



# Early life adversities and adolescent antisocial behavior: The role of cardiac autonomic nervous system reactivity in the TRAILS study

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## ABSTRACT

In the current study, the role of pre-ejection period (PEP) and respiratory sinus arrhythmia (RSA) was studied in the association between prior adversities and antisocial behavior in adolescence. PEP and RSA task reactivity and recovery to a public speaking task were assessed in adolescents from a longitudinal population-based study ( $N = 624$ ,  $M_{\text{age}} = 16.14$  years, 49.2% boys). Perinatal adversities were unrelated to antisocial behavior, but experiencing more stressful adversities between age 0 and 15 was associated with antisocial behavior at age 16 in boys with blunted PEP reactivity and smaller PEP differences from rest to recovery. Number of adversities between age 0 and 15 was associated with antisocial behavior in boys with blunted and girls with heightened RSA reactivity and larger PEP differences from rest to recovery. The association between prior adversities and antisocial behavior were small in effect size and depended upon sex and PEP and RSA reactivity and recovery.

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## 1. Introduction

Perinatal (i.e., before, during, and right after birth) and early life adversity – here defined as adversity during childhood and adolescence – have been associated with subsequent antisocial behavior in adolescence (Beck & Shaw, 2005; Hodgins, Kratzer, & McNeil, 2001; Raine, Brennan, & Mednick, 1994; Timmermans, van Lier, & Koot, 2010). One of the possible mechanisms underlying this association is the functioning of one of the major stress axes, the cardiac autonomic nervous system (ANS). It has been argued that perinatal adversities shape ANS functioning (Cohen, Vella, Jeffery, Lagercrantz, & Katz-Salamon, 2008; Jones et al., 2008; Kajantie & Raikonen, 2010). In turn, these changes in ANS functioning may co- occur with changes in emotional and behavioral reactions to environmental stressors and may therefore be associated with the development of antisocial behavior (Ortiz & Raine, 2004; Lorber, 2004). Moreover, adversities during childhood and adolescence have been shown to interact with cardiac ANS functioning (El-Sheikh, Keller, & Erath, 2007; Erath, El-Sheikh, & Cummings, 2009; Gordis, Feres, Oleszski, Rabkin, & Trickett, 2010; Shenk, Noll,

Putnam, & Trickett, 2010). In particular, these studies showed that those who experienced adversities during childhood and adolescence and showed blunted or heightened ANS functioning were at increased risk of antisocial behavior. In the current study, we examined these two processes more closely; details and directions of these two mechanisms will be discussed below.

### 1.1. Autonomic nervous system

The cardiac ANS consists of two branches, namely the parasympathetic (PNS) and sympathetic (SNS), which can be assessed by Respiratory sinus arrhythmia (RSA) and pre-ejection period (PEP), respectively (Alkon et al., 2003; Cacioppo, Tassinari, & Berntson, 2007; Camm et al., 1996). RSA is the heart rate variability due to respiratory gating of tonic vagal effects on the SA node of the heart (Berntson, Cacioppo, & Quigley, 1993), and is considered a measure of cardiac vagal control. PEP is derived as the time interval between the onset of ventricular depolarization and the opening of the semilunar valves (Sherwood et al., 1990) and commonly used as an index of myocardial contractility and sympathetic control of the heart (Berntson et al., 1994; Schachinger, Weinbacher, Kiss, Ritz, & Langewitz, 2001). These cardiac ANS measures are used as indicators of the complex processes that underlie autonomic responsiveness to a changing environment, e.g., from rest to

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a challenge or vice versa. ANS resting measures reflect a physiology state during a calm state. Challenging measures reflect physiological responses to a stressor, and stress reactivity measures indicate physiological responses to a stressor compared to a resting state, whereas recovery measures indicate physiological responses after a stressor compared to a subsequent resting state (Cacioppo et al., 2007).

### 1.2. Perinatal adversities and antisocial behavior

As suggested by evolutionary models of biobehavioral change, perinatal adversities may impact ANS reactivity and recovery because the plasticity of the ANS is strongest early in life (Boyce & Ellis, 2005; Del Giudice, Ellis, & Shirtcliff, 2011; Gunnar, Wewerka, Frenn, Long, & Griggs, 2009). Several studies support this idea by showing that perinatal adversity has an effect on cardiac ANS reactivity (Enlow et al., 2009; Jones et al., 2008; Kajantie & Raikonen, 2010). Based on these prior findings, alterations due to perinatal adversities may be expected to lead to heightened or blunted ANS reactivity in response to a stressor. In turn, empirical studies associating both PNS and SNS reactivity to antisocial behavior showed that reactivity of both branches of the ANS has been cross-sectionally associated with more antisocial behavior (i.e., aggression and externalizing behaviors) in children and adolescents (Beauchaine, Gatzke-Kopp, & Mead, 2007; Boyce et al., 2001; Calkins, Graziano, & Keane, 2007; Sijtsema, Shoulberg, & Murray-Close, 2011).

There is theoretical support for both directions, but previous research has shown more support for perinatal and early life adversities being associated with increased ANS reactivity (see Obradovic, 2013 for a discussion). However, both from a theoretical and empirical viewpoint there is reason to believe that the role ANS reactivity plays in the association between adversity and antisocial behavior is different in boys and girls. Evolutionary theorists have argued that in stressful environments it is more adaptive for females to be vigilant and attentive to environmental cues and thus show heightened ANS reactivity, with more internalizing problems as a result (Del Giudice, Hinnant, Ellis, & El-Sheikh, 2012; Glover & Hill, 2012). In contrast, in males it may be more important to respond less to environmental cues, as they are more programmed towards exploring and competing with other males, which may result in antisocial behaviors (Del Giudice et al., 2011). Previous studies investigating sex differences have indeed shown that the association between adverse environments and antisocial behavior was highest in boys with blunted ANS reactivity (Beauchaine, Hong, & Marsh, 2008; Sijtsema et al., 2013), whereas this was not the case in girls. Moreover, a recent study showed that boys high on externalizing problems showed blunted RSA withdrawal, whereas girls high on externalizing problems showed heightened RSA withdrawal (Hinnant, & El-Sheikh, 2013). In sum, perinatal adversities have been found to be associated with both ANS reactivity and antisocial behavior. However, whether ANS reactivity mediates the association between perinatal adversities and antisocial behavior is currently unknown. The first aim of the current study is to test this indirect effect. Because previous studies suggest important sex differences, we hypothesized that blunted ANS reactivity in boys and heightened ANS reactivity in girls mediates the association between perinatal adversities and antisocial behavior at age 16.

### 1.3. Adversities in childhood and adolescence and antisocial behavior

Adversities that take place later in life are less likely to impact alterations in ANS reactivity regulation mechanisms, due to decreased plasticity of the ANS (Boyce & Ellis, 2005; Del Giudice et al., 2011; Gunnar et al., 2009). However, ANS reactivity may

modify the association between adversities and antisocial behavior. Moderation by RSA reactivity of the relationship between adversities and antisocial behavior may rest on the premises that RSA withdrawal in response to stress (i.e., removing vagal control) is related to attention and emotional processing (Beauchaine, 2001; Porges, 1995). Arguably, RSA withdrawal in stressful situations reflects the ability to use attention and emotional strategies to form an appropriate reaction to stress (Bornstein, & Suess, 2000; Porges, 1995). Blunted physiological responses to stress could thus indicate inability to respond adequately to stressful situations. Moderation by PEP reactivity has been studied less frequently but may be related to the behavioral activation system (Brenner, Beauchaine, & Sylvers, 2005). As such, stressful situations or adversity may induce SNS reactivity and blunted reactivity may indicate inability to respond adequately to stressful situations (Beauchaine, 2001).

Research into the interaction between context and RSA and PEP reactivity has shown important links to antisocial behaviors (El-Sheikh, Erath, & Hinnant, 2011; El-Sheikh and Hinnant, 2007; Obradovic, Bush, & Boyce, 2011). Specifically, these studies showed that marital conflict in childhood had a stronger effect on externalizing problems (including antisocial behavior) in youth with blunted SNS and RSA reactivity. However, although marital conflict is an important stressor in childhood, these studies did not specifically examine adverse events (e.g., death/illness of a parent or divorce) and whether youth perceived these events as stressful. Moreover, previous studies largely focused on childhood behaviors and did not include adolescent behavior.

In addition, most of the studies discussed above have focused on physiological reactivity from rest to stress, but largely ignored recovery from a stressor. Recovery measures are meaningful as healthy individuals in general show elevated physiological activity to stress, but these levels typically decrease relatively quick after the stressor has passed or after habituation to the stressor (cf. Koolhaas et al., 2011). When this natural recovery process is less effective, physiological activation may remain high, even after the stressor has passed. Based on models on allostatic load, chronic or severe stress may lead to a 'wear and tear' of the ANS and hence recovery from a stressor takes longer (McEwen, 2007). ANS recovery measures may thus prove an important index for how well individuals are able to regulate their emotions or adapt to their environment after a stressor has passed. However, there is little empirical evidence regarding cardiovascular recovery and some evidence seems to go against theories of prolonged ANS activity during a stressful situation in individuals who experienced more adversity. Research on chronic stress showed that adults with greater chronic stress showed greater systolic blood pressure recovery and higher cortisol levels, with no differences between males and females (Chatkoff, Maier, & Klein, 2010). Similarly, adults who were highest on anticipatory stress, showed the greatest recovery in blood pressure and cortisol (Juster et al., 2012), though another study in adolescents showed no associations between anticipatory stress and ANS recovery (Oldehinkel et al., 2011). We aim to extend previous research by examining whether ANS recovery moderates the association between early life adversities and adolescent antisocial behavior similar to ANS task reactivity. Specifically, based on the earlier presented evolutionary perspective on stress and sex, we hypothesized that in boys, blunted ANS reactivity exacerbates the association between early life adversities and antisocial behavior at age 16, whereas in girls, heightened ANS reactivity exacerbates this association. Similarly, we expected that smaller differences between ANS rest and recovery in boys and larger differences in girls exacerbate the association between early life adversities and antisocial behavior at age 16.

We tested these hypotheses separately for number of adversities and the stressfulness of adversities. In addition, we used an ecologically valid experimental condition to induce stress. Childhood

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