



Growth hormone response to baclofen in patients with seasonal affective disorder: effects of light therapy

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Abstract

There is evidence for γ -aminobutyric acid (GABA) dysfunction in the pathophysiology and treatment response of patients with major depression, but this has not been studied in seasonal affective disorder (SAD). Growth hormone (GH) response to a challenge with a GABA_B receptor agonist, baclofen, is considered an *in vivo* index of hypothalamic GABA_B receptor function in humans. To explore the role of GABA_B receptor function in SAD, we compared the GH response to baclofen challenge in 15 patients with SAD and 20 matched healthy controls. Of the 15 patients with SAD, 14 had repeat baclofen challenge following 2-week treatment with light therapy. The results showed that baclofen administration led to a significant increase in GH release both in patients with SAD and normal controls. There was no significant difference in the GH response to baclofen between the two groups. Furthermore, 2-week treatment with light therapy did not significantly alter the baclofen-induced GH response in patients with SAD, in spite of a clear therapeutic effect. The results of this study suggest that hypothalamic GABA_B receptor function, as measured by baclofen induced GH release, is not altered in patients with SAD or by light therapy. © 1999 Elsevier Science Ltd. All rights reserved. © 1999 Elsevier Science Ltd. All rights reserved.

Keywords: GABA; GABA_B receptor; Baclofen; Growth hormone; Seasonal affective disorder; Winter depression; Light therapy

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1. Introduction

Current biochemical hypotheses of depressive disorders have predominately implicated biogenic amine neurotransmitters such as serotonin (5-HT) and norepinephrine (NE), in either the pathophysiology of depression or in the mechanisms of action of antidepressant treatments. There is an ample literature to support this. However, most antidepressant treatments in clinical use affect a number of neurotransmitter receptors in addition to those of serotonin and norepinephrine (Green and Nutt, 1983). It is plausible, therefore, that other neurotransmitter systems, such as γ -aminobutyric acid (GABA) system, may be deranged in depression, and therefore could be action sites of antidepressant treatments (Leonard, 1994).

As reviewed in our recent paper (Shiah and Yatham, 1998), several lines of evidence in the literature have accumulated to support the hypothesis of low GABA function in depression. For example, four out of eight studies reported that cerebrospinal fluid (CSF) GABA levels were significantly lower in patients with major depression compared to controls (Gerner and Hare, 1981; Gerner et al., 1984; Gold et al., 1980; Joffe et al., 1986; Kasa et al., 1982; Post et al., 1980; Roy et al., 1991; Zimmer et al., 1981). Three out of four studies showed that unipolar depressed patients have lower plasma GABA levels compared with normal controls (Petty and Schlessler, 1981; Petty and Sherman, 1984; Petty et al., 1992; Rode et al., 1991). Petty (1994) also reported that plasma GABA levels in patients with bipolar depression had lower plasma GABA compared with matched normal controls. Furthermore, the GABA synthesizing enzyme, glutamic acid decarboxylase (GAD), in plasma was shown to be lower in patients with both unipolar and bipolar depressions (Kaiya et al., 1982), further supporting a GABA deficit in depression. Perry et al. (1977) also reported that GAD activity was significantly decreased in postmortem brain of depressed patients compared with controls. In contrast, Cheetham et al. (1988) found no alterations in frontal and temporal GAD activity in 21 depressed suicide victims compared with 21 matched controls.

With regard to the contribution of GABA function to the mechanism of action of antidepressant treatments, there have been conflicting results of preclinical studies. For example, several different classes of antidepressant agents including tricyclic antidepressants (TCAs), monoamine oxidase inhibitors (MAOIs), selective serotonin reuptake inhibitors (SSRIs), and electroconvulsive shock (ECS) were reported to induce an increase in GABA_B receptor binding in rat frontal cortex (Gray and Green, 1987; Lloyd and Pichat, 1987; Lloyd et al., 1985; Pratt and Bowery, 1993; Szekely et al., 1987) or hippocampus (Lloyd and Pichat, 1987) following chronic administration. However, several other studies failed to confirm the enhanced GABA_B receptor binding with antidepressant treatments (Cross and Horton, 1987, 1988; Engelbrecht et al., 1994; McManus and Greenshaw, 1991; Szekely et al., 1987). The reasons for the discrepant results relating the effects of antidepressant treatments on GABA_B receptor binding remain unclear.

In humans, one way to assess GABA_B receptor function is to measure growth hormone (GH) release after administration of baclofen, a GABA_B receptor agonist. This endocrine challenge paradigm is based on two observations: (1) that hypothal-

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