Title

Behavioral mediators of stress-related mood symptoms in adolescence & young adulthood

Authors

Peterson, Elena C
Rosenberg, Benjamin M
Hough, Christina M
et al.

Publication Date

2021-11-01

DOI

10.1016/j.jad.2021.06.079

Peer reviewed

HHS Public Access

Author manuscript

J Affect Disord. Author manuscript; available in PMC 2022 November 01.

Published in final edited form as:

J Affect Disord. 2021 November 01; 294: 94–102. doi:10.1016/j.jad.2021.06.079.

Behavioral mediators of stress-related mood symptoms in adolescence & young adulthood

Elena C. Peterson[a], **Benjamin M. Rosenberg**[b], **Christina M. Hough**[b], **Christina F. Sandman**[b], **Chiara Neilson**[a], **David J. Miklowitz**[c], **Roselinde H. Kaiser**[a,*]

[a]Department of Psychology & Neuroscience, University of Colorado Boulder, Boulder, CO 80309, United States

[b]Department of Psychology, University of California Los Angeles, Los Angeles, CA 90095, United States

[c]Semel Institute, University of California Los Angeles, Los Angeles, CA 90024, United States

Abstract

Background: Stress is a risk factor for unipolar and bipolar mood disorders, but the mechanisms linking stress to specific symptoms remain elusive. Behavioral responses to stress, such as impulsivity and social withdrawal, may mediate the associations between stress and particular mood symptoms.

Methods: This study evaluated behavioral mediators of the relationship between self-reported intensity of daily stress and mood symptoms over up to eight weeks of daily diary surveys. The sample included individuals with unipolar or bipolar disorders, or with no psychiatric history (n = 113, ages 15–25).

Results: Results showed that higher daily stress was related to higher severity of mania, and this pathway was mediated by impulsive behaviors. Higher stress also predicted higher severity of anhedonic depression, and social withdrawal mediated this relationship. A k-means clustering analysis revealed six subgroups with divergent profiles of stress-behavior-symptom pathways.

Limitations: Given the observational study design, analyses cannot determine causal relationships amongst these variables. Further work is needed to determine how relationships between these variables may vary based on stressor type, at different timescales, and within different populations.

Conclusions: Findings support a theoretical model in which impulsivity and social withdrawal act as behavioral mediators of the relationship between stress and mood symptoms. Additionally,

*Corresponding author. roselinde.kaiser@colorado.edu (R.H. Kaiser).

Author Contributors

R.H.K. developed the study design. E.C.P. and D.J.M. contributed to study recruitment. E.C.P., B.M.R., C.M.H., and C.F.S supported data collection. C.N. contributed to data processing. E.C.P. and R.H.K. performed data analysis and interpretation. E.C.P. drafted the paper, and all co-authors provided critical revisions.

Declaration of Competing Interest

None.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jad.2021.06.079.

distinct patterns of reactivity distinguished subgroups of people vulnerable to particular types of mood symptoms. These results provide novel information about how stress-reactive behaviors relate to specific mood symptoms, which may have clinical relevance as targets of intervention.

Keywords

Adolescent; Depression; Mood; Stress; Behavior; Mediation

Unipolar and bipolar mood disorders are highly prevalent and disabling psychiatric conditions (Kessler et al., 2012; Merikangas et al., 2010; Walker et al., 2015). Despite their high prevalence, the precise timing of mood episode onsets and the longitudinal course of symptoms are hard to predict. A substantial body of work has implicated stress as a risk factor for depression (reviews in Hammen, 2005; Hammen, 2015), and a more limited but growing body of research has shown an association between stress and mania (Alloy et al., 2020; Bender & Alloy, 2011;). However, the underlying pathways by which stress contributes to mood pathology remain poorly understood, and these associations have largely been studied separately in unipolar and bipolar disorders despite substantial overlap in symptoms across patient groups and diagnoses (Angst, 2010; McIntyre et al., 2015; Moreno et al., 2012). In particular, identifying specific behaviors that may mediate the association between stress and mood can help inform our understanding of how stress contributes to mood problems across diagnoses. Understanding the nature of these associations is particularly important in youth: adolescence and young adulthood are key periods of risk for mood disorders (Paus et al., 2008) and are also a time of exposure to new social stressors and the transition to independence (Auerbach et al., 2014; Hurst et al., 2013).

While previous work has indicated that stress plays a significant role in the onset of depression (Hammen, 2005), questions remain about mechanisms of the stress-depression association. Diathesis-stress models have advanced our understanding of underlying factors that may influence an individual's vulnerability to experiencing stress-related changes in mood, pointing towards the contributions of genetic factors, physiological responses, and cognitive styles (Colodro-Conde et al., 2018; Connolly and Alloy, 2017; Li et al., 2017; Moriarity et al., 2020; Shapero et al., 2017). These models address the important question of *who* may experience stress-related changes in mood, but they do not directly address the question of *how* stress leads to changes in mood. In particular, the intermediate behavioral steps that translate experiences of stress into changes in mood are unknown: how might stress affect an individual's behavior in more or less adaptive ways, which might in turn shape mood experiences? The pathway from behavioral patterns to mood symptoms has particular relevance to behavioral therapies, which aim to alleviate symptoms by targeting behavior change (Kaiser et al., 2015). Detecting behaviors that are closely associated with mood symptoms over time can inform these therapies by identifying the most appropriate behavioral targets of such interventions.

Behavioral theories of depression implicate withdrawal behaviors as a potential mediator of the association between stress and depression. These theories propose that reduced reinforcement of positive behaviors and increased reinforcement of avoidance behaviors leads to a state of passivity and withdrawal, thereby promoting the onset and maintenance

of depression (Ferster, 1973, Lewinsohn, 1974). In particular, stress has been specifically linked with anhedonia in a body of research spanning human and animal studies, suggesting the utility of focusing on this symptom dimension when aiming to interrogate stress-reactive mood (reviews in Pizzagalli, 2014; Stanton et al., 2019). In support of behavioral theories of depression, empirical studies have found that depressed individuals engage in activities less frequently than their peers (Hopko & Mulane, 2008) and are more likely to use avoidance coping strategies in response to stressors (Connor-Smith & Compas, 2002). Furthermore, longitudinal studies have found that avoidance behavior contributes to the maintenance of depression (Holahan et al., 2005). Social withdrawal may play a role as a particularly impairing and prevalent form of avoidance behavior in depression (Kupferberg et al., 2016; Porcelli et al., 2019). Social dysfunction in depression has been associated with impaired relationships, communication, and social perception (Kupferberg et al., 2016). In particular, social withdrawal may limit access to positive experiences such as social support, which has been associated with reduced depressive symptoms (Aneshensel and Stone, 1982; Grav et al., 2012). Altogether, these results suggest a potential mediation pathway in which stress invokes withdrawal behaviors in vulnerable individuals, which in turn leads to increased anhedonic depressive symptoms. However, to the best of our knowledge, this stress-behavior-mood pathway has not been explored in the daily lives of adolescents and young adults, a population that is highly vulnerable to mood symptoms.

In parallel, researchers investigating bipolar disorders have identified stress as a potential trigger for manic symptoms, although as with depression, the potential behavioral mechanisms of this association are unclear (Bender et al., 2010, Grandin 2006; Lex et al., 2017; Urosevic et al., 2008). One possible behavioral mediator of the association between stress and mania may be impulsivity, which has been related to bipolar symptoms in prior research. For example, one study found that individuals at higher risk of mania tended to experience more impulsivity in the context of positive mood states (Giovanelli et al., 2013). Another study showed that among individuals with bipolar disorders, impulsivity increased as the severity of manic symptoms increased (Strakowski et al., 2010). Stress has also been linked to increased impulsive behaviors in other psychiatric disorders such as substance use disorders (Fox et al., 2010) which are highly comorbid with bipolar disorders (Merikangas et al., 2008). Additionally, some studies have found that individuals with bipolar disorders are more likely to use impulsive coping behaviors in response to stress (Moon et al., 2014). Together, these findings suggest a pathway in which stress leads to impulsive behaviors in daily life, which in turn lead to heightened bipolar symptoms such as mania. To our knowledge, this mediation pathway has not yet been explored in youth.

In sum, prior research has identified stress as a risk factor for both depressive and manic symptoms. However, research examining stress and mood has largely been conducted separately among individuals with unipolar or bipolar diagnoses. Investigating stress within diagnostic categories may leave gaps in our understanding of risk pathways, given ongoing debate about boundaries between diagnoses (Angst 2011; Cuthbert & Insel, 2013; Insel et al., 2010) and shared symptoms across mood diagnoses. For example, the majority of individuals with bipolar spectrum disorders experience both depressive and manic symptoms (Moreno et al., 2012) with many reporting mixed episodes (Miller et al., 2016). In turn, an estimated 20% to 40% of individuals with unipolar diagnoses may

report mixed features or subclinical manic symptoms (Angst, 2010; McIntyre et al., 2015). Therefore, a transdiagnostic perspective may help clarify how stress-mood pathways fit into a larger framework of symptom expression across diagnoses (Cuthbert & Insel, 2013; Insel, 2010). What are the intermediate steps that link stress to depression or mania, and how much do these pathways vary amongst individuals? To address these questions, data-driven approaches may help to identify transdiagnostic stress-mood pathways (or pathways unique to particular mood diagnoses), which could help further our insight into underlying mechanisms of mood disorders. Data-driven clustering approaches have been proposed as a means of identifying endophenotypes amongst heterogenous disorders, in which treatment outcomes are often challenging to predict (Rutledge et al., 2019). For example, clustering methods have been used to identify symptom profiles related to differential responses to antidepressants (Chekroud et al., 2017), and patterns of functional connectivity predictive of responses to transcranial magnetic stimulation therapy (Drysdale et al., 2017). Classifying individuals with mood disorders according to their patterns of stress-reactivity may help better match individuals with treatments that address their specific mood-related behaviors.

We examined potential behavioral mediators of the association between subjective stress intensity and mood symptoms using a prospective design in a sample of adolescents and young adults, with and without unipolar or bipolar mood disorder diagnoses. In this design, we evaluated self-reported stress, behavior, and mood via a daily diary over a period of up to eight weeks. This approach mitigates reliability issues with retrospective reporting and is designed to assess day-to-day fluctuations in stress-mood associations. The sample included subjects with unipolar and bipolar diagnoses (Tables 1 & 2) to support investigation of shared (or distinct) stress-mood symptom pathways. Based on the research evidence and models reviewed above, we hypothesized that social withdrawal would mediate the association between stress and anhedonia, and impulsivity would mediate the association between stress and manic symptoms.

Additionally, we performed an exploratory K-means clustering analysis to identify groups characterized by different patterns of stress-related behaviors and mood symptoms, that might complement or diverge from diagnostic information. While the mediation analyses tell us about group-level trends, this approach identifies subgroups that exhibit distinct stress reactivity profiles. For example, some individuals might primarily experience stress-related social withdrawal and anhedonia, while others might be more likely to experience stress-related impulsivity and mania. These subgroups can give us further insight into the potential diversity of stress, behavior, and mood associations. Additionally, these profiles could map onto diagnosis (i.e., individuals with unipolar diagnoses might only exhibit stress-related social withdrawal and anhedonia), or they may provide novel information about variation within diagnostic categories. This approach may help inform personalized approaches to medicine by identifying behavioral targets that might precipitate or correspond with changes in mood for a particular individual.

1. Methods

1.1. Participants

We recruited 154 subjects ages 15 to 25 from the Los Angeles metropolitan area including through community advertisement, the UCLA Child & Adolescent Mood Disorders Program (CHAMP), and UCLA Health System electronic health records. Participants recruited through community and clinical sources showed no significant differences in age, gender, or ethnicity. There was a significant difference in race between recruitment sources ($p <$ .001), due to fewer Asian ($z = -4.42$, $p < .001$) and more White participants ($z = 2.96$, $p = .003$) recruited from clinical sources. (Of note, controlling for race in statistical analyses did not influence results). Of this sample, 122 agreed to participate in the daily diary series. Eight individuals were excluded for poor adherence precluding statistical analysis (less than three daily diaries completed). One participant was excluded due to reporting past symptoms of anorexia nervosa but no other psychiatric symptoms, resulting in a final sample of n =113. All other participants either had a primary mood disorder diagnosis and were symptomatic at the time of recruitment, or reported no history of psychopathology, per the Diagnostic and Statistical Manual of Mental Disorders- Fifth Edition (DSM-5) criteria. This sample included individuals with current mood diagnoses, individuals with past mood disorder diagnoses reporting subclinical mood symptoms at the time of recruitment, and healthy individuals with no current or past mood disorders, to maximize variance across the sample in mood symptom severity. For additional demographic characteristics of this sample, see Table 1. Participants were excluded for ongoing use of stimulant medications, recent (past six weeks) changes in any other psychoactive medications, a history of psychosis unrelated to the primary mood disorder, neurological impairment, head injury, brain stimulation therapies, lack of English proficiency, or severe cognitive or language impairments. Psychiatric history and inclusion/exclusion criteria were evaluated by a research team member using the Structured Clinical Interview for the DSM-5(SCID; First, Williams, Karg, & Spitzer, 2015, Table 1). Individuals with comorbid diagnoses secondary to a primary mood disorder were included, to capture a range of psychopathology representative of the community. See Supplement for analyses repeated after excluding participants on the basis of comorbidities; of note, results were consistent with findings reported here in the main text. Participants gave written informed consent (for participants ages 18 and older) or written informed assent along with consent of a parent or guardian (for participants ages 17 and younger). Procedures were approved by UCLA's Institutional Review Board.

1.2. Procedures

Participants were recruited to an in-person research session consisting of cognitive testing, clinical interviews, and electronic surveys; a subset of participants also completed a neuroimaging session. These in-person procedures address separate research questions, and will be reported elsewhere. Participants were compensated separately for the initial session, neuroimaging session, and follow-up surveys. Compensation for follow-up surveys was based on the number of surveys completed, plus a bonus for completing a majority (>80%) of surveys. Following the initial in-person research session, participants received a series of electronic daily diaries to be completed on their preferred device via REDCap

(Research Electronic Data Capture), a HIPAA-compliant electronic survey platform (Harris et al., 2019; Harris et al., 2009). Daily diaries were administered on a clustered schedule of three consecutive days, once per week for six to eight weeks (Silk et al., 2011). The clustered schedule was selected to encourage participant adherence by reducing the number of requested surveys, while also allowing for day-lagged analyses. 43 participants received a diary series that lasted six weeks; 71 participants received an extended diary series that lasted eight weeks. There was no difference in daily diary adherence for participants in the six- versus eight-week series, and series duration did not moderate statistical effects. Participants completed an average of 15 daily diaries (Table 1). Controlling for daily diary count did not alter results of the mediation analyses. The first day of the diary each week was staggered to ensure coverage of all week days over the survey period (e.g. Week 1 daily diaries on Monday, Tuesday, Wednesday; Week 2 daily diaries on Tuesday, Wednesday, Thursday). At the end of the survey period, a member of the research team contacted the participant for debriefing.

1.3. Measures

The daily diary included the following measures, alongside additional measures addressing non-overlapping research goals which will be reported elsewhere. To encourage survey compliance, shorter versions of measures were selected when possible. For each day of the survey, participants were asked to answer the following measures based on their experiences in the past 24 hours. For all measures (with the exception of the single-item stress intensity measure), scores were calculated for each subject, each day of the diary, by summing item responses within each measure.

1.4. Stress

Subjective stress was assessed by the questions, “What is the most stressful thing that happened in the past 24 hours?” and “How intense was this stressful event?”. The stress intensity probe was used as the measure of daily stress in the present analyses, based on the high reliability and validity of similar single-item measures of subjective stress (Littman et al., 2006; Elo et al., 2003). This item was rated on a Likert scale ranging from 1 (not stressful at all) to 5 (extremely stressful).

1.5. Social withdrawal

To assess withdrawal behaviors, a 5-item Social Withdrawal scale was administered (Raposa & Hammen, 2018). Items were rated on a Likert scale from 1 (rarely or never) to 4 (almost always or always).

1.6. Impulsivity

Impulsivity was evaluated using the overall score across attention, motor, and self-control first-order subscales of the Barratt Impulsiveness Scale (BIS; Patton et al., 1995). These subscales were selected for their high levels of internal consistency and test-retest reliability as a measure of impulsivity (Stanford et al., 2009). Items were rated on a Likert scale from 1 (rarely/never) to 4 (almost always/always), with reverse scoring used for a subset of items.

1.7. Manic symptoms

The 11-item General Behavior Inventory (GBI; Depue, 1987) mania/hypomania subscale was used to assess manic symptoms. Items were rated on a Likert scale from 0 (never or hardly ever) to 3 (very often or almost constantly).

1.8. Anhedonic symptoms

A 7-item version (omitting the item that asks about suicidal ideation) of the Loss of Interest Anhedonia subscale of the Mood and Anxiety Symptom Questionnaire (MASQ; Watson et al., 1995a; Watson et al. 1995b) was utilized to evaluate anhedonic symptoms. For each item, participants were asked to indicate the extent to which the statements captured something they have been experiencing. Each item was rated on a Likert scale from 1 (not at all) to 5 (extremely).

2. Statistical analyses

2.1. Mixed-effects models of daily stress, maladaptive behavior, and mood

We conducted linear mixed-effects analyses to test the hypotheses that higher daily stress intensity would be related to higher levels of daily maladaptive behavior (impulsivity and withdrawal; *a* paths), and to higher severity of mood symptoms (mania and anhedonic depression; *c* paths). Linear mixed-effects analyses also tested the hypotheses that maladaptive behaviors would predict increases in mood symptoms after controlling for stress (*b* paths), i.e., daily impulsivity would predict mania, and daily withdrawal would predict anhedonic depression. Linear mixed-effects models took into account within-person variation (both intercept and slope nested within subject). Analyses were performed using the lme4 package in R. All scores were standardized (z-scored) across the sample before analyses.

2.2. Mediation analyses

We conducted mediation analyses to test the hypotheses that stress-induced increases in manic symptoms would be mediated by impulsivity, and that stress-induced increases in anhedonia would be mediated by withdrawal. Bootstrapping with 1500 simulations was used to generate 95% confidence intervals for direct and indirect effects. Indirect effects were estimated using the mediate package in R. (Of note, mediation analyses and multi-level pathways tested concurrent change in stress, behavior, and mood, i.e., how these variables track together across the daily diary. We focus on concurrent associations based on prior research showing that stress has rapid effects on behavior and mood within the same day (e.g. Fuller-Tyszkiewicz et al., 2017). For exploratory analyses that tested lagged associations, see Supplement).

2.3. Machine learning identifying symptom trajectories

An exploratory *K*-means clustering analysis was performed to identify profiles of symptom trajectories (i.e., extent to which one or both hypothesized mediation pathways were true for a given participant) that characterized subgroups within the sample. The input features for the clustering analysis were the intercepts and coefficients of mediation paths *a* (stress

predicting impulsivity or withdrawal) and *b* (impulsivity predicting mania, withdrawal predicting anhedonia). Any intercepts or coefficients more than 4 standard deviations above or below the group mean were removed to enhance cluster coherence (related discussion in Gan & Ng, 2017). *K* values ranging from 2:12 were tested (Fig. S1), and goodness-of-fit was estimated by computing silhouette scores (a measure of cluster coherence) and within-cluster sum of squares (a measure of cluster error). Analyses were performed using the cluster, tidyr, and purrr packages in R.

3. Results

3.1. Stress, withdrawal, and anhedonia across the sample

The first mixed-effects regression (*c* path, Fig. 1B) showed that higher self-reported stress was significantly related to increased anhedonia, $B = 0.11$, $F(1,88) = 34.91$, $p < .001$. Higher self-reported stress was also significantly related to increased social withdrawal, $B = 0.09$, $F(1,72) = 21.87$, $p < .001$ (*a* path, Fig. 1B). In turn, higher social withdrawal was related to higher anhedonia, over and above the effects of daily stress, $B = 0.38$, $F(1,51) = 363.18$, $p < .001$ (*b* path, Fig. 1B). Bootstrapped mediation analyses also showed that social withdrawal significantly mediated the association between stress and anhedonia (estimate of causal mediation effect = 0.03, 95% CI [0.02, 0.05], $p < .001$, Fig. 1A). Of note, this indirect pathway held in a lagged mediation model, where stress predicted social withdrawal on the next day, and withdrawal predicted anhedonia on the next day (see Supplement).

3.2. Stress, mania, and impulsivity across the sample

First, a mixed-effects regression showed that higher self-reported stress was significantly related to increased mania, $B = 0.06$, $F(1,76) = 8.69$, $p = .004$ (*c* path, Fig. 1D). Additionally, higher self-reported stress predicted increased impulsivity, $B = 0.09$, $F(1,77) = 22.27$, $p < .001$ (*a* path, Fig. 1D). Greater impulsivity was related to higher mania, controlling for daily stress, $B = 0.25$, $F(1,98) = 42.10$, $p < .001$ (*b* path, Fig. 1D). Bootstrapped mediation analyses indicated that impulsivity significantly mediated the association between stress and mania (estimate of causal mediation effect = 0.02, 95% CI [0.01, 0.04], $p < .001$, Fig. 1C). This indirect pathway also remained in a lagged mediation model (see Supplement).

3.3. Data-driven clustering of symptom trajectories

Next, we performed an exploratory *K*-means clustering analysis of the intercepts and coefficients of the *a* and *b* paths, for both *a priori* mediation pathways (stress predicting anhedonia via withdrawal; stress predicting mania via impulsivity). Outlying intercepts or coefficients (>4 SD from group mean) were excluded, resulting in $n = 107$. The optimum number of clusters was $K = 6$, (out of *K* ranging from 2:12) based on silhouette scores and elbow-plotted within-cluster sum of squares (Fig. S1). This clustering solution revealed six groups (*n*s = 31, 25, 22, 18, 8, 3) with different patterns of stress sensitivity and reactivity (Fig. 2, Table 3). This included a healthy group showing generally low stress reactivity and adaptive functioning (Cluster 1); a group that exhibited high levels of maladaptive behavior and related mood symptoms, but not in response to stress (Cluster 2); a group that appeared to show a mixed pattern of stress-reactive behavioral problems and related mood symptoms along both mediation pathways (Cluster 3); and a group showing a unipolar

pattern of stress-reactive withdrawal and withdrawal-reactive anhedonia (Cluster 4). Two smaller groups were also identified, but may reflect outlier profiles (Clusters 5 and 6). (See Supplement for additional details on cluster characteristics, including self-report measures, demographics, and diagnoses).

4. Discussion

Stress has been linked to mood disorders in youth, but there remain questions about how or for whom stress leads to symptoms of depression or mania. In this study, we tested two theoretical behavioral pathways linking stress and mood in a transdiagnostic mood sample of adolescents and young adults. First, we found that social withdrawal mediated the association between stress and anhedonic depression. Second, we found that impulsivity mediated the association between stress and mania (of note, exploratory analyses suggested that impulsivity may also mediate an association between stress and anhedonia; see Supplement). These mediated associations held in both within-day and day-lagged models (see Supplement). In addition, using an exploratory *K*-means clustering analysis, we identified six profiles of stress-mood reactivity. Together, these findings point to social withdrawal and impulsivity as viable behavioral mediators of stress-reactive mood symptoms and promising potential targets for behavioral interventions. Furthermore, the presence of these pathways in a youth sample demonstrates their relevance during a critical period of vulnerability to mood disorders and a time of heightened stress.

The present results showing a stress-withdrawal-anhedonia pathway are supported by, and converge with, previous research in depression. Prior research has previously shown that stress can lead to withdrawal (Connor-Smith & Compas, 2002), stress can lead to depression (Hammen, 2005), and withdrawal can lead to depression (Holahan et al., 2005). In complement, the results indicating a stress-impulsivity-mania pathway are supported by and build upon previous work tying stress to impulsivity (Fox et al., 2010; Moon et al., 2014) and impulsivity to mania (Giovanelli et al., 2013). Of note, exploratory analyses also suggested that impulsivity may mediate the association between stress and anhedonia, in addition to the association between stress and mania (see Supplement). Whereas withdrawal may act as a behavioral mediator specific to depressive symptoms, impulsivity may function as a non-specific behavioral mediator which can lead to mood symptoms more generally. Additional research is needed to replicate these findings and further evaluate the association between impulsivity and mood.

Notably, the results of this study demonstrated several distinct profiles of stress-behavior-symptom pathways that can characterize an individual. We used a data-driven (*K*-means) approach to identify patterns of stress-behavior and behavior-symptom associations across both symptom dimensions, yielding subgroups that varied in terms of the extent to which stress predicted maladaptive behaviors, and behaviors predicted changes in mood. Given the exploratory nature of this analysis, future studies confirming the replicability of these groups are needed. In particular, we caution interpretation of the two smallest groups (*ns* = 5 and 8). Until these profiles are replicated, it is unknown whether these smallest groups reflect a valid profile of stress-reactive behavior and symptoms or if they simply constitute outliers. The largest group (group 1) was generally low in mood symptoms and showed a

healthy (non-reactive) mood course over time. However, the next two largest groups (groups 2 and 3) were characterized by highly mixed symptom trajectories, wherein impulsivity appeared to contribute to manic (and anhedonic) symptoms, and withdrawal also appeared to contribute to anhedonia. For some (group 3), these maladaptive behaviors seemed to be evoked by stress, but for others (group 2) social withdrawal and/or impulsive behaviors seemed unrelated to stress. Notably, these groups were comprised primarily of individuals with unipolar diagnoses (see Table 2 and Supplement).

The reasons for such high prevalence of mixed symptoms in participants who have ostensibly unipolar forms of mood pathology may be complex. The daily self-report measures employed here may be more sensitive to subthreshold mania than clinical diagnoses of bipolar disorders, which have higher thresholds and rely more on retrospective reporting. Ignoring these subthreshold profiles could also be a reason for the substantial heterogeneity in depression, and may lead to underestimates of the true prevalence of bipolar symptom course (Hoertel et al., 2013). Alternatively, these day-to-day fluctuations in subclinical manic symptoms could signal risk for future conversion from unipolar to bipolar diagnoses. Altogether, these findings point to the prevalence of mixed symptomatology detectable at the level of daily fluctuations in behavior, which may or may not be accurately reflected by diagnostic categories.

In contrast with the mixed groups described above, there was another cluster (group 4) that seemed to follow a more clearly unipolar course. This group exhibited a significant stress-withdrawal-anhedonia pathway but did not exhibit a stress-impulsivity-mania pattern. Interestingly, however, this profile was not the only (or even the main) symptom profile for individuals with unipolar diagnoses across the sample; approximately a third (29.3%) of participants with unipolar diagnoses in this sample were clustered into this group (see Supplement), and the other two-thirds of participants with unipolar diagnoses were characterized by mixed symptom profiles (Table S1). Therefore, these behavioral pathways may reflect an additional way of characterizing mood disorders that may serve to supplement and refine our understanding of diagnostic categories.

A potential area of future research is examining *who* might exhibit particular stress-mood pathways. For instance, the clusters identified here could potentially reflect groups with different underlying vulnerabilities. Stress-diathesis models have indicated that genetic factors, physiological responses, and cognitive styles may influence people's sensitivity to stressors (Colodro-Conde et al., 2018; Connolly & Alloy, 2017; Li et al., 2017; Moriarity et al., 2020; Shapero et al., 2017). As an example, it could be that individuals who report more rumination are more likely to respond to stress with social withdrawal and experience higher levels of anhedonia. An important next step will be to combine what is known about moderators of stress reactivity with mechanistic models that further elaborate on the pathways linking these conditions to particular mood symptoms.

The results of these analyses suggest clinical implications for future investigation. While these mediation models cannot prove causality, they demonstrate close associations between subjective stress, social withdrawal and impulsivity, and mood symptoms on a daily level. The identification of clinically relevant behaviors has particular value for behavioral

therapies, which are based on the concept that modifying behavior can lead to changes in mood and cognition (Kaiser et al., 2015). For example, behavioral activation therapies specifically aim to reduce withdrawal and avoidance behaviors by encouraging individuals to actively seek out positive experiences (Kaiser et al., 2015; Kanter et al., 2010). In turn, impulsivity has been shown to negatively affect medication adherence within bipolar disorders, emphasizing the need to target this behavior to maximize treatment efficacy (Belzeaux et al., 2015). However, the identification of distinct clusters in this sample also suggests that it may be important to personalize treatment targets according to the individual patient's profile of stress-reactive behaviors and related symptoms. For example, individuals who exhibit stress-reactive impulsivity may benefit from interventions that specifically target impulsivity, whereas those who exhibit more stress-reactive withdrawal may not, even if they share the same primary diagnosis. Further research is needed to investigate how these stress-mood pathways may relate to treatment responses.

There are several limitations to the present study, which should be addressed in future research. First, mediation analyses cannot prove causality in observational designs. Our aim here was to demonstrate the viability of theoretical models in which maladaptive behaviors may mediate the association between stress and mood symptoms. Future studies that utilize experimental manipulations of stress and behavior will be an important complement to the present results. Second, these results show that stress, behavior, and mood track with one another on a day-to-day basis, but do not evaluate faster (within-day) or slower (across months or years) temporal sequences of stress and mood. Experience sampling methodologies that allow for measurements of these variables at more fine-grained timescales, or longer longitudinal follow-ups, may provide further insight into temporal associations between these variables. Third, this study did not evaluate the type of stressor associated with daily stress ratings. Stress is not a homogeneous construct (Dickerson & Kemeny, 2004; McEwen, 2005; McLaughlin, 2016) and it could be that specific stressors are more likely to invoke certain stress-behavior-mood patterns, or that certain individuals are more vulnerable to particular forms of stressors. Fourth, our sample was transdiagnostic across mood disorders but weighted towards individuals with lifetime unipolar diagnoses (Table 2), and consisted of adolescents and young adults. Examining these stress trajectories in other samples, e.g., in other developmental periods or samples weighted towards other diagnoses, may inform our understanding of the generalizability of these findings. Finally, the exploratory nature of the K-means analysis and the small size of some of the resulting clusters points toward the need for further replication. While K-means can be applied to a variety of sample sizes (Dalmajier et al., 2020), replication in larger samples would be a next step to confirm clinical utility of these groups.

In conclusion, this study aimed to identify daily behaviors that may mediate the association between stress and mood symptoms, or evoke mood symptoms in everyday life, in a transdiagnostic mood sample of adolescents and young adults. Altogether, the results suggest that impulsivity and social withdrawal may serve as important behavioral mediators of stress-related mood problems. However, data-driven analyses also showed heterogeneity in how these stress-behavior-symptom pathways occur for different people, identifying distinct profiles of stress and behavior reactivity. Critically, by characterizing an individual's stress-mood risk profile, we may identify individuals who have more maladaptive responses

to stress or who are especially vulnerable to certain types of mood experiences, which could guide the delivery of behavioral interventions. Future research may build upon these findings to identify individuals most vulnerable to stress-related mood problems according to their personalized profile of behavioral risk.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

The authors are grateful to the individuals who participated in this study, and the research staff who supported data collection.

Funding

This work was supported by NARSAD Young Investigator Award (24879) from the Brain & Behavior Research Foundation.

References

Alloy LB, Titone MK, Ng TH, Bart CP, 2020. Stress in bipolar disorder. The Oxford Handbook of Stress and Mental Health. 10.1093/oxfordhb/9780190681777.013.6.

Aneshensel CS, Stone JD, 1982. Stress and depression: a test of the buffering model of social support. Arch. Gen. Psychiatry 39 (12), 1392–1396. 10.1001/archpsyc.1982.04290120028005. [PubMed: 7149899]

Angst J, 2011. Problems in the current concepts and definitions of bipolar disorders. World Psychiatry 10 (3), 191–192. [PubMed: 21991272]

Angst J, Cui L, Swendsen J, Rothen S, Cravchik A, Kessler RC, Merikangas KR, 2010. Major depressive disorder with subthreshold bipolarity in the National Comorbidity Survey Replication. Am. J. Psychiatry 167 (10), 1194–1201. 10.1176/appi.ajp.2010.09071011. [PubMed: 20713498]

Auerbach RP, Admon R, Pizzagalli DA, 2014. Adolescent depression: stress and reward dysfunction. Harv. Rev. Psychiatry 22 (3), 139–148. 10.1097/HRP.0000000000000034. [PubMed: 24704785]

Belzeaux R, Boyer L, Mazzola-Pomietto P, Michel P, Correard N, Aubin V, Bellivier F, Bougerol T, Olie E, Courtet P, Etain B, Gard S, Kahn J-P, Passerieux C, Leboyer M, Henry C, Azorin J-M, French, Advanced Centers of Expertise for Bipolar Disorders Collaborators, 2015. Adherence to medication is associated with non-planning impulsivity in euthymic bipolar disorder patients. J. Affect. Disord 184, 60–66. 10.1016/j.jad.2015.05.041. [PubMed: 26070047]

Bender RE, Alloy LB, 2011. Life stress and kindling in bipolar disorder: review of the evidence and integration with emerging biopsychosocial theories. Clin. Psychol. Rev. 31 (3), 383–398. 10.1016/j.cpr.2011.01.004. [PubMed: 21334286]

Bender RE, Alloy LB, Sylvia LG, Uroševic S, Abramson LY, 2010. Generation of life events in bipolar spectrum disorders: a re-examination and extension of the stress generation theory. J. Clin. Psychol 66 (9), 907–926. 10.1002/jclp.20705. [PubMed: 20694958]

Chekroud AM, Gueorguieva R, Krumholz HM, Trivedi MH, Krystal JH, McCarthy G, 2017. Reevaluating the efficacy and predictability of antidepressant treatments: a symptom clustering approach. JAMA Psychiatry 74 (4), 370–378. 10.1001/jamapsychiatry.2017.0025. [PubMed: 28241180]

Colodro-Conde L, Couvy-Duchesne B, Zhu G, Coventry WL, Byrne EM, Gordon S, Wright MJ, Montgomery GW, Madden P.a.F., Ripke S, Eaves LJ, Heath AC, Wray NR, Medland SE, Martin NG, 2018. A direct test of the diathesis–stress model for depression. Mol. Psychiatry 23 (7), 1590–1596. 10.1038/mp.2017.130. [PubMed: 28696435]

Connolly SL, Alloy LB, 2017. Rumination interacts with life stress to predict depressive symptoms: an ecological momentary assessment study. Behav. Res. Ther 97, 86–95. 10.1016/j.brat.2017.07.006. [PubMed: 28734979]

Connor-Smith JK, Compas BE, 2002. Vulnerability to social stress: coping as a mediator or moderator of sociotropy and symptoms of anxiety and depression. Cogn. Ther. Res 26 (1), 39–55. 10.1023/A:1013889504101.

Cuthbert BN, Insel TR, 2013. Toward the future of psychiatric diagnosis: the seven pillars of RDoC. BMC Med. 11 (1), 126. 10.1186/1741-7015-11-126. [PubMed: 23672542]

Dalmaijer ES, Nord CL, Astle DE, 2020. Statistical power for cluster analysis. ArXiv:2003.00381 [Cs, q-Bio, Stat]. http://arxiv.org/abs/2003.00381.

Depue RA, 1987. General Behavior Inventory (Manual). University of Minnesota. Minneapolis.

Dickerson SS, Kemeny ME, 2004. Acute stressors and cortisol responses: a theoretical integration and synthesis of laboratory research. Psychol. Bull 130 (3), 355–391. 10.1037/0033-2909.130.3.355. [PubMed: 15122924]

Drysdale AT, Grosenick L, Downar J, Dunlop K, Mansouri F, Meng Y, Fetcho RN, Zebley B, Oathes DJ, Etkin A, Schatzberg AF, Sudheimer K, Keller J, Mayberg HS, Gunning FM, Alexopoulos GS, Fox MD, Pascual-Leone A, Voss HU, Liston C, 2017. Resting-state connectivity biomarkers define neurophysiological subtypes of depression. Nat. Med 23 (1), 28–38. 10.1038/nm.4246. [PubMed: 27918562]

Elo A-L, Leppänen A, Jahkola A, 2003. Validity of a single-item measure of stress symptoms. Scand. J. Work Environ. Health 29 (6), 444–451. 10.5271/sjweh.752. [PubMed: 14712852]

Ferster CB, 1973. A functional anlysis of depression. Am. Psychol 28 (10), 857–870. 10.1037/h0035605. [PubMed: 4753644]

First MB, Williams JBW, Karg RS, Spitzer RL, 2015. Structured Clinical Interview for DSM-5—Research Version (SCID-5 for DSM-5, Research Version; SCID-5-RV). American Psychiatric Association. Arlington, VA.

Fox HC, Bergquist KL, Gu P, Sinha R, 2010. Interactive effects of cumulative stress and impulsivity on alcohol consumption. Alcohol.: Clin. Exp. Res 34 (8), 1376–1385. [PubMed: 20491738]

Fuller-Tyszkiewicz M, Karvounis T, Pemberton R, Hartley-Clark L, Richardson B, 2017. Determinants of depressive mood states in everyday life: An experience sampling study. Motiv. Emot 41 (4), 510–521. 10.1007/s11031-017-9620-z.

Gan G, Ng MK, 2017. K-means clustering with outlier removal. Pattern Recognit. Lett 90, 8–14. 10.1016/j.patrec.2017.03.008.

Giovanelli A, Hoerger M, Johnson SL, Gruber J, 2013. Impulsive responses to positive mood and reward are related to mania risk. Cogn. Emot 27 (6), 1091–1104. 10.1080/02699931.2013.772048. [PubMed: 23472965]

Grandin LD, Alloy LB, Abramson LY, 2006. The social zeitgeber theory, circadian rhythms, and mood disorders: review and evaluation. Clin. Psychol. Rev 26 (6), 679–694. 10.1016/j.cpr.2006.07.001. [PubMed: 16904251]

Grav S, Hellzèn O, Romild U, Stordal E, 2012. Association between social support and depression in the general population: the HUNT study, a cross-sectional survey. J. Clin. Nurs 21 (1–2), 111–120. 10.1111/j.1365-2702.2011.03868.x. [PubMed: 22017561]

Hammen C, 2005. Stress and depression. Ann. Rev. Clin. Psychol 1, 293–319. 10.1146/annurev.clinpsy.1.102803.143938. [PubMed: 17716090]

Hammen CL, 2015. Stress and depression: Old questions, new approaches. Curr. Opin. Psychol 4, 80–85. 10.1016/j.copsyc.2014.12.024.

Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG, 2009. Research electronic data capture (REDCap) – A metadata-driven methodology and workflow process for providing translational research informatics support. J. Biomed. Inform 42 (2), 377–381. [PubMed: 18929686]

Harris PA, Taylor R, Minor BL, Elliott V, Fernandez M, O'Neal L, McLeod L, Delacqua G, Delacqua G, Kirby J, Duda SN, 2019. REDCap Consortium, The REDCap consortium: building an international community of software partners. J. Biomed. Inform 10.1016/j.jbi.2019.103208.

Hoertel N, Le Strat Y, Angst J, Dubertret C, 2013. Subthreshold bipolar disorder in a U.S. national representative sample: prevalence, correlates and perspectives for psychiatric nosography. J. Affect. Disord 146 (3), 338–347. 10.1016/j.jad.2012.09.016. [PubMed: 23040874]

Holahan CJ, Moos RH, Holahan CK, Brennan PL, Schutte KK, 2005. Stress generation, avoidance coping, and depressive symptoms: a 10-year model. J. Consult. Clin. Psychol 73 (4), 658–666. 10.1037/0022-006X.73.4.658. [PubMed: 16173853]

Hopko DR, Mullane CM, 2008. Exploring the relation of depression and overt behavior with daily diaries. Behav. Res. Ther 46 (9), 1085–1089. 10.1016/j.brat.2008.05.002. [PubMed: 18687422]

Hurst CS, Baranik LE, Daniel F, 2013. College student stressors: a review of the qualitative research. Stress Health 29 (4), 275–285. 10.1002/smi.2465. [PubMed: 23023893]

Insel T, Cuthbert B, Garvey M, Heinssen R, Pine DS, Quinn K, Sanislow C, Wang P, 2010. Research domain criteria (RDoC): toward a new classification framework for research on mental disorders. Am. J. Psychiatry 167 (7), 748–751. 10.1176/appi.ajp.2010.09091379. [PubMed: 20595427]

Kaiser RH, Hubley S, Dimidjian S, 2015. Behavioural Activation Theory in Treating Depression. John Wiley & Sons, Ltd, pp. 221–241. 10.1002/9781119114482.ch9.

Kanter JW, Manos RC, Bowe WM, Baruch DE, Busch AM, Rusch LC, 2010. What is behavioral activation? A review of the empirical literature. Clin. Psychol. Rev 30 (6), 608–620. 10.1016/j.cpr.2010.04.001. [PubMed: 20677369]

Kessler RC, Petukhova M, Sampson NA, Zaslavsky AM, Wittchen H-U, 2012. Twelve-month and lifetime prevalence and lifetime morbid risk of anxiety and mood disorders in the United States. Int. J. Methods Psychiatr. Res 21 (3), 169–184. 10.1002/mpr.1359. [PubMed: 22865617]

Kupferberg A, Bicks L, Hasler G, 2016. Social functioning in major depressive disorder. Neurosci. Biobehav. Rev 69, 313–332. 10.1016/j.neubiorev.2016.07.002. [PubMed: 27395342]

Lewinsohn PM, 1974. A behavioral approach to depression. The Psychology of Depression: Contemporary Theory and Research. John Wiley & Sons (pp. xvii, 318–xvii, 318).

Lex C, Bäzner E, Meyer TD, 2017. Does stress play a significant role in bipolar disorder? A meta-analysis. J. Affect. Disord 208, 298–308. 10.1016/j.jad.2016.08.057. [PubMed: 27794254]

Li YI, Starr LR, Hershenberg R, 2017. Responses to positive affect in daily life: positive rumination and dampening moderate the association between daily events and depressive symptoms. J. Psychopathol. Behav. Assess 39 (3), 412–425. 10.1007/s10862-017-9593-y.

Littman AJ, White E, Satia JA, Bowen DJ, Kristal AR, 2006. Reliability and validity of 2 single-item measures of psychosocial stress. Epidemiology 17 (4), 398–403. 10.1097/01.ede.0000219721.89552.51 (Cambridge, Mass.). [PubMed: 16641618]

McEwen BS, 2005. Stressed or stressed out: what is the difference? J. Psychiatry Neurosci 30 (5), 315–318. [PubMed: 16151535]

McIntyre RS, Soczynska JK, Cha DS, Woldeyohannes HO, Dale RS, Alsuwaidan MT, Gallaugher LA, Mansur RB, Muzina DJ, Carvalho A, Kennedy SH, 2015. The prevalence and illness characteristics of DSM-5-defined “mixed feature specifier” in adults with major depressive disorder and bipolar disorder: results from the International Mood Disorders Collaborative Project. J. Affect. Disord 172, 259–264. 10.1016/j.jad.2014.09.026. [PubMed: 25451425]

McLaughlin KA, Sheridan MA, 2016. Beyond cumulative risk: a dimensional approach to childhood adversity. Curr. Dir. Psychol. Sci 25 (4), 239–245. 10.1177/0963721416655883. [PubMed: 27773969]

Merikangas, Kathleen R, Herrell R, Swendsen J, Rössler W, Ajdacic-Gross V, Angst J, 2008. Specificity of bipolar spectrum conditions in the comorbidity of mood and substance use disorders: results from the Zurich cohort study. Arch. Gen. Psychiatry 65 (1), 47–52. 10.1001/archgenpsychiatry.2007.18. [PubMed: 18180428]

Merikangas, Kathleen Ries, He J-P, Burstein M, Swanson SA, Avenevoli S, Cui L, Benjet C, Georgiades K, Swendsen J, 2010. Lifetime prevalence of mental disorders in U.S. adolescents: Results from the National Comorbidity Survey Replication–Adolescent Supplement (NCS-A). J. Am. Acad. Child Adolesc. Psychiatry 49 (10), 980–989. 10.1016/j.jaac.2010.05.017. [PubMed: 20855043]

Miller S, Suppes T, Mintz J, Hellemann G, Frye MA, McElroy SL, Nolen WA, Kupka R, Leverich GS, Grunze H, Altshuler LL, Keck PE, Post RM, 2016. Mixed depression in bipolar disorder:

prevalence rate and clinical correlates during naturalistic follow-up in the Stanley bipolar network. Am. J. Psychiatry 173 (10), 1015–1023. 10.1176/appi.ajp.2016.15091119. [PubMed: 27079133]

Moon E, Chang JS, Choi S, Ha TH, Cha B, Cho H, Park J, Lee B, Lee YM, Choi Y, Ha K, 2014. Characteristics of stress-coping behaviors in patients with bipolar disorders. Psychiatry Res. 218 10.1016/j.psychres.2014.03.047.

Moreno C, Hasin DS, Arango C, Oquendo MA, Vieta E, Liu S, Grant BF, Blanco C, 2012. Depression in bipolar disorder versus major depressive disorder: results from the National Epidemiologic Survey on Alcohol and Related Conditions. Bipolar Disord. 14 (3), 271–282. 10.1111/j.1399-5618.2012.01009.x. [PubMed: 22548900]

Moriarity DP, Ng T, Curley EE, McArthur, Anne B, Ellman L,M, Coe CL, Abramson LY, Alloy LB, 2020. Reward sensitivity, cognitive response style, and inflammatory response to an acute stressor in adolescents. J. Youth Adolesc 49 (10), 2149–2159. 10.1007/s10964-020-01216-y. [PubMed: 32141010]

Patton JH, Stanford MS, Barratt ES, 1995. Factor structure of the Barratt impulsiveness scale. J. Clin. Psychol 51 (6), 768–774. 10.1002/1097-4679(199511)51:6≤768::aid-jclp2270510607≥3.0.co;2-1. [PubMed: 8778124]

Paus T, Keshavan M, Giedd JN, 2008. Why do many psychiatric disorders emerge during adolescence? Nat. Rev. Neurosci 9 (12), 947–957. 10.1038/nrn2513. [PubMed: 19002191]

Pizzagalli DA, 2014. Depression, stress, and anhedonia: toward a synthesis and integrated model. Ann. Rev. Clin. Psychol 10, 393–423. 10.1146/annurev-clinpsy-050212-185606. [PubMed: 24471371]

Porcelli S, Van Der Wee N, van der Werff S, Aghajani M, Glennon JC, van Heukelum S, Mogavero F, Lobo A, Olivera FJ, Lobo E, Posadas M, Dukart J, Kozak R, Arce E, Ikram A, Vorstman J, Bilderbeck A, Saris I, Kas MJ, Serretti A, 2019. Social brain, social dysfunction and social withdrawal. Neurosci. Biobehav. Rev 97, 10–33. 10.1016/j.neubiorev.2018.09.012. [PubMed: 30244163]

Raposa EB, Hammen C, 2018. A daily diary investigation of the influence of early family adversity on social functioning during the transition to adulthood. Soc. Dev 27 (2), 431–446. 10.1111/sode.12269 (Oxford, England). [PubMed: 30034119]

Rutledge RB, Chekroud AM, Huys QJ, 2019. Machine learning and big data in psychiatry: toward clinical applications. Curr. Opin. Neurobiol 55, 152–159. 10.1016/j.conb.2019.02.006. [PubMed: 30999271]

Shapero BG, McClung G, Bangasser DA, Abramson LY, Alloy LB, 2017. Interaction of biological stress recovery and cognitive vulnerability for depression in adolescence. J. Youth Adolesc 46 (1), 91–103. 10.1007/s10964-016-0451-0. [PubMed: 26923989]

Silk JS, Forbes EE, Whalen DJ, Jakubcak JL, Thompson WK, Ryan ND, Axelson DA, Birmaher B, Dahl RE, 2011. Daily emotional dynamics in depressed youth: a cell phone ecological momentary assessment study. J. Exp. Child. Psychol 110 (2), 241–257. 10.1016/j.jecp.2010.10.007. [PubMed: 21112595]

Stanton CH, Holmes AJ, Chang SWC, Joormann J, 2019. From stress to anhedonia: molecular processes through functional circuits. Trends Neurosci. 42 (1), 23–42. 10.1016/j.tins.2018.09.008. [PubMed: 30327143]

Strakowski SM, Fleck DE, DelBello MP, Adler CM, Shear PK, Kotwal R, Arndt S, 2010. Impulsivity across the course of bipolar disorder. Bipolar Disord. 12 (3), 285–297. 10.1111/j.1399-5618.2010.00806.x. [PubMed: 20565435]

Urošević S, Abramson LY, Harmon-Jones E, Alloy LB, 2008. Dysregulation of the Behavioral Approach System (BAS) in bipolar spectrum disorders: review of theory and evidence. Clin. Psychol. Rev 28 (7), 1188–1205. 10.1016/j.cpr.2008.04.004. [PubMed: 18565633]

Walker ER, McGee RE, Druss BG, 2015. Mortality in mental disorders and global disease burden implications: a systematic review and meta-analysis. JAMA Psychiatry 72 (4), 334–341. 10.1001/jamapsychiatry.2014.2502. [PubMed: 25671328]

Watson D, Weber K, Assenheimer JS, Clark LA, Strauss ME, McCormick RA, 1995a. Testing a tripartite model: I. Evaluating the convergent and discriminant validity of anxiety and depression symptom scales. J. Abnorm. Psychol 104 (1), 3–14. 10.1037//0021-843x.104.1.3. [PubMed: 7897050]

Watson D, Clark LA, Weber K, Assenheimer JS, Strauss ME, McCormick RA, 1995b. Testing a tripartite model: II. Exploring the symptom structure of anxiety and depression in student, adult, and patient samples. J. Abnorm. Psychol 104 (1), 15–25. 10.1037//0021-843x.104.1.15. [PubMed: 7897037]

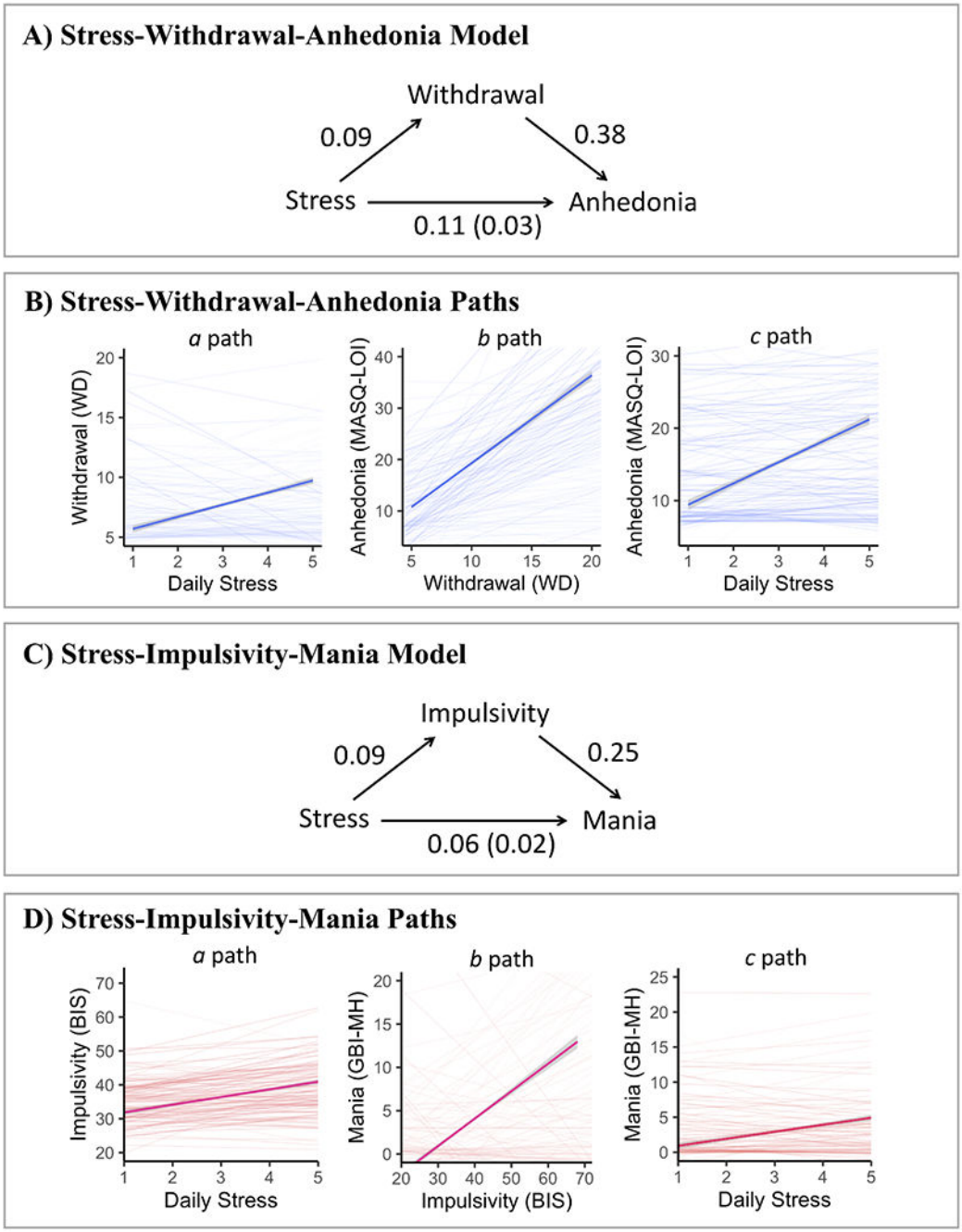

Fig. 1.

Mediation pathways.

Note. WD = Social Withdrawal scale; MASQ-LOI = Mood and Anxiety Symptom Questonnaire, Anhedonic Loss of Interest subscale; BIS = Barratt Impulsiveness Scale (attention, motor, and self-control first-order subscales); GBI-MH = General Behavioral Inventory, Mania-Hypomania subscale.

A) Stress-related anhedonia mediated by social withdrawal. Slopes of *a, b,* and *c* paths shown alongisde corresponding arrows. The estimated mediation effect is shown in

parentheses following the total effect. B) Group-level trend lines of the *a, b,* and *c* paths of the stress-withdrawal-anhedonia pathway displayed in dark blue. Lighter blue lines represent individual trend lines of the *a, b,* and *c* paths. C) Stress-related mania mediated by impulsivity. Slopes of *a, b,* and *c* paths shown alongisde corresponding arrows. The estimated mediation effect is shown in parentheses following the total effect. D) Group-level trend lines of the *a, b,* and *c* paths of the stress-impulsivity-mania pathway displayed in dark pink. Lighter pink lines represent individual trend lines of the *a, b,* and *c* paths.

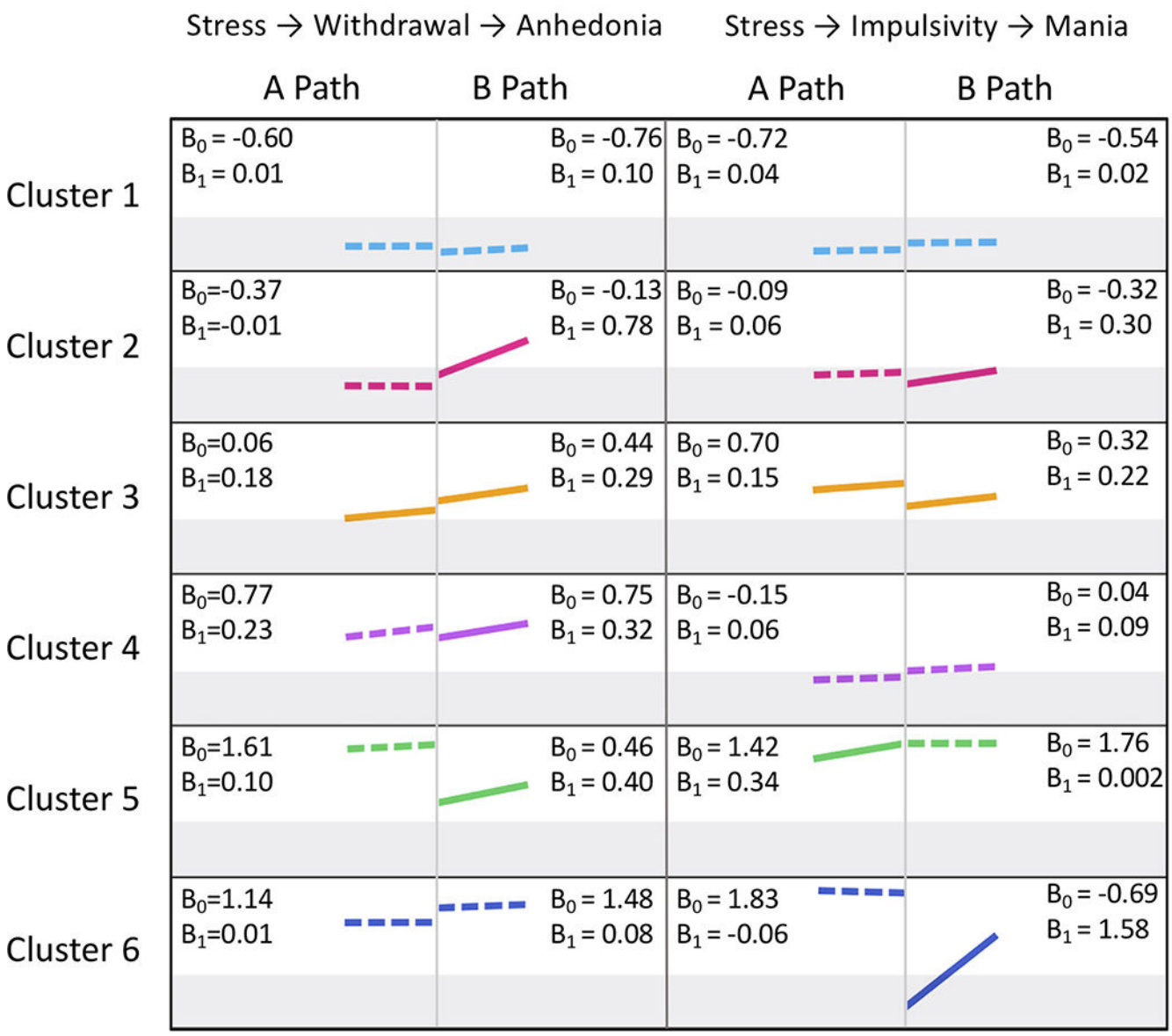

Fig. 2.

Averaged a and b paths within K-means clusters.

Note. For each K-means cluster group, displayed are a and b path intercepts and slopes. Solid lines indicate significant slopes; dashed lines indicate non-significant slopes. The zero-line on they-axis for each cell is indicated by shading gray for values below zero, and all cells are on the same (z-scored) scale. B_0 and B_1 are the cluster averages of individual intercepts (B_0 and slopes (B_1) that were estimated for each participant in the group-level (*n* = 113) mixed-effects regressions.

Table 1:

Demographic and clinical characteristics.

Total *n* = 113		
		Mean (SD)
Age, years		20.60 (2.29)
Daily diary surveys completed		15.21 (7.18)
Gender		**% of *n* = 113**
Female		71.68%
Male		26.55%
Nonbinary		1.77%
Medication Use		
Norepinephrine-dopamine reuptake inhibitor		10.62%
Selective serotonin reuptake inhibitor		19.47%
Selective serotonin-norepinephrine reuptake inhibitor		4.42%
Tetracyclics		0%
Anticonvulsants/antipsychotics		15.04%
Lithium		1.77%
Anxiolytics (non-benzodiazepine)		2.65%
Race		
African American		3.54%
American Indian/Alaskan native		0%
Asian		20.35%
Biracial or other		18.58%
White		46.02%
Ethnicity		
Hispanic		24.78%
Not Hispanic or other		75.22%
Education (Parent Highest)		
Without high school diploma		9.73%
High school graduate without college degree		5.31%
Some college education		15.04%
Degree from four-year college (or more)		69.91%
Diagnoses	**Lifetime diagnoses**	**Current diagnoses**
Mood disorders	61.06%	39.82%
Unipolar diagnoses	50.44%	32.74%
Bipolar diagnoses	10.62%	7.08%
Disorders secondary to mood disorders		
Anxiety disorders	38.94%	29.20%
Substance use disorders	29.20%	21.24%
Eating disorders	9.73%	3.54%
Attention-deficit/hyperactivity disorder	9.73%	9.73%

Note. Demographic and clinical characteristics of sample.

Table 2

Mood disorder diagnostic characteristics.

		Episode Type				
		Major Depressive Episode (MDE)	**MDE with Mixed Features**	**Dysthymic**	**Manic**	**Hypomanic**
Unipolar diagnoses (*n* = 57)						
		Current Episode (% of *n* = 57)				
Lifetime Diagnosis (% of *n* = 57)		**Major Depressive Episode (MDE)**	**MDE with Mixed Features**	**Dysthymic**	**Manic**	**Hypomanic**
MDD	54.39%	24.56%	1.75%	0%	0%	0%
PDD	45.61%	33.33%	0%	7.02%	0%	0%
Bipolar diagnoses (*n* = 12)		**Current Episode (% of *n* = 12)**				
Lifetime Diagnosis (% of *n* = 12)		**Major Depressive Episode (MDE)**	**MDE with Mixed Features**	**Dysthymic**	**Manic**	**Hypomanic**
Bipolar I	50.00%	33.33%	25.00%	0%	0%	0%
Bipolar II	25.00%	8.33%	0%	0%	0%	0%
Other	25.00%	16.67%	0%	0%	0%	0%
No mood diagnoses (*n*=44)						

Note. Mood disorder diagnoses and current episode types of sample. MDD = Major Depressive Disorder, PDD = Persistent Depressive Disorder.

Table 3

Path estimates and mediation effects within K-means clusters.

Stress → Withdrawal → Anhedonia Cluster	***a* path (stress → withdrawal)**				***b* path (withdrawal → anhedonia)**				**Mediation Effect**		
	B	***F***	***df***	***p***	***B***	***F***	***df***	***p***	***ACME***	***95% CI***	***p***
Cluster 1 (n = 31)	0.03	3.75	1,26	.06	0.15	13.38	1,21	.001	.001	−0.004, 0.01	.83
Cluster 2 (n = 25)	0.03	1.15	1,14	.30	0.59	61.98	1,16	<.001	0.02	−0.01, 0.05	.27
Cluster 3 (n = 22)	0.17	8.39	1,14	.01	0.36	35.64	1,3	.007	0.06	0.02, 0.10	.002
Cluster 4 (n = 18)	0.13	4.6	1,11	.05	0.35	56.21	1,11	<.001	0.04	0.004, 0.09	.04
Cluster 5 (n = 8)	0.10	-	-	-	0.40	-	-	-	-	-	-
Cluster 5 (n = 3)	0.01	-	-	-	0.08	-	-	-	-	-	-
Stress → Impulsivity → Mania Cluster	***a* path (stress → impulsivity)**				***b* path (impulsivity → mania)**				**Mediation Effect**		
	B	***F***	***df***	***p***	***B***	***F***	***df***	***p***	***ACME***	***95% CI***	***p***
Cluster 1 (n = 31)	0.03	1.20	1,24	.28	0.03	1.4	1,27	.20	0.001	−0.001,0.00	.29
Cluster 2 (n = 25)	0.02	0.25	1,18	.62	0.19	9.50	1,19	.006	0.002	−0.02,0.02	.81
Cluster 3 (n = 22)	0.14	6.81	1,16	.02	0.29	8.96	1,15	.009	0.04	0.004, 0.09	.02
Cluster 4 (n = 18)	0.10	4.68	1,11	.05	0.06	0.66	1,15	0.43	0.002	−0.01,0.02	.82
Cluster 5 (n = 8)	0.34	-	-	-	0.002	-	-	-	-	-	-
Cluster 5 (n = 3)	−0.06	-	-	-	1.58	-	-	-	-	-	-

Note. a and *b* path estimates and mediation effects tested within each cluster. Clusters 5 and 6 were too small to test for within-cluster effects.