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# Physical activity and respiratory behavior in daily life of patients with panic disorder and healthy controls

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ABSTRACT

Panic disorder (PD) has been linked in laboratory investigations to respiratory alterations, particularly persistent respiratory variability. However, studies of PD respiratory pattern outside the laboratory are rare, have not controlled for the confounding influence of varying levels of physical activity, and have not addressed whether abnormalities in respiratory pattern vary depending on the intensity of physical activity. Cognitive and biological theories of PD, in fact, predict that respiratory alterations may be particularly pronounced when patients are physically active. This study assessed physical activity and respiratory pattern of 26 PD patients and 26 healthy controls (HC) during two waking periods of daily life (9:00–21:00) one week apart. Respiratory data were stratified for predefined levels of physical activity (inactivity, minimal movement, slow/moderate/fast walking, and running) and analyzed using linear mixed models. Groups did not generally differ in respiratory measures, although PD patients did show elevated variability of absolute levels of tidal volume during minimal movement and slow walking (root mean squared successive differences). Other ways of analyzing tidal volume variability based on relative levels, percentage of sighing, or pooled activity levels did not substantiate this finding. Amount of time spent at different activity levels did not differ between groups, which is at variance with studies linking anticipatory anxiety with motoric agitation, and PD with self-reported avoidance of exercise. In conclusion, results provided little evidence for respiratory abnormalities or central respiratory dysregulation in PD at varying levels of activity, although instability of tidal volume regulation during low activity remains a possibility. Our research approach indicates the usefulness of stratification of real life data on the basis of levels of activity, as well as how ambulatory assessment strategies, complementarily to laboratory studies, may improve understanding of biological and psychological factors contributing to development and maintenance of PD and other anxiety disorders.



## 1. Introduction

Theoretical assumptions (Klein, 1993, Ley, 1985) and empirical evidence (Gorman et al., 1988; Gorman et al., 1994; Schwartz et al., 1996; Hegel and Ferguson, 1997; Papp et al., 1997; Abelson et al., 2001; Martinez et al., 2001; Wilhelm et al., 2001a,b,c; Caldirola et al., 2004; Blechert et al., 2007) point to trait-like persistent respiratory abnormalities in panic disorder. However, most research on panic disorder (PD) has been performed in the laboratory where PD patients are likely to be anxious and to breathe anxiously.

The few studies that have assessed respiratory pattern in the natural environment (Martinez et al., 2001; Hoehn-Saric et al., 2004) have not adequately controlled for the influence of physical activity on respiratory measures. In a previously reported study (Pfaltz et al., 2009), we adjusted for activity by restricting analyses of ambulatory respiratory data to sedentary phases. No differences between PD patients and healthy controls were found with respect to respiratory variability or other measures of ventilatory timing or volume, suggesting that previously detected respiratory alterations (Gorman et al., 1988; Schwartz et al., 1996; Abelson et al., 2001; Wilhelm et al., 2001a,b,c; Martinez et al., 2001; Caldirola et al., 2004; Papp et al., 1997; Hegel and Ferguson, 1997) reflected exaggerated emotional reactivity to experimental contexts, rather than stable trait characteristics of PD. However, the possibility remains that PD patients during daily life may display abnormal respiratory alterations related to levels of physical activity beyond sedentary states. Such alterations might be expected for several reasons.

First, PD patients tend to worry that bodily symptoms signal harmful physical consequences. According to cognitive theories of PD (Clark, 1986), this evokes anxiety that, in turn, increases bodily symptoms. In line with this theory, PD patients report increased anxiety and somatic symptoms after physical activation in the

*Abbreviations:* IA, inactivity; MM, minimal movement; SW, slow walking; MW, moderate walking; FW, fast walking; RU, running; $V_T$, tidal volume; $T_{TOT}$, total time; $V'_m$, minute ventilation.

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laboratory (Rief and Hermanutz, 1996; Ströhle et al., 2009). Given the absence of data regarding periods of activity in our previous report (Pfaltz et al., 2009), it is conceivable that physical activity might have triggered anxiety and corresponding respiratory changes among the PD patients. Second, anticipatory anxiety and panic attacks frequently occur while patients are physically active (e.g. at shopping malls or when visiting restaurants). Anxiety-induced respiratory changes might, therefore, be primarily found during episodes of physical activity and might have been missed in our previous analysis. Third, PD patients frequently try to escape anxiety-inducing situations when symptoms of panic arise. For this reason, and due to restlessness evoked by anticipatory or acute anxiety, anxiety-induced respiratory alterations might occur more frequently during physical activity than during rest. Fourth, PD patients show heightened $CO_2$ sensitivity in the laboratory (Gorman et al., 1994; Papp et al., 1997). Initially increased arterial $CO_2$ levels during the onset of physical activity might induce an exaggerated respiratory regulation, reflected by elevated minute ventilation ($V'_m$; alternatively: $V'_E$) and tidal volume ($V_T$) instabilities of respiratory pattern.

This study during everyday life explored respiratory alterations by comparing respiratory data stratified for different levels of physical activity. The results we will present represent an additional analysis of data described in our previous paper (Pfaltz et al., 2009). In this study, two ambulatory 24-h recordings of breath-by-breath respiratory pattern and physical activity were made in PD patients and healthy controls (HC). Our previous analyses were restricted to phases of physical inactivity. Here, we additionally analyzed respiratory pattern during varying levels of physical activity observed in daily life.

We hypothesized that in contrast to physical inactivity phases, PD patients would show respiratory alterations during higher levels of physical activity. Specifically, based on previous laboratory findings (Gorman et al., 1988; Schwartz et al., 1996; Abelson et al., 2001; Wilhelm et al., 2001a,b; Martinez et al., 2001; Caldirola et al., 2004), we examined whether PD patients, compared to HC, would manifest heightened variability of $V'_m$ and $V_T$ during physical activity, as well as elevations in $V'_m$ and $V_T$, and decreases in respiratory cycle total time ($T_{TOT}$). We also hypothesized group differences in the frequency of sighs at different physical activity levels, since heightened respiratory variability in PD has been linked to frequent sighing (Wilhelm et al., 2001a; Schwartz et al., 1996).

We also had two additional aims. First, we sought to investigate whether reactivity to the measurement system, demonstrated in the laboratory (Askanazi et al., 1980; Han et al., 1997), influences respiratory patterns in real life. In our previous analysis of the data set (Pfaltz et al., 2009), we averaged respiratory data across measurement days. However, reactivity effects might have occurred during the first 24-h recording, when participants were less familiar with the monitoring system. PD patients may have displayed particularly pronounced sensitivity and stress reactions to the novel and potentially uncontrollable situation (Abelson et al., 2007; Margraf et al., 1986), resulting in heightened physiologic arousal. Larsen et al. (1998) found higher heart rates in PD patients on the first of two consecutive laboratory measurements. Similar effects might occur regarding respiratory patterns outside the laboratory. We, therefore, expected to find differences in respiratory variables between measurement days that were more pronounced in PD patients, compared to HC. In particular, we expected elevated $V_T$ and $V'_m$ variability on the first, compared to the second, day, which might have reflected initially elevated respiratory dysregulation due to novelty that habituated on day 2. To assess coherence between physiologic and experiential changes, we also compared self-reported anxiety levels between days in PD patients and HC.

Our analysis approach also allowed us to examine whether the two groups spent different amounts of time at varying levels of physical activity. On the one hand, PD patients might spend a larger proportion of time during low to moderate levels of physical activity, compared to HC, due to motoric agitation brought on by anticipatory anxiety or acute panic. As demonstrated by Sakamoto et al. (2008), PD patients reporting more anxiety and panic attacks show higher daily activity levels. On the other hand, self-reported avoidance of exercise (Broocks et al., 1998) or other agoraphobic situations would suggest a decreased amount of time spent at high physical activity levels. Only one study (Clark et al., 1990) objectively assessed physical activity in daily life of PD patients in comparison to healthy controls. Clark et al. (1990) found higher mean daily activity in PD patients without phobic avoidance but not in PD patients with phobic avoidance, as compared to controls. However, they did not distinguish between different activity levels and data were collected for 1-min intervals, neglecting activity changes occurring during smaller intervals. The measurement system we used overcomes these limitations, allowing a sensitive analysis of the distribution of activity levels, in addition to respiratory behavior in daily life of PD patients.

## 2. Materials and methods

### 2.1. Participants

30 PD patients and 26 HC were recruited by means of newspaper advertisements. The study protocol was approved by the local ethics committee. Before participating, participants gave written consent. Exclusion criteria for HC were current psychiatric disorders and a history of an anxiety disorder. Four PD patients were excluded due to use of medication with strong autonomic effects or a medical history affecting the respiratory system (see Pfaltz et al., 2009, for detailed exclusion criteria). This resulted in a total sample size of 26 participants per study group. PD patients who were included took the following medications: analgesic drugs (3), benzodiazepines (4), and selective serotonin reuptake inhibitors (7). Diagnoses were assigned by means of the Diagnostic Interview for Mental Disorders (DIPS, Schneider and Margraf, 2006), which is a modified German version of the Anxiety Disorders Interview Schedule for DSM-IV–Lifetime version (ADIS-IV-L; DiNardo et al., 1994). Twenty-three of the PD patients had an additional diagnosis of agoraphobia. Other additional diagnoses in the PD group included Hypochondria (1), Posttraumatic Stress Disorder (3), Social Phobia (3), and Major Depression (4). Groups were matched for age (PD: mean = 35.5, $SD = 10.9$; HC: mean = 37.1, $SD = 9.6$, $p = .057$) and gender (PD: 84.6% female; HC: 76.9% female, $p = .43$) and did not differ regarding body mass index ($p = .31$). PD patients scored significantly higher than HC on all of the following questionnaires ($p$-values $<.001$): State-Trait Anxiety Inventory (Laux et al., 1981), Beck Depression Inventory (Hautzinger et al., 1994), Panic Disorder Severity Scale (Shear et al., 2001), Anxiety Sensitivity Index (Ehlers and Margraf, 1993), and Mobility Inventory (Ehlers et al., 2001). Further details regarding psychometric and demographic characteristics of the study groups can be found in Pfaltz et al. (2009). Participants were not allowed to drink alcohol 24 h before testing.

### 2.2. Assessment of self-reported anxiety

As described in our previous paper (Pfaltz et al., 2009), data were collected as part of a larger study during which PD patients and HC captured various attributes of psychological well being and anxiety symptoms by means of electronic diaries during one week (see Pfaltz et al., in revision). Here, only self-reported anxiety for the two physiologic measurement days will be reported for subsamples of 18 PD patients and 22 HC. For technical reasons, these data were not available for the remaining participants. Every three hours (9 am, 12 pm, 3 pm, 6 pm, and 9 pm), participants rated their anxiety on a scale from 0 (not at all) to 10 (very much). Ratings referred to the past three hours or to the time since waking up for the 9 am recording. For