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Preliminary communication

Do venlafaxine XR and paroxetine equally influence negative and positive affect?

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Abstract

Background: We assessed the therapeutic effects of venlafaxine XR and paroxetine on mood and anxiety symptoms derived from the tripartite model of mood. We hypothesized that the two antidepressants would have largely similar effects on symptoms of negative affect because both agents influence serotonergic systems. However, based on evidence indicating linkages between catecholaminergic activity and the emotional dimension of positive affect, we hypothesized that the catecholaminergic effects of venlafaxine XR would yield particularly pronounced effects on symptoms of positive affect.
Methods: Twenty depressed outpatients were randomly assigned to treatment with either venlafaxine XR (225 mg/day) or paroxetine (30 mg/day) during a 12-week treatment trial. Weekly mood ratings were collected using the Mood and Anxiety Symptom Questionnaire [Watson, D., Clark, L.A., Weber, K., Assenheimer, J.S., Strauss, M.E., McCormick, R.A., 1995. Testing a tripartite model: II. Exploring the symptom structure of anxiety and depression in student, adult, and patient samples. J. Abnorm. Psychol. 104 (1), 15–25] [Watson, D., Weber, K., Assenheimer, J.S., Clark, L.A., Strauss, M.E., McCormick, R.A., 1995. Testing a tripartite model: I. Evaluating the convergent and discriminant validity of anxiety and depression symptom scales. J. Abnorm. Psychol. 104 (1), 3–14].
Results: Consistent with predictions, analyses revealed that there were no significant differences between venlafaxine XR and paroxetine on measures of negative affect. However, contrary to predictions, the two medications produced similar changes on measures of positive affect.
Limitations: Replication and extension using a larger sample size are mandated.
Conclusions: These preliminary results suggest that two antidepressants that appear to have dissimilar mechanisms of action may nevertheless have similar effects on the positive and negative affective components of depression. Alternatively, paroxetine may have a clinically relevant noradrenergic effect at the dose tested.

Keywords: Depression; Anhedonia; Venlafaxine XR; Paroxetine; Tripartite model

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1. Introduction

We have recently proposed that a given antidepressant medication may produce a distinct profile of change across different symptom dimensions depending on its fundamental mechanisms of action (Shelton and Tomarken, 2001; Tomarken et al., 2004). In the current investigation, we assessed the effects of different antidepressant agents on symptoms of depression and anxiety derived from the tripartite model of mood disorders (e.g., Clark and Watson, 1991; Watson et al., 1995a,b). This model posits that symptoms of general distress are common to both mood and anxiety disorders, while symptoms of anhedonia are relatively specific to depression. A third dimension of somatic anxiety is primarily linked to panic disorder and perhaps other types of anxiety disorders. Watson et al., (1995a,b) have developed and validated a self-report measure, the Mood and Anxiety Symptoms Questionnaire (MASQ), which assesses these dimensions of mood.

Paroxetine, a selective serotonin reuptake inhibitor (SSRI), has a notably higher affinity for the serotonin transporter than for the norepinephrine transporter, and it demonstrates insignificant binding to postsynaptic receptors of any class (Owens et al., 1997; Reist et al., 1996). Previous findings suggest that drugs that enhance serotonin transmission such as paroxetine have a more profound effect on symptoms of negative affect than symptoms of positive affect (e.g., Bodkin et al., 1997; Knutson et al., 1998; Reist et al., 1996; Shelton and Brown, 2000; Shelton and Tomarken, 2001; van Praag et al., 1987). This evidence suggests that serotonergic agents are more likely to lower subjective anxiety and tension than relieve anhedonia. Based on these findings, we predicted that paroxetine would have stronger effects on general distress than on anhedonia.

Conversely, agents that modulate catecholaminergic activity tend to elevate forebrain dopamine activity (e.g., Karson et al., 1983) and thus increase positive affect (e.g., Depue and Collins, 1999; Depue et al., 1994). Furthermore, antidepressants with catecholaminergic mechanisms of actions have been shown to increase positive affect in individuals with depression (e.g., Bodkin et al., 1997; Tomarken et al., 2004). Venlafaxine XR is a novel antidepressant with proven efficacy for treating depression (e.g., Rudolph, 2002; Stahl et al., 2002; Thase et al., 2001). It inhibits the reuptake of serotonin, norepinephrine, and, to a lesser degree, dopamine (Muth et al., 1986), and repeated exposure increases the responsiveness of noradrenergic and dopaminergic systems (Maj and Rogoz, 1999). Because of the link between catecholaminergic transmission and positive affect, we hypothesized that venlafaxine XR would produce relatively greater decreases in anhedonic symptoms than paroxetine. We also hypothesized that the two agents would have comparable effects on negative affect because both enhance serotonin transmission. We tested these hypotheses by assessing weekly self-reported mood changes during a 12-week treatment study.

2. Method

Written informed consent was obtained from all participants. Participants were adult outpatients who met DSM-IV (American Psychiatric Association, 1994) criteria for major depression as determined by the Structured Clinical Interview for DSM-IV—patient version (First et al., 1997). Participants were recruited from advertisements and referrals by physicians at the Vanderbilt University Medical Center Department of Adult Psychiatry. Participants: (1) had scores on the 17-item version of the Hamilton Rating Scale for Depression (Hamilton, 1960) that were greater than 17; (2) were free of benzodiazepines for at least 2 weeks prior to their baseline assessment, antidepressant medication for at least 3 weeks prior to their baseline assessment, and fluoxetine, antipsychotics, lithium, carbamazepine, or valproate for at least 5 weeks prior to their baseline assessment; and (3) did not have: (a) any clinically significant physical illness that would limit treatment with either study drug; (b) a history of bipolar affective disorder; (c) any history of a psychotic Axis I disorder, including major depression with psychotic features; (d) current predominant nonpsychotic Axis I disorder, antisocial, borderline, or schizotypal Axis II personality disorders; (e) subnormal intellectual potential; (f) a history of substance abuse in the past 6 months or substance dependence in the past 12 months; (g) a known hypersensitivity to either study drug; or (h) any history of a seizure disorder.