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Brief report

## A preliminary study of dopamine-mediated prolactin inhibition in generalised social phobia

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### Abstract

The biology of social phobia has been little studied, but a possible role for dopamine has been implicated in this disorder. The aim of this study was to examine central dopaminergic function in patients with generalised social phobia using the prolactin response to quinagolide, a dopamine D2 receptor agonist, and to compare responses with those of normal controls. The study included 14 patients with moderate or severe generalised social phobia and 14 healthy age- and gender-matched comparison subjects. Quinagolide (0.5 mg) was administered orally and prolactin responses were measured over 4 h. There was no significant difference between prolactin responses in patients and healthy controls, nor was there a correlation between prolactin response and age, sex, or severity of illness. This would suggest that tuberoinfundibular dopamine D2 receptor sensitivity is normal in this disorder. © 2002 Elsevier Science Ireland Ltd. All rights reserved.

**Keywords:** Prolactin; Quinagolide; Cortisol

### 1. Introduction

Social phobia, also known as social anxiety disorder, is a common psychiatric disorder, which results in significant distress and social disability (Stein, 1998). It is characterized by a persistent fear of situations in which the individual may be exposed to the scrutiny of others, and in which he or she may act in a way that is humiliating or embarrassing (American Psychiatric Association, 1994). Social phobia has been subdivided into two

types, generalised social phobia characterised by fear and/or avoidance of most social situations (American Psychiatric Association, 1994) and 'specific' or 'discrete' social phobia, the former subtype being associated with the most severe disability (Brunello et al., 2000).

Despite 2–10% of the population being affected by this disorder (Myers et al., 1984; Davidson et al., 1994; Kessler et al., 1994; Stein et al., 1994), its biology has been little studied. Investigators have implicated a possible role for dysfunction of the serotonin, noradrenaline or GABA neurotransmitter systems (for reviews, see Stein, 1998; Bell et al., 1999). However, findings from such studies

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are by no means conclusive. Dopamine has also been implicated. Evidence for an association of social phobia with subnormal transmission in the dopamine system includes the clinical effectiveness of monoamine oxidase inhibitors but not tricyclic antidepressants (Liebowitz et al., 1987a), a report of the dopamine and noradrenaline reuptake inhibitor bupropion being used successfully in this disorder (Emmanuel et al., 1991), low cerebrospinal fluid levels of homovanillic acid among panic disorder patients with comorbid social phobia (Johnson et al., 1994), a high rate of social phobia among patients with comorbid Parkinson's disease (Stein et al., 1990) and increased symptoms of social phobia in patients suffering with Tourette's syndrome when treated with haloperidol (Mikkelsen et al., 1981). In addition, recent studies using single photon emission computed tomography (SPECT) have also implicated a possible role for this monoaminergic system in patients with social phobia. Tiihonen et al. (1997) noted markedly reduced striatal dopamine reuptake site densities in patients with social phobia in comparison to controls and speculated that this may be due to a smaller number of dopamine synapses (and neurons) or fewer dopamine reuptake sites per neuron. Schneier et al. (2000) subsequently found decreased striatal D2 receptor binding potential in these patients. However, Mathew et al. (2001) have concluded that SPECT studies of the dopamine transporter and D2 receptor in the striatum thus far are inconclusive in confirming a hypothesis of low dopamine innervation in this disorder.

To complement these studies, we attempted to examine the functional activity of dopamine D2 receptors using a neuroendocrine challenge. Plasma levels of prolactin reflect a balance between stimulation via serotonin and inhibition via dopamine. The dopamine inhibition is at the level of the pituitary (Lamberts and Macleod, 1990). The facts that dopamine receptors on the lactotrophic cells of the anterior pituitary are activated humorally via dopamine circulating in the portal vessels, and not at limited synaptic contact areas with comparatively high local dopamine concentrations, apparently results in a particularly high receptor sensitivity (Wachtel, 1991). Quinagolide is an

octahydrobenzo[g]quinoline with highly specific dopamine D2 agonist properties (Closse et al., 1988) which inhibits prolactin release (Gaillard and Brownell, 1988). This drug is used in the treatment of hyperprolactinemia and prolactinoma (Nobels et al., 2000; Rohmer et al., 2000; Schultz et al., 2000). To the authors' knowledge, it has not previously been used as a neuroendocrine probe in any psychiatric disorder. The dopamine agonist-induced decline of serum prolactin levels represents a sensitive functional test *in vivo*, which in humans responds to extremely low doses of dopamine agonists (Wachtel, 1991). An augmented decline in prolactin levels would therefore suggest hypersensitivity of D2 receptors; a diminished decline would reflect subsensitivity. The aim of this study was to examine central dopaminergic function in patients with generalised social phobia using prolactin responses to quinagolide and to compare them with those of normal controls.

## 2. Methods

Seven male and seven female patients who fulfilled DSM-IV criteria (American Psychiatric Association, 1994) for generalised social phobia were recruited via advertisement and 14 age- and sex-matched healthy controls who were known to the investigators participated in the study. The study was approved by the local ethics committee, and fully informed written consent was obtained from all subjects. All patients were physically healthy as determined by medical history, physical examination and appropriate blood and urine tests, and they suffered from no current or lifetime history of any other psychiatric disorder apart from avoidant personality. All patients were psychotropic drug-naïve and had taken no other medication that might alter dopaminergic activity in the previous year. Women who were pregnant or lactating were excluded. The diagnosis of generalised social phobia was determined by the investigator during a comprehensive psychiatric assessment and confirmed with the Structured Clinical Interview for DSM-IV Patient Edition (First et al., 1995). The Liebowitz Social Anxiety Scale (LSAS) (Liebowitz, 1987b) was used to measure the severity of social phobia, and patients were excluded from the

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