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Treatment Response for Late-Life Generalized Anxiety Disorder: Moving Beyond Symptom-Based Measures

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Abstract

Response to treatment for late-life generalized anxiety disorder has been defined by a variety of methods, all based on statistically significant reductions in symptom severity. However, it is unknown whether these improvements in symptom severity are associated with meaningful differences in everyday functioning. The current study used four methods to define response to treatment for 115 primary care patients, age 60 and older, with a principal or co-principal diagnosis of generalized anxiety disorder. The methods examined included percent improvement, reliable change index and minimal clinically significant differences. Agreement among classification methods and their associations with general and mental health related quality of life were assessed. Results indicated moderate agreement among symptom-based classification methods and significant associations with measures of quality of life.

Keywords

GAD; older adults; treatment response; quality of life

Generalized anxiety disorder (GAD) is common in late life (Blazer et al., 1991) and associated with increased sleep difficulties (Brenes et al., 2009), decreased quality of life (Bourland et al., 2000), increased disability, and greater healthcare utilization (Porensky et al., 2009). Pharmacotherapy and cognitive-behavioral therapy (CBT) are effective treatments for late-life GAD (Pinquart and Duberstein, 2007; Wetherell et al., 2005), leading to reductions in symptom severity. The clinical significance of symptom reductions, however, is equally important and represents the extent to which the effects of treatment are

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Disclosure

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meaningful in everyday life (Kazdin, 1999). Unfortunately, there is little consistency in methods used for determining response to treatment of late-life GAD, which may have important implications for conclusions drawn from intervention studies.

The most common methods of determining response to treatment for late-life GAD are percent improvement, reliable change index (RCI), and minimal clinically significant differences (MCSD). With regard to percent improvement, pharmacotherapy studies (Katz et al., 2002; Lenze et al., 2005; Lenze et al., 2009) have classified responders by a 50% reduction on the Hamilton Anxiety Scale (HAMA; Hamilton, 1959) or a rating of 1 or 2 on the Clinical Global Impression (CGI) Scale (Guy, 1976), and psychotherapy studies have defined response by a 20% reduction on three of four worry and anxiety measures (Stanley et al., 2003; Wetherell et al., 2003). The RCI assesses change in symptoms with attention to statistical reliability of the measure (Jacobson and Truax, 1991). An RCI of 1.96 is typically used to determine response status (Wetherell et al., 2005). The MCSD is the smallest difference in a score that would suggest a change in the patient's management (Jaeschke et al., 1989).

It is unclear, however, whether response as defined by these symptom-based methods is associated with perceived improvements in QOL. GAD has pervasive effects on the functioning of older adults, (Porensky et al., 2009) and is a chronic illness with long-term effects (Kessler, 2000). Associations with QOL may help validate symptom-based methods of determining response status.

Method

Participants

Participants were recruited for a randomized clinical trial of CBT for late-life GAD (described in detail by Stanley et al., 2009). Participants were age 60 and older with a principal or co-principal diagnosis of GAD (American Psychiatric Association, 2000) according to the Structured Clinical Interview for the *DSM-III-R* (SCID; Spitzer et al., 1992). Exclusion criteria included current substance abuse, bipolar disorder or psychotic symptoms, and cognitive impairment, defined by a score of 24 or less on the Mini-Mental State Exam (MMSE; Folstein et al., 1975). Participants were randomly assigned to receive CBT or enhanced usual care (EUC).

Measures

Worry—The Penn State Worry Questionnaire (PSWQ; Meyer et al., 1990) is a 16-item self-report scale with good psychometric properties among older adults (Hopko et al., 2003) and is a primary outcome measure in CBT trials of late-life GAD (Stanley et al., 2003; Stanley et al., 2009; Wetherell et al., 2003). The Generalized Anxiety Disorder Severity Scale (GADSS; Shear et al., 2006) is a six-item clinician-rated instrument with adequate psychometric properties among older adults (Weiss et al., 2007).

Anxiety—The Beck Anxiety Inventory (BAI; Beck and Steer, 1990) is a 21-item, self-report measure with strong psychometric properties among older psychiatric patients (Kabacoff et al., 1997). The Structured Interview Guide for the Hamilton Anxiety Scale (SIGH-A; Shear et al., 2001) is a 14-item clinician-rated interview developed to increase the reliability of the widely used HAMA.

QOL—General QOL was assessed using the Quality of Life Inventory (QOLI; Frisch et al., 1992), which is reliable and valid among older adults with GAD (Bourland et al., 2000). Mental health-related QOL was assessed using the mental component score (MCS) of the

Medical Outcomes Study Short Form (SF-12; Ware and Sherbourne, 1992). Evidence supports its use with older adults in primary care (Weissman et al., 2001).

Data Collection

Participants who screened positive for anxiety completed the MMSE (Folstein et al., 1975) and SCID (Spitzer et al., 1992) to determine eligibility for treatment. All measures were administered at baseline and post-treatment via telephone by an independent evaluator unaware of treatment assignment. Regular calibration meetings were held, and a random 10% were reviewed by a different evaluator to assess interrater agreement on the clinician-rated measures.

Data Analysis

Worry and anxiety symptom scores at baseline and post-treatment were used to determine response status via the following methods: (1) 20% reduction on three of four measures: PSWQ, GADSS, SIGH-A, and BAI; (2) 50% reduction on the SIGH-A; (3) RCI on the PSWQ; and (4) MCSD on the PSWQ, defined as an improvement of 8.5 points (Stanley et al., 2009). Kappas were used to assess agreement between methods. Mean differences in QOL at post-treatment between responders and nonresponders were compared, controlling for baseline scores and treatment condition.

Results

Most participants were women (79.1%) and Caucasian (67.8%), with a mean age of 67.1 years ($SD = 5.99$) and an average of 16.0 ($SD = 2.92$) years of education.

The number of participants classified as responders varied by the different methods (Table 1). Agreement between classification methods also varied. Using guidelines established by Landis and Koch (1977), the 20% reduction method had moderate agreement with other methods (k 's = .41–.46) and the 50% reduction on SIGH-A method had low to moderate agreement with other methods (k 's = .20–.23). Agreement was highest between the two methods using the PSWQ ($k = .80$).

Mean post-treatment QOL scores for responders and nonresponders are presented in Table 2. Results indicated significant differences on the QOLI and SF-12 for all methods of determining response status. Responders perceived greater improvements from baseline to post-treatment in QOL than nonresponders. QOL scores for responders and nonresponders were compared to those reported by a nonclinical control sample of older adults (Bourland et al., 2000). Results indicated that responders' scores were comparable to those of the control sample, while nonresponders' scores were significantly lower than those of the control sample ($ps < .05$).¹

Discussion

This study examined symptom-based methods of classifying response to treatment that have been used in clinical trials of GAD. Agreement between the classification methods ranged from low to high. The 20% reduction method, most frequently used in CBT trials and the most comprehensive, showed moderate agreement with other methods. The 50% reduction on SIGH-A method, most frequently used in pharmacotherapy trials, showed poor-to-moderate agreement with other methods. Even the moderate agreement between the two

¹As 51 of the 115 participants met criteria for a depressive disorder, all analyses were repeated with depression status included as a covariate, along with baseline scores and treatment group. Results of these analyses were consistent with those reported in the text; differences between responders and nonresponders were significant using all four classification methods.

percent improvement methods suggests that the ways in which response to psychotherapy and pharmacotherapy are being defined are not consistent. Comparison of outcomes across psychotherapy and pharmacotherapy trials may, therefore, be misleading. Agreement was very good, however, between the two methods involving the PSWQ, indicating greater consistency within measures than methods. Consistent use of a standard measure such as the PSWQ may help facilitate the comparison of outcomes across trials.

Each classification method demonstrated a similar pattern with regard to QOL. Treatment responders reported greater improvement in general QOL and greater reductions in the mental burden associated with illnesses and treatment. In other words, those who experienced statistically significant symptom reductions also perceived themselves to function and feel better, with QOL comparable to that of a nonclinical control sample of older adults (Bourland et al., 2000). These findings provide evidence for the validity of the various methods of determining response status.

Limitations

Lack of diversity in the current sample, with regard to age, sex, and education, may limit the generalizability of these findings. Participants as well educated as those in the current sample may respond differently to treatments than those who are not as well educated. GAD diagnosis at post-treatment would represent the “gold standard” by which to judge methods of determining response status. However, this information was not available in the current study. Future research should include a more diverse sample and diagnostic information at post-treatment.

In conclusion, there appears to be some consistency in the way in which response to treatment for GAD in late life is defined, with greater agreement within psychotherapy trials than between psychotherapy and pharmacotherapy trials. Greater consistency can be achieved, however, if researchers adopt use of a standard measure such as the PSWQ.

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Table 1

Response status and agreement

Method	Resp. (%)	Nonresp. (%)	1	2	3	4
1. 20% reduction on 3 of 4	36 (31.3)	79 (68.7)	--			
2. 50% reduction on SIGH-A	18 (15.7)	97 (84.3)	.44	--		
3. RCI PSWQ	32 (27.8)	83 (72.2)	.41	.20	--	
4. PSWQ change of 8.5	42 (36.5)	73 (63.5)	.46	.23	.80	--

Note. Resp. = responders. Nonresp. = nonresponders. SIGH-A = Structured Interview Guide for the Hamilton Anxiety Scale. Cell values are kappas. RCI = reliable change index. PSWQ = Penn State Worry Questionnaire.

Table 2

Mean post-treatment scores per group

Method	QOLI				SF-12			
	Resp.	Nonresp.	Group effect	<i>d</i> (95% CI <i>d</i>)	Resp.	Nonresp.	Group effect	<i>d</i> (95% CI <i>d</i>)
20% Reduction on 3 of 4	3.05	2.19	<i>F</i> (3, 111) = 17.19, <i>p</i> < .0001	.53 (.13 to .93)	52.40	44.98	<i>F</i> (3, 110) = 22.02, <i>p</i> < .0001	.85 (.45, 1.27)
50% Reduction on SIGH-A	3.23	2.32	<i>F</i> (3, 111) = 11.54, <i>p</i> = .0009	.56 (.05 to 1.07)	52.23	46.44	<i>F</i> (3, 110) = 7.71, <i>p</i> = .0064	.66 (.15, 1.17)
RCI PSWQ	3.14	2.21	<i>F</i> (3, 111) = 17.60, <i>p</i> < .0001	.56 (.15 to .97)	50.41	46.12	<i>F</i> (3, 110) = 5.59, <i>p</i> = .0198	.47 (.06 to .88)
PSWQ Δ of 8.5	2.99	2.16	<i>F</i> (3, 111) = 16.18, <i>p</i> = .0001	.50 (.11 to .88)	50.13	45.70	<i>F</i> (3, 110) = 7.05, <i>p</i> = .0091	.49 (.10 to .87)

Note. Group means are post-treatment scores, adjusted for baseline scores and treatment condition. Degrees of freedom vary due to missing data. Resp. = responders. Nonresp. = nonresponders. PSWQ = Penn State Worry Questionnaire. QOLI = Quality of Life Inventory. RCI = reliable change index. SF-12 = Mental Composite Score of the SF-12. SIGH-A = Structured Interview Guide for the Hamilton Anxiety Scale.