City Research Online

City, University of London Institutional Repository

This is the published version of the paper.

This version of the publication may differ from the final published version.

Permanent repository link: http://openaccess.city.ac.uk/20625/

Link to published version: http://dx.doi.org/10.1016/j.jcrimjus.2018.01.004

City Research Online: http://openaccess.city.ac.uk/   publications@city.ac.uk

Resting autonomic nervous system activity is unrelated to antisocial behaviour dimensions in adolescents: Cross-sectional findings from a European multi-centre study

Martin Prätzlich[a,*,1], Helena Oldenhof[b,1], Martin Steppan[a], Katharina Ackermann[g], Rosalind Baker[f], Molly Batchelor[c], Sarah Baumann[h], Anka Bernhard[g], Roberta Clanton[f], Dimitris Dikeos[k], Roberta Dochnal[j], Lynn Valérie Fehlbaum[a], Aranzazu Fernández-Rivas[i], Maider González de Artaza-Lavesa[i], Karen Gonzalez-Madruga[c], Silvina Guijarro[m], Malou Gundlach[h], Beate Herpertz-Dahlmann[h], Amaia Hervas[m], Lucres Jansen[b], Iñaki Kerexeta-Lizeaga[i], Linda Kersten[a], Marietta Kirchner[l], Gregor Kohls[h], Angeliki Konsta[k], Helen Lazaratou[k], Anne Martinelli[g], Willeke Martine Menks[a], Ignazio Puzzo[d], Nora Maria Raschle[a], Jack Rogers[f], Réka Siklósi[j], Areti Smaragdi[c], Noortje Vriends[a], Kerstin Konrad[h], Stephane De Brito[f], Graeme Fairchild[e], Meinhard Kieser[l], Christine M. Freitag[g], Arne Popma[b], Christina Stadler[a]

[a] University of Basel Psychiatric Hospital, Department of Child and Adolescent Psychiatry, Basel, Switzerland
[b] Departments of Child and Adolescent Psychiatry, VU University Medical Center, Amsterdam, Netherlands
[c] Department of Psychology, University of Southampton, Southampton, England, United Kingdom
[d] Broadmoor High Secure Hospital, West London Mental Health NHS Trust, Crowthorne, England, United Kingdom
[e] Department of Psychology, University of Bath, Bath, England, United Kingdom
[f] School of Psychology, University of Birmingham, Birmingham, England, United Kingdom
[g] Department of Child and Adolescent Psychiatry, Psychosomatics and Psychotherapy, University Hospital Frankfurt, Goethe University, Frankfurt am Main, Germany
[h] Department of Child and Adolescent Psychiatry, Psychosomatics and Psychotherapy, University Hospital of the RWTH, Aachen, Germany
[i] Basurto University Hospital, Bilbao, Spain
[j] Faculty of Medicine, Child and Adolescent Psychiatry, Department of the Child Health Center, Szeged University, Szeged, Hungary
[k] Children and Adolescents Mental Health Unit of Athens University, Athens, Greece
[l] Institute of Medical Biometry and Informatics, University of Heidelberg, Heidelberg, Germany
[m] Child and Adolescent Mental Health Unit, University Hospital Mutua Terrassa, Barcelona, Spain

ARTICLE INFO

ABSTRACT

Purpose: Autonomic nervous system (ANS) functioning has long been studied in relation to antisocial behaviour, but relevant measures (heart rate, heart rate variability, pre-ejection period, respiration rate) have rarely been considered together. This study investigated the relationship between these measures and antisocial behaviour.
Methods: Using a sample of 1010 youths with (47.8%) and without conduct disorder (52.2%) aged between 9 and 18 years (659 females, 351 males, mean age = 14.2 years, SD = 2.4), principal component analysis (PCA) was applied to various measures of psychopathology and antisocial behavior. Structural equation modelling was performed in order to test whether the ANS measures predicted PCA-dimensions. Cluster analysis was used in order to classify patterns of ANS activity. Analyses were performed separately for males/females and controlled for body-mass-index, age, caffeine use, cigarette smoking, sports, socioeconomic status, medication, cardiac problems.
Results: The PCA yielded three components: antisocial behaviour/comorbid psychopathology, narcissistic traits, and callous-unemotional traits. ANS measures were only weakly correlated with these components. Cluster analysis yielded high and low arousal clusters in both sexes. When controlling for covariates, all associations disappeared.

* Corresponding author at: University of Basel Psychiatric Hospital, Department of Child and Adolescent Psychiatry, Schanzenstrasse 13, CH-4056 Basel, Switzerland.
  E-mail address: martin.praetzlich@upkbs.ch (M. Prätzlich).
  [1] Both authors contributed equally.

Conclusion: Our findings suggest that resting ANS measures are only weakly related to antisocial behaviour and indicate that smoking should be considered as an important covariate in future psychophysiological studies.

1. Introduction

Autonomic nervous system (ANS) functioning has long been studied in relation to antisocial behaviour (see Portnoy et al., 2014). Antisocial behaviour can be characterized by conduct problems, aggression, psychopathic tendencies, and also comprises delinquent behaviour. Together these represent major public health and societal concerns (Portnoy & Farrington, 2015). Conduct disorder is one clinical manifestation of severe antisocial behaviour and its diagnostic criteria include aggressive (e.g., fighting, bullying, vandalism) and rule-breaking behaviour in children and adolescents (e.g., lying, theft, truancy; (American Psychiatric Association, 2013)). Due to the heterogeneity of antisocial behaviour and conduct disorder, a number of attempts have been made to characterize various subtypes or phenotypes, e.g., proactive/reactive aggression, conduct disorder with elevated psychopathic/callous-unemotional traits or in combination with internalizing symptoms or previous traumatic experiences (Steiner, Daniels, Stadler, & Kelly, 2017). Callous-unemotional traits comprising a lack of empathy, reduced guilt or reduced affective responding have been identified as important subtyping characteristics of children and adolescents with antisocial behaviour, although callous-unemotional traits can also occur in typically-developing children and adolescents (Fanti, Demetriou, & Kimonis, 2013; Herpers, Rommelse, Bons, Buitelaar, & Scheepers, 2012; Raschle et al., 2017). On a physiological level, different ANS measures have been used to identify ANS deficits in antisocial populations, and linked to some of the neurocognitive difficulties that they show, such as impairments in emotion regulation or reward processing (Fanti, 2016; Matthys, Vanderschuren, & Schutter, 2013). However, most of the studies have used just a single measure of ANS functioning, such as heart rate (Portnoy & Farrington, 2015), whereas multiple measures are needed to provide a more comprehensive assessment of ANS profiles associated with antisocial behavior. Therefore, this study aims to investigate simultaneously four cardiorespiratory ANS markers, in order to shed more light on the links between the ANS and antisocial behavior. Furthermore, the measurement of multiple ANS parameters allows for a clustering of ANS measures which might reconcile inconsistencies caused by differences in assessment of psychopathological phenotypes (Fanti, 2016). In contrast to investigating categorically defined diagnoses, we will use a comprehensive assessment approach considering a broad spectrum of antisocial behavior and adopting a dimensional approach. For a categorical approach on this dataset, please see Oldenhof et al. (this volume).

1.1. Cardiorespiratory ANS measures and antisocial behaviour

Four cardiorespiratory ANS markers measuring sympathetic (SNS) and/or parasympathetic nervous system (PNS) activity have previously been related to antisocial behavior: (1) heart rate (SNS and PNS activity), (2) heart rate variability (PNS activity), (3) pre-ejection period (SNS activity), and (4) respiration rate (SNS and PNS activity). Several meta-analyses have confirmed low resting heart rate as a robust physiological correlate of antisocial behaviour including, e.g., aggression, psychopathy and conduct and oppositional defiant disorders (Ortiz & Raine, 2004; Portnoy & Farrington, 2015). Heart rate variability, in particular respiratory sinus arrhythmia, can be an indicator of cardiac PNS activity and is commonly quantified by spectral or time-domain analytic approaches (Grossman & Taylor, 2007). These approaches can also be used to derive many other parameters of heart rate variability (Allen, Chambers, & Towers, 2007). Reduced resting heart rate variability has been linked to externalizing and antisocial behaviour

(Beauchaine, Gatzke-Kopp, & Mead, 2007; Graziano & Derefinko, 2013) and seems to be linked to lower emotion regulation abilities (Thayer, Ahs, Fredrikson, Sollers, & Wager, 2012; Williams et al., 2015). Pre-ejection period has previously been associated with reward processing which is affected in conduct and oppositional defiant disorders (Matthys et al., 2013; Sidlauskaite et al., 2017). Thereby, a lengthened resting pre-ejection period - indicating less sympathetic activity - was found in relation to conduct problems and aggression in children (Beauchaine et al., 2013). Finally, research has increasingly recognized the importance of respiration in relation to cognitive and emotional processing (Zelano et al., 2016), which are impacted in antisocial youth (Raschle, Menks, Fehlbaum, Tshomba, & Stadler, 2015). A higher respiration rate has been associated with severity of internalizing problems in girls (Blom, Serlachius, Chesney, & Olsson, 2014) and respiration rate has been linked to emotions such as anger, disgust and anxiety (Kreibig, 2010). While an association between aggressive behaviour and respiration rate has been found in animals (Carnevali, Nalivaiko, & Sgoifo, 2014), respiration rate has not yet been investigated as a correlate of aggressive or antisocial behaviour in humans. The Polyvagal Theory has been used to explain the link between the ANS and antisocial behaviour (Beauchaine et al., 2007). Despite its highly regarded, explanatory role for research findings of psychopathology and emotion dysregulation (Beauchaine et al., 2007), its biological validity has been questioned, and the basic assumptions of the theory appear to have been falsified (Farmer, Dutschmann, Paton, Pickering, & McAllen, 2016; Gourine, Machhada, Trapp, & Spyer, 2016; Grossman, 2016; Grossman & Taylor, 2007).

1.2. Biological mechanisms

Neuroimaging studies have revealed biological mechanisms behind the autonomic arousal and antisocial behaviour relationship: Brain regions involved in autonomic control and emotion regulation partly overlap (Thayer et al., 2012; Thayer & Lane, 2000) and exhibit structural and functional alterations in youths with aggression (Raschle et al., 2015) and conduct problems (Rogers & De Brito, 2016). Aggression can be considered as deficient emotion regulation which reflects abnormalities in the underlying emotion regulation network of the brain (Davidson, Putnam, & Larson, 2000). The neuro-visceral integration model elaborates on the role of one of the affected regions, the prefrontal cortex, for emotional, cognitive and autonomic regulation (Thayer & Lane, 2009). Thus, the overlap of emotion and autonomic regulation warrants the use of ANS measures for the study of aggressive behaviour.

1.3. Gaps in the literature

Overall, it can be concluded that there is substantial evidence linking ANS markers with different aspects of antisocial behaviour. However, the four ANS markers have rarely been included together in the same study. Further, many previous studies had small sample sizes. In addition, numerous studies have highlighted the importance of including sex in the description of antisocial behavior dimensions and ANS activity (e.g., Koenig & Thayer, 2016; Lehto-Salo, Närhi, Ahonen, & Marttunen, 2009), but this has rarely been done. The majority of studies on ANS activity and antisocial behaviour have not systematically controlled for lifestyle factors that may differ between typically-developing and antisocial groups (Portnoy & Farrington, 2015), even though smoking, sports, caffeine use, body mass index (BMI), medication use, and socio-economic status have all been shown to influence

ANS functioning and/or psychopathology (Alvares, Quintana, Hickie, & Guastella, 2016; Hu, Lamers, de Geus, & Penninx, 2017; Koenig et al., 2014; Martin et al., 2008; Piotrowska, Stride, Croft, & Rowe, 2015). In particular, the influence of smoking has only been examined in a few studies (Jennings, Piquero, & Farrington, 2013; Murray et al., 2016), despite evidence indicating that smoking constitutes a risk factor for the development of antisocial behaviour and impacts brain and ANS functioning (Hu et al., 2017; Pagani, Lévesque-Seck, Archambault, & Janosz, 2017).

1.4. Research aims

We aimed to disentangle the role of different ANS parameters in antisocial behaviour using data collected as part of a European multi-centre study (FemNAT-CD), with a specific focus on gender differences. We hereby aim to overcome several limitations of the previous literature by: (I) including two mixed measures capturing both SNS and PNS activity (i.e. heart rate and respiration rate) and two measures capturing PNS (i.e. heart rate variability) and SNS (i.e. pre-ejection period) activity separately. This approach allows us (II) to identify distinct physiological phenotypes and relate them to antisocial behaviour. As respiration rate has only been investigated in animal research, we also studied the link between respiration rate and antisocial behavior (III). Moreover, we consider (IV) the influence of covariates such as smoking, sports, caffeine, BMI, medication, cardiac problems and socio-economic status. We set out to investigate our research aims in a sample including individuals with and without conduct disorder. In line with previous literature, we hypothesized that we would observe negative correlations between heart rate and respiratory sinus arrhythmia and antisocial behaviour, whereas we predicted that pre-ejection period and respiration rate would be positively correlated with antisocial behaviour. Further, we hypothesized that different ANS clusters would be associated with measures of antisocial behaviour.

2. Methods

2.1. Recruitment and participants

1010 adolescents (659 females, 351 males; 47.8% with conduct disorder and/or oppositional defiant disorder) aged between 9 and 18 years (mean = 14.2, SD = 2.4) were included in the study as part of an ongoing European multi-centre study investigating female conduct disorder (FemNAT-CD). The distribution of comorbidity patterns was as follows: conduct and oppositional defiant disorder (64.5%), conduct disorder only (23.7%), oppositional defiant disorder only (11.8%). A more detailed description of the sample characteristics (including ANS values) is provided in the article by Oldenhof et al. (this volume). The participants were recruited through schools, clinics, and youth welfare institutions in seven European countries (Germany, Greece, Hungary, Netherlands, Spain, Switzerland, and United Kingdom). All participants underwent standardized clinical interviews, filled out questionnaires and took part in an ANS measurement session. All individuals had to have an IQ ≥ 70 (see Fig. 1 for inclusion and exclusion criteria). Patients were diagnosed with conduct disorder based on a semi-structured clinical interview (please see Section 2.2.2 below for details of the assessment). Written informed consent was obtained from the participants and their caretakers. The study was conducted in accordance with the Declaration of Helsinki and approved by all local ethics committees.

2.2. Materials

2.2.1. ANS measures

ANS measures were assessed using electrocardiography (ECG) and impedance cardiography (ICG) registration by the VU-AMS device (Vrije Universiteit Ambulatory Monitoring System) (de Geus, Willemsen, Klaver, & van Doornen, 1995). H98SG, ECG Micropore

electrodes (Covidien, Germany) were used and applied to the skin which was cleaned with alcohol beforehand. The R-peak time series were derived from the ECG data by an automated detection algorithm within the VU-DAMS software package version 3.9 and checked manually for missed or incorrect R-wave peaks and abnormalities in the registration. Abnormalities defined as premature ventricular contractions (PVCs), premature atrial contractions (PACs) or low quality ECG signal fragments were removed from the data. Ensemble averaged ECG and ICG complexes were derived from all valid heartbeats. In the ensemble averaged ECG, the Q-onset was detected and in the ensemble averaged ICG, the B-point, dZ/dt-min peaks and X-points were identified by an algorithm within the VU-DAMS software package. All scoring in the ensemble averaged complexes was again checked manually. Data on respiration rate was derived from the dZ-signal (thorax impedance), and identified as 'irregular respiration' when the duration of consecutive breaths reached a threshold. Whenever > 50% of the respiration data was identified as 'irregular', respiration rate data was set as missing. Data checking and scoring were performed by trained researchers and students and additional consensus meetings took place in order to discuss complex data.

Heart rate in beats per minute was derived from the ECG signal derived R-peak time series and respiration rate in breaths per minute was derived from the thorax impedance signal. To investigate heart rate variability, as a measure of PNS activity, respiratory sinus arrhythmia was assessed. Respiratory sinus arrhythmia was calculated using the peak-valley method (Grossman, Beek, & Wientjes, 1990) by subtracting the shortest heart period during inspiration minus the longest heart period during expiration; this was computed on a breath-to-breath basis. When no difference in shortest and longest beats could be detected, respiratory sinus arrhythmia was set to be zero for that particular breath. Respiratory sinus arrhythmia values were set as missing when > 50% of the breaths could not be detected or were identified as 'irregular'.

Cardiac SNS activity was measured by the pre-ejection period (in ms). This is currently the most reliable non-invasive indicator of SNS activity (van Lien, Schutte, Meijer, & de Geus, 2013) and can be derived from combined ICG and ECG recording. Pre-ejection period is defined as the time period between the onset of the left ventricular depolarization and the opening of the aortic valve. These events are marked respectively by the Q-wave onset in the ECG and the B-point in the ICG.

Baseline measurement – After the ECG/ICG electrodes were applied to the participant's body, they were given 10 min to habituate to the procedure. This enabled the participant to get accustomed to the setting in order to minimize the effect of stress induced by the experimental setting. Thereafter, a 5-minute excerpt from an aquatic video (Coral Sea
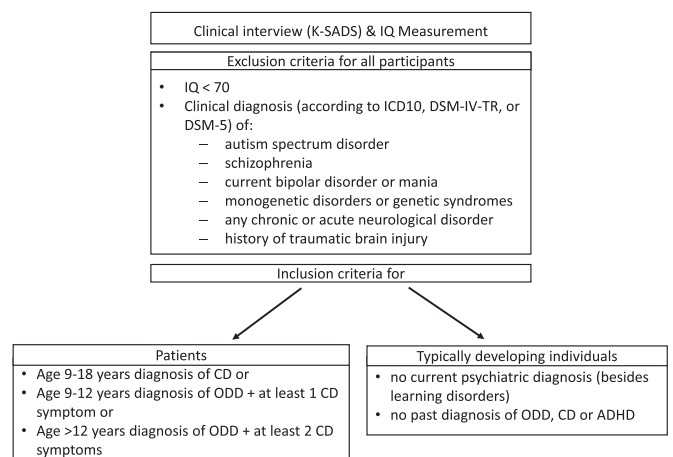

Fig. 1. Inclusion and exclusion criteria in the study. CD = conduct disorder; ODD = oppositional defiant disorder; ADHD = attention deficit hyperactivity disorder.

Dreaming, Small World Music Inc.) was presented to obtain baseline ANS measures, which was proven effective in a previous study (Piferi, Kline, Younger, & Lawler, 2000). The video was presented on a DELL Latitude E5550 Laptop and Sennheiser HD 201 earphones were used.

Prior to the physiological assessment, participants were asked whether they had smoked in the past hour or consumed alcohol or used drugs in the past 24 h. If they answered positively to any of these questions, the assessment was postponed.

2.2.2. Behavioural measures

2.2.2.1. Conduct disorder. Diagnostic information was obtained through the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL) (Kaufman et al., 1997). The K-SADS-PL is a standardized, semi-structured clinical interview assessing current and past episodes of psychopathology in children and adolescents according to DSM-IV-TR/ DSM-5 criteria (American Psychiatric Association, 2000, 2013). Interviews were conducted with the participant and their parent or caretaker separately. Additionally, information from medical files was used in some cases. Summary ratings are derived from the clinical judgment of the interviewer using all available sources.

2.2.2.2. IQ. In case of missing IQ measurements, the IQ was estimated using two subtests of the Wechsler Intelligence Scale for Children: vocabulary and block design, or for participants from the age 17 on the Wechsler Adult Intelligence Scale (Petermann & Wechsler, 2008): vocabulary and matrix reasoning. At UK sites, the Wechsler Abbreviated Scale of Intelligence (WASI) was used for all ages (Wechsler, 1999).

2.2.2.3. Psychopathic traits. We used the self-report version of the Youth Psychopathic traits Inventory (YPI) (Andershed, Kerr, Stattin, & Levander, 2002) to assess psychopathy. This questionnaire consists of 50 items scored on a 4-point Likert scale from 1 to 4, ranging from "Does not apply at all" to "Applies very well". The YPI comprises the following ten subscales: dishonest charm, grandiosity, lying, manipulation, remorselessness, unemotionality, callousness, thrill seeking, impulsiveness, irresponsibility. In our study, the subscales dishonest charm ($\alpha = 0.80$) and manipulation ($\alpha = 0.81$) showed good, the subscales lying ($\alpha = 0.77$), remorselessness ($\alpha = 0.72$), impulsiveness ($\alpha = 0.72$) and irresponsibility ($\alpha = 0.75$) acceptable, the subscales grandiosity ($\alpha = 0.68$), unemotionality ($\alpha = 0.60$) and thrill seeking ($\alpha = 0.66$) questionable and the scale callousness ($\alpha = 0.57$) poor internal consistency.

2.2.2.4. Comorbid psychopathology. We used the Massachusetts Youth Screening Instrument Version 2 (MAYSI-2) (Grisso & Barnum, 2006) to screen for a variety of comorbid psychopathological symptoms. The MAYSI-2 is a self-report tool developed to facilitate identification of youths with mental health issues within juvenile-justice facilities. The version we used in our study consists of 48 'yes' or 'no' questions regarding the past 2–3 months. The instrument contains seven scales: 'alcohol/drug use' (ADU), 'angry-irritable' (AI), 'depressed-anxious' (DA), 'somatic complaints' (SC), 'suicide ideation' (SI), 'thought disturbance' (TD), and 'traumatic experiences' (TE). The scales ADU ($\alpha = 0.89$), AI ($\alpha = 0.85$), DA ($\alpha = 0.79$), SC ($\alpha = 0.75$), SI ($\alpha = 0.89$) showed good, the TD scale ($\alpha = 0.64$) sufficient and the TE scale showed poor ($\alpha = 0.52$) internal consistencies in our study, possibly due to the use of a shortened version of this scale containing only 2 items instead of 5.

2.2.2.5. Aggression. We used the Reactive-Proactive aggression Questionnaire (RPQ) (Raine et al., 2006) to distinguish between these types of aggression. The questionnaire consists of 23 items on a 3-point Likert scale from 0 to 2, ranging from "never" to "often". The proactive and reactive scales are sum scores of the respective items. The reactive

($\alpha = 0.88$) and proactive ($\alpha = 0.86$) scales showed good internal consistency in our study.

2.2.3. Covariates

2.2.3.1. Body mass index. Weight and height were measured on the day of the physiological assessment for the calculation of participants' body mass index (BMI).

2.2.3.2. Caffeine. We assessed caffeine use on the day of the physiological assessment by asking the participants: "How many caffeine-containing drinks (e.g., coffee, tea, coke, energy drinks) have you consumed in the past 24 hours?".

2.2.3.3. Smoking. We assessed smoking on the day of the physiological assessment by asking the participants: "How many cigarettes do you smoke on an average day?" (cigarettes/day).

2.2.3.4. Sports. We asked the participants on the day of the physiological assessment "How many hours a week do you practice sports?" (hours/week).

2.2.3.5. Socioeconomic status. Socioeconomic status (SES) was estimated based on parental income, education and occupation. Assessments were based on the International Standard Classification of Occupations (International Labour Organization, 2012) and the International Classification of Education (UNESCO Institute for Statistics, 2015). Human rater and computer-based ratings were combined into a factor score using Principal Component Analysis (PCA). Reliability (internal consistency) of the composite SES score was acceptable ($\alpha = 0.74$).

2.2.3.6. Medication. We assessed psychotropic medication by asking the participant, caretaker, therapist or parent. For the analysis, we integrated the information as a dichotomous variable (0 = no medication and 1 = medication).

2.2.3.7. Cardiac problems. We assessed cardiac problems as a dichotomous variable (yes/no) by asking the participant: "Have you had any heart problems in the past?" (e.g., cardiac arrhythmia/heart surgery).

2.3. Statistical analyses

2.3.1. ANS measures – data cleaning and preparation

Statistical analyses were performed using SPSS Version 24/AMOS Version 24 and R Version 3.4.2. Before analysis, data cleaning was applied to all ANS measures. We log-transformed respiratory sinus arrhythmia (lgRSA) due to a right-skewed distribution which became closer to a normal distribution after transformation. Values higher or lower than 3 SD of the sample means were classified as outliers and excluded. For respiration rate we identified 5 outliers, for heart rate 1 missing value and 7 outliers, for pre-ejection period there were 50 missing values and 1 outlier, and for the respiratory sinus arrhythmia data 8 outliers. Additionally, for respiration rate we excluded all values which contained > 50% of irregular respiration (identified by the VU-DAMS programme) in the 5 min baseline which was the case for 6 values. The respective respiratory sinus arrhythmia values were excluded as well. Subsequently, we checked whether the number of missing values and outliers differ in a systematic way between groups (gender and patient status). Summing up the number of missing values and outliers for all four ANS measures per individual, ANOVA was performed to identify group (gender and patient status) biases. No differences were observed between the groups. The values were excluded on a single value basis, id est, if for example the pre-ejection period value was excluded, the other ANS values of this participant were still included for analysis. Several analyses were conducted to

identify potential site effects on ANS measures, e.g., due to differences in use of technical devices, climate or other local circumstances. Using a saturated model Analysis of Variance (ANOVA) on ANS measures (as dependent), patient status and gender (as fixed factors), site (as random factor) and age and testing time (as covariates), site did neither emerge as a significant main effect, nor within a significant interaction term, suggesting no bias caused by site effects.

2.3.2. Main statistical analyses

Principal Component Analysis (PCA) was performed separately for each sex, extracting orthogonal (uncorrelated) components with an Eigenvalue > 1 (Kaiser-Guttmann criterion). Standardized scores on PCA components for each individual were saved based on Bartlett-Regression. Bivariate correlations were conducted between the ANS measures, principal components and covariates. In a second step, partial correlations were used to control for the influence of covariates. Structural Equation Modelling (SEM) was performed using AMOS, with ANS measures, age and smoking as predictors and PCA components as outcome variables. Sex was included based on a two-group approach, allowing varying beta-coefficients for all paths and one common model fit for both sexes. Cluster Analysis was performed using R. At first, the R package "Mclust" (Fraley, Raftery, Murphy, & Scrucca, 2012) was used to identify the number of clusters using Bayesian Information Criterion (BIC) as a goodness-of-fit index. In a second step, k-means clustering (R package "stats") was used to assess cluster membership for each individual based on the number of identified clusters in the first step. Cluster analysis was performed only on (standardized) ANS measures as continuous input variables, no questionnaires or other psychometric variables were included for cluster identification. Analyses of Variance (ANOVA) were applied in order to test whether clusters differed on questionnaires and subscales included in the study, as well as on covariates and principal components obtained from PCA. The results obtained using cluster analysis were cross-validated with findings from Latent Class Analysis (LCA) using Mplus, based on the number of identified clusters in the first step. Phi coefficients are reported to show the agreement of the two methods.

3. Results

3.1. Dimensions of antisocial behaviour

Table 1 illustrates the results of the PCA performed separately for both sexes using measures from the antisocial behaviour spectrum, comprising conduct disorder, reactive/proactive aggression, psychopathic traits (YPI), and comorbid psychopathology (drug and alcohol use, internalizing symptoms, traumatic experiences, MAYSI). For males and females, the Kaiser-Gutmann-criterion suggested a three-component solution. For both sexes highly similar factors emerged, considering that factor loadings for each component showed a high correspondence across the sexes (r1 = 0.89; r2 = 0.99; r3 = 0.77), indicating factorial invariance in particular for component 2. Component 1 appears as a "general factor of antisocial behaviour and comorbid psychopathology" with high loadings on all scales that capture the broader spectrum of antisocial behaviour, for both sexes, with the highest loading on aggression. Component 2 was labelled "narcissistic traits" based on the highest loadings on manipulation, dishonest charm, and grandiosity (YPI). Component 3 shows similar loadings for both sexes, but considering the lowest of all correlations (r3 = 0.77) it also shows an indication of factorial non-invariance by sex. Component 3 was named "callous-unemotional" for girls as it loaded on scales of callousness (λ = 0.73) and unemotional (λ = 0.35). For boys, component 3 was named "callous-blunt" as it loaded positively on the scale callousness (λ = 0.56) and negatively on lying (λ = − 0.40). This latter dimension also showed high loadings on conduct disorder itself, alcohol and drug use and proactive aggression. All three components account for 61.4% of the variance for girls and 59.4% of the variance for boys.

3.2. Correlations between antisocial behaviour, ANS measures and covariates

Table 2 shows a correlation matrix between the three principal components of antisocial behaviour and comorbid psychopathology

Table 1
Principal Component Analysis (PCA) using measures of antisocial behavior and psychopathology.

		Females (N = 659)			Males (N = 351)		
		Component 1	Component 2	Component 3	Component 1	Component 2	Component 3
		"General factor"	"Narcissistic traits"	"Callous-unemotional"	"General factor"	"Narcissistic traits"	"Callous-blunt"
Conduct disorder	K-SADS	0.70	− 0.15	0.27	0.50	− 0.25	0.44
Dishonest charm	YPI	0.63	0.52	− 0.26	0.61	0.55	− 0.15
Grandiosity	YPI	0.36	0.54	− 0.22	0.45	0.50	− 0.26
Lying	YPI	0.59	0.34	− 0.20	0.53	0.37	− 0.40
Manipulation	YPI	0.67	0.50	− 0.24	0.62	0.57	− 0.11
Remorselessness	YPI	0.67	0.35	0.16	0.67	0.38	0.04
Unemotional	YPI	0.50	0.46	0.35	0.48	0.49	0.19
Callousness	YPI	0.41	0.18	0.73	0.39	0.24	0.56
Thrill seeking	YPI	0.70	0.23	− 0.12	0.62	0.34	− 0.09
Impulsivity	YPI	0.73	0.05	− 0.09	0.67	0.20	− 0.16
Irresponsibility	YPI	0.75	0.01	0.10	0.68	0.05	0.26
Alcohol/drug use	MAYSI	0.68	− 0.19	0.00	0.60	− 0.15	0.37
Angry-irritable	MAYSI	0.80	− 0.32	− 0.01	0.76	− 0.41	− 0.03
Depressed-anxious	MAYSI	0.74	− 0.46	− 0.02	0.66	− 0.50	− 0.27
Somatic complaints	MAYSI	0.50	− 0.48	− 0.32	0.51	− 0.52	− 0.27
Suicidal ideation	MAYSI	0.68	− 0.34	0.07	0.53	− 0.40	− 0.08
Thought disturbance	MAYSI	0.58	− 0.25	− 0.08	0.57	− 0.37	− 0.23
Traumatic experience	MAYSI	0.78	− 0.33	0.00	0.71	− 0.41	− 0.17
Proactive aggression	RPQ	0.75	0.01	0.03	0.67	− 0.12	0.30
Reactive aggression	RPQ	0.82	− 0.13	− 0.01	0.75	− 0.20	0.16
Eigenvalue		8,33	2,24	1,09	7,14	2,86	1,29
% Variance		43,9%	11,8%	5,75%	37,6%	15,0%	6,8%

Note. Component extraction based on Kaiser-Gutmann-Criterion (Eigenvalue > 1); Bold loadings > 0.30 or < − 0.30; K-SADS-PL = Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version; YPI = Youth Psychopathic traits Inventory; MAYSI-2 = Massachusetts Youth Screening Instrument 2; RPQ = Reactive-Proactive aggression Questionnaire; "General factor" (GF) of antisocial behaviour and comorbid psychopathology.

Table 2

Correlation matrix of psychopathological principal components, autonomic nervous system (ANS) measures and covariates for females (below diagonal) and males (above diagonal).

	GF	Narc.	CB	CU	lgRSA	PEP	HR	RR	BMI	Caffeine	Smoking	Sports	Age	SES	Medication	CP
GF		0 (0.11)		0 (-0.28***)	-0.03 (0.08)	0.13* (-0.00)	0.00 (0.10)	-0.02 (-0.02)	0.14*	0.27***	0.38***	0.02	0.25***	-0.16**	0.10	-0.03
Narc.	0 (0.15**)			0 (0.16*)	-0.13* (-0.12)	-0.10 (-0.03)	0.03 (0.12)	0.03 (0.00)	0.05	-0.02	-0.03	0.12	0.09	0.10	-0.05	0.01
CB	0 (-0.04)	0 (-0.03)			-0.10 (0.03)	0.18** (-0.04)	-0.07 (-0.03)	0.03 (0.01)	0.04	0.11	0.41***	-0.07	0.22***	-0.20***	0.12*	0.02
CU					0.00 (-0.03)	-0.09* (-0.05)	0.09* (0.06)	0.08* (0.04)	0.04	0.09*	0.07	0.09*	-0.14***	-0.09**	0.00	-0.03
lgRSA	-0.04 (0.04)	0.07 (0.03)				-0.10	-0.48***	-0.29***	-0.14*	-0.01	-0.12*	0.07	-0.14***	-0.03	-0.01	-0.11**
PEP	0.14*** (0.05)	0 (0.01)			-0.14**		-0.22***	-0.09	0.12**	0.05	0.12**	-0.08	0.31***	-0.06	0.01	0.03
HR	-0.02 (-0.02)	-0.03 (-0.06)			-0.54***	-0.14**		0.21***	-0.07	-0.03	-0.08	-0.09	-0.35***	-0.03	0.21***	-0.02
RR	0.12** (0.07)	-0.03 (0.00)			-0.32***	0.02 (0.02)	0.08*		-0.05	0.03	-0.01	0.04	-0.27***	-0.07	0.16**	0.02
BMI	0.21***	-0.06	0.04	0.04	-0.14*	0.12**	-0.07	0.02		0.07	0.14*	0.15***	0.39***	-0.14*	-0.11	0.04
Caffeine	0.18***	-0.07	0.11	0.09*	-0.01	0.05	-0.03	0.09*	0.15***		0.24***	0.04	0.19**	-0.10	-0.03	-0.02
Smoking	0.48***	-0.08	0.41***	0.07	-0.12*	0.12**	-0.08	-0.01	0.19***	0.31***		0.13*	0.38***	-0.21**	0.06	0.11
Sports	-0.16***	-0.05	-0.07	0.09*	0.07	-0.08	-0.09	0.04	-0.09*	0.01	-0.12**		0.12	-0.04	-0.03	0.08
Age	0.25***	-0.08*	0.22***	-0.14***	-0.14***	0.31***	-0.21***	-0.03	0.37***	0.23***	0.31***	-0.10*		-0.05	-0.14*	0.01
SES	-0.27***	0.09*	-0.20***	-0.09**	-0.03	-0.06	0.02	-0.07	-0.16***	-0.13**	-0.24***	0.12*	-0.07		-0.15**	-0.04
Medication	0.21***	-0.08*	0.12*	0.00	-0.01	0.01	0.06	0.06	0.10*	0.07	0.17***	0.00	-0.02	-0.09*		0.09
CP	0.10**	-0.07	0.02	-0.03	-0.11**	0.03	0.03	0.02	0.01	0.10*	0.16***	-0.02	0.06	-0.01	0.02	

Note. Pearson correlations. The results of partial correlations controlling for covariates are reported in parentheses and superscripted. GF = General factor of antisocial behaviour and comorbid psychopathology, Narc. = narcissistic traits, CU = callous-unemotional traits, CB = callous-blunt traits, RSA = respiratory sinus arrhythmia, PEP = pre-ejection period, HR = heart rate, RR = respiration rate, BMI = body-mass-index, CP = cardiac problems. *p < 0.05, **p < 0.01, ***p < 0.001.

[1]Antisocial and comorbid Psychopathology relates to the dimensions identified by the Principal Component Analysis (PCA), which are reported in Table 1.

identified in our analyses (see Table 1), the four ANS measures as well as covariates which are relevant for cardio-respiratory physiology and/or psychopathology. Correlations are shown for both sexes separately (females below the diagonal) and partial correlations controlled for covariates are superscripted. In females, significant correlations were observed between respiration rate and the general factor of antisocial behaviour (r = 0.12, p < 0.01) and callous-unemotional traits (r = 0.08, p < 0.05), and between heart rate and callous-unemotional traits (r = 0.09, p < 0.05), and pre-ejection period with the general factor of antisocial behaviour (r = 0.14, p < 0.001) and callous-unemotional traits (r = −0.09, p < 0.05). In males, the pre-ejection period correlated positively with the general factor of antisocial behaviour (r = 0.13, p < 0.05) and callous-blunt traits (r = 0.18, p < 0.01), while respiratory sinus arrhythmia correlated negatively with narcissistic traits (r = −0.13, p < 0.05). All significant correlations were rendered non-significant when we controlled for covariates.

Several significant correlations were observed between covariates, antisocial behaviour, and comorbid psychopathology. The most prominent association was found for smoking with the general factor of antisocial behaviour, with a higher correlation for girls (r = 0.48, p < 0.001) than for boys (r = 0.38, p < 0.001). In contrast, callous-blunt traits correlated significantly with smoking only in boys (r = 0.41, p < 0.001). Among the relation between covariates and ANS measures, age showed the strongest association with all of the ANS measures, especially in boys, whereas in females only respiration rate was not related to age. In boys, among the covariates, smoking was only related to pre-ejection period (r = 0.23, p < 0.01) whereas in girls smoking was related to respiratory sinus arrhythmia (r = −0.12, p < 0.01), pre-ejection period (r = 0.12, p < 0.01), and respiration rate (r = 0.20, p < 0.001). Among ANS measures, significant correlations were observed in the expected direction, e.g., between respiratory sinus arrhythmia and heart rate (girls: r = −0.54, p < 0.001; boys: r = −0.48, p < 0.001), except for an unexpected

negative correlation between respiratory sinus arrhythmia and pre-ejection period (r = −0.14, p < 0.01) in girls. The analyses suggest that these significant, though weak correlations between ANS measures and psychopathological components are influenced by covariates, potentially by smoking and age which show the highest correlations with these measures.

3.3. Predictors of antisocial behaviour

Fig. 2 demonstrates the result of a multi-group SEM for both sexes (CFI = 0.988 RMSEA = 0.021) using the principal components of antisocial behaviour and comorbid psychopathology from Table 1 as outcome variables. None of the ANS measures significantly predicted PCA dimensions (general factor of antisocial behaviour, narcissistic traits, callous-unemotional/blunt traits). The covariates "smoking" and "age" outperformed all ANS measures with respect to predicting PCA dimensions. Smoking showed the strongest association with the general factor of antisocial behaviour and comorbid psychopathology (girls: β = 0.44***, p < 0.001; boys: β = 0.33***, p < 0.001) and with callous-unemotional/blunt traits (girls: β = 0.12**, p < 0.01; boys: β = 0.41***, p < 0.001). Several paths are significant only for one sex, e.g., age predicts callous-unemotional traits only in girls (β = −0.18***, p < 0.001), whereas in boys the association of age and callous-blunt traits is non-significant (β = 0.06). Age is only negatively correlated with respiration rate in boys (β = −0.24***, p < 0.001) and smoking only positively correlated with respiration rate in females (β = 0.19***, p < 0.001). Residual errors (ε1, ε2, ε3) which are expected to be uncorrelated (since PCA produces uncorrelated components), are correlated in males (ε1 with ε3, r = 0.20***, p < 0.001). Fig. 2 shows that ANS measures do not function as predictors of principal components underlying antisocial behaviour and psychopathology when controlling for age and smoking behaviour.

Fig. 2. Structural Equation Model (SEM) using autonomic nervous system (ANS) measures as predictors of principal components analysis (PCA) dimensions of antisocial behavior and psychopathology controlling for age and smoking (CFI = 0.988 RMSEA = 0.021 df = 34, N = 1010) separately for females (parameters before slash) and males (parameters after slash) solid/dashed arrows represent significant paths for both sexes/significant paths only for one sex (*p < 0.05, **p < 0.01, ***p < 0.001). HR = heart rate, RR = respiration rate, RSA = respiratory sinus arrhythmia, PEP = pre-ejection period.

3.4. Physiological phenotypes

Fig. 3 illustrates the results of a k-means Cluster Analysis performed on ANS measures based on a two-cluster solution for both sexes according to the Bayesian Information Criterion. For girls, the "high arousal" cluster (40.7% of the sample) is characterized by low respiratory sinus arrhythmia, high heart rate and high respiration rate. This cluster is also characterized by significantly higher levels of caffeine consumption and lower age. The second cluster (59.3% of the sample) displays an inverse pattern and therefore appears as a "low arousal" type. For boys, both clusters show similar ANS patterns compared to girls. One difference between the two sexes, however, relates to the pre-ejection period. For boys, the pre-ejection period is significantly higher in the "low arousal" cluster (67.9% of the sample). Contrarily, the clusters in girls do not differ with regard to pre-ejection period. The "high arousal" cluster (32.1% of the sample) is characterized by significantly lower age and lower smoking levels. In females and males, there were no significant associations between cluster membership and psychopathological outcome variables (conduct disorder and principal components). Only in males, the "general factor of antisocial behaviour and comorbid psychopathology" showed evidence for a substantial difference between the two clusters. However, this association was no longer significant when controlling for multiple testing (Bonferroni correction), nor when controlling for covariates. ANOVAs were also performed on the subscales of each questionnaire, showing no significant associations between cluster membership and specific correlates of antisocial, aggressive, comorbid symptoms, callous-unemotional traits, and traumatic experiences (MAYSI, YPI, RPQ; data not shown). The cross-validation with findings from Latent Class Analysis using Mplus resulted in Phi coefficients of 0.75 for females and 0.83 for males.

4. Discussion

The aim of our study was to examine relationships between different dimensional measures of antisocial behaviour and several ANS measures determined under resting conditions. Furthermore, we investigated how different clusters of ANS activity relate to antisocial behaviour and comorbid psychopathology. We studied four ANS measures (heart and respiration rate, respiratory sinus arrhythmia and pre-ejection period) together capturing SNS and/or PNS activity. We carefully controlled for several covariates, including cigarette smoking. We studied those aspects with respect to sex using a large international sample including data acquired across seven European countries and containing not only healthy adolescents, but additionally those with clinically significant levels of antisocial behavior. This meant that we captured the full spectrum of antisocial behaviour – from very low to very high.

In our study, the weak correlations between baseline ANS measures and antisocial behaviour and psychopathology were rendered non-significant after controlling for age and smoking. Additionally, a cluster analysis suggested for both, girls and boys, a low and a high arousal cluster. Again, potentially significant (bivariate) associations between these ANS clusters and the general factor of antisocial behaviour and comorbid psychopathology were rendered non-significant when controlling for covariates.

4.1. No evidence for a relationship of low heart rate and antisocial behaviour

Some of our findings are in contrast to existing evidence regarding ANS functioning and antisocial behaviour. We did not find evidence for a relationship with low heart rate which had been shown in many previous studies (Latvala, Kuja-Halkola, Almqvist, Larsson, & Lichtenstein, 2015; Murray et al., 2016; Portnoy & Farrington, 2015). This is surprising, considering the statistical power based on a large

sample size which tends to result in even small effects to become significant. However, in line with the present findings, a recent meta-analysis reported a trend showing the relationship between low resting heart rate and antisocial behaviour to become weaker with increasing publication year (Portnoy & Farrington, 2015). They explain this trend by referring to the "proteus phenomenon" describing an effect occurring in the early phase of a scientific investigation in which most likely significant findings are published in both directions. Later, findings refuting the original results become more interesting. Thus, the findings from Ortiz and Raine (2004) might have encouraged researchers to publish null findings refuting their results. One possible explanation of the weak relationship between antisocial behaviour and ANS parameters could be related to the severity of conduct problems in our
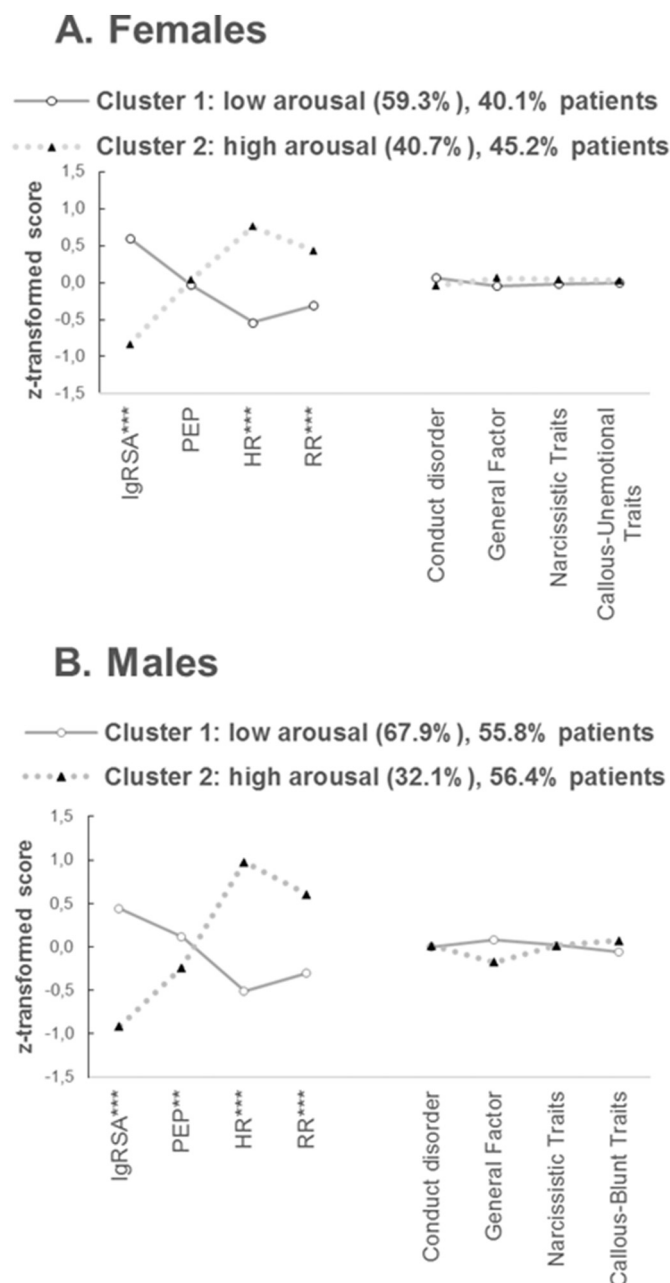

Fig. 3. K-means cluster analysis performed using autonomic nervous system (ANS) measures as clustering variables and its relation to profiles across psychopathological principal components and conduct disorder for females (fig. A) and males (fig. B). Significant p-values of ANOVAs are shown (***p < 0.001; **p < 0.01; *p < 0.05). RSA = respiratory sinus arrhythmia, HR = heart rate, PEP = pre-ejection period, RR = respiration rate.

study: Latvala et al. (2015) found a stronger relationship between violent crimes and low heart rate, as opposed to the comparison with non-violent crimes. Correspondingly, Portnoy and Farrington (2015) showed the strongest effect size (d = − 0.35) for violence compared to the other categories of antisocial behaviour (aggression, behaviour problems, conduct disorder/oppositional defiant disorder, offending, psychopathy). The conduct disorder/oppositional defiant disorder category, which is also present in our sample, only exhibited an effect size of d = − 0.19 in their analysis for low heart rate. One might also argue that the use of an inclusive sample with patients and typically developing individuals could have masked possible relationships. To investigate this, a categorical approach was performed on the same sample by Oldenhof et al. (this volume). The authors compared the conduct disorder group with controls and found no relation between antisocial behaviour and heart rate - only a higher respiration rate in female cases compared to female controls was detected.

4.2. Weak relations between the remaining ANS measures and antisocial behaviour

All remaining ANS measures showed significant, but weak associations to antisocial behaviour and psychopathology. We found positive associations between pre-ejection period and antisocial psychopathology for both sexes. A lengthened resting pre-ejection period, indicating less sympathetic activity was previously found in relation to conduct problems in children (Beauchaine et al., 2013). Further, the positive relation between respiration rate and psychopathology in females had been shown before (Blom et al., 2014). A negative association between respiratory sinus arrhythmia and our narcissistic component in males is not in line with other findings indicating a positive link (Hansen, Johnsen, Thornton, Waage, & Thayer, 2007). After controlling for covariates, none of the associations remained significant. In general, our findings of weak ANS associations with antisocial psychopathology align with previous research. For example, heart rate variability exhibited quantitatively small to moderate associations to different types of psychopathology, with the exception of schizophrenia, exhibiting a large effect size (Alvares et al., 2016), which is hypothesized to be at the peak of severity of the general psychopathology factor (Caspi et al., 2014).

4.3. Considerations on the covariate smoking

Findings regarding the covariate smoking should be considered further. The positive association between smoking and antisocial and comorbid psychopathology is in line with prior research (Jennings et al., 2013; Pagani et al., 2017; Talati, Keyes, & Hasin, 2016). Interestingly, the association of smoking and antisocial psychopathology strengthened in more recent study cohorts, whereas at the same time the prevalence of smoking decreased (Talati et al., 2016). It is argued that as social desirability of smoking decreases, the prevalence of biologically vulnerable persons among the population of smokers increases. It is further discussed by Talati et al. (2016) that the risk for deviant behaviour and for psychiatric conditions, including substance use, share common genetic variance. Accordingly, two genome-wide association studies have found genes in adults with alcohol dependence to be possibly related to conduct disorder in the past (Dick et al., 2011; Jian, Wang, Wu, Hillhouse, & Mullersman, 2011) and a strong overlap between substance abuse and antisocial behaviour has previously been shown (Krueger, Markon, Patrick, Benning, & Kramer, 2007).

4.4. ANS clusters

A further aim was to examine if reversing the common approach of relating psychopathology to physiology would benefit the investigation of the ANS and antisocial behaviour. For boys and girls a high and a low arousal cluster arose from our analysis. The results showed two

opposite and physiologically plausible clusters, i.e., the ANS measures showed the expected relationships with each other (e.g., for heart rate and respiratory sinus arrhythmia an inversed activity pattern in both clusters). Previous research would suggest differential associations to psychopathology for these patterns, e.g., internalizing symptoms being related to higher ANS activity, and callous-unemotional traits being linked to lower ANS activity (Fanti, 2016). Our data does not provide evidence for such associations. The male clusters show a significant bivariate difference on the general factor of antisocial behaviour and comorbid psychopathology. However, the difference did not remain significant, neither after correcting for multiple testing, nor when controlling for covariates. Further, from a methodological point of view, an artificial division of study populations based on continuous variables, in our study the clustering based on ANS measures, may impact on results: It has been argued that a dichotomization of continuous measures leads to a loss of information and potentially leads to spuriously increased or decreased effects (MacCallum, Zhang, Preacher, & Rucker, 2002). In conclusion, also the reversed approach of creating groups of individuals based on resting ANS activity does not account for substantial variance in antisocial behaviour and comorbid psychopathology. The finding that patients were equally distributed over both clusters highlights the limited value for classifying individuals based on baseline ANS measures.

4.5. Limitations

Limitations of this study are considered, notably that we only assessed basal ANS measures. Growing evidence highlights the importance of ANS reactivity for adaptive functioning (Graziano & Derefinko, 2013). It is possible that we would have found associations between ANS activity and antisocial behaviour if we had included ANS reactivity measures in our analyses (e.g., heart rate increases to stress or in response to aversive stimuli). Despite acceptable reliability of SES (Cronbach's Alpha = 0.74), further limitations concern the inter-rater reliability of SES.

4.6. Suggestion for future research

Our study leads to some suggestions for future research. Considering the close relationship between smoking and respiration rate, at least in females, it would be worthwhile to include other respiratory variables in future studies (e.g., tidal volume, variability, pCO_2), as they have been related to internalizing problems which are of direct relevance to the study of antisocial behaviour. Considering the strong relationship between antisocial behaviour and smoking and its relevance to ANS functioning, we recommend to assess smoking routinely in studies of ANS and antisocial behaviour. Ideally, it should be assessed as a continuous variable, given its non-linear relationship to pre-ejection period (Hu et al., 2017), allowing a more informative analysis.

5. Conclusion

In conclusion, we found that baseline ANS measures showed only weak associations with antisocial behaviour and comorbid psychopathology, all of which become insignificant when controlling for covariates. Smoking was strongly related to the general factor of antisocial behaviour and comorbid psychopathology, as well as callous-blunt traits, which implies the importance to consider this variable when studying antisocial behaviour. The finding of opposing ANS clusters for both sexes did not help to elucidate the relationship between resting ANS activity and antisocial behaviour. The positive association between respiration rate and antisocial behaviour in females warrants the inclusion of this measure in future studies on ANS activity and antisocial behaviour.

6. Practical implications

Given the small associations between the ANS and antisocial behaviour and comorbid psychopathology, our results do not support a potential of the ANS markers, as measured in a resting state, for profiling or predicting antisocial behaviour. However, future research should examine, if ANS markers examined under conditions of reactivity, for example, using an induction of emotions with film clips, provide such potential applications for the criminal justice practice. The strong relationship between smoking and antisocial behaviour suggests the relevance to target it in intervention and prevention programs, given its detrimental health effects to adolescents and their environment. Even passive smoking in households has been shown to increase the risk of antisocial behaviour (Pagani et al., 2017). Furthermore, females should be considered more carefully in intervention and prevention programs, as prenatal smoking constitutes a risk factor for the development of antisocial behaviour (Paradis, Shenassa, Papandonatos, Rogers, & Buka, 2017). Thus, the continuity of antisocial behaviour could potentially be decreased by placing a stronger focus on smoking prevention.

Competing interest

Funding

Acknowledgements

References

Allen, J. J. B., Chambers, A. S., & Towers, D. N. (2007). The many metrics of cardiac chronotropy: A pragmatic primer and a brief comparison of metrics. *Biological Psychology, 74*(2), 243–262. http://dx.doi.org/10.1016/j.biopsycho.2006.08.005.

Alvares, G. A., Quintana, D. S., Hickie, I. B., & Guastella, A. J. (2016). Autonomic nervous system dysfunction in psychiatric disorders and the impact of psychotropic medications: A systematic review and meta-analysis. *Journal of Psychiatry & Neuroscience: JPN, 41*(2), 89.

American Psychiatric Association (2000). *Diagnostic and statistical manual of mental disorders: DSM-IV-TR.* New Delhi, India: Jaypee Brothers Medical Publishers.

American Psychiatric Association (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). (Arlington).

Andershed, H. A., Kerr, M., Stattin, H., & Levander, S. (2002). *Psychopathic traits in non-referred youths: A new assessment tool.*

Beauchaine, T. P., Gatzke-Kopp, L., & Mead, H. K. (2007). Polyvagal theory and developmental psychopathology: Emotion dysregulation and conduct problems from preschool to adolescence. *Biological Psychology, 74*(2), 174–184.

Beauchaine, T. P., Gatzke-Kopp, L., Neuhaus, E., Chipman, J., Reid, M. J., & Webster-Stratton, C. (2013). Sympathetic-and parasympathetic-linked cardiac function and prediction of externalizing behavior, emotion regulation, and prosocial behavior among preschoolers treated for ADHD. *Journal of Consulting and Clinical Psychology, 81*(3), 481.

Blom, E. H., Serlachius, E., Chesney, M. A., & Olsson, E. M. G. (2014). Adolescent girls with emotional disorders have a lower end-tidal CO2 and increased respiratory rate compared with healthy controls. *Psychophysiology, 51*(5), 412–418. http://dx.doi.org/10.1111/psyp.12188.

Carnevali, L., Nalivaiko, E., & Sgoifo, A. (2014). Respiratory patterns reflect different levels of aggressiveness and emotionality in Wild-type Groningen rats. *Respiratory Physiology & Neurobiology, 204*, 28–35.

Caspi, A., Houts, R. M., Belsky, D. W., Goldman-Mellor, S. J., Harrington, H., Israel, S., ... Poulton, R. (2014). The p factor: One general psychopathology factor in the structure of psychiatric disorders? *Clinical Psychological Science: A Journal of the Association for Psychological Science, 2*(2), 119–137.

Davidson, R. J., Putnam, K. M., & Larson, C. L. (2000). Dysfunction in the neural circuitry of emotion regulation—a possible prelude to violence. *Science, 289*(5479), 591–594.

Dick, D., Aliev, F., Krueger, R., Edwards, A., Agrawal, A., Lynskey, M., ... Nurnberger, J. (2011). Genome-wide association study of conduct disorder symptomatology. *Molecular Psychiatry, 16*(8), 800–808.

Fanti, K. A. (2016). Understanding heterogeneity in conduct disorder: A review of psychophysiological studies. *Neuroscience & Biobehavioral Reviews.* http://dx.doi.org/10.1016/j.neubiorev.2016.09.022.

Fanti, K. A., Demetriou, C. A., & Kimonis, E. R. (2013). Variants of callous-unemotional conduct problems in a community sample of adolescents. *Journal of Youth and Adolescence, 42*(7), 964–979.

Farmer, D. G., Dutschmann, M., Paton, J. F., Pickering, A. E., & McAllen, R. M. (2016). Brainstem sources of cardiac vagal tone and respiratory sinus arrhythmia. *The Journal of Physiology, 594*(24), 7249–7265.

Fraley, C., Raftery, A. E., Murphy, T. B., & Scrucca, L. (2012). *Mclust version 4 for R: Normal mixture modeling for model-based clustering, classification, and density estimation [technical report].* Department of Statistics, University of Washington.

de Geus, E. J., Willemsen, G. H., Klaver, C. H., & van Doornen, L. J. (1995). Ambulatory measurement of respiratory sinus arrhythmia and respiration rate. *Biological Psychology, 41*(3), 205–227.

Gourine, A. V., Machhada, A., Trapp, S., & Spyer, K. M. (2016). Cardiac vagal preganglionic neurones: An update. *Autonomic Neuroscience, 199*, 24–28.

Graziano, P., & Derefinko, K. (2013). Cardiac vagal control and children's adaptive functioning: A meta-analysis. *Biological Psychology, 94*(1), 22–37.

Grisso, T., & Barnum, R. (2006). *Massachusetts youth screening instrument-version 2 (MAYSI-2): User's manual and technical report.* Sarasota: Professional Resource Press.

Grossman, P. (2016). Examining Porges' "Polyvagal" suppositions. Retrieved from www.researchgate.net/project/Examining-Porges-Polyvagal-suppositions, Accessed date: 25 October 2017.

Grossman, P., Beek, J. V., & Wientjes, C. (1990). A comparison of three quantification methods for estimation of respiratory sinus arrhythmia. *Psychophysiology, 27*(6), 702–714.

Grossman, P., & Taylor, E. W. (2007). Toward understanding respiratory sinus arrhythmia: Relations to cardiac vagal tone, evolution and biobehavioral functions. *Biological Psychology, 74*(2), 263–285.

Hansen, A. L., Johnsen, B. H., Thornton, D., Waage, L., & Thayer, J. F. (2007). Facets of psychopathy, heart rate variability and cognitive function. *Journal of Personality Disorders, 21*(5), 568–582.

Herpers, P. C., Rommelse, N. N., Bons, D. M., Buitelaar, J. K., & Scheepers, F. E. (2012). Callous–unemotional traits as a cross-disorders construct. *Social Psychiatry and Psychiatric Epidemiology, 47*(12), 2045–2064.

Hu, M. X., Lamers, F., de Geus, E. J., & Penninx, B. W. (2017). Influences of lifestyle factors on cardiac autonomic nervous system activity over time. *Preventive Medicine, 94*, 12–19.

International Labour Organization (2012). International standard classification of occupations. *Structure, group definitions and correspondence tables.* Geneva: International Labour Office.

Jennings, W. G., Piquero, A. R., & Farrington, D. P. (2013). Does resting heart rate at age 18 distinguish general and violent offending up to age 50? Findings from the Cambridge Study in Delinquent Development. *Journal of Criminal Justice, 41*(4), 213–219.

Jian, X.-Q., Wang, K.-S., Wu, T.-J., Hillhouse, J. J., & Mullersman, J. E. (2011). Association of ADAM10 and CAMK2A polymorphisms with conduct disorder: Evidence from family-based studies. *Journal of Abnormal Child Psychology, 39*(6), 773.

Kaufman, J., Birmaher, B., Brent, D., Rao, U., Flynn, C., Moreci, P., ... Ryan, N. (1997). Schedule for affective disorders and schizophrenia for school-age children-present and lifetime version (K-SADS-PL): Initial reliability and validity data. *Journal of the American Academy of Child & Adolescent Psychiatry, 36*(7), 980–988.

Koenig, J., Jarczok, M., Warth, M., Ellis, R., Bach, C., Hillecke, T., & Thayer, J. F. (2014). Body mass index is related to autonomic nervous system activity as measured by heart rate variability—A replication using short term measurements. *The Journal of Nutrition, Health & Aging*, 1–3.

Koenig, J., & Thayer, J. F. (2016). Sex differences in healthy human heart rate variability: A meta-analysis. *Neuroscience & Biobehavioral Reviews, 64*, 288–310.

Kreibig, S. D. (2010). Autonomic nervous system activity in emotion: A review. *Biological Psychology, 84*(3), 394–421.

Krueger, R. F., Markon, K. E., Patrick, C. J., Benning, S. D., & Kramer, M. D. (2007). Linking antisocial behavior, substance use, and personality: An integrative quantitative model of the adult externalizing spectrum. *Journal of Abnormal Psychology, 116*(4), 645.

Latvala, A., Kuja-Halkola, R., Almqvist, C., Larsson, H., & Lichtenstein, P. (2015). A longitudinal study of resting heart rate and violent criminality in more than 700,000 men. *JAMA Psychiatry, 72*(10), 971–978.

Lehto-Salo, P., Närhi, V., Ahonen, T., & Marttunen, M. (2009). Psychiatric comorbidity more common among adolescent females with CD/ODD than among males. *Nordic Journal of Psychiatry, 63*(4), 308–315.

van Lien, R., Schutte, N. M., Meijer, J. H., & de Geus, E. J. (2013). Estimated preejection period (PEP) based on the detection of the R-wave and dZ/dt-min peaks does not adequately reflect the actual PEP across a wide range of laboratory and ambulatory

conditions. *International Journal of Psychophysiology, 87*(1), 60–69.

MacCallum, R. C., Zhang, S., Preacher, K. J., & Rucker, D. D. (2002). On the practice of dichotomization of quantitative variables. *Psychological Methods, 7*(1), 19.

Martin, C. A., Cook, C., Woodring, J. H., Burkhardt, G., Guenthner, G., Omar, H. A., & Kelly, T. H. (2008). Caffeine use: Association with nicotine use, aggression, and other psychopathology in psychiatric and pediatric outpatient adolescents. *The Scientific World Journal, 8*, 512–516.

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.

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.

Oldenhof, H., Prätzlich, M., Ackermann, K., Baker, R., Batchelor, M., Baumann, S., ... Popma, A. Baseline autonomic nervous system activity in female children and adolescents with conduct disorder: Psychophysiological findings from the FemNAT-CD study. Journal of Criminal Justice (this volume).

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.

Pagani, L., Lévesque-Seck, F., Archambault, I., & Janosz, M. (2017). Prospective longitudinal associations between household smoke exposure in early childhood and antisocial behavior at age 12. *Indoor Air, 27*(3), 622–630.

Paradis, A. D., Shenassa, E. D., Papandonatos, G. D., Rogers, M. L., & Buka, S. L. (2017). Maternal smoking during pregnancy and offspring antisocial behaviour: Findings from a longitudinal investigation of discordant siblings. *Journal of Epidemiology and Community Health, 71*(9), 889–896. http://dx.doi.org/10.1136/jech-2016-208511.

Petermann, F., & Wechsler, D. (2008). *HAWIK-IV: Hamburg-Wechsler-Intelligenztest für Kinder-IV: Verlag Hans Huber.* Testverlag: Hogrefe.

Piferi, R. L., Kline, K. A., Younger, J., & Lawler, K. A. (2000). An alternative approach for achieving cardiovascular baseline: Viewing an aquatic video. *International Journal of Psychophysiology, 37*(2), 207–217.

Piotrowska, P. J., Stride, C. B., Croft, S. E., & Rowe, R. (2015). Socioeconomic status and antisocial behaviour among children and adolescents: A systematic review and meta-analysis. *Clinical Psychology Review, 35*, 47–55.

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.

Portnoy, J., Raine, A., Chen, F. R., Pardini, D., Loeber, R., & Jennings, J. R. (2014). Heart rate and antisocial behavior: The mediating role of impulsive sensation seeking.

Criminology, 52*(2), 292–311.

Raine, A., Dodge, K., Loeber, R., Gatzke-Kopp, L., Lynam, D., Reynolds, C., ... Liu, J. (2006). The reactive–proactive aggression questionnaire: Differential correlates of reactive and proactive aggression in adolescent boys. *Aggressive Behavior, 32*(2), 159–171.

Raschle, N. M., Menks, W. M., Fehlbaum, L. V., Steppan, M., Smaragdi, A., Gonzalez-Madruga, K., ... Stadler, C. (2017). *Callous-unemotional traits and brain structure: Sex-specific effects in anterior insula of typically-developing youths.* NeuroImage: Clinical.

Raschle, N. M., Menks, W. M., Fehlbaum, L. V., Tshomba, E., & Stadler, C. (2015). Structural and functional alterations in right dorsomedial prefrontal and left insular cortex co-localize in adolescents with aggressive behaviour: An ALE meta-analysis. *PLoS One, 10*(9), e0136553.

Rogers, J. C., & De Brito, S. A. (2016). Cortical and subcortical gray matter volume in youths with conduct problems: A meta-analysis. *JAMA Psychiatry, 73*(1), 64–72.

Sidlauskaite, J., González-Madruga, K., Smaragdi, A., Riccelli, R., Puzzo, I., Batchelor, M., ... Fairchild, G. (2017). Sex differences in risk-based decision making in adolescents with conduct disorder. *European Child & Adolescent Psychiatry,* 1–10.

Steiner, H., Daniels, W., Stadler, C., & Kelly, M. (2017). *Disruptive Behavior: Development, Psychopathology, Crime, and Treatment.* Oxford University Press.

Talati, A., Keyes, K., & Hasin, D. (2016). Changing relationships between smoking and psychiatric disorders across twentieth century birth cohorts: Clinical and research implications. *Molecular Psychiatry, 21*(4), 464–471.

Thayer, J. F., Ahs, F., Fredrikson, M., Sollers, J. J., & Wager, T. D. (2012). A meta-analysis of heart rate variability and neuroimaging studies: Implications for heart rate variability as a marker of stress and health. *Neuroscience and Biobehavioral Reviews, 36*(2), 747–756. http://dx.doi.org/10.1016/j.neubiorev.2011.11.009.

Thayer, J. F., & Lane, R. D. (2000). A model of neurovisceral integration in emotion regulation and dysregulation. *Journal of Affective Disorders, 61*(3), 201–216.

Thayer, J. F., & Lane, R. D. (2009). Claude Bernard and the heart–brain connection: Further elaboration of a model of neurovisceral integration. *Neuroscience & Biobehavioral Reviews, 33*(2), 81–88.

UNESCO Institute for Statistics (2015). *International standard classification of education fields of education and training 2013 (ISCED-F 2013): Detailed field descriptions.*

Wechsler, D. (1999). *Wechsler abbreviated scale of intelligence.* Psychological Corporation.

Williams, D. P., Cash, C., Rankin, C., Bernardi, A., Koenig, J., & Thayer, J. F. (2015). Resting heart rate variability predicts self-reported difficulties in emotion regulation: A focus on different facets of emotion regulation. *Frontiers in Psychology, 6*(261), http://dx.doi.org/10.3389/fpsyg.2015.00261.

Zelano, C., Jiang, H., Zhou, G., Arora, N., Schuele, S., Rosenow, J., & Gottfried, J. A. (2016). Nasal respiration entrains human limbic oscillations and modulates cognitive function. *Journal of Neuroscience, 36*(49), 12448–12467.