J Physiol Sci (2013) 63:87–94
DOI 10.1007/s12576-012-0238-3

ORIGINAL PAPER

Inattentive and hyperactive preschool-age boys have lower sympathetic and higher parasympathetic activity

Tzong-Shi Wang · Wei-Lieh Huang · Terry B. J. Kuo · Guo-She Lee · Cheryl C. H. Yang

Received: 19 July 2012 / Accepted: 25 September 2012 / Published online: 18 October 2012

Abstract The presented study aimed to clarify the relationship between the autonomic nervous system and disruptive behaviors among preschoolers. Possible gender differences in autonomic activity were also examined. A total of 88 preschool-age children were enrolled in this study. Autonomic activities were measured by power spectrum analysis of heart rate variability (HRV). The Swanson, Nolan and Pelham parents and teachers rating scale (SNAP-IV) was applied to evaluate each subject's severity of disruptive behavior. The relationship between the HRV results and the SNAP-IV was evaluated by correlation analysis, which disclosed that the scores for inattention, hyperactivity/impulsivity and oppositional defiant disorder showed a negative association with LF % and LF/HF. The above scales, except for the hyperactivity subscale, also showed a positive association with HF. On separating the two genders, only boys showed the above correlations. Preschool-age boys who show more inattentive and hyperactive features have lower sympathetic and higher parasympathetic activity.

Keywords Preschool age children · Autonomic activity · Heart rate variability · SNAP-IV · Gender difference

T.-S. Wang and W.-L. Huang contributed equally to this study.

T.-S. Wang · W.-L. Huang · T. B. J. Kuo · G.-S. Lee · C. C. H. Yang (✉)
Institute of Brain Science, National Yang-Ming University, No. 155, Sec. 2, Li-Nong St., Taipei 11221, Taiwan
e-mail: cchyang@ym.edu.tw

T.-S. Wang
Department of Psychiatry, Tri-Service General Hospital, Taipei, Taiwan

W.-L. Huang
Department of Psychiatry, National Taiwan University Hospital, Yun-Lin Branch, Yunlin, Taiwan

W.-L. Huang
Department of Psychiatry, National Taiwan University Hospital, Taipei, Taiwan

T. B. J. Kuo · C. C. H. Yang
Sleep Research Center, National Yang-Ming University, No. 155, Sec. 2, Li-Nong St., Taipei 11221, Taiwan

T. B. J. Kuo · G.-S. Lee · C. C. H. Yang
Department of Education and Research, Taipei City Hospital, Taipei, Taiwan

G.-S. Lee
Faculty of Medicine, School of Medicine, National Yang-Ming University, Taipei, Taiwan

Introduction

Attention-deficit and hyperactivity disorder (ADHD) is a syndrome of inattention, restless overactivity and impulsiveness [1]. It is one of the most common childhood-onset psychiatric disorders and affects 5–12 % of children worldwide [2]. ADHD is a disorder with prominent biological components [3]. Its core mechanism involves dopamine and norepinephrine dysregulation in the frontal lobe [4, 5]. The frontal cortex is involved in the activities of the limbic area and autonomic nervous system (ANS) [6]. In this context, norepinephrine is the major neurotransmitter in sympathetic nervous system (SNS) [7], and there is also significant evidence supporting various neuroimaging, neurophysiological and neuropsychological biomarkers of ADHD [8, 9]; however, whether ANS manifestations can be used as biomarkers of ADHD still awaits clarification.

The activity of the ANS can be measured by non-invasive tools such as heart rate variability (HRV) and skin conductance [10, 11]. High frequency power (HF, also called respiratory sinus arrhythmia, RSA) of the HRV represents parasympathetic activity, while normalized low frequency power (LF %) and the ratio of low frequency power to high frequency power (LF/HF) are considered sympathetic parameters [10, 12]. The pre-ejection period (PEP) is another commonly used index that reflects sympathetic function [13]. Using these tools, some studies have suggested that autonomic dysregulation plays a role in the pathogenesis of disruptive behavior disorders [14–19]. Decreased sympathetic modulation has been reported in subjects with ADHD or conduct disorder (CD) [14, 15, 17], while changes in the parasympathetic activity of ADHD subjects remains controversial [15, 16, 18, 19]. A low sympathetic tone has been suggested to be associated with disinhibition and reward insensitivity [15, 20]. However, most of these studies distinguished the disruptive behavior disorder group and the control group using a perspective that was categorical in nature. We believe a dimensional approach may provide more information on the relationship between disruptive behavior in its many facets in relation to ANS activity and that the results ought to be extendable to healthy subjects. Rating using Swanson, Nolan and Pelham-IV (SNAP-IV), a self-rated inventory based on DSM-IV criteria, has been applied worldwide to measure inattention, hyperactivity/impulsivity and ODD dimensions [21–23]. We believe that SNAP-IV is a suitable means of exploring the relationships between symptom dimensions and the various HRV indexes.

Another interesting issue is whether there are gender differences, originating from autonomic influence, that are associated with various aspects of disruptive behavior. Gender difference in ADHD subjects has been investigated in previous studies [24–26]. ADHD boys show more externalization of behavior (presentations of hyperactivity/impulsivity/ODD), while ADHD girls show more inattentive symptoms [27]. Our past studies also disclosed that male and female adults show distinct ANS patterns [10]. It is possible that the different ADHD symptoms in boys and girls are also influenced by variations in ANS features. Since low SNS activity is associated with disinhibited behavior, we hypothesize that the ADHD boys have lower sympathetic tone than the ADHD girls. Gender differences in skin conductance level and electroencephalographic presentation have been found among ADHD adolescents and adults [28, 29]. However, to our knowledge, a similar design focusing on preschool-aged children has yet been carried out.

The presented study has two major goals. The first is to understand the relationship among preschool-age children between the severity of disruptive behavior and various HRV parameters. Additionally, the data sets from the two genders were analyzed separately to examine whether gender differences exist. We hypothesized that SNS activity is negatively correlated with each of the various SNAP-IV dimensions. We also hypothesize that lower SNS activity among preschool-aged boys than preschool-aged girls is a contributing factor to their different patterns of disruptive behavior.

Method

Subjects

The subjects recruited for this study were preschool-age children. These children were studying in the senior classes of two kindergartens that covered both urban and rural areas. The epidemiological and physical information on the subjects was gathered via questionnaires, which were completed by their parents and by their kindergarten teachers. Subjects with a history of congenital heart disease, neuropathy, cardiac arrhythmia, other cardiovascular diseases or who had used any medication within the last week were excluded. The subjects did not have any psychiatric history, but the possibility of individuals having an ADHD/ODD diagnosis had not been ruled out. We explored their ADHD and ODD symptoms by self-administered questionnaire. In total, 88 subjects, made up of 41 boys (46.59 %) and 47 girls (53.41 %), were enrolled in the study. Informed written consent was obtained from the parents of all participants, and the procedures used in this study were approved by the Institutional Review Board of National Yang-Ming University.

The Swanson, Nolan and Pelham-IV (SNAP-IV) Rating Scale

SNAP-IV is a rating scale completed by both parents and teachers [30]. It was developed for use with DSM-III-defined ADHD and has been updated with each DSM revision. The short version of the SNAP-IV includes the core DSM-IV-derived ADHD subscales of inattention, hyperactivity/impulsivity and ODD along with summary questions for each domain. The longer version includes these scales together with items selected from other scales measuring ADHD and associated features, including the Conners Index Questionnaire, the IOWA Conners Questionnaire and the Swanson, Kokin, Agler, M-Flynn, and Pelham rating scale (SKAMP). SNAP-IV in its final form contains 40 items extracted from DSM-IV-based criteria for other disorders, including symptoms related to other externalizing behaviors, internalizing symptoms and motor disturbances. Thus, this scale incorporates multiple dimensions into a single scale.

The SNAP-IV has frequently been used in ADHD research. Its coverage of other behaviors and symptoms offers an abbreviated assessment of comorbidity. Furthermore, the multiple published applications are able to give potential users a good idea of its utility [31]. The short version of the Chinese version of the SNAP-IV teacher and parent rating scales has been applied to evaluate individual subject's severity of symptoms in relation to ADHD and ODD. A total of 26 items and four subscales are included and are made up of inattention (items 1–9), hyperactivity/impulsivity (items 10–18) and ODD (items 10–26). The SNAP-IV is based on a 0–3 rating scale, namely not at all (0), just a little (1), quite a bit (2) and very much (3). The sum of the scores for the inattention and hyperactivity/impulsivity subscales is used to provide a score for ADHD. The validity and reliability of the Chinese version have been established previously [32].

Processing of electrocardiogram signals

The procedure for HRV analysis was based on the standard method [10, 12, 33] and has been reported previously [10, 33, 34]. In brief, a precordial electrocardiogram (ECG) was taken for 5 min. The subjects were asked to lie in a relaxed position and breath normally, but not to fall asleep. Conditions that might cause discomfort (including being too hot or too cold) were avoided. The time of examination was between 9 a.m. to 12 a.m., which was designed to limit the influence of meals and circadian rhythm. One electrode was placed over the jugular notch of the sternum, between the collarbones, another was placed 4 cm under the left breast between the ribs, and the third electrode was placed on the right lateral side between two lower ribs. ECG signal acquisition, storage and processing were performed using a HRV analyzer (SS1C, Enjoy Research Inc., Taiwan). Signals were recorded using an 8-bit analog-to-digital converter with a sampling rate of 512 Hz. The digitized ECG signals were analyzed online and were simultaneously stored on a hard disk for offline verification. The computer algorithm then identified each QRS complex and rejected each ventricular premature complex or noise according to likelihood using a standard QRS template. Normal and stationary R–R interval values (RR) were resampled and interpolated at a rate of 7.11 Hz to produce continuity in the time domain. This interpolation produced 2,048 data points over 288 s, which was used for the subsequent Fourier transformation.

Frequency-domain analysis of the HRV

Power spectral analysis of the HRV was performed using a nonparametric method of fast Fourier transformation (FFT). The direct current component was deleted and a Hamming window was used to attenuate the leakage effect [35]. For each time segment (228 s, 2048 data points), our algorithm estimated the power spectrum density based on FFT. The resulting power spectrum was corrected for attenuation resulting from the sampling and the Hamming window. The power spectrum was subsequently quantified and modified to fit children based on standard frequency-domain measurements as defined previously [12, 36], including variance of R–R intervals (Var), very low-frequency power (VLF, 0.003–0.04 Hz), LF (0.04–0.15 Hz), HF (0.15–1.0 Hz), LF/HF and LF %, and total power (TP) of HRV. Var, VLF, LF, HF and LF/HF were logarithmically transformed to correct for skewness [10]. The HF component is modulated by respiratory sinus arrhythmia and is considered to represent vagal control of heart rate [37, 38]. LF % and LF/HF are considered by some investigators to reflect sympathetic modulations or to mirror the sympathovagal balance [12, 39, 40]. TP and LF heart oscillations are under joint sympathetic and parasympathetic control.

Statistical analysis

Student's *t* tests and chi-square tests were performed to compare data (including demographics, SNAP-IV scores, HRV profiles) of the boys and girls. Continuous variables are expressed as the mean ± standard deviation (SD), and categorical variables are expressed as frequencies (percentage). To identify associations between HRV parameters and SNAP-IV scale values, Pearson's correlation analysis was used. For the Pearson's correlation analysis, if the p value was less than 0.05, the variables were regarded as having a significant relationship. Finally, Fisher transformation was used to compare the correlation coefficients of boys and girls.

Results

Table 1 and Fig. 1 show the characteristics of all subjects. The children's average age was 5.61 ± 0.56 years old and consisted of 41 boys and 47 girls. The gestational age and birth weight of the two genders were not significantly different. After dividing all subjects into two groups based on gender, the boys' group had significantly higher scores for both the parent and teacher SNAP-IV scales compared to the girls, except for the ODD subscale of the SNAP-IV parent form (Fig. 1). Nevertheless, no statistically significant gender differences were found for the HRV measurements (Table 1).

In order to determine whether there are significant correlations between the SNAP-IV values and HRV parameters for the parent and teacher forms, Pearson's correlation

Table 1 Subject characteristics and HRV profiles in boys and girls

	All subjects ($N = 88$)	Boys	Girls	p value
Male/female	41/47	41	47	0.06
Age (years)	5.61 ± 0.56	5.59 ± 0.51	5.64 ± 0.56	0.62
Gestational age (weeks)	37.90 ± 4.82	37.31 ± 6.54	38.49 ± 2.05	0.29
Birth weight (kg)	3.15 ± 0.35	3.15 ± 0.35	3.17 ± 0.38	0.79
HRV measurements				
R–R intervals (ms)	616.70 ± 17.65	616.20 ± 19.44	617.20 ± 15.98	0.85
Var [ln(ms^2)]	7.78 ± 0.93	7.96 ± 0.83	7.69 ± 0.99	0.39
VLF [ln(ms^2)]	6.71 ± 8.54	6.77 ± 0.79	6.65 ± 0.92	0.47
LF [ln(ms^2)]	6.49 ± 0.94	6.67 ± 0.88	6.40 ± 0.97	0.82
HF [ln(ms^2)]	6.44 ± 1.30	6.71 ± 1.20	6.37 ± 1.35	0.53
TP [ln(ms^2)]	7.79 ± 0.95	7.94 ± 0.88	7.63 ± 0.99	0.95
LF % (v)	47.03 ± 15.84	45.54 ± 16.17	48.52 ± 15.04	0.35
LF/HF [ln(ratio)]	0.69 ± 0.74	−0.01 ± 0.75	0.14 ± 0.72	0.35

Data are presented as mean ± standard deviation

Analysis of the data was by Student's t test (for continuous variables) and by chi-square test (for categorical variables)

HRV heart rate variability, *Var* variance of R–R intervals, *VLF* very low frequency power, *LF* low frequency power, *HF* high frequency power, *TP* total power, *LF %* normalized LF, *LF/HF* ratio of LF to HF

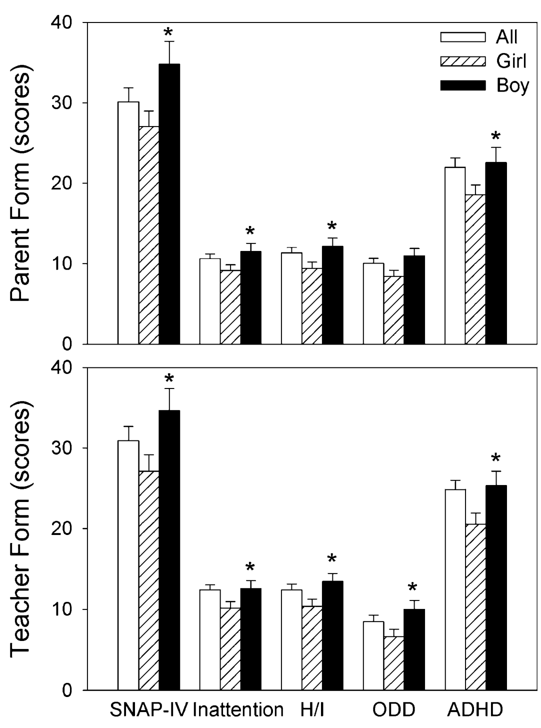

Fig. 1 Comparison of SNAP-IV scores of boys and girls. Analysis of the data was by Student's t test. *SNAP-IV* Swanson, Nolan and Pelham rating scale-IV, *ODD* oppositional defiant disorder, *ADHD* attention-deficit and hyperactivity disorder; $*p < 0.05$ versus girls

analysis was performed. In the first step of correlation analysis, the data from all subjects (including both boys and girls) were analyzed. For the SNAP-IV parent form scores and the HRV measurements, the results of Pearson's correlation analysis revealed that all four subscales and the total scale of the SNAP-IV parent form, except for the hyperactivity/impulsivity subscale, showed a positive correlation with HF. In addition, the four subscales and the total SNAP-IV parent form scale showed a negative correlation with LF % and LF/HF (Table 2). However, when the SNAP-IV teacher form scores and HRV measurements were examined, there were some differences compared to the parent results. The hyperactivity and ODD subscales of the SNAP-IV teacher form merely showed a negative but non-significant correlation with LF %, but the four subscales and the total SNAP-IV teacher form scale still showed a significantly negative correlation with LF/HF (Table 3).

In order to determine whether there are gender differences for the correlation between the SNAP-IV results and the HRV parameters, in the second step of the correlation analysis we divided the subjects by sex. We found that, among the boys' group, the Pearson's correlation analysis revealed that the total scale and the four subscales of the boys' SNAP-IV parent and teacher forms, except for the ODD subscale of SNAP-IV teacher form, showed a significant negative association with LF % and the LF/HF ratio. For the boys' group, only the inattention and ADHD subscales and the total scale of SNAP-IV parent form showed a positive correlation with HF. (Tables 2, 3). However, the girls' group did not produce the same findings and all results were not significant (Tables 2, 3).

Finally, Fisher transformation was performed to compare the correlation coefficients of the boys and girls. Considering the parent form SNAP-IV, we found that

Table 2 Pearson's correlation analysis of the SNAP-IV scores rating (parents) and the heart rate variability parameters

	Inattention subscale score	Hyperactivity/impulsivity subscale score	ODD subscale score	ADHD subscale score	SNAP-IV total score
All					
LF	0.110 (0.258)	−0.002 (0.982)	0.059 (0.557)	0.056 (0.579)	0.059 (0.554)
HF	0.246* (0.013)	0.167 (0.093)	0.209* (0.035)	0.220* (0.027)	0.226* (0.022)
LF %	−0.319** (0.001)	−0.368** (0.000)	−0.209* (0.003)	−0.371** (0.000)	−0.359** (0.000)
LF/HF	−0.425** (0.000)	−0.468** (0.000)	−0.393** (0.000)	−0.479** (0.000)	−0.467** (0.000)
Boys					
LF	0.116 (0.420)	−0.089 (0.530)	0.009 (0.950)	0.020 (0.891)	0.011 (0.942)
HF	0.392* (0.004)	0.228 (0.108)	0.209 (0.142)	0.293* (0.037)	0.331* (0.018)
LF %	−0.496** (0.000)	−0.483** (0.000)	−0.479** (0.000)	−0.449** (0.001)	−0.523** (0.000)
LF/HF	−0.507** (0.000)	−0.459** (0.000)	−0.467** (0.001)	−0.442** (0.000)	−0.513** (0.000)
Girls					
LF	0.234 (0.098)	0.042 (0.768)	0.109 (0.448)	0.149 (0.296)	0.143 (0.317)
HF	0.260 (0.065)	0.077 (0.590)	0.128 (0.372)	0.183 (0.199)	0.173 (0.224)
LF %	−0.153 (0.248)	−0.094 (0.531)	−0.075 (0.601)	−0.135 (0.344)	−0.121 (0.399)
LF/HF	−0.154 (0.281)	−0.067 (0.641)	−0.080 (0.575)	−0.120 (0.400)	−0.113 (0.432)

Data are presented as correlation coefficient (test of significance)

SNAP-IV Swanson, Nolan and Pelham rating scale-IV, *ODD* oppositional defiant disorder, *ADHD* attention-deficit and hyperactivity disorder, *LF* low frequency power [ln(ms^2)], *HF* high frequency power [ln(ms^2)], *LF %* normalized LF [in normalized units (v)], *LF/HF* ratio of LF to HF [ln(ratio)]

* $p < 0.05$, ** $p < 0.001$

Table 3 Pearson's correlation analysis of SNAP-IV scores rating (teachers) and the heart rate variability parameters

	Inattention subscale score	Hyperactivity/impulsivity subscale score	ODD subscale score	ADHD subscale score	SNAP-IV total score
All					
LF	−0.023 (0.822)	0.069 (0.493)	0.064 (0.525)	0.030 (0.765)	0.046 (0.645)
HF	0.085 (0.398)	0.170 (0.088)	0.140 (0.161)	0.149 (0.134)	0.154 (0.122)
LF %	−0.275* (0.005)	−0.189 (0.058)	−0.164 (0.100)	−0.263* (0.008)	−0.236* (0.017)
LF/HF	−0.380** (0.000)	−0.431** (0.000)	−0.359** (0.000)	−0.469** (0.000)	−0.446** (0.000)
Boys					
LF	0.035 (0.810)	0.069 (0.631)	0.063 (0.661)	0.045 (0.752)	0.033 (0.812)
HF	0.209 (0.141)	0.249 (0.078)	0.227 (0.110)	0.227 (0.110)	0.205 (0.148)
LF %	−0.290* (0.039)	−0.314* (0.025)	−0.271 (0.054)	−0.303* (0.031)	−0.288* (0.040)
LF/HF	−0.331* (0.020)	−0.342* (0.014)	−0.297* (0.038)	−0.338* (0.011)	−0.318* (0.026)
Girls					
LF	0.257 (0.068)	−0.024 (0.866)	0.184 (0.195)	0.133 (0.353)	0.162 (0.257)
HF	0.151 (0.219)	0.112 (0.432)	0.202 (0.156)	0.157 (0.270)	0.185 (0.746)
LF %	0.045 (0.753)	−0.238 (0.092)	0.096 (0.504)	−0.124 (0.386)	0.121 (0.397)
LF/HF	0.045 (0.752)	−0.246 (0.081)	−0.155 (0.276)	−0.129 (0.367)	0.110 (0.444)

Data are presented as correlation coefficient (test of significance)

SNAP-IV Swanson, Nolan and Pelham rating scale-IV, *ODD* oppositional defiant disorder, *ADHD* attention-deficit and hyperactivity disorder, *LF* low frequency power [ln(ms^2)], *HF* high frequency power [ln(ms^2)], *LF %* normalized LF [in normalized units (v)], *LF/HF* ratio of LF to HF [ln(ratio)]

* $p < 0.05$; ** $p < 0.001$

boys showed significantly higher correlation coefficients for LF %-inattention ($p = 0.039$), LF %-hyperactivity ($p = 0.026$), LF %-ODD ($p = 0.022$), LF/HF-inattention ($p = 0.034$), LF/HF-hyperactivity ($p = 0.026$) and LF/HF-ODD ($p = 0.027$) than girls. On the other hand, for HF-inattention, HF-hyperactivity and HF-ODD, the correlation coefficients of boys and girls were not significantly different. The result provides further support for the hypothesis that there is a gender difference associated with the correlation between sympathetic modulation and disruptive behavior symptoms.

Discussion

This is the first study to attempt to connect gender difference to the relationship between disruptive behaviors and HRV. Our study has three major findings. First, according to SNAP-IV scores, boys show more disruptive behavior (in the dimensions of inattention, hyperactivity/impulsivity and ODD) than girls, whereas the HRV manifestations of the two sexes are not significantly different. Second, the sympathetic indices LF % and LF/HF are negatively correlated with all dimensions of the parent form SNAP-IV. Separating the two genders, only the boys showed a significant correlation. This finding was true for both the parent and the teacher form of SNAP-IV. Third, HF, the parasympathetic index, revealed a positive correlation with inattention and the ODD dimensions of the parent form SNAP-IV. Considering the gender issue, only boys revealed a positive correlation between HF and inattention scores.

In this study, the sympathetic indices LF % and LF/HF showed a significant negative correlation with the dimensions of inattention, hyperactivity/impulsivity and ODD. The findings support our first hypothesis, namely that underarousal of the sympathetic tone is likely to be a contributing factor to disruptive behavior. Our results are similar to past studies using PEP and electrodermal activity as sympathetic indices [15, 17]. Frontal dysregulation and reduced sympathetic activity both involve the norepinephrine system. We hypothesize that the sympathetic dysregulation is a result of the frontal dysfunction, or, alternatively, the two systems that are involved noradrenergic dysfunction have a shared etiology. These two hypotheses need a well-designed experiment to differentiate them.

Unexpectedly, HF, the parasympathetic index, is positively correlated with inattention and ODD dimensions of the parent form SNAP-IV. Past studies have shown discrepancies in the parasympathetic activity of ADHD. Some research has suggested that the autonomic features of subjects with externalizing behaviors are due to reduced parasympathetic activity [15, 18, 41]. However, other studies have found that RSA is maintained at an elevated level during psychological tasks [19]. Lenard et al. [42] investigated the maturation of cardiovagal autonomic function from childhood to young adulthood. They found that cardiovagal activity may serve as an indicator of the efficiency of central parasympathetic signal processing. Cardiovagal activity increases during early ontogeny and reaches a peak value at adolescence [42], then declines with advancing age. Therefore, the different findings across the previous studies may be attributable to the different ages of the study groups. It is well known that ADHD symptoms change during maturation. Whether maturation of the autonomic system parallels fluctuations in disruptive behavior awaits further investigation. Furthermore, the average SNAP-IV scores in this study do not fulfill a diagnosis of ADHD or ODD. Another explanation is that "non-pathological" inattentive and ODD behaviors mainly originate from a low sympathetic tone, and the parasympathetic system has a modulating effect during the process. In subjects with ADHD or conduct disorder, dysregulation of the vagal system may cause more severe externalizing behaviors.

The HRV values for boys and girls did not show any significant differences. This implies that the different behavior patterns of boys and girls cannot solely be attributed to autonomic activity. This finding does not support our second hypothesis. The correlation analysis revealed that no matter which of the sympathetic or parasympathetic indices is explored, boys show a higher correlation with disruptive behaviors than girls. Thus, disruptive behavior can be predicted by ANS activity only in boys. Several hypotheses have been proposed to explain the gender difference in ADHD including hormonal effects, differences in the maturation curve, the influence of nurture, peer relationships and observer bias [27]. These issues need to be considered in future studies that are aimed at clarifying gender differences in relation to ANS activities and disruptive behavior.

Among our subjects, boys having a diagnosis of ADHD/ODD may be greater in number than girls based on the higher ADHD/ODD scores for boys. Based on this, there is a need to discuss whether the gender difference is actually based on the different proportion of disorders. The major finding of our study is the difference in the HRV-ADHD/ODD score correlation for the two genders and not the difference in HRV between the two genders. If the HRV profiles in boys and girls were different, this could easily be explained by the disorder. However, the HRV results for the two genders are not significantly different. Thus, the key point of our study is that the high correlation between HRV and ADHD/ODD scores is only found in boys, and we must assume that gender is a moderator in the above relation; this will need further research.

Both the parent and teacher form of SNAP-IV indicate that boys have a higher score for each dimension than girls. Parent scoring is lower for inattention and hyperactivity, while teacher scoring is lower for ODD. This implies that awareness of disruptive behavior may be different between teachers and parents, or that children show distinct behavioral patterns at home and school. Considering the correlation between SNAP-IV and ANS activity, the parent form and the teacher form show similar results for the sympathetic indexes. However, the parasympathetic index HF only shows a significant correlation for the parent form SNAP-IV. It is possible that children show higher vagal modulation in a familiar environment such as their home. This difference needs further investigation.

Several limitations of this study need to be highlighted. First, although we measured disruptive behavior symptoms using SNAP-IV, clinical evaluation by a psychiatrist was not performed. Therefore, whether a high score for SNAP-IV represents a diagnosis of ADHD or ODD is questionable. Second, this study did not provide standardized psychological stimuli, such as psychological tasks, and the HRV presentations are baseline rather than "reactivity." Some studies have found ADHD symptoms show a better correlation with the latter [19]. Third, some factors known to affect HRV, such as body mass index, emotional state and sleep patterns [43–45], were not gathered in this study. Finally, the cross-sectional design and correlation analysis used in this study are unable to show causation.

Our results support the connection between disruptive behavior and the ANS, especially the sympathetic system. In pre-school boys, ADHD and ODD behaviors may be related to sympathetic underarousal. A larger sample size, an investigation of other possible mechanisms that may affect disruptive behaviors in girls and the combining of psychological tasks with the measurement of autonomic reactivity need to be considered when future studies are conducted. Whether the autonomic features of ADHD and ODD change with the disease's course and with fluctuation in symptoms also warrants clarification.

Acknowledgments This work was supported by a grant (101AC-B3) from the Ministry of Education, Aim for the Top University Plan and a grant (NSC 100-2627-B-010-002), from the National Science Council (Taiwan). We thank Ms. Ying-Hua Huang and Wan-Han Hsu for their manuscript production support.

References

1. Association AP (1994) Diagnostic and statistical manual of mental disorders, fourth edition (DSM-IV). American Psychiatric Association, Washington, D.C.
2. Fayyad J, De Graaf R, Kessler R, Alonso J, Angermeyer M, Demyttenaere K, De Girolamo G, Haro JM, Karam EG, Lara C, Lepine JP, Ormel J, Posada-Villa J, Zaslavsky AM, Jin R (2007) Cross-national prevalence and correlates of adult attention-deficit hyperactivity disorder. Br J Psychiatry 190:402–409
3. Durston S (2003) A review of the biological bases of ADHD: what have we learned from imaging studies? Ment Retard Dev Disabil Res Rev 9:184–195
4. Biederman J, Spencer T (1999) Attention-deficit/hyperactivity disorder (ADHD) as a noradrenergic disorder. Biol Psychiatry 46:1234–1242
5. Levy F (1991) The dopamine theory of attention deficit hyperactivity disorder (ADHD). Aust N Z J Psychiatry 25:277–283
6. Groenewegen HJ, Uylings HB (2000) The prefrontal cortex and the integration of sensory, limbic and autonomic information. Prog Brain Res 126:3–28
7. Esler M, Turbott J, Schwarz R, Leonard P, Bobik A, Skews H, Jackman G (1982) The peripheral kinetics of norepinephrine in depressive illness. Arch Gen Psychiatry 39:295–300
8. Doyle AE, Faraone SV, Seidman LJ, Willcutt EG, Nigg JT, Waldman ID, Pennington BF, Peart J, Biederman J (2005) Are endophenotypes based on measures of executive functions useful for molecular genetic studies of ADHD? J Child Psychol Psychiatry 46:774–803
9. Bidwell LC, Willcutt EG, Defries JC, Pennington BF (2007) Testing for neuropsychological endophenotypes in siblings discordant for attention-deficit/hyperactivity disorder. Biol Psychiatry 62:991–998
10. Kuo TBJ, Lin T, Yang CCH, Li CL, Chen CF, Chou P (1999) Effect of aging on gender differences in neural control of heart rate. Am J Physiol 277:H2233–H2239
11. Loggia ML, Juneau M, Bushnell MC (2011) Autonomic responses to heat pain: heart rate, skin conductance, and their relation to verbal ratings and stimulus intensity. Pain 152:592–598
12. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology (1996) Heart rate variability: standards of measurement, physiological interpretation and clinical use. Circulation 93:1043–1065
13. Schachinger H, Weinbacher M, Kiss A, Ritz R, Langewitz W (2001) Cardiovascular indices of peripheral and central sympathetic activation. Psychosom Med 63:788–796
14. Scarpa A, Raine A (1997) Psychophysiology of anger and violent behavior. Psychiatr Clin North Am 20:375–394
15. Beauchaine TP, Katkin ES, Strassberg Z, Snarr J (2001) Disinhibitory psychopathology in male adolescents: discriminating conduct disorder from attention-deficit/hyperactivity disorder through concurrent assessment of multiple autonomic states. J Abnorm Psychol 110:610–624
16. Boyce WT, Quas J, Alkon A, Smider NA, Essex MJ, Kupfer DJ (2001) Autonomic reactivity and psychopathology in middle childhood. Br J Psychiatry 179:144–150
17. Crowell SE, Beauchaine TP, Gatzke-Kopp L, Sylvers P, Mead H, Chipman-Chacon J (2006) Autonomic correlates of attention-deficit/hyperactivity disorder and oppositional defiant disorder in preschool children. J Abnorm Psychol 115:174–178
18. Tonhajzerova I, Ondrejka I, Adamik P, Hruby R, Javorka M, Trunkvalterova Z, Mokra D, Javorka K (2009) Changes in the cardiac autonomic regulation in children with attention deficit hyperactivity disorder (ADHD). Indian J Med Res 130:44–50
19. Musser ED, Backs RW, Schmitt CF, Ablow JC, Measelle JR, Nigg JT (2011) Emotion regulation via the autonomic nervous system in children with attention-deficit/hyperactivity disorder (ADHD). J Abnorm Child Psychol (in press)
20. Luman M, Tripp G, Scheres A (2010) Identifying the neurobiology of altered reinforcement sensitivity in ADHD: a review and research agenda. Neurosci Biobehav Rev 34:744–754
21. Conners CK, Epstein JN, March JS, Angold A, Wells KC, Klaric J, Swanson JM, Arnold LE, Abikoff HB, Elliott GR, Greenhill LL, Hechtman L, Hinshaw SP, Hoza B, Jensen PS, Kraemer HC, Newcorn JH, Pelham WE, Severe JB, Vitiello B, Wigal T (2001) Multimodal treatment of ADHD in the MTA: an alternative outcome analysis. J Am Acad Child Adolesc Psychiatry 40: 159–167

22. Swanson JM, Sandman CA, Deutsch C, Baren M (1983) Methylphenidate hydrochloride given with or before breakfast: I. Behavioral, cognitive, and electrophysiologic effects. Pediatrics 72:49–55
23. Kieling C, Roman T, Doyle AE, Hutz MH, Rohde LA (2006) Association between DRD4 gene and performance of children with ADHD in a test of sustained attention. Biol Psychiatry 60:1163–1165
24. Rucklidge JJ (2008) Gender differences in ADHD: implications for psychosocial treatments. Expert Rev Neurother 8:643–655
25. Gershon J (2002) A meta-analytic review of gender differences in ADHD. J Atten Disord 5:143–154
26. Biederman J, Kwon A, Aleardi M, Chouinard VA, Marino T, Cole H, Mick E, Faraone SV (2005) Absence of gender effects on attention deficit hyperactivity disorder: findings in nonreferred subjects. Am J Psychiatry 162:1083–1089
27. Arnold LE (1996) Sex differences in ADHD: conference summary. J Abnorm Child Psychol 24:555–569
28. Hermens DF, Williams LM, Lazzaro I, Whitmont S, Melkonian D, Gordon E (2004) Sex differences in adult ADHD: a double dissociation in brain activity and autonomic arousal. Biol Psychol 66:221–233
29. Hermens DF, Kohn MR, Clarke SD, Gordon E, Williams LM (2005) Sex differences in adolescent ADHD: findings from concurrent EEG and EDA. Clin Neurophysiol 116:1455–1463
30. Swanson JM (1992) School-based assessments and interventions for ADD students. K.C. Publishing, Irvine
31. Collett BR, Ohan JL, Myers KM (2003) Ten-year review of rating scales. V: scales assessing attention-deficit/hyperactivity disorder. J Am Acad Child Adolesc Psychiatry 42:1015–1037
32. Liu YC, Liu SK, Shang CY, Lin CH, Tu CL, Gau SF (2006) Norm of the Chinese version of the Swanson, Nolan, and Pelham, version IV scale for ADHD. Taiwan J Psychiatry 20:209–304
33. Liu CC, Kuo TBJ, Yang CCH (2003) Effects of estrogen on gender-related autonomic differences in humans. Am J Physiol Heart Circ Physiol 285:H2188–H2193
34. Chen CJ, Kuo TBJ, Tseng YJ, Yang CCH (2009) Combined cardiac sympathetic excitation and vagal impairment in patients with non-organic erectile dysfunction. Clin Neurophysiol 120:348–352
35. Kuo TBJ, Chan SHH (1993) Continuous, on-line, real-time spectral analysis of systemic arterial pressure signals. Am J Physiol 264:H2208–H2213
36. Toweill DL, Kovarik WD, Carr R, Kaplan D, Lai S, Bratton S, Goldstein B (2003) Linear and nonlinear analysis of heart rate variability during propofol anesthesia for short-duration procedures in children. Pediatr Crit Care Med 4:308–314
37. Fouad FM, Tarazi RC, Ferrario CM, Fighaly S, Alicandri C (1984) Assessment of parasympathetic control of heart rate by a noninvasive method. Am J Physiol 246:H838–H842
38. Kuo TBJ, Lai CJ, Huang YT, Yang CCH (2005) Regression analysis between heart rate variability and baroreflex-related vagus nerve activity in rats. J Cardiovasc Electrophysiol 16:864–869
39. Malliani A, Pagani M, Lombardi F, Cerutti S (1991) Cardiovascular neural regulation explored in the frequency domain. Circulation 84:482–492
40. Pagani M, Montano N, Porta A, Malliani A, Abboud FM, Birkett C, Somers VK (1997) Relationship between spectral components of cardiovascular variabilities and direct measures of muscle sympathetic nerve activity in humans. Circulation 95:1441–1448
41. Mezzacappa E, Tremblay RE, Kindlon D, Saul JP, Arseneault L, Seguin J, Pihl RO, Earls F (1997) Anxiety, antisocial behavior, and heart rate regulation in adolescent males. J Child Psychol Psychiatry 38:457–469
42. Lenard Z, Studinger P, Mersich B, Kocsis L, Kollai M (2004) Maturation of cardiovagal autonomic function from childhood to young adult age. Circulation 110:2307–2312
43. Vallejo M, Marquez MF, Borja-Aburto VH, Cardenas M, Hermosillo AG (2005) Age, body mass index, and menstrual cycle influence young women's heart rate variability—a multivariable analysis. Clin Auton Res 15:292–298
44. Carney RM, Saunders RD, Freedland KE, Stein P, Rich MW, Jaffe AS (1995) Association of depression with reduced heart rate variability in coronary artery disease. Am J Cardiol 76:562–564
45. Jurysta F, Lanquart JP, Sputaels V, Dumont M, Migeotte PF, Leistedt S, Linkowski P, van de Borne P (2009) The impact of chronic primary insomnia on the heart rate—EEG variability link. Clin Neurophysiol 120:1054–1060