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Panic disorder: the role of the balance system

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Abstract

Experimental evidences suggest that Panic Disorder (PD) is characterized by abnormalities in respiratory and vestibular functions. We studied balance system function in patients with PD and its relationships with CO_2 reactivity and clinical characteristics. Nineteen patients with PD with/without agoraphobia underwent static posturography and the 35% CO_2 challenge. The severity of clinical symptomatology was measured by standardized psychometric scales. Patients were free of psychotropic medications during the 2 weeks before the study. Different investigators blind to each other carried out the CO_2 challenge, static posturography and clinical assessment. Nineteen age and sex-matched healthy controls underwent static posturography. Body sway velocity and length were significantly higher in panic patients than in controls and patients showed high percentages of abnormal scores. Patients with two or more abnormal scores on static posturography were significantly more agoraphobic than those with less than two. Abnormal posturography scores under the eyes-opened was related to high anticipatory anxiety, whereas those under eyes-closed was related to phobic avoidance. Symptomatological reactivity to CO_2 was significantly correlated to abnormal functions of the balance system in the eyes-closed condition. Our findings suggest that (1) many patients with PD (5–42%) have abnormalities in their balance system function compared with healthy controls (0–5%), (2) symptomatological reactivity to CO_2 and balance system function in patients with PD are correlated only in the eyes-closed condition and (3) there is a significant link between agoraphobic avoidance and subclinical abnormal function of the balance system network.

Keywords: PD; Respiration; Balance system; Agoraphobia; Panic provocation; Anxiety; Brainstem

1. Introduction

Significant relationships between balance function disorders and panic disorder (PD) has been repeatedly reported (Jacob, 1988; Jacob et al., 1989, 1992; Sklare et al., 1990; Clark et al., 1994; Frommberger et al., 1994; Hoffman et al., 1994; Stein et al., 1994; Yardley et al., 1994, 1995; Furman and Jacob, 1997; Gordon et al., 1998; Asmundson et al., 1998). The studies into these relationships have focused on two main areas: vestibular abnormalities in patients with PD, and anxiety symptoms or disorders among patients with abnormalities in the vestibular system. Jacob and co-workers (Jacob et al., 1985, 1989) reported vestibular abnormalities in patients with PD who complained of dizziness. This finding has been replicated in patients with PD non-specifically selected for the presence of dizziness (Sklare et al., 1990; Hoffman et al., 1994; Jacob et al., 1997), where the abnormalities were not the expression of a full-blown vestibular disorder. Similarly, patients with vestibular disorders have psychiatric syndromes with a particular reference to PD and agoraphobia (Hallam and Stephens, 1985).

Yardley and co-workers (1995) reported an association between vestibular abnormalities and phobic avoidance. Jacob and co-workers (1996) showed that patients with PD and agoraphobia had more vestibular abnormalities than patients with PD but without

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agoraphobia, patients with depressive disorders or with anxiety disorders other than panic or healthy controls. We (Allevi et al., 1997) found a significant relationship between the presence of dizziness during panic attacks and agoraphobia. It seems that in some patients phobic avoidance might not be a mere consequence of panic attacks but rather the result of a more complex interaction.

Abnormalities in the respiratory function may play a central role in the pathogenetic mechanisms underlying PD and has been mainly associated with panic attacks (Klein, 1993; Bellodi and Perna, 1998). Some observations have indicated that the vestibular and the respiratory systems may work in complex interrelationships with one another. Dizziness is one of the main symptoms induced by CO_2 inhalations (Perna et al., 1994a) and by hyperventilation (Fried and Grimaldi, 1993).

Balance and respiratory systems seem to influence two different aspects of panic disorder, respectively agoraphobia and panic attacks. Control centers of both, however, are located nearby in the brainstem with significant reciprocal influences and there is evidence of vestibular-respiratory functional interconnections (Furman et al., 1998). We hypothesize that balance function might play a role in the development of agoraphobia and that respiratory reactivity might influence this process. To test this hypothesis we evaluated the balance system function by posturography and respiratory reactivity by CO_2 inhalation test in a sample of patients with PD.

2. Methods and materials

2.1. Subjects

Nineteen patients with PD with/without agoraphobia were included in the study [13 women and six men, mean age 27.1 ± 9.1 years (17–46 years), age at onset: 20.1 ± 4.8]. The patients were consecutively recruited over 8 months at the outpatient facilities of the Anxiety Disorders Clinical and Research Unit at San Raffaele Hospital in Milan. Eighteen patients (95%) admitted to the study had a lifetime history of agoraphobia. Since no normative data for the Italian general population on static posturography are available in international peer-reviewed journals, a sample of 19 sex- and age-matched healthy controls were recruited by advertisements placed around the University and tested with static posturography. Controls had never fit any lifetime psychiatric diagnoses and had never experienced panic attacks. Consensus diagnoses according to DSM IV criteria were established by two senior psychiatrists who independently assessed patients by a clinical interview and the MINI International Neuropsychiatric Interview-Plus (Sheehan et al., 1994). Exclusion criteria for all the patients were the presence of psychiatric disorders other than PD with/without agoraphobia.

Both patients and controls underwent a physical and neuro-ophthalmologic examinations. Accurate medical history taking were performed to exclude any subjects with substantial current medical disorders, especially respiratory and balance systems disorders, neurological deficits, signs of polyneuropathies, personal and familial history of cerebral aneurysm, significant hypertension (systolic $>$ 180 mm Hg, diastolic $>$ 100 mm Hg), pregnancy or epilepsy. No subject included in the study had been treated with ototoxic drugs such as aminoglycosides. The procedure of this study has been carried out in accordance with the Declaration of Helsinki and all subjects gave their informed consent to the study after receiving a detailed explanation of the entire procedure. During the 2 weeks before the start of the study, all subjects were free of psychotropic medications. They were asked to refrain from alcohol and any kind of medication for at least 2 days, beverages containing xanthines for at least 12 hours and food or smoking for at least 2 hours before both static posturography and CO2 challenge.

2.2. General procedure

The patients underwent a series of tests according to the following schedule:

Day 0: psychometric tests and interviews for diagnostic evaluation and clinical assessment.
Day 1: static posturography.
Day 3: the 35% CO_2 challenge.

2.2.1. Clinical assessment

The severity of PD was evaluated by the Panic Associated Symptoms Scale (PASS) to obtain a global score (PASS-tot) and subscores for panic attacks, phobic avoidance and anticipatory anxiety (Argyle et al., 1991). Patients also completed the following self-administered scales:

- The Fear Questionnaire (FQ) to obtain a global score (FQ-tot) and subscores for agoraphobia (FQ-AGO), blood-injury phobia (FQ-BI) and social phobia (FQ-SP; Marks and Mathews, 1979).
- The Sheehan Disability Scale (SDS) to obtain a global score (Leon et al., 1992).
- The Dizziness Handicap Scale (DHI) to obtain a global score (Jacobson and Newman, 1990).

2.2.2. Static posturography (stabilometry)

In general, static posturography gives information on the ability to integrate the multiple inputs that contribute to the control of posture. Although posturography is not able to give any specific neuroanatomical information it can point out the need for re-education of the sensory integration when the system does not