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Information processing bias and pharmacotherapy outcome in older adults with generalized anxiety disorder

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ABSTRACT

Information processing bias was evaluated in a sample of 25 older adults with generalized anxiety disorder (GAD) over the course of 12 weeks of escitalopram pharmacotherapy. Using the CANTAB Affective Go/No Go test, treatment response (as measured by the Hamilton Anxiety Rating Scale, Penn State Worry Questionnaire, and Generalized Anxiety Disorder Severity Scale) was predicted from a bias score (i.e., difference score between response latencies for negative and positive words) using mixed-models regression. A more positive bias score across time predicted better response to treatment. Faster responses to positive words relative to negative words were associated with greater symptomatic improvement over time as reflected by scores on the GADSS. There was a trend toward significance for PSWQ scores and no significant effects related to HAMA outcomes. These preliminary findings offer further insights into the role of biased cognitive processing of emotional material in the manifestation of late-life anxiety symptoms.

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Information processing biases have been implicated as both causal and maintenance factors in cognitive models of anxiety (e.g., Beck & Clark, 1997; Mogg & Bradley, 2005). For example, among younger and middle-aged adults, attention bias for threat-related stimuli has been linked to anxiety symptomatology, including symptoms of generalized anxiety disorder (GAD; Becker, Rinck, Margraf, & Roth 2001; Bradley, Mogg, Millar, & White, 1995; Bradley, Mogg, White, Groom, & de Bono, 1999; Mogg, Bradley, Williams, & Mathews, 1993). In fact, it has been demonstrated that measures of attention bias can predict treatment outcome among persons with GAD (Mogg, Bradley, Millar, & White, 1995). There is also some evidence that information-processing biases can be altered with pharmacotherapy (Mogg, Baldwin, Brodrick, & Bradley, 2004). Preliminary research on attention training programs suggests that reductions in the magnitude of an attention bias toward threatening information can lead to reductions in anxiety symptoms, further suggesting that information processing biases play a role in the development or maintenance of GAD (e.g., Amir, Beard, Burns, & Bomyea, 2009; Hazen, Vasey, & Schmidt, 2009). Although progress has been made in this area, we know very little about whether these relationships between affective biases and anxiety are observed in older populations.

Among older adults without anxiety disorders, there is evidence for a bias toward positive material. Research on healthy aging suggests that older adults tend to attend to and remember positive information relative to neutral or negative information, a phenomenon that has been dubbed "the positivity effect" (cf. Mather & Carstensen, 2005). According to *Socioemotional Selectivity Theory*, this bias for positive information is not accidental; rather, it is theorized to reflect a shift of motivational goals with age from a focus on the acquisition of knowledge and information to the maintenance of emotional well-being (Carstensen, Isaacowitz, & Charles, 1999; Charles & Carstensen, 2007). It is thought that this change occurs due to age-related shifts in time perspective, such that individuals become more acutely aware of the limited nature of time as they grow older.

Despite the general developmental trend to focus upon the positive in later life, many older adults struggle with anxiety. The prevalence of anxiety in community-living older adults is as high as 10%, with most research indicating that GAD is the most common anxiety disorder in late life (Bryant, Jackson, & Ames, 2008; Flint, 2005). Onset of the disorder typically occurs in early adulthood, though some individuals develop it in later life (Chou, 2009). Among the elderly, GAD is associated with increased functional impairment and poorer quality of life (e.g., Porensky et al., 2009; Wetherell et al., 2004). The onset or maintenance of later-life GAD has been

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attributed to the quality and quantity of psychosocial stressors that are commonly faced by the elderly (e.g., deBeurs et al., 1999), as well as vulnerability to cognitive decline (particularly in the domain of executive functioning; e.g., Mohlman & Gorman, 2005) due to advanced age.

Although evidence supports the use of various elements of cognitive behavioral therapy for treating anxiety disorders, including GAD, in younger and middle-aged adults, these interventions are substantially less effective in older adults, with effect sizes approximately half of those detected in younger or middle-aged samples (Covin, Ouimet, Seeds, & Dozois, 2008; Gould, Coulson, & Howard, 2012). This suggests the possibility of age-related differences in factors affecting the development and maintenance of anxiety.

One such factor could be information processing biases, yet research in this area is relatively new. To date, completed studies have examined the associations between attention bias and anxiety in older people. Two published studies (Fox & Knight, 2005; Lee & Knight, 2009) showed that older adults (who underwent an anxious mood induction or were high in trait anxiety, respectively) showed greater attention to anxiety-related or negatively valenced stimuli. Another study examining selective attention in fear of falling showed that older adults with fear of falling had greater difficulty disengaging from fall-relevant words than did those without fear of falling (Brown, White, Doan, & de Bruin, 2011). Utilizing an emotional Stroop paradigm to evaluate attention bias among anxious older adults, Price, Siegle, and Mohlman (2012) found that older adults who habitually worry demonstrated a bias for threat-related information. Price, Eldreth, and Mohlman (2011) also used the Stroop task to examine the neural substrates of attention bias among older adults with GAD. This latter study was the first to include a clinically diagnosed sample. Results indicated that late-life GAD is associated with an attention bias for negative information. The aforementioned findings are largely consistent with the biases for threat-related information observed among anxious younger adults.

The present study is part of a larger project examining the efficacy of treatment for older adults with GAD. We were interested in whether information processing biases serve as a predictor of treatment outcome. Harmer, Goodwin, and Cowen (2009) have suggested that"antidepressants work by remediating negative affective biases [. . .] relatively quickly following drug administration" (p. 102). Given evidence that interpretation biases among patients with GAD can be changed through short-term SSRI pharmacotherapy (e.g., Mogg et al., 2004), and that information processing biases can predict treatment outcome (e.g., Mogg et al., 1995), we sought to explore whether information processing biases over the course of a 12-week open-label medication trial for anxiety were associated with treatment outcome among older adults with GAD. We chose to use the Cambridge Neuropsychological Test Automated Battery (CANTAB) Affective Go-No Go (AGN) test (Cambridge Cognition, 2006; Murphy et al., 1999) to evaluate differences in speed of classifying positive and negative words. The CANTAB AGN is aset-shifting task requiring affective labeling and inhibitory control (see further description below, under "Section 1.3"). Specifically, we hypothesized that faster processing of positive words relative to negative words would be associated with better treatment outcome (i.e., lower levels of anxiety over time) among treatment-seeking patients with GAD.

1. Method

1.1. Participants

Participants in the present study were 25 older adults (age 60 years or older) with a principal or co-principal (i.e., most severe) diagnosis of GAD according to criteria established by the *Diagnostic and Statistical Manual of Mental Disorders*, *4th edition*, *Text Revision* (DSM-IV-TR; American Psychiatric Association, 2000) who were awaiting randomization into a study evaluating the effects of cognitive-behavioral therapy as an augmentation to pharmacotherapy. GAD diagnosis was established using the Structured Clinical Interview for DSM-IV (First, Spitzer, Gibbon, & Williams, 1995); the interclass correlation coefficient for the GAD diagnosis among raters was 0.70, indicating acceptable reliability. All participants were treated with 12 weeks of open-label escitalopram (10 mg, increased to 20 mg at 4 weeks as tolerated if response was not achieved at the lower dose). Participants were not permitted to receive psychotherapy or other anxiolytic pharmacotherapy, although some participants who were taking benzodiazepines or sleep medications were allowed to remain on these medications at a consistent low dose. A board-certified geriatric psychiatrist monitored the participants' response to escitalopram and made adjustments as needed. Participants were recruited from clinics at the University of California, San Diego, as well as other community medical practices, senior centers, and through flyers, posters, and advertisements. Exclusion criteria were dementia or cognitive impairment (as defined as a score of 25 or less on the Mini-Mental Status Exam, or MMSE; Folstein, Folstein, & McHugh, 1975), history of bipolar disorder or psychosis, substance abuse within the past 6 months, inability or unwillingness to discontinue other pharmacotherapy or psychotherapy, and serious medical conditions that would interfere with study participation or result in contraindication to escitalopram (e.g., oxygen-dependent chronic obstructive pulmonary disease, congestive heart failure, active cancer treatment, end-stage liver or kidney disease). Informed consent was obtained and documented on signed forms for all participants. Enrolled participants were compensated $100 for their participation.

Participants were 15 women and 10 men with a mean age of 68.8 years (SD = 7.6). The racial composition of the sample was predominantly White (80%), with 12% Latino, 4% Asian, and 4% African-American. Participants had a mean of 16.4 years (SD = 2.5) of education. A plurality of participants were married (36%), and 20% were never married, 20% were widowed, 16% were divorced, 4% were separated, and 4% were cohabitating. Sixteen percent had a comorbid diagnosis of major depression and 40% had any comorbid Axis I disorder. Enrolled participants reported taking other medications in addition to the escitalopram prescribed for this study, some of which belong in classes that may affect cognition. These medication classes, along with percentage of participants who reported taking a medication in the class, include: analgesic combination (12%), anticonvulsant (4%), antihistamine (24%), benzodiazepine (24%), beta blocker (12%), cholinergic receptor blocker (4%), opiate agonist (4%), and sedative/hypnotic (8%).

1.2. Measures

Anxiety symptoms were monitored by three trained raters over a 12 week period using the Hamilton Anxiety Rating Scale (HAMA; Hamilton, 1959), Penn State Worry Questionnaire (PSWQ; Meyer, Miller, Metzger, & Borkovec, 1990), and Generalized Anxiety Disorder Severity Scale (GADSS; Shear, Belnap, Mazumdar, Houck, & Rollman, 2006). Two of the raters had masters degrees in psychology. A third rater earned a masters degree over the course of the study.

The HAMA is a 14-item interview-rated measure of anxiety primarily assessing somatic symptoms (i.e., physical complaints related to anxiety). It is considered the "gold standard" outcome measure in studies of GAD pharmacotherapy treatment. It has been validated in samples of older patients with GAD and normal community volunteers (Beck, Stanley, & Zebb, 1999; Diefenbach et al.,