Is the Looming Maladaptive Cognitive Style a Central Mechanism in the (Generalized) Anxiety–(Major) Depression Comorbidity: An Intra-Individual, Time Series Study

Dana Tzur-Bitan and Nachshon Meiran
Ben Gurion University of the Negev

David M. Steinberg
Tel Aviv University

Golan Shahar
Ben Gurion University of the Negev;
Yale University School of Medicine

The authors examined the unfolding of anxiety-depression comorbidity while emphasizing its multifaceted and intra-individual nature. An intensive time series design was employed, whereby three young adult patients with diagnosed comorbid Generalized Anxiety Disorder (GAD) and Major Depression Disorder (MDD) were followed daily for a period of 6 months. Daily reports included affective states, cognitive vulnerability, and symptoms of depression and anxiety. The Looming Maladaptive Style (LMS), pertaining to the tendency to generate mental scenarios of potentially threatening situations as rapidly rising in risk, prospectively predicted anxiety, depression, and hopelessness, a dimension of depressive vulnerability. Effects of anxiety and depression on cognitive vulnerability were also documented. Findings suggest that LMS confers vulnerability to emotional disorders, broadly defined, and emphasize the need to include an intra-individual analysis for the purpose of elucidating the nature of psychopathological comorbidity.

Anxiety-Depression comorbidity is the rule rather than the exception in psychopathology (Kessler et al., 1996; Maser & Cloninger, 1990; Mineka, Watson, & Clark, 1998; Zimmerman, Chelminski, & McDermut, 2002). Such comorbidity is impli...
cated in (a) a more severe course of illness, (b) elevated social, marital, and occupational impairment, (c) risk for suicide, and (d) a poor treatment response (Coryell et al., 1988; Cox, Direnfeld, Swinson, & Norton, 1994; Noyes et al., 1993; Ormel, Oldehinkel, Brilman, & van den Brink, 1993; Weissman, Klerman, Markowitz, & Ouellette, 1989). Nevertheless, the underlying mechanisms of this comorbidity are still poorly understood.

Two dominant groups of explanatory models of this comorbidity are the shared factor hypothesis and the causal relationships explanation. The shared factor explanation pertains to the possibility that a higher order psychopathological factor underlies both anxiety and depression, such as the negative affectability factor of the Tripartite Model (Clark & Watson, 1991), or neuroticism as a shared genetic predisposition (Gray & McNaughton, 2000). Conversely, the causal relationships explanation targets one disorder as the cause of the other, or, alternatively, suggests reciprocal causality. Such causal relations are usually established by the temporal precedence of one disorder over the other, yet while most studies suggest that anxiety proceeds, and might even bring about, depression (Breslau, Schultz, & Peterson, 1995; Hettema, Prescott, & Kendler, 2003; Kessler et al., 1996; Lewinsohn, Zinbarg, Seeley, Lewinsohn, & Sack, 1997), other studies are consistent with the supposition that both disorders are equally likely to be the first in a comorbidity sequence (Moffit et al., 2007). Thus, should such a relationship exist, standard longitudinal studies fail to clearly determine its directionality.

Two important considerations in comorbidity research, which, in our opinion, have not been fully addressed, are the multifaceted nature of anxiety and depression and their dynamic, intra-individual, unfolding over time. With respect to their multifaceted nature, both anxiety and depression are presumed to include mood states (e.g., fear, sadness), clinical symptoms (e.g., hypervigilance, anhedonia), and distinct cognitive vulnerability. Regarding the latter, our focus was on helplessness, hopelessness, rumination, and looming. Helplessness is theorized to be a vulnerability dimension shared by both anxiety and depression, whereas Hopelessness appears to be a distinct depressive vulnerability (Alloy, Kelly, Mineka, & Clements, 1990). Rumination, a focal cognitive vulnerability, pertains to the tendency for self-reflection and repetitive and passive focus on one's negative emotions (Morrow & Nolen-Hoeksema, 1990; Nolen-Hoeksema, 1991). While rumination was demonstrated to be implicated in depressive vulnerability, it was also shown to be involved in the co-occurrence of depression and anxiety (Cox, Enns, & Taylor, 2001; Rector, Antony, Laposa, Kocovski, & Swinson, 2008).

Another important dimension of cognitive vulnerability is the Looming Maladaptive Style (LMS), pertaining to individuals' tendency to generate mental scenarios of potentially threatening situations as rapidly rising in risk or intensifying in danger. This style was shown to be a distinct dimension of cognitive vulnerability to anxiety disorders (Riskind, Rector, & Cassin, 2011; Riskind, Tzur, Williams, Mann, & Shahar, 2007; Riskind & Williams, 2006; Riskind, Williams, Gessner, Chrosniak, & Cortina, 2000; Williams, Shahar, Riskind, & Joiner, 2005). LMS was also proposed as a depressive vulnerability dimension, mainly through its derailment of perceived ability to cope with life problems, thereby generating helplessness and hopelessness (Rector, Kamkar, & Riskind, 2008).

A second consideration in comorbidity research is the dynamic, time variant, nature of each disorder (Tzur-Bitan, Meiran, & Shahar, 2010). Exploring the dynamic unfolding of depression and anxiety over time may enable the detection of causal re-
relationships, not only with respect to *disorders*, but also in terms of *components* of each disorder, for example, between a cognitive vulnerability dimension of anxiety and a mood component of depression. An analogy demonstrating the promise of this approach comes from intelligence research. In this field, the dominant theory posits a general intelligence factor (Spearman, 1904). According to this theory, the abilities that are measured in individual tests indicate this general ability to a certain degree. However, new studies that emphasized the development of abilities suggest a drastically different account. According to this alternative account, the correlations between abilities reflect the influence of one ability on the acquisition of another, rather than reflecting the fact that these abilities are determined by a general factor (Van der Mass et al., 2006).

Such dynamics are best captured using intra-individual research methodology (Molenaar, 2004; Molenaar & Campbell, 2009), preferably relying on a time series (TS) design (Ford & Lerner, 1992; Gottlieb, 1992, 2003; Granic & Hollenstein, 2003; Molenaar, Sinclair, Rovine, Ram, & Corneal, 2009; Wohlwill, 1973). Extensively used designs, such as cross-lagged Structural Equation Modeling (e.g., Shahar & Davidson, 2003) or Latent Difference Scores Modeling (LDS; McArdle & Hamagami, 2001), do allow for the investigation of dynamic unfolding of psychological conditions. However, these designs are limited in several important respects. First, they test hypothesized causal relationships across—rather than within—individuals. As such, they make the assumption that causal relationships are identical across all, or most, of the individuals, an assumption that might be (grossly) oversimplified (Granic & Hollenstein, 2003). Second, rank order designs such as cross-lagged SEM or LDS do not examine changes in absolute levels of a symptom (e.g., changes in depression symptoms) but rather estimate rank-order change, namely, change in the relative positioning of participants in comparison to others. Finally, although rank order designs permit intense measurement over time, in practice such intensity is difficult to employ because of the need to assess a large sample of participants. The end result is comprised of studies employing up to five or so waves of measurement, as compared to approximately 180 in this study.

TS designs circumvent these shortcomings. Such designs consist of assessments employed at short intervals (e.g., one day, in the present case). Data pertaining to each variable (e.g., depression) per each participant is then considered as a series. Each level of a variable within a series is related to the level predicted by previous fluctuations of that variable *within the same individual*, rather than to the sample mean or to other participants. Then, series are linked to each other intra-individually, allowing one to empirically examine the extent to which causal patterns are identical versus different across individuals.

Integrating the two considerations, namely, the multifaceted nature of anxiety and depression and the distinction between rank-order and intra-individual changes, we examined the direction of relationships between affective, symptomatic, and cognitive components of anxiety and depression. Our participants were three patients diagnosed with comorbid Generalized Anxiety Disorder (GAD) and Major Depressive Disorder (MDD). Such comorbidity was selected because it is quite prevalent (Massion, Wershaw, & Keller, 1993; Wittchen, Beesdo, Bittner, & Goodwin, 2003). These patients were assessed daily over a 6-month period. TS analyses were conducted to disentangle directionality pertaining to the three disorder components, whereby each participant served as an entire study (e.g., Brossart, Willson, Patton, Kivilighan, & Mufon, 1998;
Our main focus was on within-participant findings replicated across the three patients.

METHOD

Participants

Two hundred and twenty-six female undergraduate students were evaluated for anxiety and depression using the Beck Depression Inventory (BDI; Beck, Steer, & Brown, 1996) and the Beck Anxiety Inventory (BAI; Beck, Epstein, Brown, & Steer, 1988). Students high in anxiety and depression, as evident by a higher than cutoff score of 15 on the BDI and BAI, were invited for a structured clinical interview (SCID; First, Spitzer, Gibbon, & Williams, 1996), and were assessed for the presence of current GAD and MDD. Of this sample, four were invited to a clinical interview, and two were found to meet SCID criteria for comorbid GAD and MDD. These participants were recruited to the follow up study and completed a 6-month follow-up.

Students treated at the counseling services of Ben Gurion University were also invited to participate. An initial screening was conducted by a clinician from the counseling services based on a clinical interview and MMPI data (Butcher, Dahlstrom, Graham, Tellegen, & Kaemmer, 1989). From this pool of candidates, eight students were evaluated using the SCID. However, only one met criteria for a diagnosis of comorbid anxiety and depression. This student participated in the next stage. Thus, a total of three participants with a SCID diagnosis of both MDD and GAD completed the 6-month longitudinal daily evaluation.

Procedure

Upon signing an informed consent form, the above three participants began a 6-month follow-up which included daily assessment via phone conversations with the study coordinator. Each phone conversation was documented. In cases where participants reported elevated distress, a risk assessment and crisis intervention was conducted by Golan Shahar, who is an experienced clinical psychologist. Due to repeated administration of the experience report form, it was necessary to shorten the form as much as possible, while still including the necessary items for the evaluation of the different dimensions. Therefore, specific items were included in the experience report form.

Assessment

Participants' daily level of affect, symptoms, and cognitions were measured via a report form, developed for this study. The affective component of anxiety and depression was derived from the Positive and Negative Affect Scale-Expanded Form (PANAS-X; Watson & Clark, 1994). It is a 60-item adjective checklist designed to measure two higher order effects of negative and positive affect along with 11 specific affects such as guilt, self-assurance, fear, sadness, etc. For the purpose of the current study, 11 items addressing two specific affects were included: six items related to fear and five related...
to sadness. For all variables, participants were requested to report their feelings and experiences from last measurement. Specifically, they were asked, “Since last report, to what degree have you been feeling...”

Symptoms of depression and anxiety were assessed using items from the Beck Depression Inventory (BDI; Beck et al., 1996) and the Beck Anxiety Inventory (BAI; Beck et al., 1988). Each consists of 21 self-report items each, designed to measure symptoms of depression (BDI) or anxiety (BAI), respectively. Five items addressing depression symptoms were chosen from the BDI, and included: sadness, anhedonia, sleep disturbances, appetite, and energy. An additional four items addressing anxiety symptoms were chosen from the BAI, and included: fear of the worst happening, feelings of panic, increased heartbeat, and difficulty breathing.

Cognitive vulnerability to anxiety and depression was assessed by the items from the short version of the Hopelessness Helplessness Questionnaire (Lester, 2001), an eight-item Likert scale, measuring helplessness, hopelessness, and haplessness (the feeling of having bad luck or bad fortune). This questionnaire was adopted from the Pessimism Scale (Beck, Weissman, Lester, & Trexler, 1974), and was shortened by the aid of Principal Components Analysis to include four items of each subscale (Lester, 2001). In the current study, eight items of the short version subscales of helplessness and hopelessness were used, and included items such as “I can't think of reasonable ways to reach my current goal” for helplessness, and “I look forward to the future with hope and enthusiasm” for hopelessness.

Cognitive vulnerability to anxiety was also assessed using items from the Looming Maladaptive Style Questionnaire (LMSQ, Riskind et al., 2000), a measure of individuals’ tendency to generate mental scenarios of potentially threatening situations that are rapidly rising in risk or intensifying in danger. The LMSQ consists of six items describing potentially stressful situations (such as hearing a strange noise from the engine of your car while driving on the highway) and participants are asked to complete four questions for each description using a 5-point Likert scale (such as: “To what extent do you feel worried or anxious due to imagining this scenario?”; “Are your chances of having difficulties with your car increasing or decreasing with each moment?”). In the current study, the description was removed in order to fit the daily experience structure of our questionnaire. Therefore four items were redesigned to address increasing feelings of worry from a general daily event (e.g., “To what degree have you felt worried or anxious?”; “Are your chances of having difficulties increasing or decreasing each moment?”).

Cognitive vulnerability to depression was derived from the Ruminative Response Scale of the Response Style Questionnaire (RRS-RSQ; Nolen-Hoeksema & Morrow, 1991). The RRS-RSQ is a 22-item self-report measure aimed at assessing rumination in response to depressed mood such as focusing on either the meaning of rumination or the subjective feelings related to the depressed mood (“I think about how I feel”), on symptoms and on consequences and causes (“I think I won't be able to do my job if I won't snap out of it”). For the current study, three items were chosen to represent ruminative response style, and included Items 1, 17, and 26.

In summary, the questionnaire that the participants filled in on a daily basis yielded the following scale scores: Fear, Sadness, Depression Symptoms, Anxiety Symptoms, Hopelessness, Helplessness, Rumination, and Looming.
Data Analysis

A detailed description of the TS analysis is provided in supplementary materials available online. TS analysis evaluates a series of observations pertaining to a specific variable (e.g., Depression Symptoms). TS enables the examination of the influence of past values of the series on its current value, referred as "auto-influences." These auto influences are represented by the three components of what is known as the Autoregressive Integrated Moving Average (ARIMA) model (Box, Jenkins, & Reinsel, 2008). The first component, the autoregressive one, represents partial accumulation from past values (e.g., today's depression is likely to spill over to tomorrow's). The second component is needed when the mean level of the variable changes over time (i.e., there is an increase or decrease, etc.). The third is the moving average component, which represents the influences of random changes in the past (also called "random shocks") on the current level. These changes or "shocks" are said to be random because they cannot be predicted on the basis of the past behavior of the sequence.

The underlying principle of TS is that the three auto components, or sources of influence, represented in ARIMA, should be taken into account prior to estimating the effect of X on Y. This is done as follows. First, the second ARIMA component, representing the mean change pattern, is addressed by differencing, in which the preceding value is subtracted from the current value. The other two components (i.e., autoregressive and moving average) are addressed via "pre-whitening," a procedure tantamount to residualization in regression. The procedure is somewhat analogous to hierarchical regression in which the first block of predictors includes the ARIMA components (representing Y influences upon itself) and the second block includes X.

Importantly for our purposes, TS enables the examination of directional (i.e., causal) relations between two series. Assessment of causal relations is conducted by evaluating an input-output model consisting of a predictor (X) and outcome (Y). Both are "cleaned" from their respective auto influences. Causal examination is conducted via Granger Causality Test (Granger, 1969), followed by fitting a "Transfer Function" (TF). The Granger Causality Test examines whether past levels of variable X determine current levels of variable Y. Specifically, X is said to Granger-cause Y if previous levels of X are significantly correlated with the current level of Y, meeting the requirement for temporal precedence in determining causality. This test includes a comparison between the residuals of two regression models, one containing only past values of variable Y, the other containing both past values of X and past values of Y. A significant reduction in unexplained variance, as determined by the F-test difference, comparing the two residual series, means that residuals are significantly lower when adding past values of X into the regression model, thereby, X Granger-causes Y.

Once Granger causality is determined, it is important to determine and quantify its directionality (e.g., whether an increase in depression causes subsequent increase or decrease in anxiety) using TF. In the TF, the current level of the variable Y is estimated as a function of the mean level of that variable (represented by an intercept term), and the influence of current and past levels of X. Additional influences of past values of the output series, after accounting for influences of variable X, are assessed by an additional ARMA procedure (also referred to as "noise function"), and are added to

1. https://docs.google.com/file/d/0B7Oll2h3HcwONmEzNzN2MzBzTNjMDzLzksOGIrTnxcOjFmZmUyN2Zm/edit
Thus, the modeling process in TS involves a sequential testing of various influences. When a given influence is found not to be significant, it is dropped from the model. Model fitting is done by evaluating different combinations of parameters for the series until the residuals show no additional information (such series is referred to as "white noise"). Missing values accounted for less than 1% of the overall data across all 3 participants. Since Time Series Analysis cannot handle missing data, all missing values were replaced by the mean value of previous and following reports of the specific measured item.

RESULTS

Modeling Each Series Separately

Table 1 summarizes the data collected and analyzed for each of the three participants. Each of the variables in Table 1 was computed as the sum of its items in any given day. Table 2 summarizes results of TS modeling the separate series. It presents the models selected for each of the eight series estimated in all three participants. Below we will describe patterns that are similar in at least two out of the three participants.

For Fear, there was an autoregressive component in two participants, indicating that levels of Fear accumulated. For Helplessness and Hopelessness, all three participants corresponded to a moving average pattern indicative of a local influence of past cognitions. Additionally, Rumination had a dominant autoregressive component, showing that its level persisted over time. Looming had a dominant moving average component in two out of three participants, indicative of local influence of past levels of Looming, rather than a persistent pattern.

Granger Causality Tests

All models were examined with a time lag of 1 (p = 1 autoregressive order), due to the fact that most ARIMA models pointed to the order of 1. In series showing high autocorrelation, indicative of a trend (non-stationary series), differencing was employed prior to the Granger causality test, and the differenced series as fitted in the ARIMA modeling stage was entered into the regression. Table 3 presents a summary of all pairs showing statistically significant Granger’s causality (based on the F-test). Note that Table 3 presents the direction of causality. We restrict the description of causal rela-
DEPRESSION ANXIETY COMORBIDITY: A TSA STUDY

TABLE 2. Summary of ARIMA Models Fitted to Eight Collected Series of Each Participant

<table>
<thead>
<tr>
<th></th>
<th>RS</th>
<th>HB</th>
<th>RG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fear</td>
<td>(1,0,0)</td>
<td>Low variance</td>
<td>(4,1,0)</td>
</tr>
<tr>
<td>Sadness</td>
<td>(0,0,1)</td>
<td>Low variance</td>
<td>(4,1,0)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>(0,0,1)</td>
<td>(2,0,0)</td>
<td>(1,1,1)</td>
</tr>
<tr>
<td>symptoms</td>
<td>(0,1,1)</td>
<td>(1,0,0)</td>
<td>(1,1,1)</td>
</tr>
<tr>
<td>Helplessness</td>
<td>(0,1,1)</td>
<td>(1,0,1)</td>
<td>(0,1,1)</td>
</tr>
<tr>
<td>Hopelessness</td>
<td>(0,1,1)</td>
<td>(1,0,0)</td>
<td>(0,0,1)</td>
</tr>
<tr>
<td>Looming</td>
<td>(0,0,1)</td>
<td>(1,0,0)</td>
<td>(2,0,0)</td>
</tr>
<tr>
<td>Rumination</td>
<td>Random</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: ARIMA (p, d, q) representation as follows: p is the order of the autoregressive component, such that (1,0,0) represents a pure autoregressive process by which variable X is determined by accumulation of its past values going back p times. d is the order of differencing (in which time t is subtracted from t-I). When d=1, for example, this would mean that the previous level of t is subtracted from its current level, i.e., t - t-1. In case of series exhibiting a trend, q is the order of the moving average component, representing local influence/random shock going back q times. Series showing low variance cannot be analyzed due to violation of normal distribution assumption.

Within Depression. Hopelessness Granger-caused Depression Symptoms in two of three participants (HB, RG), while showing the reversed causal direction in the third (RS).

Within Anxiety. Looming was Granger-related to Anxiety Symptoms in two of three participants, showing a unidirectional pattern in which Looming Granger-caused Anxiety Symptoms in one participant (RG), and indicating bidirectional causal relations in the other (HB).

Between Disorders. Looming Granger-caused some aspects of depression in all three participants. Specifically, it caused Depression Symptoms in two out of three participants and caused Hopelessness in another two of the three participants. In one participant (HB) this causal relationship was bidirectional, showing a feedback loop involving Looming and Depression Symptoms. Helplessness was also found to Granger-cause Depression Symptoms in two participants and in one of them there was also a reverse causality, indicative of a feedback loop involving Helplessness and Depression Symptoms.

Transfer Functions

Pairs of variables showing statistically significant Granger causality results were further analyzed using TE. Each pair was first pre-whitened using the filter of the input series (i.e., the ARMA process fitted to the input series). The Cross Correlation Function (CCF), which evaluates the similarity between each input-output series as a function of the time-lag, was evaluated to gain an appreciation of the lag structure to be fitted, as well as for re-examining directionality. Competing models were tested for the optimal information criterion (AICC, SBC; Akaike, 1979; Schwarz, 1978. For further elaboration see supplementary materials). Parameter estimates were evaluated.
<table>
<thead>
<tr>
<th>Dependant</th>
<th>Fear</th>
<th>Sadness</th>
<th>Anxiety Symptoms</th>
<th>Depression Symptoms</th>
<th>Helplessness</th>
<th>Hopelessness</th>
<th>Looming</th>
<th>Rumination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fear</td>
<td></td>
<td></td>
<td>4.01**(H)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sadness</td>
<td>3.74 p = .052**(H)</td>
<td></td>
<td>3.95**(H)</td>
<td>9.81***(H)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anxiety symptoms</td>
<td>3.16 p = .07**(H)</td>
<td></td>
<td>4.71**(H)</td>
<td>43.46***(H)</td>
<td>3.25 p = .06(RG)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression symptoms</td>
<td>3.51 p = .06**(H)</td>
<td></td>
<td>4.82**(H)</td>
<td>3.20 p = .07(RG)</td>
<td>3.25 p = .06(RG)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Helplessness</td>
<td>7.57***(H)</td>
<td></td>
<td>4.20***(H)</td>
<td>6.86***(H)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hopelessness</td>
<td>6.42***(H)</td>
<td></td>
<td>3.93**(H)</td>
<td>3.93**(H)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Looming</td>
<td>3.66 p = .055**(H)</td>
<td>12.99***(H)</td>
<td>9.71***(H)</td>
<td>8.95***(H)</td>
<td>3.29 p = .06(H)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rumination</td>
<td>13.90***(H)</td>
<td>22.21***(H)</td>
<td>3.29 p = .06(H)</td>
<td>2.93 p = .08(RG)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note. *p < .05, **p < .001. Blank cells indicate nonsignificance, for results approaching significance, p value is detailed. Case initials are reported in the parentheses.
FIGURES 1-3. Visual representation of causal network as detected by Granger Causality Test in participants RS, HB, RG, respectively. Black arrows represent unidirectional causality, broken arrows represent marginal significance.
TABLE 4. Transfer and Noise Function Models of Pairs Showing Granger Causality within Each Disorder Construct

<table>
<thead>
<tr>
<th>Case</th>
<th>Output</th>
<th>Intercept</th>
<th>Transfer Function (Input)</th>
<th>Noise Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>RS</td>
<td>(1-B)hopeless</td>
<td>-0.05</td>
<td>1.09 sad, - 1.07 sad,</td>
<td>(1-0.93)(e)</td>
</tr>
<tr>
<td>RS</td>
<td>(1-B)hopeless</td>
<td>-0.30</td>
<td>0.47(1-B) dep.symp,</td>
<td>(1-0.74)(e)</td>
</tr>
<tr>
<td>HB</td>
<td>loom</td>
<td>1.81</td>
<td>1.80(anx.sym, + 0.99 anx.sym, + 0.51 anx.sym, + 0.37 anx.sym, + 0.38 anx.sym),</td>
<td>1/(1-0.70)(e)</td>
</tr>
<tr>
<td>HB</td>
<td>anx.sym</td>
<td>-0.20</td>
<td>0.10(hopeless, ,</td>
<td>1/(1-0.83)(e)</td>
</tr>
<tr>
<td>HB</td>
<td>loom</td>
<td>3.60</td>
<td>0.27(hopeless,</td>
<td>1/(1-0.72)(e)</td>
</tr>
<tr>
<td>HB</td>
<td>rum</td>
<td>3.74</td>
<td>1.11(dep.symp, + 0.38(dep.symp, ,</td>
<td>(1-0.26)(e)</td>
</tr>
<tr>
<td>HB</td>
<td>dep.sym</td>
<td>-1.48</td>
<td>0.20(hopeless, + 0.17(hopeless, ,</td>
<td>1/(1-0.50)(e)</td>
</tr>
<tr>
<td>RG</td>
<td>anx.sym</td>
<td>-0.98</td>
<td>0.22(loom, + 0.07(loom,</td>
<td>1/(1-0.50)(e)</td>
</tr>
<tr>
<td>RG</td>
<td>(1-B)sad</td>
<td>-0.05</td>
<td>0.12(1-dep.sym,</td>
<td>1/(1-0.71)(e)</td>
</tr>
<tr>
<td>RG</td>
<td>dep.sym</td>
<td>-10.55</td>
<td>0.44(hopeless, + 0.49(hopeless,</td>
<td>1/(1-0.38)(e)</td>
</tr>
</tbody>
</table>

Note: Variables names have been shortened for formula simplification: Sadness−sad, Anxiety Symptoms−anx.sym, Depression Symptoms−dep.sym, Helplessness−helpless, Hopelessness−hopeless, Looming−loom, Rumination−rum. The Backshift operator is commonly used as an abbreviation in TS literature, and represents an index for lagging the expression in parenthesis, e.g., (1-B) Output, represents a series that has undergone differencing procedure of Order 1, and is factored into: (1-B) Output = Output, − Output, (see supplementary materials for a detailed explanation). \(e\), represents the residuals (noise series) of the output series after accounting for the input variance.

for significance and white noise diagnostics were applied to ensure that all the relevant variation in the series was modeled. Note that the models selected were those best fitting the data.

TF results are presented in Tables 4 and 5. These results are presented as regression models so as to enable simple and accessible format for readers more familiar with multiple regression. Full diagnostics, information criterion, model fitting procedure and pre-transformations are detailed in the supplementary material. Note that pairs with Granger test results approaching significance and random cross-correlation functions were not further analyzed (see Table 5).

The following sections are subdivided into between disorders, within depression and within anxiety. Each subsection consists of two parts: the causality pattern and the influences of a series on itself (indicating accumulation over time vs. local influences) once causality was considered (Noise Functions).

Within Disorders: Table 4 represents the TF and Noise Functions for all pairs showing significant causality within each disorder.

Within Depression

Causal Relations Between Series. In Participants HB and RG, Hopelessness positively caused Depression Symptoms at Times t and t-1, \(\omega(\text{hopeless}_{t}) = .20, p < .001, \omega(\text{hopeless}_{t-1}) = .17, p < .05; \omega(\text{hopeless}_{t}) = .44, p < .001, \omega(\text{hopeless}_{t-1}) = .40, p < .01\), respectively. For participant RS, the inverse temporal-causal direction prevailed, showing that changes in Depression Symptoms from day before yesterday to yesterday positively caused changes in Hopelessness, \(\omega(\text{hopeless}_{t-1} | \text{hopeless}_{t}) = .47, p < .01\).
DEPRESSION ANXIETY COMORBIDITY: A TSA STUDY

TABLE 5. Transfer and Noise Function Models of Pairs Showing Granger Causality Between Anxiety Components and Depression Components

<table>
<thead>
<tr>
<th>Case</th>
<th>Output</th>
<th>Intercept</th>
<th>TF (Input)</th>
<th>AR</th>
<th>MA</th>
</tr>
</thead>
<tbody>
<tr>
<td>RS</td>
<td>hopeless</td>
<td>16.77</td>
<td>0.27loom, -0.10loom,</td>
<td>1/(1-0.41B)</td>
<td></td>
</tr>
<tr>
<td>RG</td>
<td>(1-B)hopeless,</td>
<td>0.05(1-B)loom,</td>
<td>(1-0.798)e,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RS</td>
<td>(1-B)dep.symp,</td>
<td>0.12(1-B)loom,</td>
<td>1/(1-0.31B)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HB</td>
<td>dep.symp,</td>
<td>1.88</td>
<td>0.10helpless, +0.13helpless,</td>
<td>1/(1-0.72B)</td>
<td></td>
</tr>
<tr>
<td>HB</td>
<td>dep.symp,</td>
<td>-1.10</td>
<td>0.28loom, -0.13loom,</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Noise Function. The inclusion of Hopelessness in the models (reported in the above section) revealed additional influences of series on themselves. In Participant RS, an MA component showed that Depression Symptoms were influenced by local past influences, \( \theta_{(dep.symp,)} = 0.95, p < 0.01 \). In Participant RG, Depression symptoms accumulated as indicated by an AR component, \( \phi_{(dep.symp,)} = 0.38 \).

Within Anxiety

Causal Relations Between Series. Looming positively caused Anxiety Symptoms at Times t and t-1 in Participant RG, \( \omega_{(loom,)} = 0.22, p < 0.01, \omega_{(loom,)} = 0.07, p < 0.05 \). In Participant HB Anxiety Symptoms positively caused Looming going back t-4 days, \( \omega_{(loom,)} = 1.80, p < 0.01, \omega_{(loom,)} = 0.99, p < 0.01, \omega_{(loom,)} = 0.51, p < 0.01, \omega_{(loom,)} = 0.37, p < 0.05, \omega_{(loom,)} = 0.38, p < 0.05 \).

Noise Function. When the inter-series causal relations (reported in the preceding section) were included in the model, we identified additional influences of series on themselves. In Participant HB, LMS both accumulated and was influenced by local past influences as indicated by an ARMA (1,1) model, \( \phi_{(loom,)} = 0.70, \theta_{(loom,)} = 0.38, p < 0.001 \). In Participant RG, Anxiety Symptoms accumulated (AR component), \( \phi_{(anx.symp,)} = 0.50, p < 0.001 \). Model fitting diagnostics and further details of transfer models are described in the supplementary materials.

Between Disorders

Causal Relations Between Series. Results presented in Table 5 confirm those yielded by the Granger causality test. In two participants (RG, HB), Looming positively Granger-caused Depression Symptoms, with the most apparent effect seen for t-1 and t. These results mean that yesterday's and today's looming predicts today's depression symptoms in 2 participants. In participant RG, the output series represents different values (i.e., level of change from yesterday to today) rather than absolute values, making the interpretation slightly more complex. Nonetheless, the essentially positive causal direction remained. Specifically, changes in Looming from yesterday to today positively caused changes in Depression Symptoms from today to tomorrow, \( \omega_{(loom,)} = 0.12, p < 0.001 \). In Participant HB, the same trajectory prevails, in which changes in Looming from day-before-yesterday to yesterday positively caused changes in Depression Symptoms from yesterday to today, \( \omega_{(loom,)} = 0.28, \omega_{(loom,)} = 0.38 \).
In Participant RS, elevated Looming today and yesterday predicted high current level of Hopelessness, \( \rho(\text{loom}_t) = .26, p < .001 \), \( \rho(\text{loom}_{t-1}) = .012, p < .005 \). In Participant RG, changes in Looming from day-before-yesterday to yesterday positively caused changes in Hopelessness, \( \rho(\text{loom}_{t-2} - \text{loom}_{t-1}) = .05, p < .001 \). In addition, changes in Helplessness 5 and 6 days ago positively caused changes in today's Depression Symptoms in Participant HB, \( \rho(\text{helplessness}_{t-5}) = .13, \rho(\text{helplessness}_{t-6}) = .09, p < .001 \).

Noise Function. The Noise Functions reveal influences of a series on itself that are seen only after causal relations from other variables are entered into the model in the TFM. In Participant RS, there was an AR component indicating accumulating effects of Hopelessness; after the influence of Looming was included in the model, \( \rho(\text{hopelessness}_{t}) = .41, p < .001 \). A similar accumulating effect (AR component) for Depression Symptoms was apparent in Participants RG and HB; after Looming was entered into the model, \( \rho(\text{depression}_{t}) = .31, .72 \) correspondently, \( p < .001 \). In Participant RG, local leaps in either Depression Symptoms, \( \theta(\text{depression}_{t}) = .90, p < .001 \), or Hopelessness, \( \theta(\text{hopelessness}_{t}) = .79, p < .001 \), caused the reverse effect the following day (an MA component).

DISCUSSION

Espousing a multidimensional, within-individual, TS study of the associations between aspects of anxiety and depression in three participants with comorbid MDD and GAD, we found evidence consistent with causal relations in each of our three participants. Focusing on patterns emerging for at least two participants, we found that LMS was predictive of Depression Symptoms in two participants. We also found that LMS predicted Hopelessness, a cognitive vulnerability marker of depression, in another two participants. This pattern of results provides a very strong test for the vulnerability status of the LMS, not only in the context of anxiety, but also—consistent with Rector, Kamkar, & Riskind's (2008) clinical case illustration—in the context of depressive symptoms and cognitive vulnerability to depression.

Within each disorder component, we identified directional (i.e., Granger-causal) relationships involving Hopelessness and Depression Symptoms across all three participants. In two participants, these relationships were unidirectional, leading from Hopelessness to Depression Symptoms. In the third participant, an opposite pattern, leading from Depression Symptoms to Hopelessness, was found.

The importance of these findings is twofold. First, they provide, to the best of our knowledge for the first time, support for the Hopelessness Theory for Depression using an intra-individual, TS design. Second, our findings show that hopelessness, as a cognitive vulnerability factor, may also be influenced by depression symptoms, an effect that is consistent with the highly debated scarring hypothesis (Lewinsohn, Steinmetz, Larson, & Franklin, 1981; Shahar & Davidson, 2003; Shahar & Henrich, 2010).

The fact that each individual had her own specific causal network, with specific trajectories not always congruent with known literature, highlights the limitations inherent in cross-sectional and "snap shot" longitudinal designs in terms of capturing clinical dynamics. As such, the present findings are in line with theoretical models suggesting the need for more complex, novel tools of analysis (Essex & Smythe,
DEPRESSION ANXIETY COMORBIDITY: A TSA STUDY

The most salient limitation of this study should be acknowledged. Because we focused on an intra-individual network of causal relations, each participant was treated as a separate study, leading to a sample of N = 3. While this is common in Time Series studies (Brossart et al., 1998; Dunn et al., 1987; Pole et al., 2008), replications with additional participants are needed. As well, our exclusive reliance on self-report measures might have inflated shared method variance, inadvertently boosting the associations between the study variables. Third, whereas the time scale employed in the present study was based on days, important changes in depression, anxiety, and their interrelations might have occurred on other time scales (hours, weeks, months), and our findings could not be generalized to these time scales. Within the context of these limitations, however, the present study provides a detailed examination of the anxiety-depression comorbidity by differentiating between symptoms, affective, and cognitive vulnerability dimensions that characterize each of the disorders, using—for the first time to our knowledge—a sophisticated, intra-individual TSA.

REFERENCES


Molenar, P. C. M. (2007). Psychological methodology will change profoundly due to the necessity to focus on intra-individual variation. Integrative Psychological and Behavioral Science, 41, 35-40.


