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Early improvement in positive rather than negative emotion predicts remission from depression after pharmacotherapy

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Abstract

Knowledge on mechanisms involved in early prediction of response to antidepressant medication may help optimize clinical decision making. Recent studies regarding response to pharmacotherapy implicate resilience-like mechanisms and involvement of positive, rather than negative emotions. The aim of the current study is to examine the contribution of early change in positive affect to the prediction of response to pharmacotherapy. Positive and negative emotions were measured at baseline and during the first week of pharmacotherapy, using experience sampling techniques. The association between early change in positive and negative emotions and severity of depressive symptoms at week six was examined in a sample of 49 depressed patients. The added benefits of measuring early change in positive emotions compared to early Hamilton Depression Rating Scale (HDRS) change alone were evaluated through model comparisons. Early improvement in positive affect during the first week of treatment predicted the continuous HDRS score (β=−0.64, p<0.001), response (50% reduction; OR=4.32, p<0.01), and remission (HDRS ≤7; OR=9.29, p<0.001) at week six with moderate to large effect sizes. Effects of early change in negative emotions were only half as large and disappeared when evaluated simultaneously with early change in positive emotions. When early change in positive emotions was added to the models including early HDRS change only, all three models improved significantly. In conclusion, early change in positive rather than negative emotions best predicted response to treatment, supporting the notion that antidepressants activate resilience-like mechanisms. Moreover, monitoring of positive emotions in early stages of treatment may improve clinical decision making.

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1. Introduction

The efficiency of depression treatment can be considerably improved if current trial and error strategies are enriched with accurate outcome predictors at an early stage of treatment. In contrast to previous hypotheses on delayed onset of treatment response (Quitkin et al., 1984), evidence suggests that about 60% of the improvement occurring on active antidepressant and placebo takes place during the first two weeks of treatment (Posternak and Zimmerman, 2005). Several randomized or naturalistic studies as well as meta-analyses have shown that early improvement after one or two weeks of treatment strongly predicts later treatment outcome (e.g., Henkel et al., 2009; Stassen et al., 2007; Szegedi et al., 2009; Tadic et al., 2010). However, all these studies on early improvement assessed symptom severity with the Hamilton Depression Rating Scale (HDRS; Hamilton, 1960). The HDRS is a multidimensional instrument that covers only a selected number of clinical symptoms and neglects the assessment of positive emotions (Bagby et al., 2004). Investigations that rely on the HDRS therefore provide little information on the nature of emotional changes driving long-term improvement in early responders. Better knowledge on the emotional mechanisms involved in early response may aid the development of better strategies for assessing early response to treatment, thereby optimizing clinical decision making and improving quality of life for patients suffering from depression.

Although studies show that antidepressant use affects both positive and negative emotion processing (e.g. Harmer et al., 2010; Rawlings et al., 2010), recent studies suggest that changes in positive rather than negative emotions may be important in predicting recovery from depression. First, recovery from depression was associated with increases in the ability to experience reward in daily life, rather than decreases in sensitivity to stress (Wichers et al., 2009). Second, a high ability to experience positive emotions in daily life was associated with both reduced risk of becoming depressed in individuals with high genetic loading for depression and increased resilience against the development of affective symptoms (Geschwind et al., 2010; Wichers et al., 2007, 2010). Third, Stassen et al. (2007) concluded that antidepressants appear to trigger and maintain a common, resilience-like mechanism that controls recovery from depression. Psychological resilience can be defined as the ability to bounce back from negative emotional experiences (Block and Kremen, 1996; Tugade and Fredrickson, 2004), and recent studies show that positive, but not negative emotions, predict psychological resilience (Cohn et al., 2009).

Based on the findings outlined above, we hypothesized that early change in positive affect, rather than early change in negative affect, would be an important predictor of response to antidepressant treatment. Furthermore, we expected that adding information on early change in positive affect to information on early change in HRSD would significantly improve early prediction models of recovery from depression. We tested this hypothesis in a pre-existing longitudinal dataset on depressed patients starting pharmacotherapy. Early change in positive and negative emotions was measured using the experience sampling method (ESM) at baseline and at the end of the first week of pharmacotherapy. ESM is a momentary assessment technique in which participants are prompted to report on current emotions at random moments during the day, and is ideally suited for investigating change in emotions in daily life (Csikszentmihalyi and Larson, 1987).

2. Experimental procedures

2.1. Sample

Eighty-three patients with a DSM-IV diagnosis of current major depressive disorder (MDD) were recruited in eight primary care practices in the Netherlands (for full details concerning diagnosis and screening, see Barge-Schaapveld and Nicolson, 2002). Data were collected in the period between 1995 and 1996. Inclusion criteria were aged between 18 and 65 years and a score at study entry of ≥ 18 on the 17-item Hamilton Depression Rating Scale (HDRS; Hamilton, 1960). Exclusion criteria included major medical disorders and current use of psychotropic medications, except for the occasional use of temazepam. All participants gave written informed consent. The study was approved by the standing medical ethics committee.

2.2. Study design

During an initial baseline week, participants received no treatment in any form and took part in the experience sampling procedure during 6 days. Those who had completed at least 30 valid experience sampling assessments (for rationale see Experience sampling method below) were randomly assigned to twice-daily, double-blind, six-week treatment with either a tricyclic antidepressant or placebo (imipramine: starting dose of 50 mg/day, increased to 200 mg/day over the first week of treatment; placebo: starting with one capsule per day, increased to 4 capsules over the first week of treatment). In case of intolerance, the dose could be decreased to either 100 mg/day of imipramine or 2 placebo capsules per day. Participants then took part in a second period of experience sampling during the last three days of the first week of treatment. In addition, patient's general practitioners (GPs) administered the HDRS at screening, and at the end of baseline, week 1, week 2, week 4 and week 6. The current report used data from baseline, week 1 and week 6.

2.3. Experience sampling method

The experience sampling method (ESM) is a momentary assessment method to assess participants in their daily living environment, providing repeated in-the-moment assessments of affect in a prospective and ecologically valid manner (Csikszentmihalyi and Larson, 1987). Participants received a digital wristwatch and a set of ESM self-assessment forms collated in a booklet for each day. The wristwatch was programmed to emit a signal ("beep") at an unpredictable moment in each of ten 90-minute time blocks between 7:30 and 22:30, on consecutive days, resulting in a maximum of 60 beeps per person for the baseline measurement and a maximum of 30 beeps for the last three days of the first week. After each beep, participants were asked to fill out the ESM self-assessment, collecting reports of current mood and context. All self-assessments were rated on 7-point Likert scales. Participants were instructed to complete their reports immediately after the beep, thus minimizing memory distortion, and to record the time at which they completed the form. Participants with less than one third of valid reports were excluded from the analysis, and all reports not completed within 15 min after the actual beep were considered invalid, as previous work (Delespaul, 1995) has shown that reports completed after this interval are less reliable and consequently less valid.