ELSEVIER

European Neuropsychopharmacology 15 (2005) 663 – 671

EUROPEAN NEURO-PSYCHOPHARMACOLOGY

www.elsevier.com/locate/euroneuro

Subjective and neurovegetative changes in healthy volunteers and panic patients performing simulated public speaking

Alexandre C.B.V. Parente[a], Cybele Garcia-Leal[a], Cristina M. Del-Ben[a], Francisco S. Guimarães[b], Frederico G. Graeff[a,*]

[a]*Department of Neurology, Psychiatry and Medical Psychology, Medical School of Ribeirão Preto, University of São Paulo, FMRP-USP, Av. 9 de Julho 980, 14025-000, Ribeirão Preto, SP, Brazil*

[b]*Department of Pharmacology, Medical School of Ribeirão Preto, University of São Paulo, Ribeirão Preto, SP, Brazil*

Received 9 November 2004; received in revised form 3 May 2005; accepted 3 May 2005

Abstract

Drug-free symptomatic panic patients, drug-treated nonsymptomatic patients and healthy controls were submitted to simulated public speaking. Subjective anxiety, cognitive impairment and discomfort measured by the visual analog mood scale as well as skin conductance level were higher in symptomatic patients than in controls at the beginning of the experimental session, nonsymptomatic patients lying in between. Subjective sedation, spontaneous fluctuations of skin conductance, heart rate and blood pressure were similar in the three groups. Preparation and performance of speech decreased sedation while increasing anxiety, cognitive impairment, level and fluctuations of skin conductance, heart rate and blood pressure. Anxiety, cognitive impairment and conductance level were less increased in symptomatic patients than in controls. Electrodermal activity, but not cardiovascular measures of sympathetic arousal correlated with anticipatory anxiety. Chronic treatment with serotonin uptake inhibitors attenuated the differences between panic patients and controls, supporting the participation of serotonin in panic disorder.

Keywords: Experimental anxiety; Panic disorder; Skin conductance; Heart rate; Blood pressure; Serotonin uptake inhibitors

1. Introduction

Public speaking is the most frequent social fear (Furmark et al., 1999; Stein et al., 1994), and is especially prominent in patients with social anxiety disorder (Stein et al., 1996; Brunello et al., 2000). The most used procedure to study public speaking in the laboratory is the Simulated Public Speaking (SPS) test, in which the subject is requested to prepare a speech and then speak in front of a videocamera, the performance being recorded on videotape; at different moments, the subject fills self-evaluation rating scales that measure anxiety and other subjective states (McNair et al., 1982). A comparative study has shown that SPS enhanced anxiety in healthy volunteers irrespective of trait anxiety level (Palma et al., 1994). In contrast, another procedure that induces experimental anxiety, the Stroop Color-Word Test, was anxiogenic only in persons with high trait anxiety. In addition, the prevalence of the fear of speaking in public is high among students (Geer, 1965) and is independent of gender, ethnic group or age (Phillips et al., 1997). For these reasons, SPS is believed to induce a species-specific emotional reaction (Deakin and Graeff, 1991; Deakin et al., 1994).

Although in terms of face validity SPS reminds social anxiety rather than panic disorder (PD), pharmacological evidence indicates that the pharmacological profile of SPS is akin to that of PD (for a review, see Graeff et al., 2003). In this regard, the enhancement of SPS-induced anxiety by a single dose of the serotonin (5-HT) reuptake inhibitor (SRI) clomipramine (Guimarães et al., 1987) as well as of nefazodone (Silva et al., 2001) has been related to the worsening that occurs during the initial phase of PD

* Corresponding author. Tel./fax: +55 16 635 0713.
E-mail address: fgraeff@keynet.com.br (F.G. Graeff).

0924-977X/$ - see front matter © 2005 Elsevier B.V. and ECNP. All rights reserved.
doi:10.1016/j.euroneuro.2005.05.002

treatment with SRIs. Also, a connection between the lengthening of SPS-induced anxiety caused by the 5-HT_2-receptor antagonist ritanserin (Guimarães et al., 1997) and the absence of therapeutic effect of the same drug on PD (Deakin et al., 1990; Den Boer and Westenberg, 1990) has been suggested. Moreover, the 5-HT releaser and reuptake inhibitor D-fenfluramine has been shown to markedly decrease SPS-induced anxiety (Hetem et al., 1996). Accordingly, the results of an open clinical study (Solyom, 1994) and a case report (Hetem, 1996) indicate that fenfluramine improves PD.

On the basis of the above pharmacological evidence as well as of results obtained with animal models of anxiety disorders (Graeff and Zangrossi, 2002), a neurobiological hypothesis has been elaborated, proposing that SPS activates the same neural networks that control panic attacks (Deakin and Graeff, 1991; Deakin et al., 1994). These neural systems have evolved to organize defensive responses, such as fight or flight for coping with danger that is very close or in actual contact with the threatened animal (Blanchard and Blanchard, 1988). The critical neural structure for integrating such defensive reactions is the periaqueductal gray matter (PAG) of the midbrain (see, e.g., Fanselow, 1991) and, as a consequence the PAG has been implicated in PD. It has been further assumed that a deficit of the serotonergic input that comes from the dorsal raphe nucleus and inhibits escape induced by PAG stimulation would result in PD and its enhancement by SRIs would be the chief mechanism of their antipanic action (for a review, see Graeff, 2004).

If SPS indeed mobilizes the same neural systems that command panic attacks, PD patients should react differently from healthy controls to the SPS challenge. To test this hypothesis, a comparative study has been performed by Del-Ben et al. (2001b). As expected, the obtained results have shown that symptomatic non-drug-treated panic patients reacted less than healthy controls to SPS.

The main purpose of the present study is to carry on this line of inquiry by introducing a third group of panic patients that became nonsymptomatic following SRI chronic administration. Since neurovegetative changes are prominent symptoms of PD (American Psychiatric Association, 1994), psychophysiological indexes of neurovegetative functioning have been measured at selected times of the experimental session, in addition to the usual evaluation of subjective states. The selected variables were electrodermal activity, heart rate and arterial blood pressure, because they have been used as indexes of sympathetic arousal in the study of anxiety and related emotions (see, e.g., Lader, 1975).

In addition, methodological changes have been introduced in the present study to minimize possible biases that could affect preferentially panic patients. First, information necessary for consent was given in two occasions, namely before a screening interview and just before the SPS test, only the latter providing a full description of the SPS procedure. In the former study (Del-Ben et al., 2001b), the subjects were informed about the test from the beginning, a procedure that might induce more anxiety in panic patients than in controls. Second, the healthy volunteers were chosen among the acquaintances of the panic patients, thus ensuring a similar socio-cultural background for the two experimental groups. In the study by Del-Ben et al. (2001b), healthy volunteers belonged to the hospital staff, and therefore came from different social categories than the patients. In addition, they were already familiar with the experimental setting.

With the exception of a few subjects, the participants of this investigation had their salivary cortisol measured before and after the SPS test. The obtained results have been reported elsewhere (Garcia-Leal et al., 2005).

2. Experimental procedures

2.1. Subjects

Informed consent was obtained from all volunteers. The Regional Ethics Committee approved the study.

The subjects were selected on the basis of a screening interview (see below). All participants were at least 18 years old and had at least 6 years of formal education. Panic patients with other psychiatric disorders were excluded, except for current depressive disorder and agoraphobia that are often comorbid with PD. Other exclusion criteria were pregnancy, somatic disease, and current use of oral contraceptives or other medication, except for antidepressants. Healthy controls did not meet criteria for any category of psychiatric disorder.

The participants were divided into three experimental groups: (1) symptomatic patients (SP): 14 patients with the diagnosis of symptomatic PD with and without agoraphobia by DSM-IV criteria (American Psychiatric Association, 1994), who were drug free for at least 2 weeks; (2) nonsymptomatic patients (NSP): 16 patients with the same diagnosis, but who were nonsymptomatic for at least 3 months and were receiving either a selective serotonin reuptake inhibitor or clomipramine, without association with any benzodiazepine; (3) healthy controls (HC): 16 healthy volunteers. To match for socio-economic level, the patients who participated in the study have indicated the healthy volunteers among their acquaintances.

Information about the drug treatment of the NSP is summarized in Table 1.

2.2. Screening interview

Clinical diagnosis was made through the Structured Clinical Interview for DSM-IV, clinical version (SCID-CV, First et al., 1997), translated to Portuguese by Del-Ben et al. (2001a). The Panic and Agoraphobia Scale (Bandelow, 1995) translated to Portuguese by Ito and Ramos (1998) was used to evaluate the severity of PD.