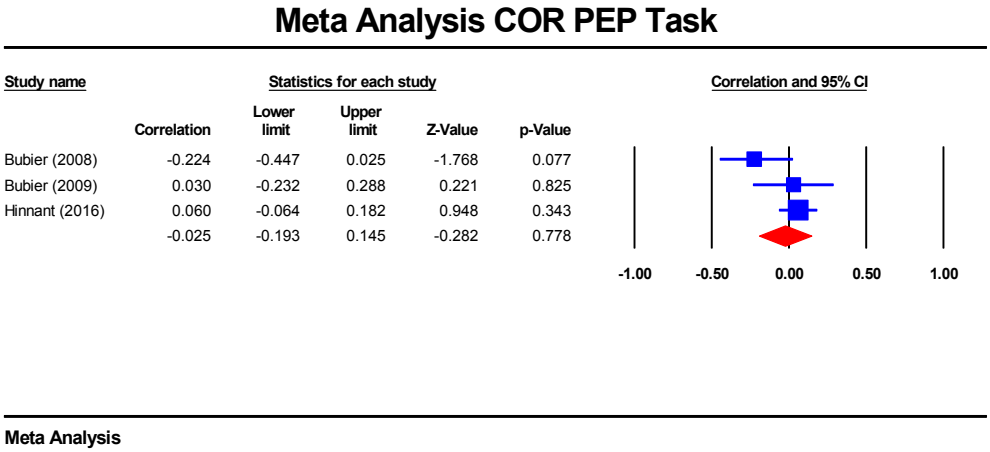
Suppl. Figure 17: Boys, Correlational HR During Task, r = 0.159, CI [0.055; 0.259], I^2: 0.000



Suppl. Figure 18: Girls, Correlational HR During Task, r = -0.004, CI [-0.135; 0.127], I^2: 0.000

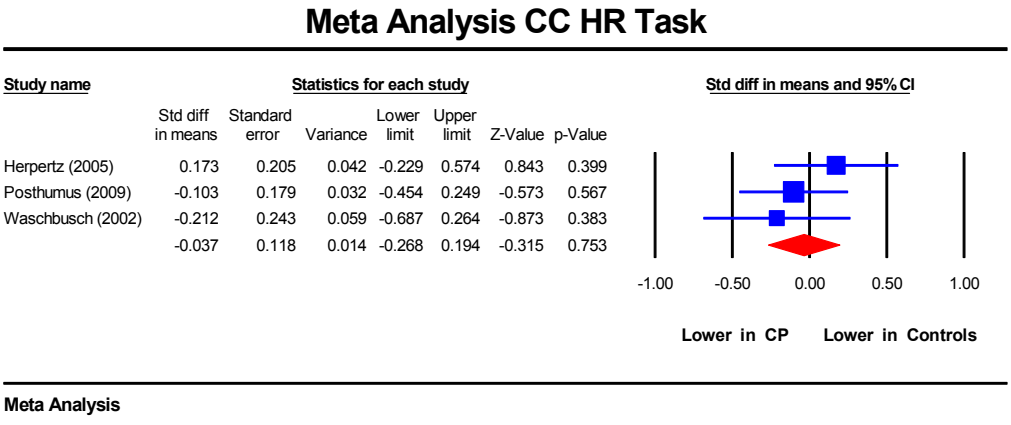


Suppl. Figure 19: Correlational PEP Baseline, *r* = -0.020, CI [-0.115; 0.077], I²:0.000

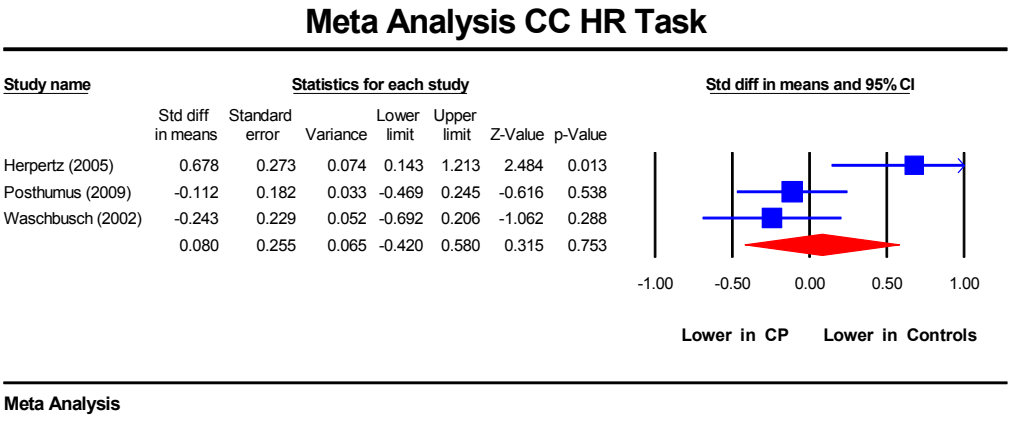


Suppl. Figure 20: Correlational PEP Task, *r* = -0.025, CI [-0.193; 0.145], I²:50.631, Egger: p= .518

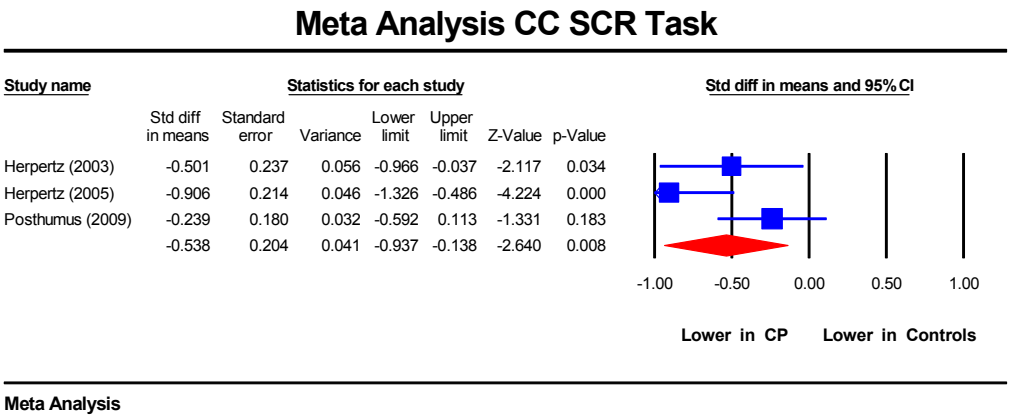
Subgroup Meta Analyses: ADHD



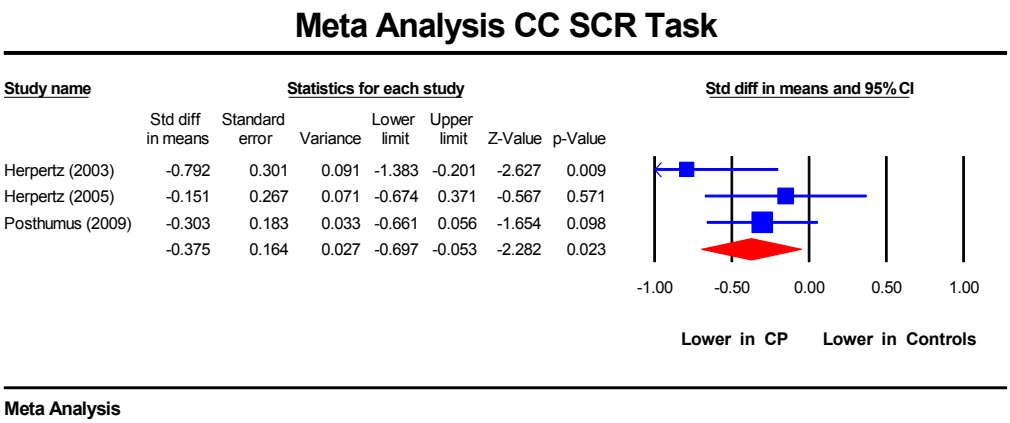
Suppl. Figure 21: With ADHD, Case-Control HR During Task, SMD: -0.037, CI [-0.268; 0.194], I^2: 0.000, Egger: p=.429



Suppl. Figure 22: Without ADHD, Case-Control HR During Task SMD: 0.080, CI [-0.420; 0.580], I^2: 73.887, Egger: p=.241

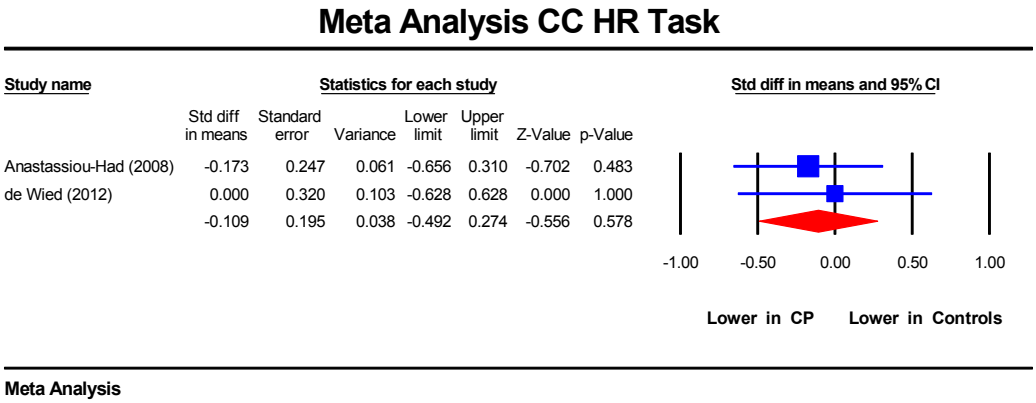


Suppl. Figure 23: With ADHD, Case-Control SCR During Task, SMD: -0.538, CI[-0.937; -0.138], I^2: 64.773, Egger: p=.292

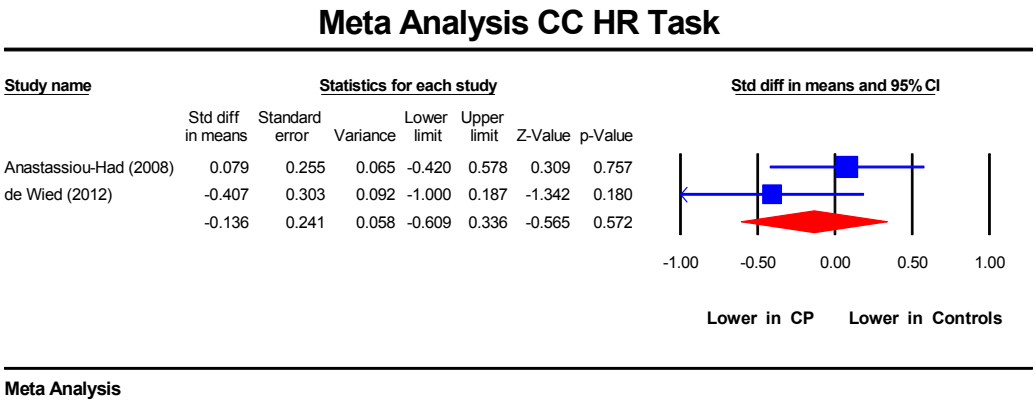


Suppl. Figure 24: Without ADHD, Case-Control SCR During Task, SMD: -0.375, CI [-0.697; -0.053], I^2: 27.666, Egger: p=.333

Subgroup Meta-Analyses: Callous-Unemotional Traits

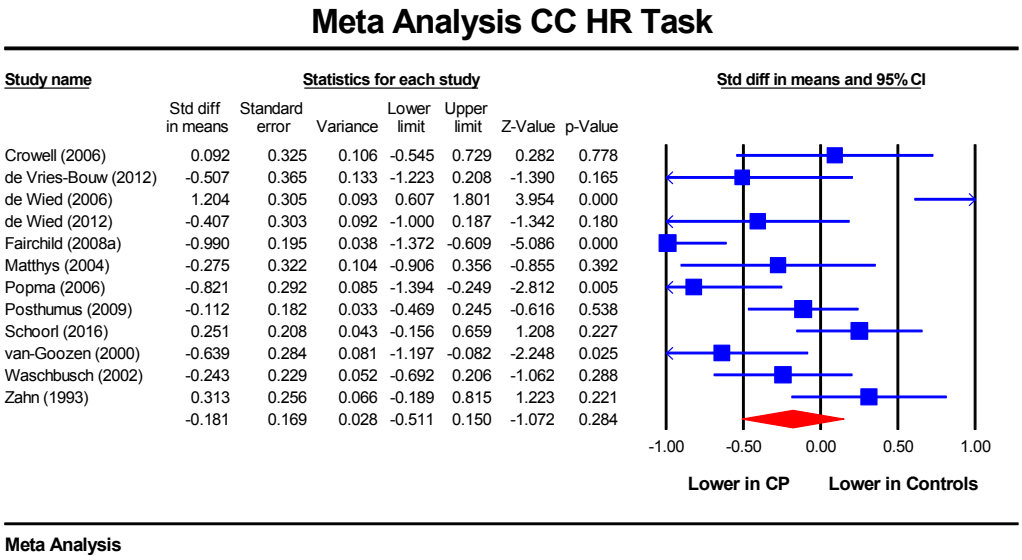


Suppl. Figure 24: CP/CU+ Case-Control HR During Task, SMD: -0.109, CI [-0.492; 0.274], I^2: 0.000

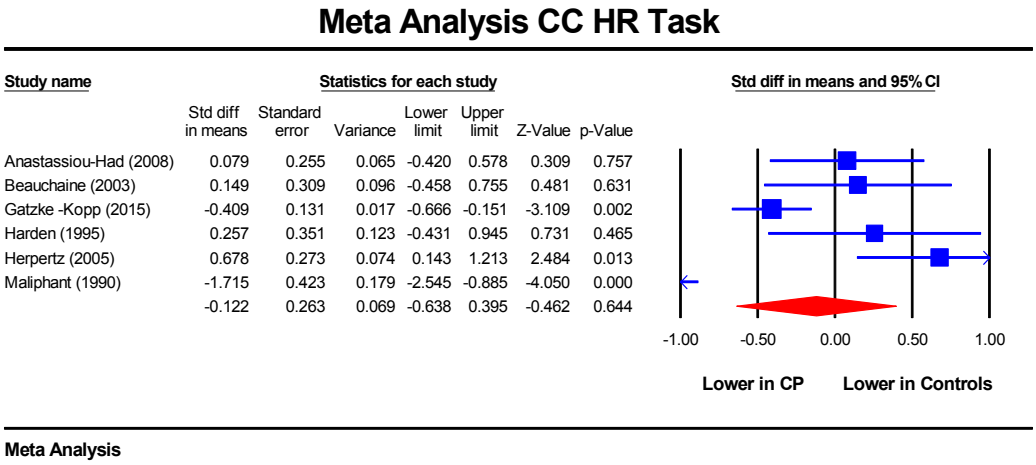


Suppl. Figure 25: CP/CU- Case-Control HR During Task, SMD: -0.136, CI [-0.609; 0.336], I^2: 33.514

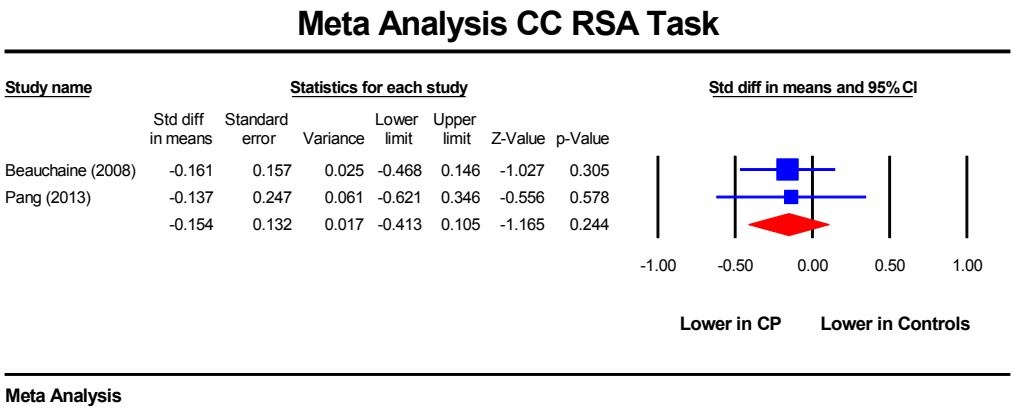
Subgroup Meta-Analyses: Clinical versus Non -Clinical CC samples



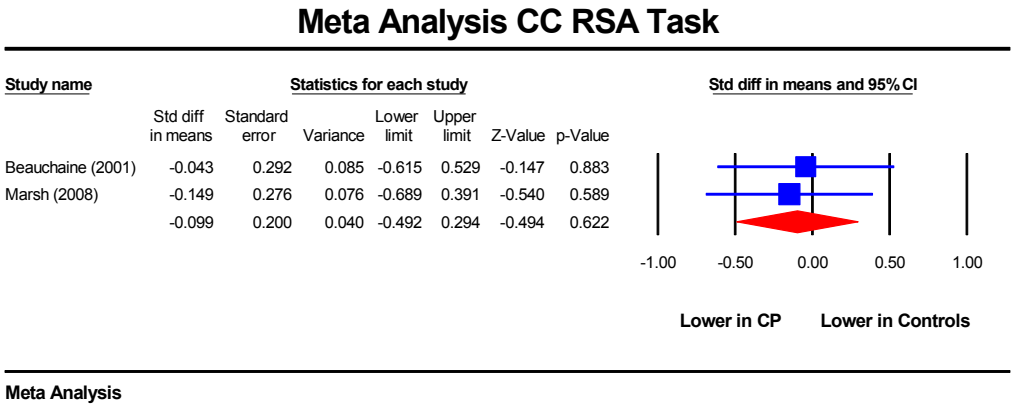
Suppl. Figure 26: Clinical Case-Control HR During Task, SMD: -0.181, CI [-0.511; 0.150], I^2: 0.802



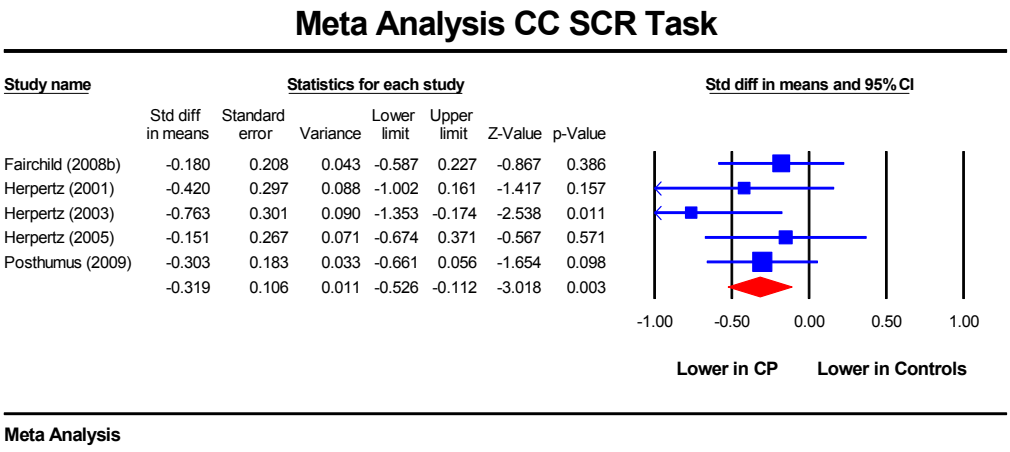
Suppl. Figure 27: Non-Clinical Case-Control HR During Task, SMD: -0.122, CI [-0.638; 0.395], I^2: 0.832



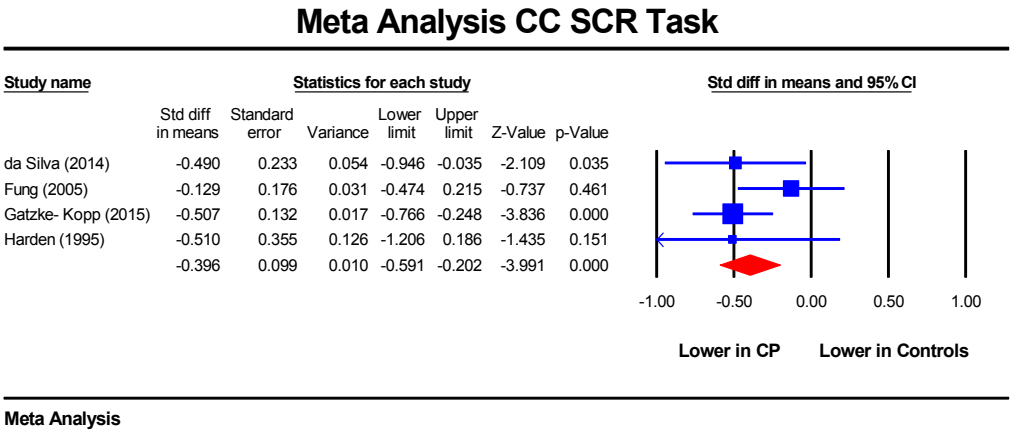
Suppl. Figure 28: Clinical Case-Control RSA During Task, SMD: -0.154, CI [-0.413; 0.105], I^2: 0.000



Suppl. Figure 29: Non-Clinical Case-Control RSA During Task, SMD: -0.099, CI [-0.492; -0.294], I^2: 0.000

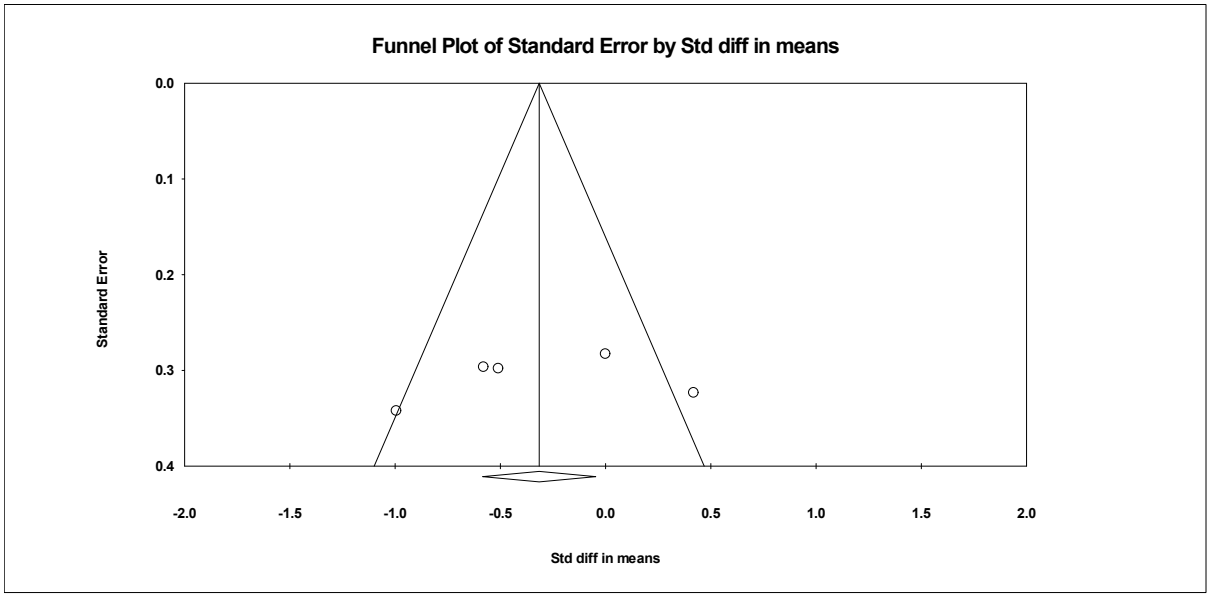


Suppl. Figure 30: Clinical Case-Control SCR During Task, SMD: -0.319, CI [-0.526; -0.112], I^2: 0.000

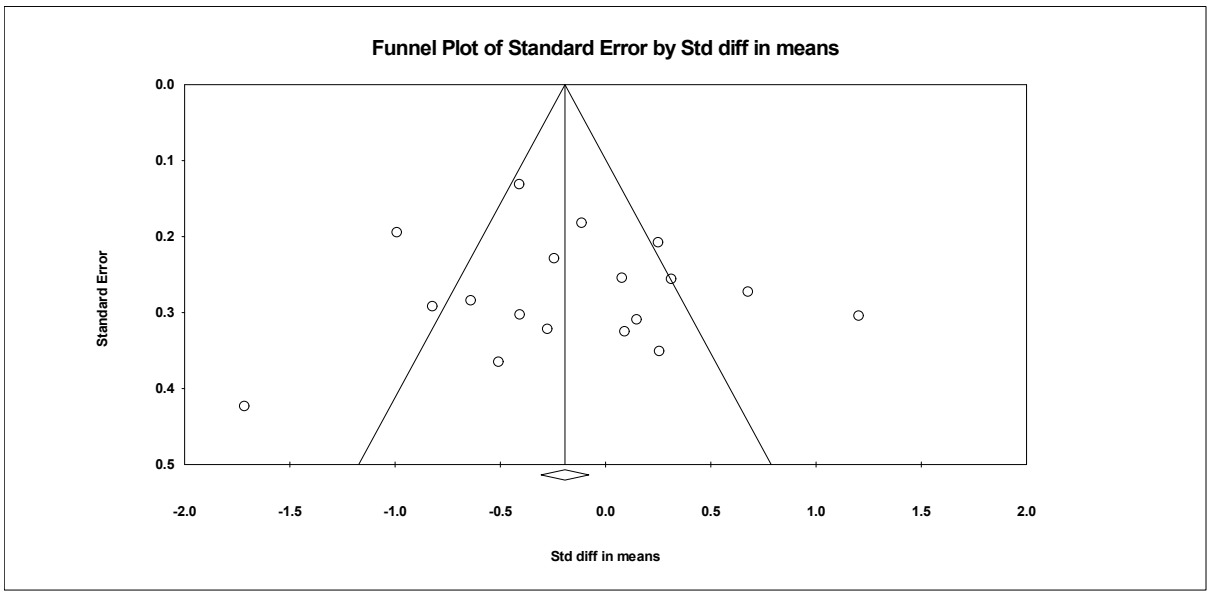


Suppl. Figure 31: Non-Clinical Case-Control SCR During Task, SMD: -0.396, CI [-0.591; -0.202], I^2: 0.084

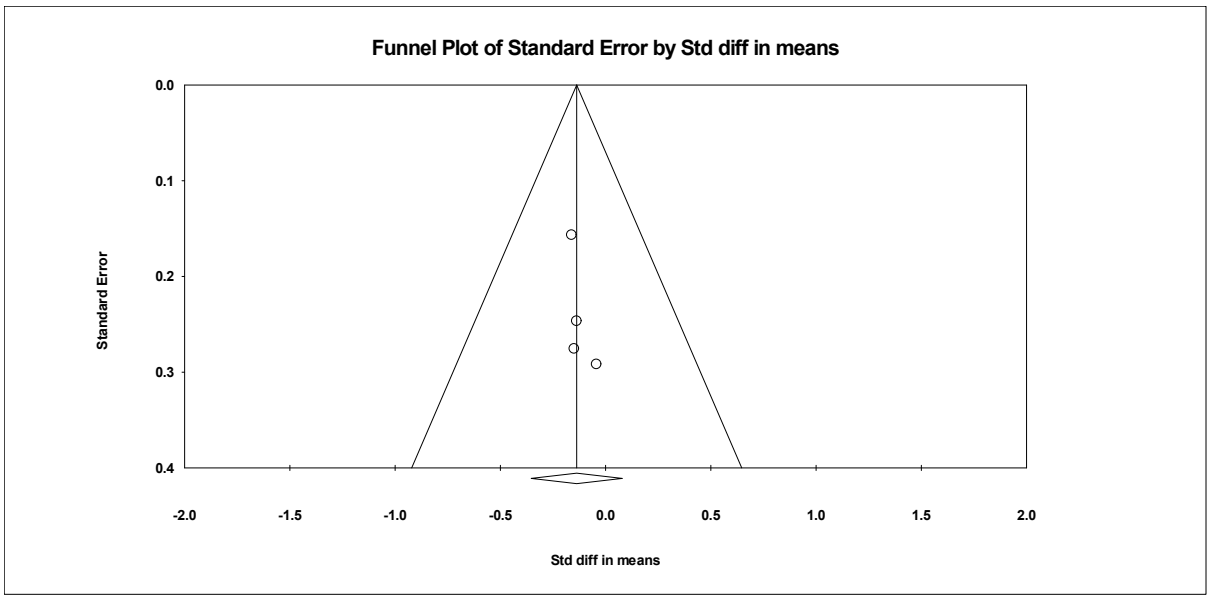
Supplemental Figures 32-42. Funnel plots for each outcome



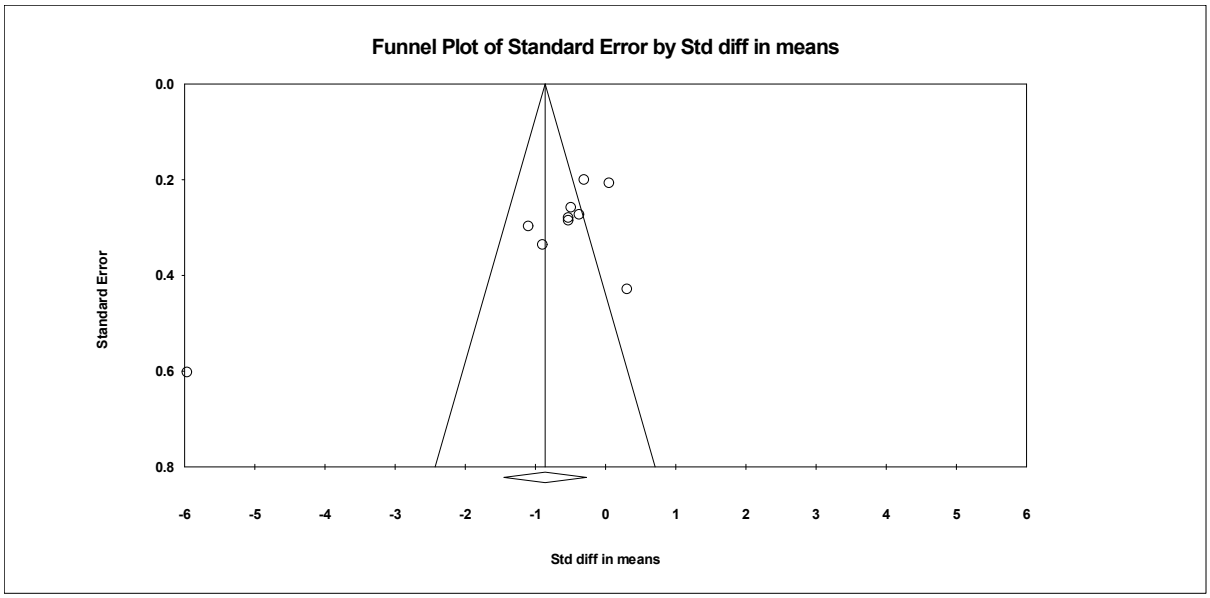
Suppl. Figure 32: Funnel Plot for Case-control HR Baseline studies



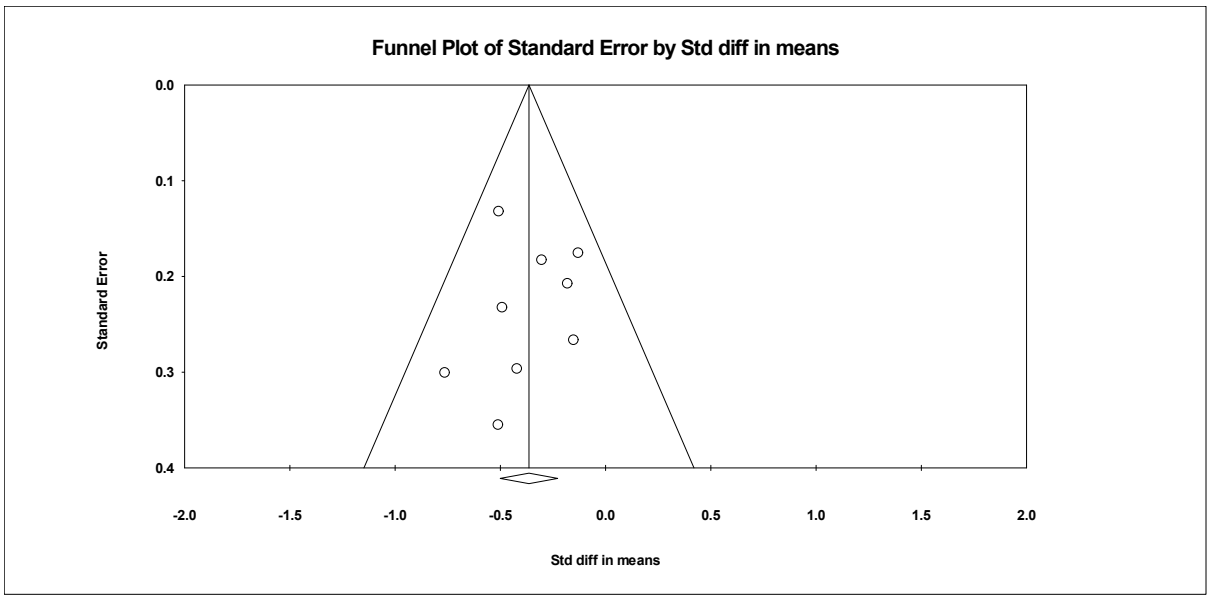
Suppl. Figure 33: Funnel plot for Case-control HR during Task studies



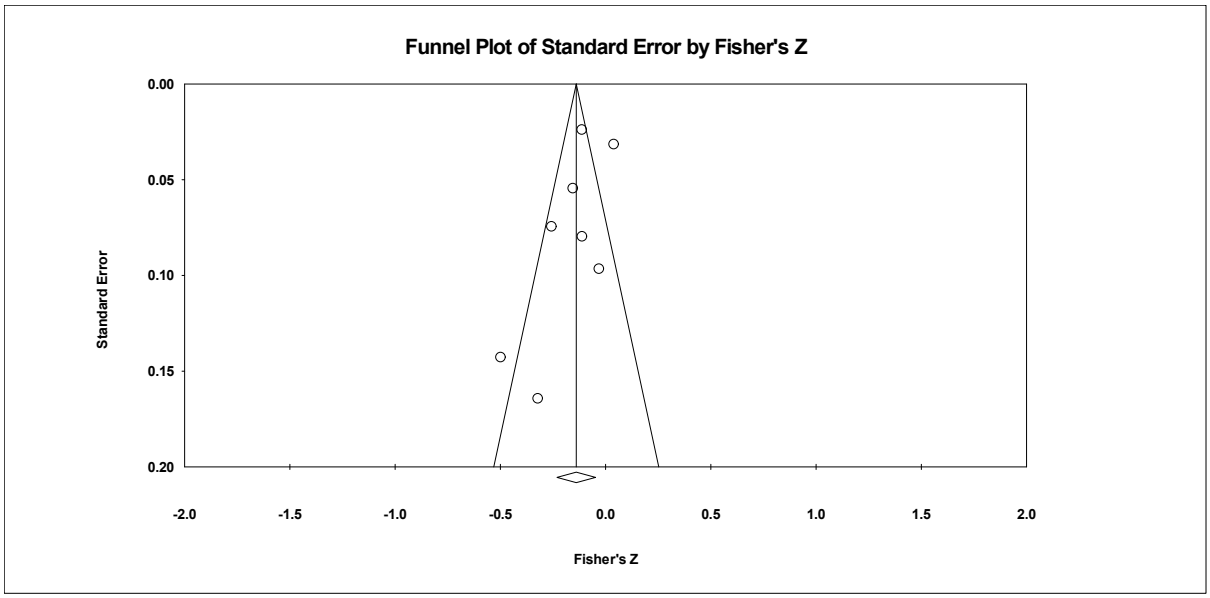
Suppl. Figure 34: Funnel plot for Case-control RSA during task studies



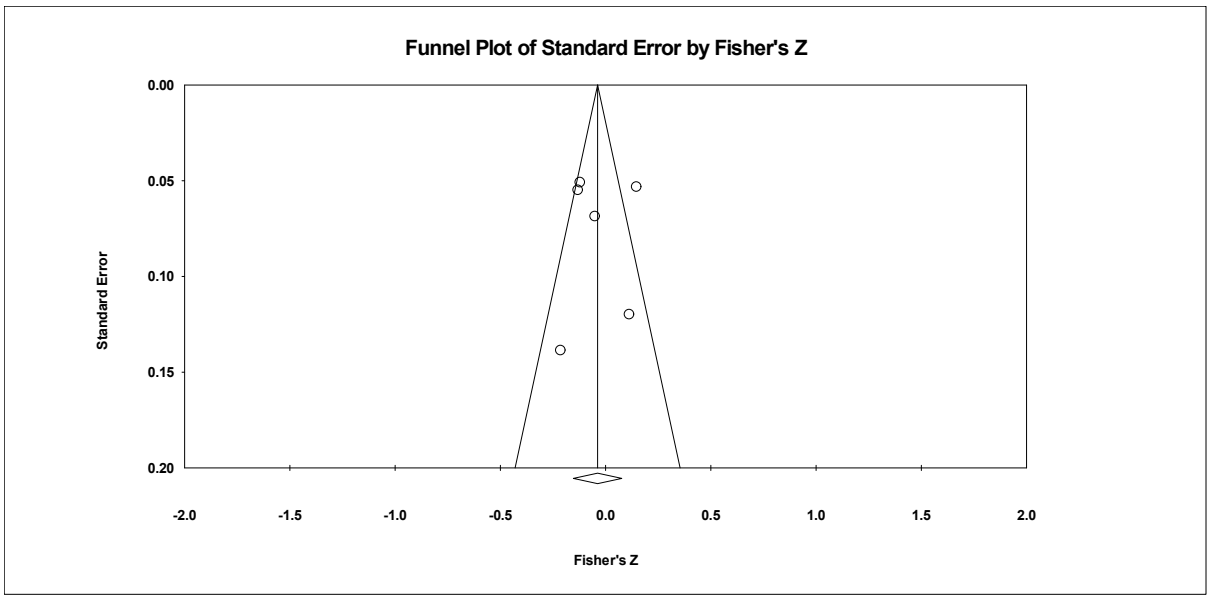
Suppl. Figure 35: Funnel plot for Case-control SCL during Task studies



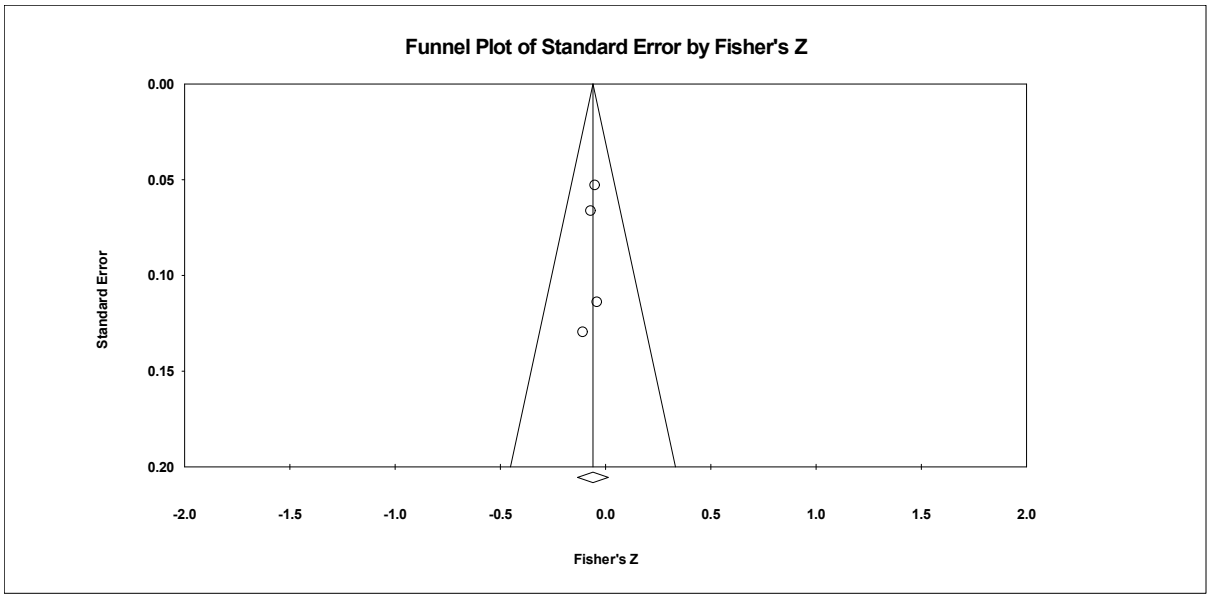
Suppl. Figure 36: Funnel plot for Case-control SCR during Task studies



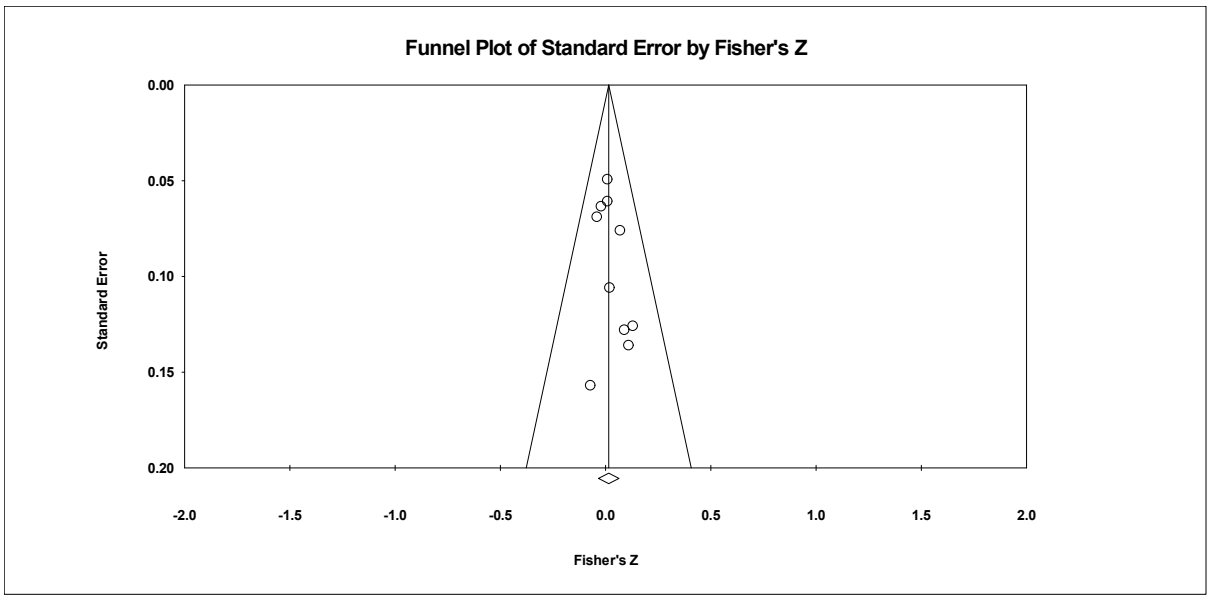
Suppl. Figure 37: Funnel plot for Correlational HR Baseline studies



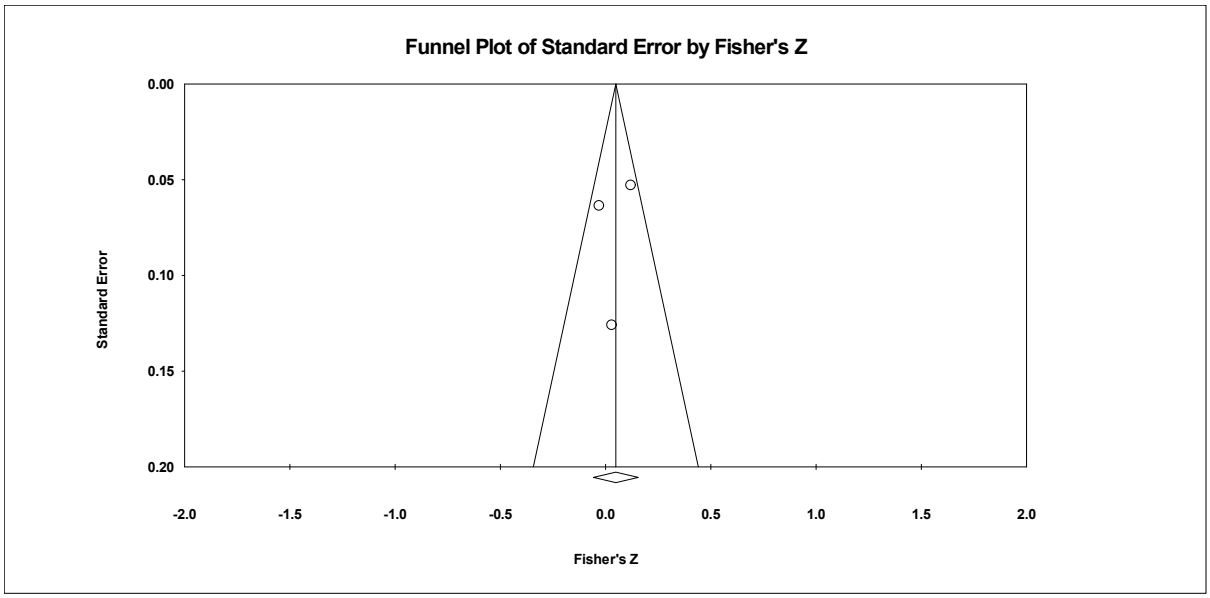
Suppl. Figure 38: Funnel plot for Correlational HR during Task studies



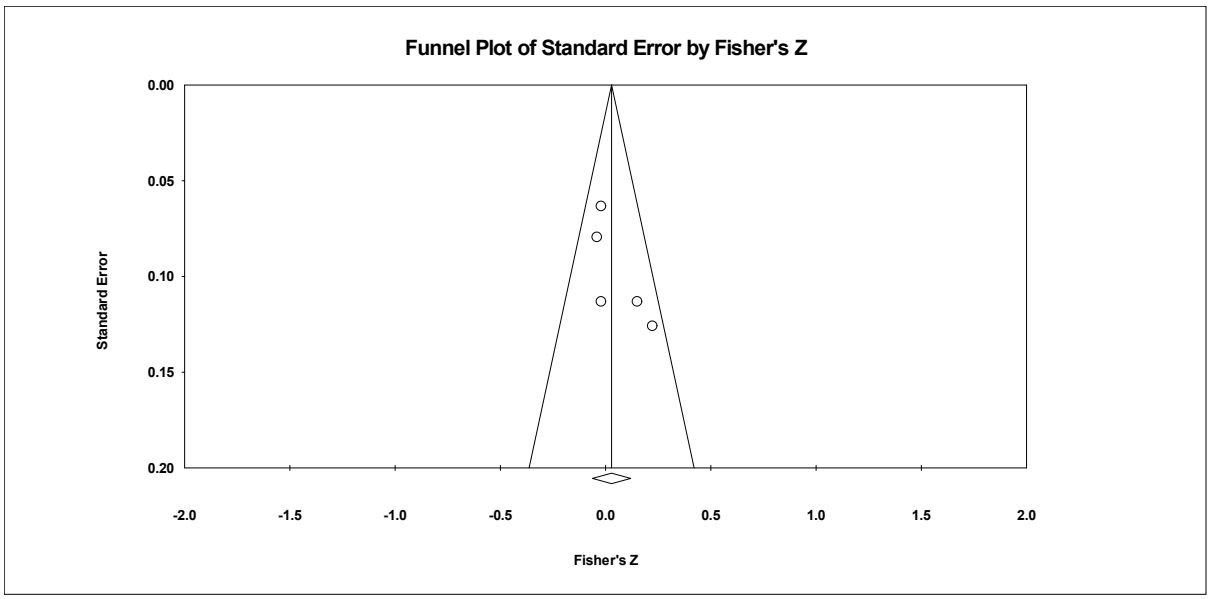
Suppl. Figure 39: Funnel plot for Correlational RSA Baseline studies



Suppl. Figure 40: Funnel plot for Correlational RSA during Task studies



Suppl. Figure 41: Funnel plot for Correlational SCL Baseline studies



Suppl. Figure 42: Funnel plot for Correlational SCL during Task studies