Internalizing Problems and Attentional Control: Effects on Cardiac Autonomic Responses After the Induction of Negative Affect

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Abstract

Individuals with internalizing problems differ in levels of attentional control (AC), and this heterogeneity could be associated with differences in autonomic arousal. The present study investigated whether AC moderated the effect of internalizing problems on self-reported experience and autonomic nervous system (ANS) responses after the induction of negative affect. Children aged 9-13 years were recruited into a patient group (29) and a healthy control group (25). AC was measured by the Early Adolescent Temperament Questionnaire. Heart rate, heart rate variability (HRV) and pre-ejection period (PEP) were recorded during baseline, a sad film clip and recovery, and analyzed using a marginal linear model. Children reported their experienced emotion, valence and arousal in response to the film. A significant interaction effect showed increased HRV and longer PEP from baseline to recovery for patients with higher AC. Patients with lower AC showed increased HRV followed by a return to baseline values after the film clip and no significant changes in PEP. Healthy controls showed no significant changes in HRV or PEP independent of level of AC. There were no differences between groups in self-reported experience. The results indicate that AC moderated the effect of internalizing problems on ANS regulation. Increased HRV and longer PEP from baseline to recovery were uniquely associated with higher AC and internalizing problems. This physiological response might indicate a cognitive avoidance strategy. AC could be an important factor explaining heterogeneity in ANS activity among individuals with internalizing problems. Clinical implications of the present findings are discussed.

Keywords: Internalizing problems – Attentional Control – Autonomic Nervous System – Heart Rate Variability – Pre-ejection Period

Internalizing problems include symptoms of anxiety and depression and are characterized by *"a core disturbance in intropunitive emotions and moods (e.g., sorrow, guilt, fear and worry)"* (Zahn-Waxler, Klimes-Dougan, & Slattery, 2000, p. 443). Anxiety and depression are common in childhood, comorbidity rates are high and investigations have described longitudinal stability in symptoms (Costello, Mustillo, Erkanli, Keeler, & Angold, 2003). While the identification of predictors is crucial for increasing our current understanding of internalizing problems, investigations that focus on intragroup variability could provide equally important information on the nature of these problems. For instance, different paths in the development and maintenance of internalizing problems might be related to different levels of attentional control (AC) – the ability to focus and shift attention voluntarily (Derryberry & Rothbart, 1997; Vasey, Chriki, & Toh, 2017).

Effortful control, an overarching concept that includes AC, develops during preschool years (Derryberry & Rothbart, 1997), and Polderman et al. (2007) found longitudinal stability in AC from the age of 5-12. While AC has been reported to be lower in individuals with internalizing problems compared to healthy controls (Armstrong, Zald & Olatunji, 2011; Eisenberg et al., 2001), children and adults with internalizing problems also show heterogeneity in levels of AC (Derryberry & Reed, 2002; Lonigan & Vasey, 2009; Toh & Vasey, 2017; Vasey et al., 2017). Heterogeneity in AC could be associated with differences in the capability for dealing with negative affect (Derryberry & Rothbart, 1997). For instance, it was found that anxious adults with lower AC were slower at disengaging attention from threatening stimuli compared to their higher AC counterparts (Derryberry & Reed, 2002), and attentional bias to threat cues was found in children who had high levels of negative affect and low levels of effortful control (Lonigan & Vasey, 2009). The implications could be that anxious individuals with lower AC and attentional bias toward threat might experience an amplification of negative affect. Their higher AC counterparts can more easily redirect

attention away from threat and experience less negative affect, which is presumably a more favorable outcome. However, higher AC could also facilitate maladaptive coping strategies, for instance the use of cognitive avoidance such as worry (Derryberry & Reed, 2002). Vasey et al. (2017) suggest that, in the face of threatening stimuli, individuals with higher levels of cognitive control might more often manage to make a shift to verbal worry, while individuals with lower levels of cognitive control might struggle to disengage from a more imagery-based worry. Interestingly, worrisome *thinking* has been associated with a lower heart rate response compared to processing fear imagery (Borkovec, Lyonfields, Wiser & Deihl, 1993; Vrana, Cuthbert & Lang, 1986), and efforts to decrease autonomic arousal were more effective if a verbal compared to an imaginal strategy was used (Tucker & Newman, 1981). The present study explores the relationship between heterogeneity in AC and heterogeneity in autonomic arousal in children with internalizing problems and discusses how the interplay between these factors could be important for the understanding and treatment of internalizing problems.

The autonomic nervous system (ANS) controls the mobilization of bodily resources in response to rest or threat and is essential for emotion regulation. The neurovisceral integration model (Thayer & Lane, 2000, 2009) delineates how prefrontal-subcortical inhibitory circuits inhibit sympathetic nervous system (SNS) activity during rest to avoid excess energy use and how a resting state dominated by parasympathetic nervous system (PNS) activity is associated with behavioral flexibility and adaptability to changing environmental demands. Conversely, both lower PNS activity during rest and a disinhibition of cardiac sympathoexcitatory mechanisms are associated with a defensive state marked by increased heart rate and hypervigilance toward threat. Numerous studies have shown that lower cardiac PNS activity during rest, indicated by lower heart rate variability (HRV), is associated with symptoms of anxiety and depression in both children and adults (e.g.,

Chalmers, Quintana, Abbott, & Kemp, 2014; Greaves-Lord et al., 2007; Koenig, Kemp, Beauchaine, Thayer, & Kaess, 2016; Rottenberg, 2007). Although far less investigated, higher cardiac SNS activity during rest, indicated by a shorter pre-ejection period (PEP) (Newlin & Levenson, 1979), was found in children and adults with internalizing problems (Kossowsky, Wilhelm, Roth & Schneider, 2012; Light, Kothandapani, & Allen, 1998); however, nonsignificant differences have also been reported (Byrne et al., 2010; Licht, Penninx & de Geus, 2012).

Despite the extensive literature reporting lower resting HRV among individuals with internalizing problems, inconsistent findings have been reported among adults (e.g., Fisher & Newman, 2013; Kogan, Gruber, Shallcross, Ford & Mauss, 2013; Licht, de Geus, Van Dyck & Penninx, 2009; Licht et al., 2008) and children (as reviewed by Koenig et al., 2016). These publications showed either nonsignificant, positive or nonlinear associations between resting HRV and internalizing problems. Such heterogeneity is evident in autonomic responses to negative affect as well. For instance, in response to sad film clips, depressive symptoms in children and adults have been associated with both blunted and greater HRV-reactivity (Hamilton & Alloy, 2016).

Taken together, these findings indicate a complex relationship between internalizing problems and ANS activity. There could be a number of reasons explaining the inconsistencies; for instance, the severity of internalizing problems (e.g., Beauchaine & Thayer, 2015; Koenig et al., 2016) or confounding factors such as medication (Licht et al., 2009; Licht et al., 2008). There are indications that developmental processes alone cannot account for the inconsistent findings among children, as both baseline measures and reactivity measures of HRV and PEP have been found to be moderately stable individual difference variables in middle childhood (El-Sheikh, 2005; Matthews, Salomon, Kenyon & Allen, 2002). Vasey et al. (2017) propose an additional way of understanding some of this

heterogeneity, namely, by individual differences in cognitive control. The authors review inconsistencies in research on self-reported and objectively measured autonomic arousal in response to worry and among individuals with generalized anxiety disorder (GAD). In recent studies, the authors found that lower effortful control was associated with higher self-reported autonomic arousal in individuals with high GAD symptom severity (Vasey et al., 2017). Furthermore, there was an indication that individuals with high GAD symptom severity and high effortful control reported a higher percentage of verbal thoughts compared to images during worry, which in turn predicted lower self-reported autonomic arousal (Toh & Vasey, 2017). In short, individuals with internalizing problems and higher AC might more often and more efficiently redirect their attention from negative stimuli to verbally-based worry and limit or suppress the activation of autonomic arousal. Lower AC counterparts might more often struggle to disengage attention from negative stimuli, process threat as images and experience increased autonomic arousal. Both responses could be maladaptive and serve to maintain internalizing problems (Toh & Vasey, 2017).

To our knowledge, no published studies have tested the moderating effect of AC on the relationship between internalizing problems and *objectively* measured autonomic arousal. However, some studies have linked higher levels of executive function to higher baseline HRV in healthy adults and children (Hansen, Johnsen & Thayer, 2003; Marcovitch et al., 2010; Suess, Porges & Plude, 1994), in patients with panic disorder (Hovland et al., 2012) and to moderate levels of HRV-withdrawal in healthy children (Marcovitch et al., 2010). In the present study, ANS activity during baseline, a sad film clip and resting recovery was assessed in children with internalizing problems and healthy controls at higher and lower levels of AC. Using both a sad film clip and a resting recovery phase after the film clip allows for the evaluation of prolonged adaptive or maladaptive responses. A return to physiological baseline values after a stressor has subsided is associated with energy

conservation and marks flexible, healthy behavior (Santucci et al., 2008). Both increased PNS activity and decreased SNS activity to baseline values during recovery from a stressor have been associated with positive psychosocial outcomes (Bazhenova, Plonskaia, & Porges, 2001; Willemen, Schuengel, & Koot, 2009).

The present study

In the present study, it was assumed that patients with internalizing problems would show different ANS responses to negative affect, depending on the level of AC. Specifically, the following hypotheses were investigated:

(1) AC will moderate the effect of internalizing problems on ANS regulation after the induction of negative affect. Patients with lower AC will show increased HR, decreased HRV and shorter PEP throughout recovery, compared to baseline values. Patients with higher AC will show decreased HR, increased HRV and longer PEP throughout recovery. Healthy controls will show a return to baseline values of HR, HRV and PEP during recovery.

(2) AC will moderate the effect of internalizing problems on self-reported experience of a sad film clip, where lower AC internalizers will report the sad film clip as more negative (more negative valence, higher arousal) compared to higher AC internalizers and controls.

Methods

Participants

In total, 68 subjects participated in the study. Healthy controls and patients between 9 and 13 years were considered for inclusion. Patients presenting with internalizing symptoms (N=40) were recruited at the outpatient clinic at the Norwegian University of Science and

Technology in Trondheim (NTNU), Norway (N=28) and at the Akershus university hospital's child and adolescent psychiatric outpatient clinic in Furuset, Oslo, Norway (BUP Furuset) (N=12). Prior to intake, children were evaluated by licensed psychologists and specialists in Clinical Child and Adolescent Psychology. Only children presenting with internalizing symptoms who scored above the subclinical threshold for either anxiety or affective problems (either Syndrome- or DSM-oriented scales) on the Child Behavior Checklist (CBCL) were included in the patient group. The included patients showed symptoms of both anxiety and depression: 24 patients scored above subclinical levels on the DMS-oriented CBCL Anxiety Problems scale, and 22 scored above subclinical levels on the DSM-oriented CBCL Affective Problems scale. Exclusion criteria included developmental disorders, mental disorders not in the internalizing spectrum, medication potentially affecting ANS activity and somatic illness affecting the circulatory system. Two participants were excluded because of equipment malfunction during the assessment, and two participants had missing data on BMI. A total of 29 children were included in the patient group (15 girls). Twenty-one of the mothers and 18 of the fathers had completed higher (tertiary) education.

Healthy controls (N=28) were mainly recruited from local schools. Parents were informed about the research project in a parent meeting at their children's school. Parents interested in participating gave their contact information and were contacted by telephone to arrange for participation. The included healthy controls did not score above the subclinical cut-off on either anxiety or affective problems on the CBCL, and parents reported no current or previous mental illness or referral for mental health care. Similar to the patient group, controls had no somatic illness affecting the circulatory system and did not use medication potentially affecting ANS activity. A total of 25 children were included in the control group (14 girls). Twenty-three of the mothers and 20 of the fathers had completed higher education.

All parents and children were given verbal and written information about the research project, and parents signed an informed consent. All children received a 300 NOK gift certificate to go to the movies after participation. The study is part of a larger research project where all participants were assessed at two time points as follows: before and after patients received a psychotherapeutic treatment and at two time points of similar spacing for the healthy controls. The present study is based on data from the first assessment only. The study was approved by the Regional Committees for Medical and Health Research Ethics in Norway, region North (ref. 2013/953), and was in compliance with the Declaration of Helsinki (World Medical Association, 2001).

Parent-reported measures

Early Adolescent Temperament Questionnaire – revised (EATQ-R). The EATQ-R is a measure of temperamental traits in adolescents (9-15 years of age) (Ellis, 2002). AC is commonly included as a factor in models of temperament, and in the present study, AC was measured using the attention subscale in the EATQ-R. In the EATQ-R, items were answered on a 5-point Likert scale as follows: 5 = almost always true, 4 = usually true, 3 = sometimes true, sometimes untrue, 2 = usually untrue, and 1 = almost always untrue. The questionnaire includes 10 subscales. Only the attention subscale was used (6 items). A higher score reflects a greater capacity to focus and shift attention when desired (sustained and selective attention) (e.g., *Has a difficult time tuning out background noise and concentrating when trying to study* – reverse item). Father-report was used where mother-report was missing (3 cases). The Chronbach's alpha for attention was .745 (mother-report) and .738 (combined mother- and father-reports). As no Norwegian translation of the questionnaire exists that we were aware of, in the present study, we translated the EATQ-R into Norwegian. Two clinical

psychologists translated the questionnaire independently, and a native English speaker with a high proficiency in Norwegian did a back-translation. The questionnaire developer approved the back-translation (personal communication, Ellis, 2014). In a large population sample of preadolescents, the attention scale of the parent-reported EATQ-R loaded on the effortful control factor (Oldehinkel, Hartman, De Winter, Veenstra, & Ormel, 2004), and studies have presented support for the construct validity of this factor (Oldehinkel et al., 2004; Verstraeten, Vasey, Claes, & Bijttebier, 2010).

Child behavior checklist (CBCL). The CBCL is a measure of parent-reported behavioral/emotional problems and adaptive characteristics for 6- to 18-year-old children. The CBCL has demonstrated good validity and reliability (Achenbach, 2011; Ebesutani et al., 2010). In the present study, levels of Anxiety and Affective problems for the DSM-oriented scales were reported. Father-report was used where mother-report was missing (3 cases). The Cronbach's alpha for Anxiety problems (6 items) was .796 (mother-report) and .789 (combined mother- and father-reports). The Cronbach's alpha for Affective problems (13 items) was .777 (mother-report) and .778 (combined mother- and father-reports).

Experimental protocol

Experiments were conducted at different locations in rooms with similar properties; rooms were temperature controlled, visually sparse and quiet. All experimenters were female. Experiments were conducted between 08:30 a.m. and 18:00 p.m. Participants did not eat during the entire lab visit; however, we did not control for meal status prior to entering the lab. Participants and parents were given a tour of the lab together before parents were seated in the waiting area to fill out questionnaires. Participants were shown to the bathroom and asked to empty their bladder and to change into a loose t-shirt. Upon return their height and

weight (Coline brand scale) were measured. They were seated in a comfortable chair in front of a computer monitor. All electrode sites were thoroughly prepared using abrasive gel that was washed off with lukewarm water, and last, the skin was cleaned with alcohol wipes. Preparation lasted approximately 30 minutes and participants acclimated to sitting in the chair for approximately 10 minutes before the protocol started.

In the experiment proper, participants first completed the resting baseline condition, resting quietly in a seated upright position with their eyes open for 5 minutes. The statistical analyses in the present study are based on the last 2 minutes of the baseline condition. Participants watched film clips from two animated movies, either The Lion King or The Land Before Time. Both film clips have been used in previous psychophysiological studies with children (Davis, Quiñones-Camacho, & Buss, 2016; Fortunato, Gatzke-Kopp, & Ram, 2013). Participants were randomly assigned the film clips. Two film clips were introduced to eliminate test-retest bias in the second assessment. Data from the second assessment are not included in the present study. The total duration of the film clips was 7-8 minutes, and the clips had similar content: a neutral beginning with a transition into a chase, and a sad part where the parent figure dies. Both film clips were chosen to induce negative affect, specifically, sadness. The death of a parent figure could also represent a threatening scenario. Recordings that lasted 2 minutes were analyzed. The selected clips were identical in length (2 minutes) and content (death of parent figure). Participants were instructed to sit quietly and to try to engage emotionally with the film. In the 2-minute recovery period immediately after the sad clip ended, participants were in advance asked to sit quietly in an upright position and look at the blank screen. Participants had no contact with the experimenter until the recovery period had ended. Immediately after the end of the recovery period, participants completed an experimenter-led self-report on how the films were experienced.

Self-reported experience

Participants reported what emotions the film clips induced and could specify several emotions but using predefined emotional categories read aloud by the experimenter. The following emotions were included: sad, scared/anxious, happy, angry, surprised, disgusted, and no feeling. The reports from both films were comparable; 81.3% of the participants watching The Lion King and 86.4% watching The Land Before Time reported feeling sad, and 15.6% of the participants watching The Lion King and 13.6% watching The Land Before Time reported feeling scared/anxious. We interpret this as an indication that the sad film clips successfully induced negative affect, and in particular sadness.

Children also evaluated the valence and arousal of the films using the Self-Assessment Manikin (SAM). The SAM consists of a 9-point scale with explanatory pictures where children report valence (negative/neutral/positive) and arousal (how much could you feel the emotion in your body?) (Bradley & Lang, 1994). The SAM was administered once, after the recovery period had ended. The results of group differences on the SAM are presented in the results section.

Psychophysiological measures

All psychophysiological data were collected using the Biopac MP 150-system (Biopac Systems Inc., Goleta, CA). The ECG100C was used to record an electrocardiogram (ECG) (1 Hz high pass filter, 35 Hz low pass filter) and the Bionomadix/NICO to record impedance cardiography (10 Hz low pass filter). To control for power line artifacts, a 50 Hz notch filter was used. For the recordings of ECG, three disposable Ag-AgCl electrodes (11 mm) were placed on the clavicles and lower left rib in a lead II configuration. Electrode contact impedance was checked to ensure an optimal signal at acquisition. The ECG signal

was sampled at 1000 Hz. The ECG signal for each participant was saved, extracted from the Biopac AcqKnowledge software (version 4.4), and analyzed off-line using the Kubios HRV analysis package, version 2.2 (Biosignal Analysis and Medical Imaging Group, University of Eastern Finland) to obtain a time domain analysis of the R-R interval (HR and HRV). Smoothness priors (500 Lambda) were selected for detrending the data. The ECG signal was visually inspected to ensure that all R-waves were identified correctly. The tachogram was inspected for artifacts, and in one subject, two R-R intervals showed clear deviation and were corrected by cubic spline interpolation using the lowest possible filter for correction.

The root mean square of successive differences (RMSSD) between adjacent R-R intervals was the chosen HRV-variable in the present study. RMSSD is an index of vagally mediated cardiac control and a common measure of short-term HRV (Malik et al., 1996). Although 5-minute recordings have commonly been used in HRV research, recent studies indicate that ultrashort recordings of RMSSD are valid (Munoz et al., 2015). Two-minute recordings during resting baseline, sad film clip and resting recovery were used in the present study. When comparing recordings in HRV studies, similar recording lengths are recommended (Laborde, Mosley & Thayer, 2017). A 2-minute recovery condition has been used in previous studies assessing HRV recovery (Santucci et al., 2008) and the length was considered sufficient, as cardiovascular changes occur relatively swiftly (Linden, Earle, Gerin & Christenfeld, 1997).

Impedance cardiography was used to measure PEP. Pre-ejection period (PEP) is mainly a measure of the influence of the SNS on the contractile force of the heart, mediated primarily by beta-adrenergic mechanisms. A shorter PEP (in milliseconds) indicates higher sympathetic influence (Newlin & Levenson, 1979). Four paired Ag-AgCl impedance electrodes (11 mm) placed bilaterally on the neck and torso produced measures of baseline impedance (Z0) and rate of change in impedance (dZ/dt). Electrode contact impedance was

checked to ensure an optimal signal at acquisition. The Z0 and dZ/dt signal was sampled at

1000 Hz. The signal was saved and analyzed off-line using MindWare IMP version 3.1.4.

Scale factors were set to 0.09 V/ohm for Z0 and 1.0 V/Ohm/s for dZ/dt. The 50 Hz notch

filter and a baseline and muscle noise filter was applied. As visual inspection is

recommended in addition to automated routines (Lozano et al., 2007), the first author visually

inspected all ECG and dZ/dt-waveforms, excluding waveforms considerably affected by

motion artifacts from analysis, as recommended by Sherwood et al. (1990). PEP values for

each 2-minute condition were calculated by averaging values from four 30-second ensemble

averages. PEP was calculated based on the interval between the Q-peak/R-onset (Berntson,

Lozano, Chen, & Cacioppo, 2004) of the ECG signal and the B-point of the dZ/dt signal. The

Q-peak/R-onset was estimated using the minimum value K-R interval (K value 35). The B-

point was estimated using percent of dZ/dt time (55%).

Statistical analyses

Statistical analyses were conducted using IBM SPSS Statistics, version 25. Normality

was evaluated by inspecting the Q-Q plots of residuals and residual plots in all linear models.

A generalized linear model (maximum likelihood estimation) tested whether there was a

moderating effect of AC on the relationship between internalizing problems and self-reported

valence and arousal. AC was included as a continuous moderator variable, internalizing

problems as a dichotomous independent variable (group), and a moderating effect was tested

by including the interaction term AC × group, while controlling for age, sex and film.

A repeated measures marginal linear model tested whether AC moderated the effect of

internalizing problems on ANS regulation in response to the sad film clip and recovery phase,

assessing both within- and between-group differences. Restricted maximum likelihood was

chosen as the final estimation method, as it produces unbiased estimates of covariance parameters (West, Welch, & Galecki, 2014). Covariance structures were chosen on the basis of covariance pattern, parsimony and model fit. A heterogeneous compound symmetry covariance structure provided the best fit for the models. Fit was evaluated using information criteria (lower - 2 Restricted Log Likelihood and Schwarz's Bayesian Criterion indicate better fit). Models were run with all predictors included and consequently reduced by removing nonsignificant covariates to assess model fit, using maximum likelihood estimation (model fit by - 2 Log Likelihood) in this step. Reduced models showed the same results for the interaction as for the full models. The full models showed slightly better model fit. The results from the full models are presented.

The analyses included three conditions: baseline, sad film clip and recovery. In the marginal models, condition and group were treated as factors. AC was treated as a continuous moderator variable. The control variables sex and film were treated as factors, and time of day, age and body mass index (BMI) as continuous control variables. The marginal models included control variables, main variables, all lower order interactions and, lastly, a three-way interaction between Group $\times$ AC $\times$ Condition in order to test the moderating effect of AC.

Simple effects tests of the estimated marginal means were used to investigate interactions, using Sidak correction for multiple comparisons. As AC was defined as a continuous moderator variable, we interpreted interactions defining higher and lower levels of AC as $\pm$ 1 standard deviation (SD) from the mean. Thus, the estimated marginal means provide estimated group means with AC fixed at $\pm$ 1 SD from the mean. The terms lower/higher AC patients/controls were based on this analysis and do not represent actual groupings of participants.

Results

Descriptive statistics and between-group differences

Table 1 shows descriptive statistics and between-group differences. Table 2 shows the descriptive statistics of the psychophysiological measures and between-group differences. There were no significant differences between groups in baseline HR ($U = 419$, $z = 0.98$, $p = .327$) or HRV (RMSSD) ($U = 322$, $z = -0.70$, $p = .482$); however, there was a significant difference in baseline PEP, where patients had longer PEP ($U = 210$, $z = -2.50$, $p = .012$).

HR – marginal linear model

A marginal linear model tested whether AC moderated the relationship between internalizing problems and HR across conditions. There was no significant effect of the three-way interaction (Group $\times$ AC $\times$ Condition) ($F(2, 93.7) = 0.08$, $p = .923$), indicating no significant moderating effect. No main variables, interactions or covariates were significant. The results are shown in figures 1 and 2.

HRV (RMSSD) – marginal linear model

A marginal linear model tested whether AC moderated the relationship between internalizing problems and HRV (RMSSD) across conditions. There was a significant effect of the three-way interaction (Group $\times$ AC $\times$ Condition) ($F(2, 98.9) = 3.61$, $p = .031$), indicating a significant moderating effect. Groups showed different HRV-responses to the film clip at different levels of AC. Age was a significant control variable ($F(1, 44.9) = 4.40$, $p = .042$); higher age was associated with lower HRV. No other control variables were significant including sex ($F(1, 44.9) = 0.003$, $p = .959$), BMI ($F(1, 44.9) = 0.36$, $p = .552$),

film ($F(1, 44.9) = 0.09$, $p = .760$), and time of day ($F(1, 44.9) = 0.33$, $p = .570$). The significant interaction was interpreted with the estimated marginal means: with AC fixed at 1 SD above the mean, patients showed significant changes in HRV ($F(2, 82.5) = 4.17$, $p = .019$); HRV increased significantly from baseline to recovery (16.3±6.14, 95% CI [1.37, 31.3], $p = .028$). With AC fixed at 1 SD below the mean, patients also showed significant changes in HRV ($F(2, 82.5) = 5.42$, $p = .006$); HRV increased significantly from baseline to the sad film clip (15.9±5.20, 95% CI [3.23, 28.5], $p = .009$) and decreased significantly from the sad film clip to recovery (-13.4±5.08, 95% CI [-25.8, -1.05], $p = .029$). The control group showed no significant changes in HRV, neither when AC was fixed at 1 SD below ($F(2, 82.5) = 1.67$, $p = .195$) nor at 1 SD above the mean ($F(2, 82.5) = 1.03$, $p = .361$). There were no differences in HRV between patients and controls with AC fixed at ±1 SD during any of the conditions. The results from the HRV analysis are shown in figures 1 and 2.

PEP – marginal linear model

A marginal linear model tested whether AC moderated the relationship between internalizing problems and PEP across conditions. The three-way interaction (Group × AC × Condition) was significant ($F(2, 93.5) = 4.26$, $p = .017$), indicating a significant moderating effect. Groups showed different PEP-responses to the film clip at different levels of AC. No control variables were significant including sex ($F(1, 44.2) = 3.44$, $p = .07$), age ($F(1, 44.2) = 0.04$, $p = .836$), BMI ($F(1, 44.2) = 0.29$, $p = .594$), film ($F(1, 44.2) = 0.94$, $p = .337$), and time of day ($F(1, 44.2) = 1.49$, $p = .228$). The significant interaction was interpreted with the estimated marginal means: at 1 SD above mean levels of AC, a significant change in PEP across conditions was found among patients ($F(2, 85.7) = 10.6$, $p < .001$). In this group (patients, higher AC), PEP increased significantly from baseline to the sad film clip

(3.89±0.86, 95% CI [1.80, 5.98], $p < .001$) and from baseline to recovery (2.65±0.86, 95% CI [0.56, 4.74], $p = .008$). Patients with lower AC showed no significant changes in PEP ($F(2, 85.7) = 1.24$, $p = .293$) nor did lower AC controls ($F(2, 85.7) = 0.79$, $p = .456$) or higher AC controls ($F(2, 85.7) = 0.45$, $p = .639$). The results from the PEP analysis are shown in figures 1 and 2.

The estimated marginal means showed significant differences in PEP between the patients and controls when AC was fixed at 1 SD above mean levels. PEP was significantly longer in patients with higher AC compared to higher AC controls during the sad film clip ($F(1, 45.4) = 8.59$, $p = .005$) and recovery ($F(1, 45.4) = 7.39$, $p = .009$) (figure 1). There were no significant differences between patients and controls when AC was fixed at 1 SD below mean levels.

Self-reported valence and arousal – generalized linear model

A generalized linear model tested whether AC moderated the relationship between internalizing problems and self-reported valence (SAM Valence) and arousal (SAM Arousal). The omnibus test was not significant for either the model predicting SAM Valence (Likelihood ratio $\chi2$ (6) = 8.8, $p = .185$) or the model predicting SAM Arousal (Likelihood ratio $\chi2$ (6) = 6.83, $p = .337$), suggesting that the overall effect was not significant. Thus, there was no significant effect of group status, AC or its interaction on self-reported valence or arousal.

Discussion

In the present study, the first hypothesis was supported. AC moderated the effect of internalizing problems on ANS regulation after the induction of negative affect; patients with internalizing problems showed different ANS responses during the sad film clip and recovery depending on the level of AC. Healthy controls showed no significant changes in ANS responses and displayed similar levels and direction of responses independent of AC level.

Patients with higher AC showed significantly longer PEP from baseline to the sad film clip and recovery and significantly increased HRV from baseline to recovery, indicating a PNS-dominated resting state during recovery. This could be interpreted as an adaptive response as a PNS-dominated resting state has been associated with adaptive functioning (Thayer & Lane, 2000, 2009). However, healthy controls did not display a similar response, and patients with higher AC showed significantly longer PEP during the sad film clip and recovery compared to higher AC controls. Thus, the increased PNS- and decreased SNS activity could represent a coping strategy. The results are interpreted in line with the predictions in the cognitive control model presented by Vasey et al. (2017); individuals with internalizing problems and higher AC might limit or suppress autonomic arousal in response to negative affect. The mechanism behind this response could be the efficient direction of attention to verbally-based worry. Worrisome thinking has previously been associated with inhibited heart rate response (Borkovec et al., 1993) and verbal compared to imaginal processing of negative stimuli has been associated with a greater decrease in SNS activity (Tucker & Newman, 1981). In individuals with GAD and higher levels of effortful control, a higher percentage of thoughts during worry predicted lower levels of self-reported autonomic arousal (Toh & Vasey, 2017). Predictions in the cognitive control model resonate well with the proposed importance of prefrontal top-down inhibitory control of ANS regulation presented in the neurovisceral integration model (Thayer & Lane, 2000, 2009).

Contrary to expectations, patients with lower AC showed no increased autonomic arousal; there were no significant changes in PEP or HRV from baseline to recovery. This group displayed a nonsignificant shortening in PEP values from baseline to recovery. Furthermore, they displayed significantly increased HRV in response to the sad film clip, and significantly decreased HRV from the sad film clip to resting recovery, approaching baseline values. On the one hand, HRV did return to baseline values during recovery, which could indicate a healthy response (Santucci et al., 2008). On the other hand, only patients with lower AC displayed significantly increased HRV during the sad film clip, which complicates the interpretation of the HRV response. A recent review points to the possibility that increased HRV in response to stressors could be associated with self-regulatory processes (Balzarotti, Biassoni, Colombo & Ciceri, 2017). Davis et al. (2016) found that children instructed to use either distraction or reappraisal showed a greater increase in HRV during both a sad film clip and a scary film clip, compared to controls who were only instructed to pay attention to the film. In the present study, patients with both higher and lower AC showed significant changes in ANS activity in response to the sad film clip, but in different branches of the ANS. Future studies could assess whether specific coping strategies or modes of worry are differentially associated with PNS or SNS activation.

There was no significant moderating effect in the prediction of HR. At both higher and lower levels of AC, patients and controls showed a decrease in HR during the sad film clip and an increase in HR from the sad clip to recovery (nonsignificant in the marginal model). Interestingly, patients with higher and lower AC displayed a similar decrease in HR, despite different responses in HRV and PEP. This could be an example in which the ANS can show different modes of activation, and in addition to a reciprocal activity of the PNS and SNS, activity of the two branches can be nonreciprocally coupled or uncoupled (Berntson, Cacioppo & Quigley, 1991).

The second hypothesis assumed that patients with lower AC would report the sad film clip as more negative (more negative valence, higher arousal) compared to patients with higher AC and controls. This hypothesis was not supported. There were no differences between groups on self-reported valence or arousal. Thus, the differences in ANS responses were not reflected in self-reported experience. A lack of coherence between sadness experience and cardiovascular activity has been reported previously (Mauss, Levenson, McCarter, Wilhelm, & Gross, 2005). Average ratings of valence and arousal indicated that children experienced a moderate level of arousal and a moderately negative-to-neutral valence. A stimulus experienced as more negative could perhaps have revealed significant differences between the groups on self-reported experience.

There were no significant differences between patients and healthy controls on baseline HRV. These results stand in contrast to the extensive literature showing a negative association between HRV and internalizing problems (e.g., Chalmers et al., 2014; Greaves-Lord et al., 2007; Koenig et al., 2016; Rottenberg, 2007). The nonsignificant difference in HRV between patients and controls could be explained by the small sample size. Moreover, patients in the present study were included at subclinical levels of internalizing problems, and the negative relationship between internalizing problems and HRV found in previous studies might be associated with more severe psychopathology (Beauchaine & Thayer, 2015; Koenig et al., 2016). As indicated in the introduction, inconsistent findings in the literature on HRV (Fisher & Newman, 2013; Hamilton & Alloy, 2016; Koenig et al., 2016; Kogan, et al., 2013; Licht et al., 2009; Licht et al., 2008) and PEP (Byrne et al., 2010; Licht et al., 2012) point to a greater complexity in the relationship between ANS activity and internalizing problems. Interestingly, the finding in the present study that patients showed significantly longer baseline PEP compared to controls was not significant in the marginal linear model. In this model, patients showed significantly longer PEP during the sad film clip and recovery, and

only at higher levels of AC. Furthermore, AC moderated the relationship between internalizing problems and HRV, and the effect was particularly evident during the sad film clip and recovery. This could indicate that, as suggested by Vasey et al. (2017), aspects other than internalizing symptoms, such as level of AC, can contribute to explaining variance in autonomic arousal.

Conclusion and Clinical implications

The main finding in the present study was that AC moderated the effect of internalizing problems on ANS regulation after the induction of negative affect. Patients with lower or higher AC displayed activation in different branches of the ANS in response to the film clip, and a PNS-dominated state continued throughout recovery for patients with higher AC only. These responses might indicate self-regulatory efforts to deal with negative affect, which is a plausible explanation given that responses differed from healthy controls. The exact interpretation of these results remains unclear, especially what strategies were employed and how they were linked to the heterogeneous levels of AC and ANS activity. One interpretation could be that patients with lower AC employed distraction or reappraisal in response to the film, as these strategies have been associated with increased HRV (Balzarotti et al., 2017; Davis et al., 2016). Patients with higher AC showed a continued decrease in autonomic activity throughout recovery and might have redirected attention from the negative stimulus to verbal worry. Worrying in a verbal manner, or verbal processing of negative stimuli, has been associated with inhibited autonomic arousal (Borkovec et al., 1993; Tucker & Newman, 1981). These interpretations are speculative and could be explored in future studies.

A central proposition in the present study was that individuals with internalizing problems might use different strategies when they experience negative affect depending on their capability for top-down cognitive control. The field should continue to explore how individuals with internalizing problems could benefit from adjustments of psychotherapy according to individual differences in cognitive control. If patients frequently switch to cognitive coping strategies to avoid unpleasant autonomic arousal, they might need to practice how to direct attention properly to adequately deal with negative thoughts and feelings (Derryberry & Reed, 2002; Hirsch & Mathews, 2012). If patients frequently struggle to disengage attention from negative stimuli and are overwhelmed by negative affect, as has been indicated by other studies (Derryberry & Reed, 2002; Vasey et al., 2017), they might need a different type of support during therapy, perhaps intensively directed at the intersubjective regulation of both ANS activity and attention (Bentzen, 2015). Shirk, Talmi, and Olds (2000) emphasize that from a developmental psychopathology perspective, treatment guidelines should not exclusively depend on diagnosis. Instead, they suggest flexible treatment guidelines that consider the pathogenic processes implicated in the development and maintenance of a clinical problem. Different patients with the same diagnosis may require different adjustments of therapy – or different treatments.

Limitations

Our sample size was modest and only powered to detect large effect sizes (Quintana, 2017), and the results should be evaluated against this limitation. The hypotheses in the present study should be explored in future studies with larger samples.

The present study did not control for respiration. While controlling for respiration has been recommended (Quintana & Heathers, 2014), Penttilä et al. (2001) found that RMSSD

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was less affected by respiration compared to frequency domain measures of HRV. Time since last meal was not included in the present study, which could be a limitation. Food intake was shown to significantly affect both HRV and PEP in a study of healthy adults (Sauder, Johnston, Skulas-Ray, Campbell & West, 2012). Including measures of attentional performance in addition to parent-reported AC would have strengthened the design. However, parent-reported temperament (including AC) is generally considered a fruitful and valid way of measuring temperamental constructs (Wachs & Bates, 2010), and parent-reported effortful control was associated with performance on a standardized clinical battery assessing attention in children (Verstraeten et al., 2010).

The present study did not include a structured diagnostic interview to assess diagnosis and relied only on results from the parent-reported Child Behavior Checklist (CBCL) and the unstructured clinical assessment of specialists in Clinical Child and Adolescent Psychology. The chosen procedure was considered sufficient; however, we acknowledge that the study could have benefited from a structured diagnostic interview. There are both similarities and distinctive features characterizing depression and anxiety disorders (Brown, Chorpita & Barlow, 1998), and the question of whether or not it is more meaningful to study internalizing disorders in childhood in separate diagnostic categories remains an empirical question (Tandon, Cardeli, & Luby, 2009). The present study included children with high levels of both anxiety and depressive symptoms, which are assumed to represent a population commonly seen in mental health care. The cognitive control model (Vasey et al., 2017) is specifically centered on GAD and worry, and future studies could assess the moderating effect of AC on ANS regulation within specific diagnostic groups. Furthermore, the present study did not assess worry. While worry has been associated with lower HRV in some studies (e.g. Chalmers, Heathers, Abbott, Kemp, & Quintana, 2016), there are inconsistencies in this literature as well (as reviewed by Vasey et al., 2017). The association between different

modes of worry (i.e. imaginal vs. verbal) and ANS activity could be a topic for future investigation.

There were no baseline measures of self-reported valence and arousal. Furthermore, valence and arousal were not measured directly after the sad film clip but immediately after the recovery period. Contact with the experimenter prior to recovery could have represented a second stressor, thus complicating the interpretation of the results. The chosen procedure has important limitations: First, self-reports were not compared to a baseline, which could mask important differences. Second, self-report after recovery could be a measure of self-regulation, rather than experiences directly related to the film clip, as valence and arousal levels could be affected by how well participants coped with the negative affect during recovery. We suggest that future studies consider the inclusion of self-reported valence and arousal at several time points throughout the experiment.

The design of the present study allows for no definitive conclusions concerning the directionality of the relationship between the included variables. The neurovisceral integration model delineates the interconnectedness among the CNS, the ANS and affective and attentional processes, serving as an important theoretical framework for future studies (Thayer & Lane, 2000, 2009).

Conflicts of Interest

The authors declare that there are no conflicts of interest related to this article.

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Table 1. Descriptive statistics and between-group differences

Variable	Group	N	M (SD)	Median	P-value*
Age (years)	Patients	29	10.7 (1.27)	10.5	.060
	Controls	25	10.1 (1.08)	10	
BMI	Patients	29	17.2 (2.95)	16.6	.435
	Controls	25	17.5 (2.46)	17.5	
CBCL *Anxiety problems*	Patients	29	68.5 (4.85)	70	**<.001**
	Controls	25	51.6 (3.27)	50	
CBCL *Affective problems*	Patients	29	66.9 (7.29)	67	**<.001**
	Controls	25	52.2 (3.50)	50	
AC (EATQ-R)	Patients	29	3.28 (0.69)	3.33	.188
	Controls	25	3.57 (0.60)	3.50	
SAM Valence – after film clip	Patients	29	4.16 (1.47)	4	.218
	Controls	25	4.64 (1.78)	5	
SAM Arousal – after film clip	Patients	29	4.97 (1.94)	5	.944
	Controls	25	5.16 (1.70)	5	

Note: BMI = body mass index, CBCL = Child Behavior Checklist (T Scores), AC = attentional control, EATQ-R = Early Adolescent Temperament Questionnaire – Revised, SAM = Self-Assessment Manikin, M = mean, SD = standard deviation. * Statistical significance for differences between patients and control group from Mann-Whitney U-test. Bold = $p < .05$.

Table 2. Psychophysiological variables and between-group differences

Variable	Group	N	Baseline M (SD)	Sad film clip M (SD)	Recovery M (SD)	P-value* between groups
HR	Patients	29	78.4 (8.12)	73.7 (7.50)	79.4 (7.85)	Baseline: .327
	Controls	25	80.5 (8.98)	78.1 (7.91)	80.7 (7.67)	Sad film: .069
						Recovery: .684
HRV (RMSSD)	Patients	29	75.6 (45.3)	86.0 (53.2)	83.7 (41.4)	Baseline: .482
	Controls	25	66.9 (39.8)	61.8 (30.1)	70.3 (31.9)	Sad film: .103
						Recovery: .362
PEP	Patients	28	122.2 (6.19)	123.4 (6.94)	122.6 (6.71)	Baseline: **.012**
	Controls	25	117.6 (6.00)	118.5 (5.25)	117.7 (5.29)	Sad film: **.004**
						Recovery: **.004**

Note: HR = heart rate, HRV = heart rate variability, RMSSD = root mean square of successive differences, PEP = pre-ejection period. M = mean, SD = standard deviation. * Statistical significance for differences between patients and control group from Mann-Whitney U-test. Bold = $p < .05$.
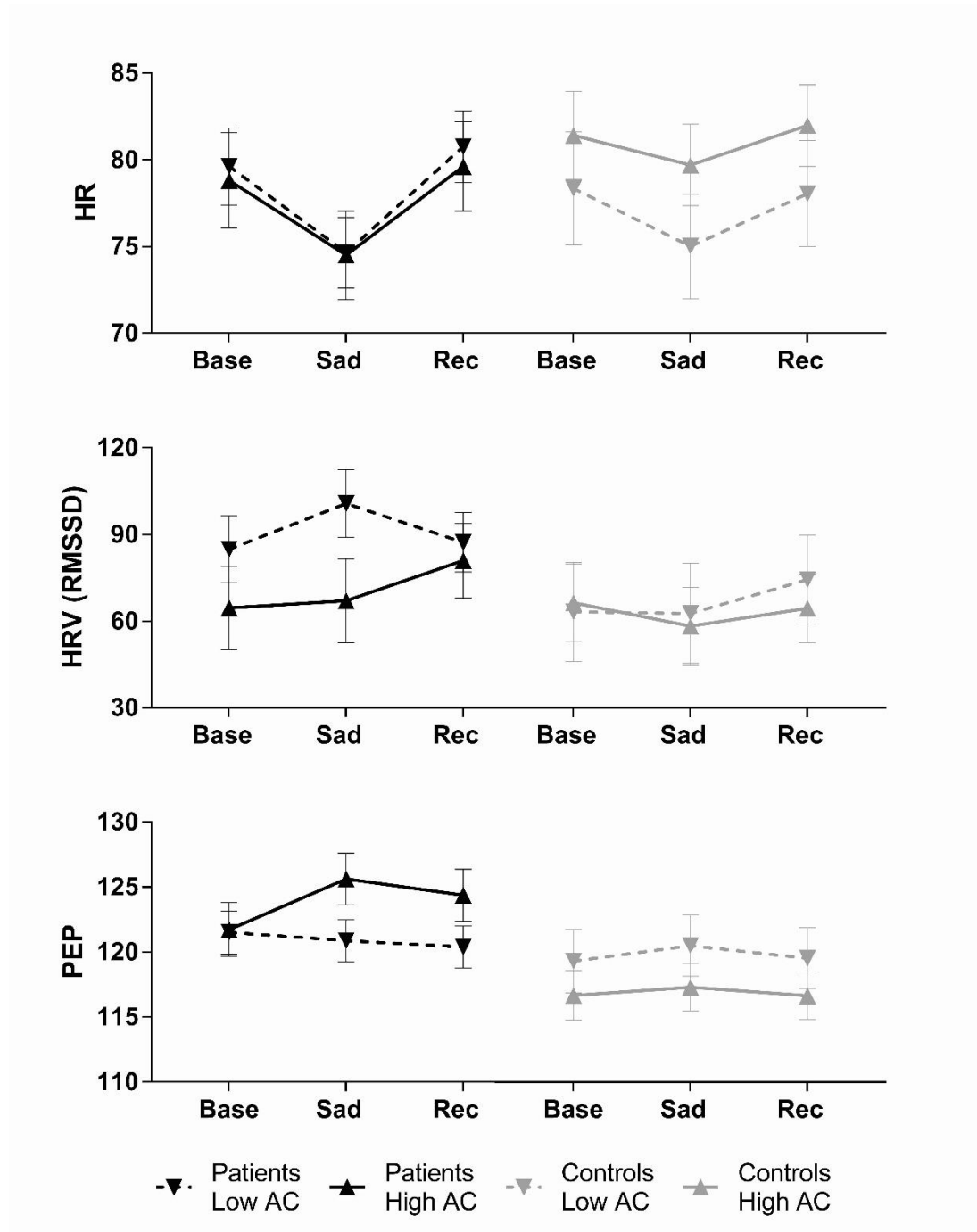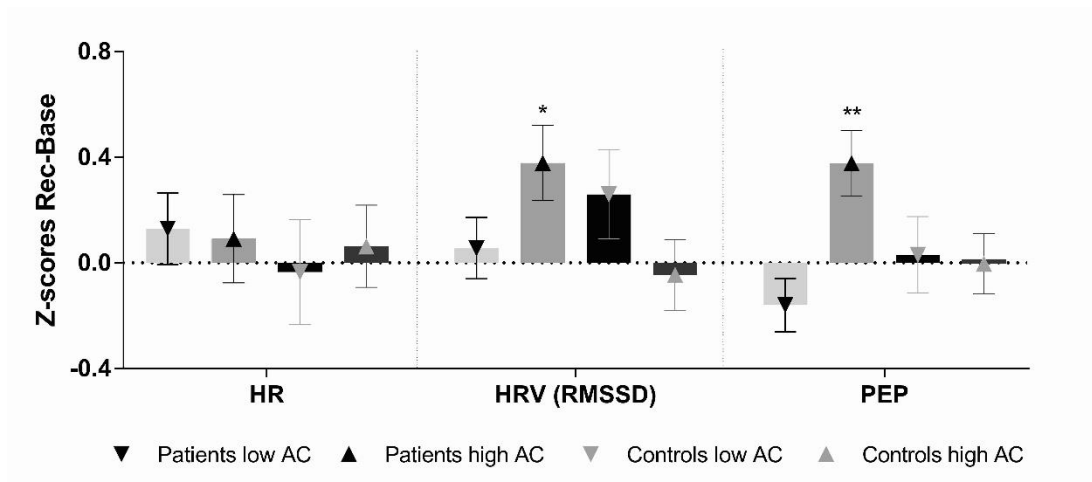
Figures

Figure 1.

Figure 2.

Figure legends

Figure 1. Moderating effect of attentional control (AC) on the relationship between group status (patients/controls) and heart rate (HR), heart rate variability (HRV) and pre-ejection period (PEP). RMSSD = root mean square of successive differences. Base = baseline, Sad = sad film clip, Rec = recovery. Low/high AC = the value of AC fixed at ±1 SD in the estimated marginal means. Triangles represent estimated means and error bars represent standard error of the mean.

Figure 2. Standardized reactivity scores (z-scores) of estimated mean differences in heart rate (HR), heart rate variability (HRV) and pre-ejection period (PEP) between recovery – baseline (positive scores indicate higher levels during recovery) for patients and controls at lower and higher levels of attentional control (AC). RMSSD = root mean square of successive differences. Low/High AC = value of AC fixed at ±1 SD in the estimated marginal means. *p < .05. **p < .01.