Prospective Clinical Research Report

Journal of INTERNATIONAL MEDICAL RESEARCH

Journal of International Medical Research
2022, Vol. 50(9) 1–14

DOI: 10.1177/03000605221127104
journals.sagepub.com/home/imr
SAGE

The association between heart rate variability and skin conductance: a correlation analysis in healthy individuals and patients with somatic symptom disorder comorbid with depression and anxiety

Wei-Lieh Huang[1,2,3], Li-Chin Ko[4] and Shih-Cheng Liao[2,5]

Abstract

Objective: To investigate the correlations between heart rate variability (HRV) and skin conductance (SC) in two populations under three different situations.

Methods: This cross-sectional study enrolled patients with somatic symptom disorder comorbid with depression and anxiety and healthy individuals without a psychiatric history. The biological signals were measured under three conditions: resting state, during a cognitive task and during paced breathing. Pearson's correlation analysis and the generalized estimating equation were used to examine the correlations between SC and HRV in the two populations under the three situations.

Results: The study enrolled 97 patients with somatic symptom disorder comorbid with depression and anxiety and 96 healthy individuals. In healthy individuals, the ratio of low-frequency power to high frequency power (LF/HF) and normalized LF (LF%) were significantly correlated with SC in the resting state and during a cognitive task, but the correlation coefficients were low level. In patients with somatic symptom disorder comorbid with depression and anxiety, LF/HF and LF% did not show significant correlations with SC under any situation.

[1]Department of Psychiatry, National Taiwan University Hospital Yunlin Branch, Yunlin
[2]Department of Psychiatry, College of Medicine, National Taiwan University, Taipei
[3]Graduate Institute of Clinical Medicine, College of Medicine, National Taiwan University, Taipei
[4]Department of Neurology, National Taiwan University Hospital, Taipei
[5]Department of Psychiatry, National Taiwan University Hospital Hsin-Chu Branch, Hsin-Chu Hospital, Hsin-Chu City

Corresponding author:
Shih-Cheng Liao, Department of Psychiatry, National Taiwan University Hospital Hsin-Chu Branch, No. 2, Sec. 1, Shengyi Road, Zhubei City, Hsinchu County 302.
Email: scliao@ntu.edu.tw

Conclusions: The two different populations and three situations might have affected the significance of the LF/HF-SC and LF%-SC correlations. The generally low correlations indicate that LF/HF and LF% cannot fully reflect the sympathetic cholinergic activity represented by SC.

Keywords

Heart rate variability, skin conductance, autonomic activity, psychiatry

Date received: 9 May 2022; accepted: 1 September 2022

Introduction

Heart rate variability (HRV) has been widely applied in the psychiatric field. It is viewed as a candidate biomarker of many psychiatric disorders and often considered as an index of psychological pressure, the observing target in biofeedback therapy.[1,2] The biological meaning of HRV is often viewed as an indicator of autonomic activity; for example, high-frequency power (HF) and root mean square of successive differences (RMSSD) are considered as parasympathetic indices, whereas total power and standard deviation of normal-to-normal RR intervals (SDNN), which represent the total variability, are also suggested to reflect mainly parasympathetic modulation.[1–3] With regard to sympathetic activity, some scholars suggested that normalized low-frequency power (LF%) and the ratio of low-frequency power to high-frequency power (LF/HF) can reflect sympathetic function, but this is still controversial; low-frequency power (LF) is often considered to be modulated by both sympathetic and vagal systems.[2,4]

The controversy about LF/HF can be understood from the physiological aspect. The proportion of sympathetic activity in LF is not fixed; it would fluctuate in different situations.[2] Under a resting sitting condition, LF is mainly contributed by parasympathetic and baroreflex activities rather than sympathetic activity.[2] Low respiratory rate causes LF to reflect more parasympathetic activity.[2] LF/HF with recording times of 24 hr and 5 min were found to correlate poorly.[5] Because LF is modulated by several systems, and the activity of these systems fluctuated in different situations, it is hard to extract a quantitative value of sympathetic tone in mathematical ways. Therefore, even HF is widely accepted as a valid parasympathetic biomarker, viewing LF/HF as an index of sympathovagal balance or sympathetic index may be an over-simplified approach. Clarifying the biological mechanisms of the distinct HRV indicators should be meaningful for understanding the neurological process related to the psychological phenomena.

Along with the flourishing of biofeedback therapy, there are now convenient instruments that can measure HRV and other biological signals concurrently.[6,7] Among these biological signals, some are considered more representative for reflecting sympathetic activity than HRV, such as skin conductance (SC);[8,9] although SC cannot be viewed as the gold standard of sympathetic activity. Therefore, if SC and HRV can be recorded at the same time, correlation analyses can be performed to clarify their associations. In this manner, the question of whether HRV can provide meaningful data about sympathetic activity can be further clarified.

Another interesting issue is whether the associations between HRV and SC are affected by different populations and conditions. In the psychiatric field, HRV is often applied in patients with depression, anxiety and somatic symptoms; these emotional and somatic problems have a high tendency for comorbidity.[10–14] Besides the resting state HRV, the HRV reactivity design has been studied increasingly in recent years.[15–17] Common approaches to HRV reactivity designs include the biological and psychological challenging of subjects.[8,13] As mentioned above, short-term stress and changing respiratory rate may change the proportion of the sympathetic component in LF.[2] Thus, this current study was interested in whether the correlations between HRV and SC have distinct patterns with different populations and situations. The current study also aimed to investigate whether the respiratory rate affects the above correlations.

The main objective of the present study was to investigate the correlations between HRV (especially LF/HF and LF%) and SC in two different populations under three different situations. The situations included resting state, during cognitive tasks and during paced breathing. The populations included healthy individuals and patients with somatic symptom disorder comorbid with depression and anxiety.

Patients and methods

Participants

This cross-sectional study enrolled consecutive psychiatric patients visiting the outpatient clinic at of the National Taiwan University Hospital Yunlin Branch (NTUHYL), Yunlin with somatic symptom disorder comorbid with depression and anxiety; and consecutive healthy individuals without psychiatric history living in the communities near the NTUHYL by posting advertisements between January 2019 and December 2020. The inclusion criteria were as follows: (i) somatic symptom disorder; or (ii) healthy population without psychiatry history. The exclusion criteria were as follows: (i) <20 or >70 years old; (ii) psychotic symptoms; (iii) difficulty completing the questionnaires or measurement of signals; (iv) lethal physical illness; (v) diseases that obviously affect HRV or SC (arrhythmia, heart diseases, diabetes mellitus); (vi) medications that obviously affect HRV or SC (anti-arrhythmic agents, tricyclic antidepressants, multi-acting-receptor-targeted-antipsychotics). After providing informed consent, eligible participants completed questionnaires on their psychological states and demographic data and then received biological signal measurement in three situations (i.e. resting state, under cognitive task and under paced breathing).

The diagnosis of somatic symptom disorder was confirmed by a board-certified psychiatrist (W.L.H.). Common comorbidities in these patients included major depressive disorder, panic disorder and generalized anxiety disorder. Because of the high tendency of these comorbidities, questionnaires that reflected the level of somatic distress (Patient Health Questionnaire-15), hypochondriacal ideation (Health Anxiety Questionnaire), depression (Beck Depression Inventory-II) and anxiety (Beck Anxiety Inventory) were used for presenting their psychological features.[18–21] This approach was considered to be more suitable than separating them according to the dichotomous diagnosis.[22,23] The data used for analysis were de-identified.

The Institutional Review Board of National Taiwan University Hospital, Taipei approved the study (Approval number: 201607029RIND). All study participants provided written informed consent. The reporting of this study conforms to STROBE guidelines.[24]

Heart rate variability

The study participants, in clear consciousness and a sitting position, were subjected to three 5-min HRV measurements using ProComp5 Infiniti™ (Thought Technology, Montreal, Canada); similar equipment that had been applied in other HRV studies.[25,26] The raw signals of heart rate were from lead I electrocardiography and were gathered at a sample rate of 2048 Hz. The raw signals were then managed via the CardioPro Infiniti HRV analysis module (Thought Technology). In this step, non-periodic signals were removed and the inter-beat intervals (IBI) were generated. Electrocardiographic signals were inspected manually for excluding the obvious artifacts. Only a low proportion of signals was removed; the mean data length after this step was 289 s. SDNN was calculated from the IBI data and fast Fourier transformation was performed to generate the frequency-domain HRV data: the three frequency bands were <0.04 Hz (very-low-frequency power, VLF), 0.04–0.15 Hz (low-frequency power, LF) and 0.15–0.4 Hz (high-frequency power, HF). The LF/HF ratio, LF% and normalized HF (HF%) were calculated from the above data.[25,26]

Skin conductance

The values of SC were gathered at the same time as HRV using ProComp5 Infiniti™. For measuring SC, two electrodes were connected to the participant's two fingers of one hand.[27] Ethanol was used to prepare the skin area before recording signals. No conductive gel was used. The main parameter of SC is the amplitude of the electrodermal activity with the unit μS. Manual inspection was performed for removing obvious artifacts of SC also. SC for the present study (the mean value over 5 min) mainly corresponded to the 'tonic' rather than the 'phasic' SC response.[28–30] The sampling rate of the SC was 256 Hz.

Situations of measurement

The change of biological signals in three 5-min situations were measured, with a 1-min interval between each. The similar protocol (including 1-min interval) has been adopted in other studies.[16] The first situation was the resting state, where participants were subjected to measurement without any specific physiological or psychological manipulation. The second situation was during a cognitive task, where participants performed a computer-based colour-word Stroop task. There were three colours (red, blue, green) revealed in Chinese characters in the task; the participants were asked to answer the correct colour verbally as soon as possible. The purpose of doing a mental task was to increase the pressure during the process; therefore, the participant's performance of the task was not recorded. The third situation was paced breathing. All participants were asked to breath slowly (the respiratory rate was 0.1 Hz) by computer instruction. This frequency is commonly used in biofeedback therapy and has been reported to enhance relaxation.[31] In this current study, no participants reported overt discomfort during this process. The durations of inspiration and expiration were 4 s and 6 s, respectively. Slow breathing is considered to elevate HRV and parasympathetic activity, but the main frequency band of vagal activity moves from HF to LF.[2] The measured mean respiratory rates of the three conditions were 14.36/min, 13.21/min and 7.08/min, respectively.

Statistical analyses

All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA). The available case method was adopted for handling missing data. Independent t-test and χ^2-test were used to compare the demographic data, scores of psychological questionnaires, SC and some HRV values in the two populations. Because the possible skewness of the frequency domain HRV indices (VLF, LF, HF, LF/HF), they were logarithmically transformed first. Shapiro–Wilk test was then used to examine the distribution normality. Mann–Whitney U-test was used to compare the values between the two groups for the indices that were not normally distributed. Pearson's correlation analysis was used to explore the relationships between HRV and SC. The values $r < 0.3$, $0.3 \leq r < 0.5$, $0.5 \leq r < 0.7$, $0.7 \leq r < 0.9$, ≥ 0.9 are often considered to represent negligible, low, moderate, high and very high level of correlation, respectively.[32] In this step, the data of healthy individuals and psychiatric patients in different situations were analysed separately. Considering the repeated measurement in the three situations, the generalized estimating equation (GEE) was used to analyse whether the association between HRV and SC was affected by situations or populations. The model was: SC as dependents; LF/HF, situations and populations as independents. The unstructured working correlation matrix and the robust standard error estimator were used in the GEE. The above analyses were all two-sided and a P-value <0.05 was considered statistically significant.

Results

This cross-sectional study analysed the data from 97 patients with somatic symptom disorder comorbid with depression and anxiety and 96 healthy individuals. The demographic and psychological features of the two groups are shown in Table 1. Patients with somatic symptom disorder comorbid with depression and anxiety showed significantly lower educational years, a lower proportion having a steady job and a lower body mass index than the healthy individuals ($P < 0.05$ for all comparisons). As expected, all psychopathological scores (somatic distress, health anxiety, depression, general anxiety) were significantly higher in patients with somatic symptom disorder comorbid with depression and anxiety than in healthy individuals ($P < 0.001$ for all comparisons). Table 2 presents the HRV and SC data in the two populations under three situations. Under the three situations, SC was not significantly different in the two populations. Most HRV indices were also not significantly different between the two groups, but there were two exceptions. LF% was significantly lower in patients with somatic symptom disorder comorbid with depression and anxiety than in healthy individuals under all three situations ($P < 0.05$ for all comparisons); and VLF was significantly lower in patients with somatic symptom disorder comorbid with depression and anxiety than in healthy individuals in the resting state ($P = 0.037$).

The associations between HRV and SC in each group and under the three situations are shown in Table 3 and Figure 1. SDNN, VLF and HF did not show significant correlations with SC in any situation and group. LF was significantly associated with SC in the resting state in patients with somatic symptom disorder comorbid with depression and anxiety, but the correlation coefficient was low ($r = 0.215$; $P < 0.05$). In healthy individuals, LF/HF, LF% and HF% were significantly correlated with SC in the resting state ($r = 0.368$, $r = 0.360$, $r = –0.367$, respectively; $P < 0.05$ for all correlations) and under the cognitive task ($r = 0.227$, $r = 0.229$, $r = –0.311$, respectively; $P < 0.05$ for all correlations). The significance was not observed under paced breathing. In patients with somatic symptom disorder comorbid with depression

Table 1. Demographic and psychological characteristics of patients ($n = 97$) with somatic symptom disorder comorbid with depression and anxiety and healthy individuals ($n = 96$) that were included in a cross-sectional study investigating the correlation between heart rate variability and skin conductance.

Characteristic	All study participants $n = 193$	Patients with somatic symptom disorder comorbid with depression and anxiety $n = 97$	Healthy individuals $n = 96$	Statistical analysis[a] t/X^2	P-value
Age, years	43.21 ± 11.26	44.31 ± 11.94	42.10 ± 10.48	1.364	NS
Sex, male	72 (37.3%)	40 (41.2%)	32 (33.3%)	–1.289	NS
Educational level, years	14.33 ± 2.81	13.21 ± 3.01	15.47 ± 2.05	–6.112	$P < 0.001$
Marital status, married	115 (59.6%)	60 (61.9%)	55 (57.3%)	–0.417	NS
Employment status, having a steady job	143 (74.1%)	60 (61.9%)	83 (86.5%)	–15.215	$P < 0.001$
Exercise habits, having exercise habits	61 (31.6%)	28 (28.9%)	33 (34.4%)	–0.677	NS
Body mass index, kg/m^2	23.56 ± 4.25	22.96 ± 3.92	24.16 ± 4.50	–1.981	$P = 0.049$
Psychological status scores					
PHQ-15	7.93 ± 6.20	11.77 ± 5.49	4.04 ± 4.11	11.084	$P < 0.001$
HAQ	18.83 ± 14.11	26.91 ± 14.25	10.59 ± 7.81	9.865	$P < 0.001$
BDI-II	14.01 ± 12.88	21.80 ± 12.40	6.13 ± 7.42	10.673	$P < 0.001$
BAI	12.64 ± 12.43	21.18 ± 11.47	4.02 ± 5.46	13.283	$P < 0.001$

Data presented as mean ± SD or *n* (%).
[a]Continuous data were compared using independent *t*-test and categorical data were compared using χ^2-test; NS, no significant difference ($P \geq 0.05$).
PHQ-15, Patient Health Questionnaire-15; HAQ, Health Anxiety Questionnaire; BDI-II, Beck Depression Inventory-II; BAI, Beck Anxiety Inventory.

and anxiety, only under paced breathing were HF% and SC significantly correlated ($r = 0.204$; $P < 0.05$). LF% and LF/HF did not show significant correlations with SC in any situations in patients with somatic symptom disorder comorbid with depression and anxiety.

In the GEE models considering the effects of the three situations, LF/HF and SC did not show any significant association and neither did the interaction items between situation*LF/HF and population*LF/HF (Table 4). The main effects of situation on SC were significant ($P < 0.001$ for both correlations).

Discussion

The major findings in this present study were that in some situations (i.e. the resting state and under a cognitive task), LF/HF and LF% were significantly correlated with SC in healthy individuals, but the correlations were not significant in any situation for patients with somatic symptom disorder comorbid with depression and anxiety.

In the literature, whether LF% and LF/HF can represent sympathetic modulation is controversial. Some authors support their sympathetic tendency,[4] whereas others suggest them to reflect sympathovagal balance or an unclear meaning.[15] Despite some studies suggesting that LF-related indices do not accurately reflect sympathetic tones,[33] interpreting them as sympathetic indices is not rare in clinical situations.[34] This current study found that LF% and LF/HF did not show moderate or higher

Table 2. Skin conductance and heart rate variability data under three situations in patients ($n = 97$) with somatic symptom disorder comorbid with depression and anxiety and healthy individuals ($n = 96$).

	All study participants $n = 193$	Patients with somatic symptom disorder comorbid with depression and anxiety $n = 97$	Healthy individuals $n = 96$	Statistical analysis[a]	
				t/U	*P*-value
(a) Resting state					
Skin conductance, μS	0.59 ± 0.50	0.55 ± 0.43	0.62 ± 0.57	–0.916	NS
SDNN, ms	48.80 ± 36.75	45.76 ± 37.78	51.87 ± 35.61	−1.157	NS
VLF, ln[ms^2]	4.10 ± 1.04	3.94 ± 1.12	4.26 ± 0.95	–2.105	$P = 0.037$
LF, ln[ms^2]	4.25 ± 1.30	4.11 ± 1.41	4.37 ± 1.18	−1.362	NS
HF, ln[ms^2]	3.97 ± 1.51	3.93 ± 1.56	4.02 ± 1.46	4564.500[#]	NS
LF/HF, ln[ratio]	0.27 ± 0.91	0.19 ± 0.93	0.35 ± 0.88	−1.241	NS
LF%	32.30 ± 14.10	30.07 ± 14.70	34.55 ± 13.18	–2.227	$P = 0.027$
HF%	29.63 ± 16.03	29.63 ± 17.85	29.63 ± 14.05	0.001	NS
(b) Under cognitive task					
Skin conductance, μS	1.13 ± 0.92	1.07 ± 0.73	1.18 ± 1.08	–0.804	NS
SDNN, ms	61.29 ± 45.93	56.94 ± 48.45	65.68 ± 43.05	−1.325	NS
VLF, ln[ms^2]	4.11 ± 1.04	3.99 ± 1.07	4.22 ± 1.01	4994.000[#]	NS
LF, ln[ms^2]	4.61 ± 1.23	4.49 ± 1.26	4.72 ± 1.19	4776.000[#]	NS
HF, ln[ms^2]	4.54 ± 1.43	4.50 ± 1.44	4.57 ± 1.42	4483.000[#]	NS
LF/HF, ln[ratio]	0.07 ± 0.71	–0.00 ± 0.74	0.14 ± 0.67	4828.000[#]	NS
LF%	33.74 ± 12.20	31.91 ± 13.21	35.59 ± 10.85	−2.116	$P = 0.036$
HF%	31.78 ± 12.27	31.68 ± 14.01	31.89 ± 10.28	–0.121	NS
(c) Under paced breathing					
Skin conductance, μS	1.20 ± 1.17	1.14 ± 0.90	1.27 ± 1.40	–0.769	NS
SDNN, ms	72.97 ± 48.65	70.54 ± 52.16	75.42 ± 44.97	–0.696	NS
VLF, ln[ms^2]	3.91 ± 1.11	3.81 ± 1.26	4.01 ± 0.96	4883.000[#]	NS
LF, ln[ms^2]	5.81 ± 1.12	5.75 ± 1.18	5.86 ± 1.07	–0.679	NS
HF, ln[ms^2]	4.48 ± 1.50	4.50 ± 1.56	4.47 ± 1.45	0.141	NS
LF/HF, ln[ratio]	1.32 ± 1.07	1.25 ± 1.13	1.39 ± 1.00	–0.915	NS
LF%	63.21 ± 20.57	60.05 ± 24.04	66.41 ± 15.84	–2.170	$P = 0.031$
HF%	18.60 ± 12.58	19.22 ± 14.13	17.98 ± 10.83	0.688	NS

Data presented as mean ± SD.

[a]Continuous data were compared using independent *t*-test; NS, no significant difference ($P \geq 0.05$); [#]Mann–Whitney *U*-test was used when data were not normally distributed.

SDNN, standard deviation of normal to normal RR intervals; VLF, very low-frequency power; LF, low-frequency power; HF, high-frequency power; LF/HF, ratio of low-frequency power to high-frequency power; LF%, normalized low-frequency power; HF%, normalized high-frequency power.

correlations with SC in either group or under any of the three situations. Therefore, if viewing SC as a valid sympathetic index, using LF% and LF/HF as sympathetic indicators is not supported by these current results. In the resting state and for healthy individuals, the values of LF%-SC and LF/HF-SC were the highest. This implies that in this population and situation, LF% and LF/HF may be more similar with the rhythm SC reflects, but considering the low level of correlation, simply viewing them as sympathetic biomarkers is still questionable. In addition, in all situations the correlation between LF/HF and LF% was moderate to high,

Table 3. Correlations between skin conductance (SC) and heart rate variability data under three situations in patients ($n = 97$) with somatic symptom disorder comorbid with depression and anxiety and healthy individuals ($n = 96$).

Group	Situation		SDNN	VLF	LF	HF	LF/HF	LF%	HF%
Healthy individuals	Resting state	SC	0.040	0.150	0.156	0.046	0.368***	0.360***	–0.367***
Healthy individuals	Under cognitive task	SC	–0.025	–0.081	–0.059	–0.049	0.227*	0.229*	–0.311**
Healthy individuals	Under paced breathing	SC	–0.004	0.001	0.016	–0.009	0.062	0.055	–0.141
Patients with somatic symptom disorder comorbid with depression and anxiety	Resting state	SC	0.180	0.158	0.215*	0.197	0.031	0.141	0.159
Patients with somatic symptom disorder comorbid with depression and anxiety	Under cognitive task	SC	0.093	–0.100	–0.018	0.058	0.085	0.137	0.125
Patients with somatic symptom disorder comorbid with depression and anxiety	Under paced breathing	SC	0.116	–0.091	–0.014	0.054	–0.020	0.048	0.204*

SDNN, standard deviation of normal to normal RR intervals; VLF, very low-frequency power; LF, low-frequency power; HF, high-frequency power; LF/HF, ratio of low-frequency power to high-frequency power; LF%, normalized low-frequency power; HF%, normalized high-frequency power.
$*P < 0.05$, $**P < 0.01$, $***P < 0.001$.

which is similar to the result of a previous study.[4]

Another issue is that whether there is a sympathetic index reflecting the 'general' sympathetic tone. Both HRV and SC are generated from peripheral effectors; their values cannot be directly viewed as the central autonomic activity. It is possible that their low associations were originated from the distinct natures of the effectors. For example, SC is related to sympathetic cholinergic regulation; and HRV is modulated by both sympathetic noradrenergic and vagal cholinergic mechanisms.[35] This point may also explain the distinct correlation patterns in healthy individuals and in patients with somatic symptom disorder comorbid with depression and anxiety. Although patients taking tricyclic antidepressants were excluded in the current study, some patients took medications involving noradrenergic mechanism, such as serotonin–norepinephrine reuptake inhibitors (SNRIs). Although SNRIs are not usually found to increase or reduce HRV values, the possibility that these drugs had different impacts on the distinct effectors cannot be excluded.[36]

The significant correlation between HF% and SC under paced breathing in patients with somatic symptom disorder comorbid with depression and anxiety is an accidental finding, though the level of correlation was low. HF% is sometimes viewed an index of vagal activity, but from the mathematical viewpoint, it is closer to LF% and LF/HF.[37] This can explain the significant negative associations between HF% and SC under the resting state and cognitive task in healthy individuals. But it is difficult to draw a mechanism for their positive correlation in the somatic symptom disorder group under paced breathing. Whether the significance is associated with the probabilistic reason awaits further clarification.

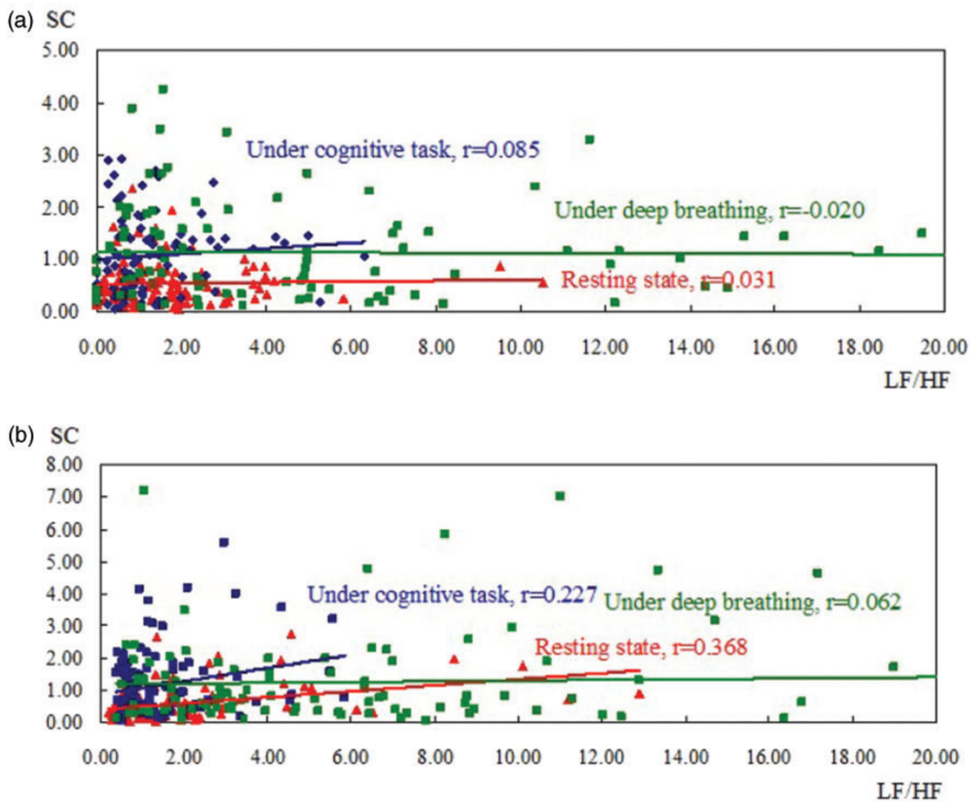

Figure 1. Correlations between the ratio of low-frequency power to high-frequency power (LF/HF) and skin conductance (SC) under three situations in patients ($n = 97$) with somatic symptom disorder comorbid with depression and anxiety (a) and healthy individuals ($n = 96$) (b). The colour version of this figure is available at: http://imr.sagepub.com.

Under a cognitive task, SC showed negligible correlations with LF/HF and LF%; under paced breathing the correlations SC-LF/HF and SC-LF% were even lower. Slow paced breathing has been reported to change the physiological meaning of LF.[2] It would cause the respiratory-based vagal tone to move to the lower frequency band.[2] Therefore, LF would reflect more parasympathetic activity in this condition; it is rational that the meaning of LF/HF and LF% also changes. According to these current results, the sympathetic component of LF/HF and LF% would be lower under paced breathing. Recording biological signals during cognitive tasks is a common study design to investigate the physiological reactivity; and LF/HF is one of the frequently used indicators.[13] These current results imply that it is not suitable to interpret LF/HF as the sympathetic biomarker under tasks. A similar viewpoint has been mentioned in other studies.[8,38]

Although low HRV (vagal based, such as HF, RMSSD and SDNN) has been reported in patients with depression, anxiety and somatic symptoms in meta-analyses, the effect sizes were usually low to medium.[13,39] Therefore, in studies with a low sample size, HRV between these patients and healthy individuals was often not significantly different.[13,40] Another

Table 4. Generalized estimating equation models about the correlations between the ratio of low-frequency power to high-frequency power (LF/HF) and skin conductance (SC) in patients ($n = 97$) with somatic symptom disorder comorbid with depression and anxiety (A) and healthy individuals ($n = 96$).

Outcome		SC	
Variable	Level	Estimate (SE)	*P*-value
Situation	2 versus 1	0.536 (0.148)	P < 0.001
	3 versus 1	0.561 (0.130)	P < 0.001
Population	1 versus 0	–0.151 (0.104)	NS
LF/HF	–	–0.045 (0.070)	NS
Situation*LF/HF	2 versus 1	–0.018 (0.082)	NS
	3 versus 1	0.043 (0.070)	NS
Population*LF/HF	1 versus 0	–0.009 (0.005)	NS

NS, no significant correlation ($P \geq 0.05$).
Situation 1: resting state; situation 2: under cognitive task; situation 3: under paced breathing; population 0: healthy individuals; population 1: patients with somatic symptom disorder comorbid with depression and anxiety.

explanation for the non-significant HRV difference is the effect of confounders. For example, body mass index has been reported to affect HRV;[41] and it was significantly different in the two populations of the current study. The current results further indicate that SC is unlikely to be an index that can distinguish patients with depression, anxiety and somatic symptoms from healthy individuals. However, the current study found that LF% was significantly higher in patients with somatic symptom disorder comorbid with depression and anxiety than in healthy individuals; this is not a frequently mentioned finding in the literature and may have potential for future investigation.

This current study had several limitations. First, SC was adopted as a valid sympathetic indicator in this study, but it cannot be considered as the gold standard of autonomic activities.[42] SC can be affected by skin temperature and skin texture.[43] Several different concepts can be separated from SC or epidermal activity.[44,45] For example, not only skin conductance level reflects sympathetic activity; the spontaneous fluctuations of SC are also sympathetic-driven and may represent more association with psychological stimuli.[46] But they were not investigated in detail in the present study. Pre-ejection period may be a more valid measurement of sympathetic modulation on the heart, but it is less frequently used in the literature than SC.[8] The current study chose to use SC because of its wide application in clinical situations and relatively clear biological meaning, which might be enough to clarify the core question of this current research. Secondly, although somatic symptom disorder is quite common in the clinical practice of psychosomatic medicine and is frequently comorbid with anxiety/depression, the results cannot necessarily be extended to patients with other psychiatric disorders. In addition, the current sample might also be different to those patients only having somatic symptom disorder (no depression/anxiety comorbidities). Depression and anxiety may have an influence on autonomic activities. Thirdly, although individuals taking medications with autonomic influence were excluded, not all participants in this study were drug naïve. In the population with somatic symptom disorder comorbid with depression and anxiety, many people were taking selective serotonin reuptake inhibitors, SNRIs or benzodiazepines. But these three types of medications were not found to significantly affect autonomic activity in previous studies.[36,39,47] Some other conditions may also interfere with the results, such as being overweight, underweight, smoking, activity level, detailed medications and having endocrinological diseases other than diabetes mellitus; but these were not exclusion criteria for this current study. Because age is an important factor affecting autonomic activity,[48] the wide age range (20–70 years) of this current study is another potential limitation. These potential confounders might also contribute to the non-significant difference of most HRV and SC indices between the two groups. Fourthly, the performance of the Stroop task was not recorded. The level of psychological pressure was hence hard to quantify. It was not possible to analyse the influence of pressure on autonomic activity. As the participants answered the task verbally, HF might be affected by modified respiratory rate during vocalization.

In conclusion, the biological meaning and applicability of HRV in different situations and populations were examined in this current study. No HRV index demonstrated a moderate or high correlation with SC. The correlation between LF/HF and SC was >0.3 only in healthy individuals and in the resting state, which indicates that simply viewing LF/HF as a sympathetic index may be a questionable approach. These current findings may provide a clearer understanding on the application of HRV in the psychiatric field.

Acknowledegments

The authors thank Huei-Mei Ma and Yi-Ling Lin for their administrative work during manuscript preparation.

Author contributions

Conceived and designed the experiments: Wei-Lieh Huang, Shih-Cheng Liao. Performed the experiments: Wei-Lieh Huang. Analysed the data: Wei-Lieh Huang, Li-Chin Ko. Wrote the paper: Wei-Lieh Huang, Li-Chin Ko, Shih-Cheng Liao.

Declaration of conflicting interests

The authors declare that there are no conflicts of interest.

Funding

The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported by the National Taiwan University Hospital Yunlin Branch (grant number: NTUHYL108.X001).

ORCID iD

Shih-Cheng Liao https://orcid.org/0000-0003-4129-0879

References

1. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Heart rate variability: standards of measurement, physiological interpretation and clinical use. *Circulation* 1996; 93: 1043–1065.
2. Shaffer F and Ginsberg JP. An Overview of Heart Rate Variability Metrics and Norms. *Front Public Health* 2017; 5: 258. DOI: 10.3389/fpubh.2017.00258.
3. Kuo TB, Lai CJ, Huang YT, et al. Regression analysis between heart rate variability and baroreflex-related vagus nerve activity in rats. *J Cardiovasc Electrophysiol* 2005; 16: 864–869. DOI: 10.1111/j.1540-8167.2005.40656.x.
4. Kuo TB, Lin T, Yang CC, et al. Effect of aging on gender differences in neural control of heart rate. *Am J Physiol* 1999; 277: H2233–H2239.
5. Shaffer F, McCraty R and Zerr CL. A healthy heart is not a metronome: an integrative review of the heart's anatomy and heart rate variability. *Front Psychol* 2014; 5: 1040. 2014/10/18. DOI: 10.3389/fpsyg.2014.01040.
6. Schoenberg PL and David AS. Biofeedback for psychiatric disorders: a systematic

review. *Appl Psychophysiol Biofeedback* 2014; 39: 109–135. DOI: 10.1007/s10484-014-9246-9.

7. Banerjee S and Argaez C. Neurofeedback and Biofeedback for Mood and Anxiety Disorders: A Review of Clinical Effectiveness and Guidelines. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health, https://www.ncbi.nlm.nih.gov/books/NBK531603/ (2017, accessed 21 February 2021).
8. Cheng YC, Huang YC and Huang WL. Heart rate variability in individuals with autism spectrum disorders: A meta-analysis. *Neurosci Biobehav Rev* 2020; 118: 463–471. DOI: 10.1016/j.neubiorev.2020.08.007.
9. Wickramasuriya DS, Amin MR and Faghih RT. Skin Conductance as a Viable Alternative for Closing the Deep Brain Stimulation Loop in Neuropsychiatric Disorders. *Front Neurosci* 2019; 13: 780. DOI: 10.3389/fnins.2019.00780.
10. Huang WL, Chen TT, Chen IM, et al. Depression and anxiety among patients with somatoform disorders, panic disorder, and other depressive/anxiety disorders in Taiwan. *Psychiatry Res* 2016; 241: 165–171. DOI: 10.1016/j.psychres.2016.05.008.
11. Li CT, Chou YH, Yang KC, et al. Medically unexplained symptoms and somatoform disorders: diagnostic challenges to psychiatrists. *J Chin Med Assoc* 2009; 72: 251–256. DOI: 10.1016/S1726-4901(09)70065-6.
12. Koch C, Wilhelm M, Salzmann S, et al. A meta-analysis of heart rate variability in major depression. *Psychol Med* 2019; 49: 1948–1957. DOI: 10.1017/S0033291719001351.
13. Cheng YC, Huang YC and Huang WL. Heart rate variability in patients with somatic symptom disorders and functional somatic syndromes: A systematic review and meta-analysis. *Neurosci Biobehav Rev* 2020; 112: 336–344. DOI: 10.1016/j.neubiorev.2020.02.007.
14. Chalmers JA, Quintana DS, Abbott MJ, et al. Anxiety Disorders are Associated with Reduced Heart Rate Variability: A Meta-Analysis. *Front Psychiatry* 2014; 5: 80. DOI: 10.3389/fpsyt.2014.00080.
15. Laborde S, Mosley E and Thayer JF. Heart Rate Variability and Cardiac Vagal Tone in Psychophysiological Research – Recommendations for Experiment Planning, Data Analysis, and Data Reporting. *Front Psychol* 2017; 8: 213. DOI: 10.3389/fpsyg.2017.00213.
16. Huang WL, Liao SC, Tu YK, et al. Autonomic reactivity during reading of a somatic distress script in patients with somatic symptom disorder. *J Psychosom Res* 2019; 123: 109729. DOI: 10.1016/j.jpsychores.2019.05.007.
17. Lee D, Kim SJ, Cheon J, et al. Characteristics of Autonomic Activity and Reactivity During Rest and Emotional Processing and Their Clinical Correlations in Somatic Symptom Disorder. *Psychosom Med* 2018; 80: 690–697. DOI: 10.1097/PSY.0000000000000622.
18. Che HH, Lu ML, Chen HC, et al. Validation of the Chinese Version of the Beck Anxiety Inventory. *Formosan J Med* 2006; 10: 447–454 [In Chinese, English abstract].
19. Chen IM, Huang WL, Lee MB, et al. Chinese Version of Health Anxiety Questionnaire: psychometric properties and is association with DSM-IV/DSM-5 systems. *Formosan J Med* 2019; 23: 21–30 [In Chinese, English abstract]. https://www.airitilibrary.com/Publication/alDetailedMesh?docid=10281916-201901-201901300007-201901300007-21-30.
20. Liao SC, Huang WL, Ma HM, et al. The relation between the patient health questionnaire-15 and DSM somatic diagnoses. *BMC psychiatry* 2016; 16: 351. DOI: 10.1186/s12888-016-1068-2.
21. Lu ML. Reliability and validity of the Chinese version of the Beck Depression Inventory-II. *Taiwanese Journal of Psychiatry* 2002; 16: 301–310.
22. Huang WL and Liao SC. Subgrouping Somatic Symptom Disorder: An Analysis Based on the Diagnostic Criteria for

Psychosomatic Research. *Psychother Psychosom* 2018; 87: 316–318. DOI: 10.1159/000492227.
23. Tu CY, Liu WS, Chen YF, et al. Is severity a clinically meaningful specifier of somatic symptom disorder? *J Psychosom Res* 2020; 133: 110108. DOI: 10.1016/j.jpsychores.2020.110108.
24. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Ann Intern Med* 2007; 147: 573–577. 2007/10/17. DOI: 10.7326/0003-4819-147-8-200710160-00010.
25. Lin IM, Fan SY, Yen CF, et al. Heart Rate Variability Biofeedback Increased Autonomic Activation and Improved Symptoms of Depression and Insomnia among Patients with Major Depression Disorder. *Clin Psychopharmacol Neurosci* 2019; 17: 222–232. DOI: 10.9758/cpn.2019.17.2.222.
26. Lin IM, Ko JM, Fan SY, et al. Heart Rate Variability and the Efficacy of Biofeedback in Heroin Users with Depressive Symptoms. *Clin Psychopharmacol Neurosci* 2016; 14: 168–176. DOI: 10.9758/cpn.2016.14.2.168.
27. Ogorevc J, Geršak G, Novak D, et al. Metrological evaluation of skin conductance measurements. *Measurement* 2013; 46: 2993–3001.
28. Bach DR, Flandin G, Friston KJ, et al. Modelling event-related skin conductance responses. *Int J Psychophysiol* 2010; 75: 349–356. DOI: 10.1016/j.ijpsycho.2010.01.005.
29. Clark DJ, Chatterjee SA, McGuirk TE, et al. Sympathetic nervous system activity measured by skin conductance quantifies the challenge of walking adaptability tasks after stroke. *Gait Posture* 2018; 60: 148–153. DOI: 10.1016/j.gaitpost.2017.11.025.
30. Sugimine S, Saito S and Takazawa T. Normalized skin conductance level could differentiate physical pain stimuli from other sympathetic stimuli. *Sci Rep* 2020; 10: 10950. DOI: 10.1038/s41598-020-67936-0.
31. Szulczewski MT. Training of paced breathing at 0.1 Hz improves CO2 homeostasis and relaxation during a paced breathing task. *PloS One* 2019; 14: e0218550. 2019/06/21. DOI: 10.1371/journal.pone.0218550.
32. Mukaka MM. Statistics corner: A guide to appropriate use of correlation coefficient in medical research. *Malawi Med J* 2012; 24: 69–71.
33. Hayano J and Yuda E. Pitfalls of assessment of autonomic function by heart rate variability. *J Physiol Anthropol* 2019; 38: 3. DOI: 10.1186/s40101-019-0193-2.
34. Sands KE, Appel ML, Lilly LS, et al. Power spectrum analysis of heart rate variability in human cardiac transplant recipients. *Circulation* 1989; 79: 76–82. DOI: 10.1161/01.cir.79.1.76.
35. Wang Y, Hensley MK, Tasman A, et al. Heart Rate Variability and Skin Conductance During Repetitive TMS Course in Children with Autism. *Appl Psychophysiol Biofeedback* 2016; 41: 47–60. 2015/09/06. DOI: 10.1007/s10484-015-9311-z.
36. Huang WL, Liao SC, Kuo TB, et al. The Effects of Antidepressants and Quetiapine on Heart Rate Variability. *Pharmacopsychiatry* 2016; 49: 191–198. DOI: 10.1055/s-0042-102964.
37. Burr RL. Interpretation of normalized spectral heart rate variability indices in sleep research: a critical review. *Sleep* 2007; 30: 913–919. 2007/08/09. DOI: 10.1093/sleep/30.7.913.
38. Cheng YC, Su MI, Liu CW, et al. Heart rate variability in patients with anxiety disorders: A systematic review and meta-analysis. *Psychiatry Clin Neurosci* 2022; 76: 292–302. 2022/03/28. DOI: 10.1111/pcn.13356.
39. Alvares GA, Quintana DS, Hickie IB, et al. Autonomic nervous system dysfunction in psychiatric disorders and the impact of psychotropic medications: a systematic review and meta-analysis. *J Psychiatry Neurosci* 2016; 41: 89–104.
40. Huang WL, Liao SC, Yang CC, et al. Measures of Heart Rate Variability in

Individuals With Somatic Symptom Disorder. *Psychosom Med* 2017; 79: 34–42. DOI: 10.1097/PSY.0000000000000362.

41. Huang WL, Chang LR, Kuo TB, et al. Gender differences in personality and heart-rate variability. *Psychiatry Res* 2013; 209: 652–657. DOI: 10.1016/j.psychres.2013.01.031.
42. Ziemssen T and Siepmann T. The Investigation of the Cardiovascular and Sudomotor Autonomic Nervous System – A Review. *Front Neurol* 2019; 10: 53. DOI: 10.3389/fneur.2019.00053.
43. Grossman P and Taylor EW. Toward understanding respiratory sinus arrhythmia: relations to cardiac vagal tone, evolution and biobehavioral functions. *Biol Psychol* 2007; 74: 263–285. DOI: 10.1016/j.biopsycho.2005.11.014.
44. Novak P. Autonomic Disorders. *Am J Med* 2019; 132: 420–436. DOI: 10.1016/j.amjmed.2018.09.027.
45. Buchmann SJ, Penzlin AI, Kubasch ML, et al. Assessment of sudomotor function. *Clin Auton Res* 2019; 29: 41–53. DOI: 10.1007/s10286-018-0530-2.
46. Bach DR, Friston KJ and Dolan RJ. Analytic measures for quantification of arousal from spontaneous skin conductance fluctuations. *Int J Psychophysiol* 2010; 76: 52–55. 2010/02/11. DOI: 10.1016/j.ijpsycho.2010.01.011.
47. Huang WL, Chang LR, Kuo TB, et al. Impact of antipsychotics and anticholinergics on autonomic modulation in patients with schizophrenia. *J Clin Psychopharmacol* 2013; 33: 170–177. DOI: 10.1097/JCP.0b013e3182839052.
48. Nunan D, Sandercock GR and Brodie DA. A quantitative systematic review of normal values for short-term heart rate variability in healthy adults. *Pacing Clin Electrophysiol* 2010; 33: 1407–1417. DOI: 10.1111/j.1540-8159.2010.02841.x.