

Brief report

Psychic and somatic anxiety symptoms as predictors of response to fluoxetine in major depressive disorder

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Abstract

The purpose of this study was to examine whether the presence/severity of psychic and somatic anxiety symptoms predicted clinical response following a 12-week, flexible-dose (20–60 mg daily), open-label trial of fluoxetine for major depressive disorder (MDD). The presence and severity of psychic and somatic anxiety symptoms were assessed with the use of select subscales of the Symptom Questionnaire and the Hopkins Symptom Checklist among 518 outpatients with MDD. With the use of separate logistic regressions, we tested for the relationship between clinical response, baseline Hamilton Depression Rating Scale (HAM-D-17) scores, and subscale scores at baseline entered separately as independent variables. Overall completion, response and remission rates for the trial were 64.2%, 55.4%, and 48.9%, respectively. All subscale scores selected for this analysis significantly predicted treatment response to fluoxetine. The presence/severity of psychic and somatic anxiety symptoms of MDD at baseline predicted an increased likelihood of non-response to fluoxetine in MDD. Studies examining whether specific treatment strategies are more effective than the selective serotonin reuptake inhibitors for MDD patients with high levels of co-morbid psychic and somatic anxiety symptoms are warranted.

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1. Introduction

Despite the progressive increase in the number of available antidepressants (Papakostas and Fava, 2005), many patients suffering from major depressive disorder

(MDD) continue to be symptomatic. For example, as many as half of all patients enrolled in two academic-based depression specialty clinics did not achieve remission despite receiving numerous adequate antidepressant trials (Petersen et al., 2005). To complicate matters further, residual symptoms among remitters are common, and associated with poorer psychosocial functioning (Papakostas et al., 2004a), as well as increased relapse rates (Paykel et al., 1995). Yet, there is little consensus among psychiatrists regarding optimizing treatment for patients with MDD. In light of the

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challenge MDD poses to clinicians and patients alike, there is a need to develop novel treatment strategies that are both safer and more effective than those currently employed.

Two general approaches exist to develop novel, pharmacotherapy-based treatment strategies for MDD (Petersen et al., 2006). The first is to develop individual treatments or treatment combinations which are, overall, more effective than the ones currently available. The second is to use those treatments currently available, but to develop strategies to better match each treatment with a specific MDD subtype. Such efforts have focused on examining the impact of various symptoms, symptom clusters, or depressive subtypes (Danish University Antidepressant Group, 1986, 1990; Liebowitz et al., 1988; Quitkin et al., 1990, 1991; Winokur et al., 2005; Papakostas et al., 2006, in press; Thase et al., 2007) on differential treatment outcome during the administration of two antidepressant monotherapies involving distinct mechanisms of action including the tricyclic antidepressants (TCAs), monoamine oxidase inhibitors (MAOIs), selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRI), and the norepinephrine-dopamine reuptake inhibitor (NDRI) bupropion. The latter approach, however, has been limited due to the paucity of feasible, reliable, and robust agent-specific clinical or biological predictors of response, particularly with regards to treatment with newer agents including the SSRIs and SNRIs. In previous trials conducted by our group, we had found a relationship between the presence of psychological (Fava et al., 1997) as well as physical anxiety symptoms (Papakostas et al., 2003; Papakostas et al., 2004b; Denninger et al., 2006; Fava et al., 2008) and poorer response to pharmacotherapy in MDD. The goal of the present work is to either confirm or refute these preliminary studies with the use of a newer dataset. Specifically, we sought to examine whether the presence/severity of psychic and somatic anxiety symptoms predicted clinical response following a 12-week, flexible-dose (20–60 mg daily), open-label trial of fluoxetine for MDD.

2. Methods

2.1. Overview and study population

Six hundred twenty-seven patients, aged 18–65, with major depressive disorder (MDD) diagnosed with the use of the Structured Clinical Interview for DSM-IV Axis I Disorders — Patients Edition (SCID-I/P) (First et al., 1995), were enrolled in a 1-week, medication-free washout period followed by a 12-week, flexible-dose, open-label

trial of up to 60 mg/day of fluoxetine. Patients were enrolled at either of two hospital-based, academic sites: the Depression Evaluation Service Center of the New York State Psychiatric Institute ($n=372$), an affiliate of Columbia University, or the Depression Clinical and Research Program (DCRP) at Massachusetts General Hospital (MGH) ($n=254$), an affiliate of Harvard Medical School. Patients who experienced adequate symptom improvement following the 12-week treatment period were then randomized in a double-blind fashion to either continue their treatment with fluoxetine or switch to placebo for a 52-week follow-up period. The present report focuses on the acute phase of the study (the primary results from this study are reported in McGrath et al., 2006).

2.2. Exclusion criteria

The following patients were excluded from the study: pregnant women, women of child-bearing potential who were not using a medically accepted means of contraception, women who were breast-feeding, patients with serious suicidal risk, with history of seizure disorder, with serious and unstable medical disorders, with clinical or laboratory evidence of hypothyroidism without adequate stable replacement, or with a history of an allergy to fluoxetine, or patients who were concurrently using any of a list of exclusionary drugs. Exclusionary drugs included: terfenadine and astemizole, oral steroids (corticosteroids and androgens), anticoagulants (with the exception of aspirin), antiarrhythmics, and psychotropic medications (including antidepressants, hypnotics, anxiolytics, sedatives, antipsychotics and mood stabilizers).

Patients meeting criteria for the following DSM-IV diagnoses: organic mental disorders, alcohol or substance use disorders which were active within the past 6 months, schizophrenia, delusional disorder, psychotic disorders, bipolar disorder, or the presence of psychotic features were also excluded. Finally, we excluded: patients with a history of non-response to an adequate trial of fluoxetine, defined as a 4-week trial of fluoxetine with a minimum dosage of 40 mg/day for at least 2 weeks; patients treated with fluoxetine within the last 4 weeks prior to the screen visit, or with any other antidepressant or benzodiazepine within the last week prior to the screen visit; and patients treated with psychotherapy for less than 1 month before the screen visit.

2.3. Study procedures

Once patients had agreed to participate in the study by signing an IRB-approved informed consent document, the

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