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# Effect of emotion regulation training in patients with panic disorder: Evidenced by heart rate variability measures☆

Sheng-Min Wang, M.D. [a,b], Hae-Kook Lee, M.D., Ph.D. [c], Yong-Sil Kweon, M.D., Ph.D. [c], Chung Tai Lee, M.D., Ph.D. [c], Jeong-Ho Chae, M.D., Ph.D. [b], Jung-Jin Kim, M.D., Ph.D. [b,*,1], Kyoung-Uk Lee, M.D., Ph.D. [c,**,1]

[a] International Health Care Center, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea
[b] Deparment of Psychiatry, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea
[c] Department of Psychiatry, Uijeongbu St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea

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ABSTRACT

*Objective:* We aimed to examine the effect of emotion regulation training in patients with panic disorder (PD) by measuring heart rate variability (HRV).
*Methods:* Forty-eight patients with PD were randomly divided into emotion regulation group ($n=25$) and no-regulation group ($n=23$). Three five-minute ECG recordings were taken in the following states: 1) baseline, 2) while subjects viewed 15 aversive pictures (active stimulus), 3) resting state after aversive pictures (post-stimulus). The emotion regulation group briefly received acceptance technique training for five minutes before performing the experimental task. Spectral analysis measures included a high-frequency (HF; 0.15–0.4 HZ) component, a low-frequency (LF; 0.04–0.15 Hz) component, and an LF/HF ratio.
*Results:* The mean change in LF/HF ratio from baseline to active stimulus was significantly lower in the emotion regulation group than in the no-regulation group (emotion regulation group, 0.13; no-regulation group, 2.31; $t=-2.67$; $P<.05$).
*Conclusion:* This suggests that brief emotion acceptance training could decrease aversive stimulus-induced sympathetic hyperactivity in patients with PD.



## 1. Introduction

Panic disorder (PD) is characterized by recurrent unexpected panic attacks accompanied by fear of panic recurrence, their consequence or significant change in behavior in order to avoid further episodes [1,2]. Increased sensitivity to threat, persistent and repetitive thoughts, physiological arousal, and avoidance behaviors could result in "fear of fear," leading patients with PD to have functional impairment in various areas [3,4].

Psychotherapy, especially cognitive behavioral therapy (CBT), is considered first line treatment for PD, along with pharmacotherapy [5–7]. American Psychiatric Association (APA) guidelines for PD showed that, despite the efficacy of first-line treatments, non-response, attrition, and relapse are problems in 20–30% of patients [7]. Therefore, it is important to more clearly understand the effects of other novel treatment modalities for PD. Recent research specifically suggests that a panic attack, which is the core, defining feature of PD, is associated with difficulties in emotion regulation. The experience of a panic attack is associated with decreased emotional clarity, and patients with PD are reported to have greater difficulty labeling emotions and have a higher level of alexithymia than healthy controls [8,9]. Patients with PD also feared and avoided panic-related internal sensations, and this fear of bodily sensations might generalize to stimuli that produce physiological reactions similar to those associated with panic attacks [10]. For example, when a certain emotion is perceived as threatening because of its accompanied internal bodily sensations, those who experience panic attacks might be less accepting of their emotions and more likely to utilize avoidant coping strategies. Thus, these studies suggest that patients with PD exhibit emotion regulation difficulties in the form of emotional non-acceptance, experiential avoidance, and decreased emotional clarity, which are associated with the fear of bodily sensations culminating in un-cued panic attacks [11,12]. In this respect, a large and consistent body of research demonstrates that emotion regulation strategies can suppress the "fear of fear" and help improve the symptoms of PD [13].

☆ Conflicts of interest: none.

* Correspondence to: J.-J. Kim, M.D., Ph.D., Deparment of Psychiatry, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, 222, Ban-Po Dae Ro, Seocho-gu, Seoul, 06591, Republic of Korea. Tel.: +82 2 2258 6084; fax: +82 2 2258.
** Correspondence to: K.-U. Lee, M.D, Ph.D, Department of Psychiatry, Uijeongbu St. Mary's Hospital, College of Medicine, The Catholic University of Korea, 271, Cheonbo-Ro, Uijeongbu-si, Gyeonggi-do, 11765, Republic of Korea. Tel.: +82 31 820 3609; fax: +82 31 847 3630.
*E-mail addresses:* jjean@catholic.ac.kr (J.-J. Kim), mindcure@catholic.ac.kr (K.-U. Lee).
[1] Equally contributed to the paper as the corresponding author.

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Among the various emotion regulation strategies available, one of the most studied within clinical populations is the strategy of "acceptance" [14]. Acceptance is widely used in newer generation CBTs or "third wave CBTs" such as Acceptance and commitment therapy (ACT), Mindfulness-based cognitive therapy (MBCT), Dialectical behavior therapy (DBT), and others [15,16]. The aim of acceptance is to facilitate psychological flexibility or "the ability to contact the present moment more fully" [17]. By doing so, it can significantly reduce anxiety symptoms in patients with PD [18,19]. Emotional acceptance can also decrease self-reported negative affect and physiologic response during emotional provocation [20,21].

Heart rate variability (HRV), or the fluctuation in heart rate over a period of time, is often used to investigate autonomic dysregulation in various anxiety disorders [22]. Many studies have suggested that there is autonomic dysfunction and reduced HRV in patients with PD [23–27]. Reduced HRV observed in PD is also associated with increased risk of cardiac events and cardiac mortality [28,29]. Among frequency domain and time domain measures of HRV, frequency domain measures are especially useful in providing information on sympathovagal change after exposure to various stimuli [22]. In this respect, we previously showed a significantly greater threatening stimuli-induced increase of sympathetic tones (i.e. LF/HF ratios) in PD than in healthy controls. Our previous study illustrated that patients with PD exhibit a sympathetic predominance when faced with threatening stimuli compared to normal control subjects [30].

A large number of studies have investigated the effect of acceptance training in diverse anxiety disorders [12,15]. A previous study showed that patients with anxiety disorder who received acceptance training were less avoidant and reported less intense fear, fewer cognitive symptoms, and fewer catastrophic thoughts during carbon dioxide inhalations (an important panicogen) than those who did not receive acceptance training [31]. Another study further compared the effects of acceptance and suppression of emotion in patients with PD [32], which showed that the acceptance group reported less anxiety than the suppression group during a carbon dioxide challenge test. In particular, Campbell-Sills et al. found that the suppression group exhibited increased heart rate in response to an emotion-provoking film, while the acceptance group showed decreased heart rate [20]. However, the study included patients with both anxiety and mood disorders, rather than panic disorder alone. More importantly, HRV is known to more accurately reflect sympathetic hyperactivity than do heart rate and skin temperature, but previous studies used simple heart rate and skin temperature as objective measures [33,34]. Cardiac vagal tone measured from HRV could quantify the effectiveness of central–peripheral neural feedback systems and so can serve as an index of emotion regulation, as it represents physiological flexibility [33]. In this respect, decreased HRV is known to be closely related to difficulties in emotion regulation [35,36]. Thus, HRV is considered an important, objective biological marker when investigating symptom severity or the effects of pharmacotherapy and psychotherapy in PD [37–39].

Despite these facts, no previous study has investigated the effect of acceptance training in threat-induced autonomic hyperactivity in PD using HRV. Thus we aimed to extend our previous work by examining effect of emotion acceptance strategies training in patients with PD by measuring their heart rate variability (HRV). We hypothesized that PD patients who received emotion acceptance strategy would have lower sympathetic activity, as measured by lower sympathovagal ratios (LF/HF), than PD patients who did not receive acceptance strategy in response to threatening stimuli.

## 2. Methods

### 2.1. Subjects

Patients aged 20–65 years and diagnosed with PD based on the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, Text Revision (DSM-IV-TR) criteria were recruited from the Outpatient Psychiatry Clinic at Uijeongbu St. Mary's Hospital, College of Medicine, Catholic University of Korea. A comprehensive psychiatric interview was conducted by two board-certified psychiatrists using the Structured Clinical Interview for DSM-IV (SCID-IV) in order to confirm the diagnosis of PD with or without agoraphobia and to exclude patients with bipolar disorder, psychotic symptoms, cognitive deficits, and neurological conditions. The two board-certified psychiatrists asked all patients meeting above criteria to participate in the study from September 1st, 2011, to August 31st, 2012. Patients were randomly divided into two groups: those receiving emotion acceptance strategy training (emotion regulation group) and those not receiving emotion acceptance strategies (no-regulation group). The training was modified from the skills used in MBCT. All subjects provided written, informed consent. This study was approved by the Institutional Review Board of Uijeongbu St. Mary's Hospital, College of Medicine, Catholic University of Korea.

### 2.2. Clinical measures

All patients provided demographic data and clinical measures before performing the experimental task. Demographic data included age, gender, marital status, religion, and socio-economic status. Clinical measures included Beck Depression Inventory (BDI), Cognitive Emotion Regulation Questionnaire (CERQ), Mindfulness Awareness Attention Scale (MAAS), Positive and Negative Affect Schedule (PANAS), Panic Disorder Severity Scale (PDSS), State–Trait Anxiety Inventory (STAI), Toronto Alexithymia Scale (TAS). In addition, PANAS was measured once more immediately after the experimental task to rate participants' subjective distress scores.

### 2.3. Experimental task

We have modified our previous study's experimental task to fit the purpose of this study [30]. In the present study, four separate ECGs were recorded with a limb lead placed on the index finger. Five-minute breaks were provided before all four ECGs in order to provide signal stabilization. All participants first sat in a semi-supine position with their back leaning comfortably against a chair in order to allow visual contact with a computer screen. The first five-minute ECG was recorded while remaining in the semi-supine position (baseline). Another five-minute ECG was recorded while participants were presented with 15 aversive pictures on the computer screen. Thereafter, a third five-minute ECG recording was conducted while the subjects were viewing another set of 15 similarly aversive pictures (active stimulus). The 15 aversive pictures (e.g., a person with a severe leg injury) were intended to provoke negative emotions. When we used the set of pictures prepared in our previous study, all 20 healthy volunteers reported that the aversive pictures induced negative emotions (threatened and/or disgusted) [30]. Finally, another ECG was recorded while the subjects remained in the semi-supine position without viewing threatening pictures (post-stimulus). The second five-minute ECG recording was not included in the analysis because HRV tends to not be stationary within the first three minutes of stimulus exposure [40,41]. Thus, a total of three five-minute ECG recordings were included: 1) before subjects began the experimental task and were in a resting state (baseline), 2) during the aversive stimuli (active stimulus), and 3) at a resting state after participants completed the task involving aversive pictures (post-stimulus). A digital arterial pulse-wave analyzer (McPulse, Meridian, Seoul, Korea) was used to record the ECGs, and the E-Prime software package (Psychology Software Tools Inc., Pittsburgh, PA, USA) was used to present pictures. All participants were prohibited from drinking caffeinated beverages for at least eight hours before the ECG recordings. Please see Fig. 1 for a summary of the experiment.