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Autonomic activity and somatic symptoms in response to success versus failure on a cognitive task: A comparison of chronic abdominal pain patients and well children

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Abstract

Objectives—To compare autonomic nervous system (ANS) activity and somatic symptoms in chronic abdominal pain (CAP) patients and well children during (a) resting baseline, (b) training in a cognitive task, and (c) random assignment to success vs. failure on the task.

Methods—The ECG was continuously recorded with a dual lead system (Biopac) in 45 CAP patients and 22 well children, ages 9–16 years (mean age = 12.3). Heart rate variability (HRV) was analyzed during the 5 minute resting baseline, training, and success/failure on the task. Performance expectations were assessed before the task. Gastrointestinal (GI) and non-GI somatic symptoms were assessed before and after the task.

Results—Compared to well children, CAP patients reported lower expectations for their task performance and higher GI symptoms (p 's < 0.05). During success, CAP patients exhibited significant increases in both sympathetic (p < 0.05) and parasympathetic (p < 0.05) activity whereas well children exhibited no change in ANS activity. During failure, CAP patients exhibited significant increases in somatic symptoms (< 0.05) but no change in ANS activity.

Conclusions—The lower performance expectations of CAP patients compared to well children may have influenced their experience of success and contributed to differences in their autonomic activity.

Keywords

chronic abdominal pain; heart rate variability; co-activation; autonomic nervous system; stress

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Introduction

Chronic abdominal pain (CAP) is a common pediatric problem that often occurs without evidence of organic disease [1,2]. Medical evaluations show that the majority of CAP patients meet diagnostic criteria for a functional gastrointestinal disorder [3–5]. Psychological evaluations link CAP to emotional distress, primarily anxiety [6,7]. For many children, somatic and emotional symptoms associated with pediatric CAP continue into adolescence and young adulthood [1,8–10].

Psychological stress is widely believed to precipitate or exacerbate abdominal pain and other somatic symptoms associated with CAP. Several studies have shown that CAP patients more frequently experience major stressful life events than children without CAP [11–13]. In addition, a diary study found that, in comparison to well children, CAP patients reported significantly more hassles (i.e., minor stressors) during school hours [14]; moreover, the within-subject correlation between school day hassles and somatic symptoms was significantly higher for CAP patients than well children. These findings suggest that school may be an important source of recurring acute stress for CAP patients. Studies that expose CAP patients to acute stress under controlled laboratory conditions are needed to further our understanding of the behavioral and physiological impact of stress on CAP patients.

Stress can be defined as a real or perceived threat to homeostasis that triggers adaptive responses including behavior as well as neuromuscular, endocrine, immune, autonomic and visceral functions [15,16]. Dorn and colleagues conducted one of the few laboratory studies of CAP patients' physiological responses to stressors [17]. The laboratory stressors in their study -- public speaking and mental arithmetic -- were similar to those children experience at school. Their physiological measures included heart rate, blood pressure, and salivary cortisol. Results indicated that both CAP patients and patients with anxiety disorders had higher levels of systolic blood pressure following the laboratory stressors, although the comparison to well children did not achieve statistical significance. The authors recommended that future research with larger samples of CAP patients examine autonomic nervous system (ANS) activity during acute stress. Another study [18] found no ANS differences between CAP patients and well children during rest and also recommended study of ANS activity in CAP patients during acute stress. The ANS provides essential communication between the central nervous system and the gastrointestinal tract [19,20]. Thus, ANS activity is particularly relevant to understanding mechanisms linking psychological stress to symptoms in CAP patients.

Heart rate variability (HRV) -- the beat-to-beat alterations in heart rate -- serves as a non-invasive, indirect measure of ANS activity [21,22]. HRV is sensitive to acute stress [23–25]. Spectral analysis of the electrocardiogram (ECG) partitions the total variance in HRV into rhythms that occur at different frequencies. The high frequency (HF) component of HRV is mediated by parasympathetic nervous system activity and serves as an index of vagal tone. Its measurement is proposed as a method to assess an individual's vulnerability to stress [26]. Low vagal tone (low HF) reflects lack of ANS flexibility and has been associated with a variety of poor health outcomes [27,28]. The low frequency (LF) component of HRV has been used as an index of sympathetic influences on the heart but this perspective has been challenged [29,30] and the autonomic correlates of LF remain uncertain. By assessing ANS influences on cardiovascular activity, spectral analysis provides a "window" onto the interaction of sympathetic and parasympathetic tone and gives more detailed information about ANS activity than heart rate itself.

The present laboratory study investigated ANS activity and somatic symptoms in CAP patients and healthy children at rest and during a task similar to a classroom assignment. Using

electrocardiogram (ECG), we assessed participants' ANS activity while they learned a novel cognitive task and subsequently performed the task. Participants were randomly assigned, without their awareness, to succeed or fail on the task. Thus, we manipulated children's exposure to a stressor – task failure -- and evaluated the impact of the stressor by assessing changes in ANS activity and somatic symptoms from pre- to post-performance following randomization to success versus failure conditions.

Other investigators have observed vagal withdrawal (i.e., decreases in HF) in response to laboratory stressors such as mental arithmetic [31]. Therefore, in this study we hypothesized that CAP patients would exhibit decreased HF (parasympathetic) activity, i.e., vagal withdrawal, and a reciprocal increase in LF activity in response to task failure. We expected that these changes in autonomic activity would be significantly greater in CAP patients than Well children because of CAP patients' greater vulnerability to stress. Immediately prior to beginning the task, we assessed children's performance expectations, i.e., how well they expected to perform on the task compared to other children their age. Because CAP is associated with somatization [32,33] and school stress has been linked to both GI and non-GI symptoms in CAP patients [14], we also assessed GI symptoms and non-GI somatic symptoms before and after task performance. We hypothesized that CAP patients would experience greater increases in GI and non-GI somatic symptoms than well children in response to failure on the task.

Materials and Methods

Study Sample

The study population consisted of 45 consecutive new patients referred for evaluation of chronic abdominal pain at the pediatric gastrointestinal (GI) clinic of the Children's Hospital at Vanderbilt University and 22 Well children recruited from participants in a health survey conducted in the local public schools.

Patients were eligible for participation if they met the following criteria: (a) primary presenting complaint of at least three episodes of abdominal pain interfering with activities during the last three months; (b) no chronic illness (e.g., Crohn's disease, pancreatitis, diabetes, epilepsy); (c) not on tricyclic antidepressant or beta blocker medications (d) child and parent able to communicate in English; and (e) child between the ages of 9 and 16 years. The same eligibility criteria (b–e) were applied to well children; those well children who reported more than two episodes of abdominal pain in the past 2 weeks were excluded.

The majority (92%) of both CAP patients and well children were Caucasian. Forty-six percent of participants came from two-sibling and 32% from three-sibling families. Neither family size nor the child's birth order differed between CAP patients and well children. The gender distribution of participants (55% female) did not differ significantly between CAP patients and well children. Participants ranged in age from 9 to 16 years. The mean age of well children ($M = 13.6$ years) was significantly greater than that of CAP patients ($M = 11.6$ years), $p < 0.001$, due to an equipment failure that resulted in the loss of data from several younger children in the well group.

Procedure

Parents of eligible patients and well children were contacted by telephone, the study was described to them, and those who were interested in participating were scheduled for the study. Informed consent procedures for parent and child were conducted in our laboratory prior to beginning the study protocol.

All participants (patients and well children) were tested on the same equipment in the same room with lighting and temperature kept constant (71.3 F). Participants were instructed not to drink any caffeinated beverages before the laboratory session. The majority of participants were tested in the mid-afternoon on a weekend. Parents left the testing room following consent procedures and placement of ECG leads.

The study protocol was the same for all participants. First, study participants were seated in a chair while we recorded resting ECG activity for five minutes. Next, participants received instructions from the experimenter in a cognitive problem-solving task administered by computer. This task (modified from Diener and Dweck [34]) involved identifying the next pattern in a sequence of shapes and colors. Training for the task lasted approximately 20 minutes and included practice trials. All participants demonstrated success on a practice trial prior to beginning the task. Following training, participants completed a brief questionnaire assessing their current level of GI symptoms and non-GI somatic symptoms. They also responded to a question assessing their performance expectations, that is, how well they expected to perform on the task compared to other children their age. Finally, participants were randomly assigned to either the “success” or “failure” condition on the task, which had three trials. Participants in the success condition succeeded on all three trials; those in the failure condition failed on all three trials. Participants were not aware that their success versus failure was manipulated by the experimenters. Following completion of the task, participants again completed a questionnaire assessing their current level of GI symptoms and non-GI somatic symptoms. Prior to leaving the laboratory, participants and their parents were debriefed regarding the manipulation of success and failure on the task.

The proportion of CAP patients and well children was similar in the success and failure conditions. The experimenter was blind to the randomly assigned condition (success or failure) and to the participant’s health status (CAP, well).

The study was approved by the Vanderbilt University Medical Center Institutional Review Board.

ECG Recording

Dual-lead ECG was recorded at 1 kHz sample rate (Biopac Systems Inc. ®) throughout the study.

Signal Processing—R-peak detection in recorded ECG and analysis of R-R intervals and HRV time and frequency variables were performed by a customized MATLAB analysis program (*HRV Analyzer*® André Diedrich and Rob Brychta, Vanderbilt University, Autonomic Dysfunction Center) using guidelines of the Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology [35]. Correct identification of the R-peak was visually verified and edited if necessary. Four participants with excessive noise in the ECG recording were excluded.

Spectral Analysis of HRV frequency domain measures—Beat-to-beat values of R–R intervals were interpolated, low-pass filtered (cutoff 0.5 Hz), and re-sampled at 4 Hz. Data segments of 300 seconds were used for spectral analysis. Linear trends were removed and power spectral density was estimated with the FFT-based Welch algorithm using segments of 256 data points with 50% overlapping and Hanning window [11]. The power in the frequency range of low frequencies (LF: 0.04 to 0.15 Hz) and high frequencies (HF: 0.15 to 0.40 Hz) as well as total power (TP) were calculated following Task Force recommendations [31]. For short-term stationary recordings such as those obtained in this study, HRV frequency domain measures (LF, HF, TP) are more frequently used and interpreted in terms of physiological

response than time domain measures (e.g., R-R intervals) [31]; therefore, we followed the Task Force recommendation and focused data analysis on frequency domain measures.

Self-report Measures

GI and Non-GI Somatic Symptoms were assessed by asking participants to rate the severity of four GI symptoms (e.g., stomach ache, nausea) and eight non-GI somatic symptoms (e.g., headache, dizzy, tired) commonly reported by CAP patients (Walker et al., 2006). Participants were asked, “How much do you feel _____ right now?” They responded on a 5 point scale (0 = not at all; 1 = a little; 2 = some; 3 = a lot; 4 = a whole lot). Total scores for the GI Symptom Index and the Non-GI Somatic Symptom Index were calculated as the mean rating for symptoms on each measure. Internal consistency reliability was adequate for the GI Symptom Index ($\alpha = .78$) and the non-GI Symptom Index ($\alpha = .77$). Symptom ratings were administered preceding the computer task and immediately following success or failure on the task.

Performance Expectations were assessed prior to beginning the task with the question: “How well do you think you’ll do compared to other kids your age?” Participants’ responded to a 5 point Likert-type scale (much worse; somewhat worse; the same as; somewhat better; much better).

Statistical Analysis

All HRV measures were non-parametric; therefore, we conducted data analysis using medians and ranges rather than means and SD’s. Medians and ranges were calculated for all HRV measures at rest, during training, and during the success and failure conditions.

Differences between CAP patients and well children were assessed at each of three periods: baseline period; training period; and success (vs. failure) period. Because the HRV measures were heavily skewed to the right, the Wilcoxon rank-sum and Kruskal-Wallis tests were used to test for differences between the CAP and well groups.

Changes over time in HRV measures were assessed in the following periods of the experiment: baseline to instruction period; baseline to the success arm of the cognitive task; and baseline to the failure arm of the cognitive task. To analyze the individual-level data and account for repeated measures over time, we used generalized estimating equations (GEE’s). [36] This approach, considered superior to ANOVA, allowed us to adjust for baseline measures and age differences. We used the natural logarithm of the HRV measures in these analyses to account for their skewness. In our GEE models, we considered independence, first-order autocorrelation, and exchangeable working correlation matrices. Since all three produced similar results, we report the findings using the independence working correlation matrix.

The scores of CAP patients and well children on measures of GI and non-GI symptoms were compared before and after randomization using two-sample t-tests. All analyses were performed using the statistical software package Stata version 9.0 (Stata Corp, College Station, TX).

Results

Table 1 presents HR and HRV measures for CAP patients and well children during all phases of the study (baseline resting period; instruction period; success vs. failure on computer task).

Figure 1 shows examples of Power Spectral Density HRV measures for CAP patients and well children at baseline and during the failure and success conditions.

Baseline resting period

During the baseline resting period, CAP patients and well children did not differ on any HRV measure (see Table 1 and Figure 1).

Instruction period

Heart rate variability measures—For both CAP patients and well children, the instruction period was associated with increased HF and LF compared to the baseline resting period (Table 1). The increase in LF from baseline to instruction period was statistically significant for CAP patients ($z = -3.018$; $p < 0.01$) but not for well children. Levels of both HF and LF were significantly higher in CAP patients than well children during the instruction period (p 's < 0.01). When adjusted for baseline and age, these differences between CAP and well during the instruction period were attenuated but approached significance for LF ($p > 0.05$).

Self reported symptoms and performance expectations prior to task

performance—CAP patients reported significantly more GI symptoms than well children immediately prior to randomization into success vs. failure conditions (mean 1.5 vs. 1.1; $t = -2.29$; $p < 0.01$) but did not differ on non-GI symptoms (mean 1.9 vs. 1.6; $t = -1.89$; $p > 0.05$). Prior to beginning the task, CAP patients reported significantly lower expectations for their performance than well children (mean = 3.3 vs. 3.7; $t = 3.11$; $p < 0.01$).

Task Performance Period: Success and Failure Conditions

Differences in median heart rate variability measures between CAP patients and well children during task failure and task success are illustrated in Figure 2.

Failure condition—In both groups the task failure period was associated with further increases in LF and HF compared to the instruction period. However, these increases did not reach statistical significance. Moreover, CAP patients did not differ significantly from well children on any HRV measure assessed during the failure period.

Success condition—CAP patients exhibited a three-fold increase in HF from the resting baseline period to the period of successful task performance ($z = -3.27$; $p = 0.001$). In contrast, levels of HF in well children were not significantly different between the baseline and success periods ($z = -0.065$; $p > 0.05$). CAP patients also exhibited a significant increase in LF from baseline to the success period ($z = -3.48$; $p < 0.001$). Levels of LF in well children did not change significantly from the baseline to success periods ($z = -0.079$; $p > 0.05$).

Adjusting for age and baseline, levels of LF, HF, and TP during the success period were significantly higher for CAP patients than well children, as shown in Table 2.

Self reported symptoms after success vs. failure on the task—In the failure condition, the increase in non-GI somatic symptoms from pre- to post- failure was significantly greater in CAP patients compared to well children (mean difference = 0.227 versus 0.001, $t = -2.31$; $p < 0.05$). GI symptoms, however, did not increase significantly from pre- to post- failure for CAP patients. In the success condition, no significant increases in GI or non-GI somatic symptoms were observed for CAP patients or well children.

Discussion

The most striking finding of this study was unexpected: CAP patients randomized to the success condition on a cognitive task exhibited a significant, three-fold increase from baseline in the HF component of HRV while the LF component simultaneously increased. Well children, in contrast, exhibited no significant change in HF or LF during successful performance of the

same task. Controlling for age and baseline levels, both HF and LF components of HRV were significantly higher in CAP patients than well children during successful task performance. Thus, successful task performance appears to have produced co-activation of sympathetic and parasympathetic activity in CAP patients comparable to driving full throttle while slamming on brakes.

Sympathetic and parasympathetic activity traditionally are viewed as acting reciprocally, as observed in both the baroreceptor reflex and in response to behavioral demands such as a mental arithmetic. Co-activation of sympathetic and parasympathetic activity, however, is associated with several other reflexes [37] and also has been observed during laboratory tasks associated with focused attention [31] and social touch [38]. The functional significance of co-activation is not well understood, although it appears to be associated with increased cardiac output [39]. Berntson and colleagues' [40] doctrine of autonomic space provides an overarching conceptual framework for understanding multiple modes of autonomic control, including reciprocal, co-activation, and co-inhibition. As noted by Wilhelm [38], personal meaning may play an important role in determining a person's mode of autonomic control in a particular situation.

Findings from psychological measures administered in the present study suggest that differences in the meaning of successful task performance for CAP patients and well children might underlie differences in their ANS activity during success. Prior to the task, CAP patients endorsed significantly lower performance expectations than well children. This is consistent with evidence that CAP patients are less confident of their ability to cope with daily stress compared to healthy peers [41]. If CAP patients were less confident than well children of their ability to maintain successful performance throughout all three trials of the task, their increased autonomic activity during success may have reflected greater vigilance and anticipation of potential failure. This possibility should be explored in future studies that include more extensive assessment of children's expectations and subjective experience during tasks involving success versus failure.

Of course, interpretation of co-activation of HF and LF components of HRV as increased sympathetic and parasympathetic response should be made with caution, as the level of modulation of low frequency heart rate variability by the sympathetic branch is still debated. Correlations with other clearly sympathetic measures, such as blood pressure, skin conductance, skin temperature or muscle sympathetic nerve activity, should be investigated in the future.

We had predicted that changes in HRV would occur for CAP patients randomized to failure rather than to success, and that those changes would be characterized by vagal withdrawal - decreases in the HF component of HRV. This prediction was based on the assumption that task failure would constitute a psychological stressor for CAP patients and that their autonomic response would be similar to that observed in other laboratory studies of ANS responses to mental stressors. For both CAP patients and well children, however, differences in ANS activity between the baseline resting period and the failure period were minimal. Perhaps the task was not sufficiently stressful to activate a physiological stress response. Low performance expectations also may have protected the CAP patients from experiencing task failure as stressful. Finally, others have demonstrated considerable variability in patterns of ANS responses to different types of laboratory tasks [31]. It is possible that we would indeed have observed vagal withdrawal in CAP patients if we had used the mental arithmetic or public speaking paradigms employed in other studies. We chose the computer task for this study because it allowed us to compare responses to a positive versus negative outcome (success versus failure) in a challenge similar to those children experience in the classroom. Future research should examine autonomic responses by CAP patients to a variety of laboratory tasks.

Although CAP patients did not exhibit significant changes in ANS activity during task failure, they appear to have experienced increased subjective distress. Specifically, they reported significantly greater increases in non-GI somatic symptoms than well children following failure. This finding is consistent with the observation that school stress is associated with increases in somatic symptoms in CAP patients [14]. It is possible that increases in somatic symptoms in CAP patients in this study reflected a behavioral response to failure that was not manifest in ANS activity. Divergence of subjective experience and physiological responding is not uncommon [38]. Amplification of somatic symptoms is characteristic of somatization and functional somatic syndromes such as CAP [42,43] and might function to elicit sympathy from others.

During the baseline resting period in this study, we observed no differences in HRV measures between CAP patients and well children. Similarly, Olafsdottir [18] found no ANS differences between CAP patients and well children during rest. Results of studies of resting ANS activity in adults with functional gastrointestinal symptoms have been mixed. Compared to healthy controls, vagal tone was significantly lower during rest in patients with functional dyspepsia [44,45], but did not differ in women with irritable bowel syndrome (IBS) [46]. Heitkemper's subgroup analysis of patients with the most severe IBS symptoms, however, indicated that low vagal tone may have been related to constipation-predominant IBS and high vagal tone to diarrhea-predominant IBS. Subgroup analysis was beyond the scope of the present study but, as Heitkemper suggested, the pattern and severity of symptoms may be important to consider in future studies of HRV in pediatric patients with functional gastrointestinal disorders. Psychological characteristic such as trait anxiety also might explain individual differences in CAP patients' physiological responses in the laboratory.

This study had limitations similar to those of the few other studies of ANS activity in pediatric patient populations. It was beyond the scope of the study to control for the numerous factors that may affect ANS activity including gender, pubertal status, body mass index, and time of day [47]. In addition, in our effort to minimize any risks to our child participants, we may have designed a failure condition that was not sufficiently stressful to affect children's physiological activity. Finally, although we investigated responses to two experimental conditions (success vs. failure), these were in the context of a single laboratory task. Different types of laboratory tasks may elicit different patterns of ANS activity [31].

Future research on ANS activity in CAP patients should investigate not only laboratory conditions presumed to evoke stress but also other behavioral contexts that may elicit distinctive modes of ANS activity that distinguish CAP patients from their peers. Our findings suggest that it will be critical to include measures of the subjective meaning of the laboratory experience in these studies in order to fully understand the participants' autonomic responses. Finally, future studies should include collateral physiological measures to assess the level of cardiac efficiency or inefficiency caused by co-activation and other modes of ANS control.

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Figure 1.

Examples of a typical Power Spectral Density (PSD) estimated with the FFT-based Welch algorithm and Hanning window in CAP patients and well children (a) at baseline, (b) during success condition, and (c) during failure condition.

Figure 2.

Differences in median heart rate variability measures between CAP patients and well children during task failure and task success.

Table 1

Mean heart rate and median scores on heart rate variability measures for CAP patients and well children during initial resting period, instruction period and success and failure periods of the computer task

	Mean Heart rate (bpm)			Median Low Frequency (msec2)			Median High Frequency (msec2)			Median Total Power (msec2)		
	CAP	Well	p	CAP	Well	p	CAP	Well	p	CAP	Well	p
Baseline	87.1	86.8	ns	930.0	765.4	ns	539.3	510.1	ns	2457.3	1887.6	ns
Instruction	86.3	86.9	ns	1042.4	862.2	0.04	660.0	534.7	0.004	2788.6	2301.4	0.06
	CAP	Well	p	CAP	Well	p	CAP	Well	p	CAP	Well	p
Success	84.3	90.2	ns	1635.5	831.1	0.03	1624.0	600.1	0.04	4264.5	2750.4	0.02
Failure	88.0	84.5	ns	1129.0	1233.5	ns	867.0	915.1	ns	3132.4	3517.7	ns

Note: During baseline and instruction: CAP n =45, well n =22;

In success condition: CAP n =23, well n =11;

In failure condition: CAP n =22, well n =11

Table 2

Differences in heart rate variability measures between CAP patients and well children during the success condition, adjusted for age and baseline measures using the GEE model

	Mean Difference CAP-Well	95% CI	<i>p</i>	<i>z</i>
logLF	0.50	−0.04, 0.97	0.03	2.12
logHF	0.54	−0.14, 0.95	0.01	2.42
logTP	0.41	−0.03, 0.86	0.06	1.83