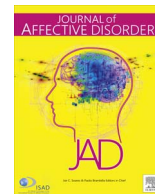




Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Research paper

Trait liabilities and specific promotive processes in psychopathology: The example of suicidal behavior

Jennifer M. Buchman-Schmitt*, Sarah J. Brislin, Noah C. Venables, Thomas E. Joiner, Christopher J. Patrick*

Florida State University, United States

ARTICLE INFO

Keywords:

Research Domain Criteria
Suicidal behavior
Threat sensitivity
Disinhibition
Interpersonal Theory of Suicide

ABSTRACT

Background: The RDoC matrix framework calls for investigation of mental health problems through analysis of core biobehavioral processes quantified and studied across multiple domains of measurement. Critics have raised concerns about RDoC, including overemphasis on biological concepts/measures and disregard for the principle of multifinality, which holds that identical biological predispositions can give rise to differing behavioral outcomes. The current work illustrates an ontogenetic process approach to addressing these concerns, focusing on biobehavioral traits corresponding to RDoC constructs as predictors, and suicidal behavior as the outcome variable.

Method: Data were collected from a young adult sample ($N=105$), preselected to enhance rates of suicidality. Participants completed self-report measures of traits (threat sensitivity, response inhibition) and suicide-specific processes.

Results: We show that previously reported associations for traits of threat sensitivity and weak inhibitory control with suicidal behavior are mediated by more specific suicide-promoting processes—namely, thwarted belongingness, perceived burdensomeness, and capability for suicide.

Limitations: The sample was relatively small and the data were cross-sectional, limiting conclusions that can be drawn from the mediation analyses.

Conclusions: Given prior research documenting neurophysiological as well as psychological bases to these trait dispositions, the current work sets the stage for an intensive RDoC-oriented investigation of suicidal tendencies in which both traits and suicide-promoting processes are quantified using indicators from different domains of measurement. More broadly, this work illustrates how an RDoC research approach can contribute to a nuanced understanding of specific clinical problems, through consideration of how general biobehavioral liabilities interface with distinct problem-promoting processes.

1. Introduction

The Research Domain Criteria (RDoC) matrix system was introduced in 2012 as an impetus and concrete point of reference for improving integration of biobehavioral concepts and measures into mental health research and practice (Morris and Cuthbert, 2012). Critics have argued (e.g., Lilienfeld, 2014) that the RDoC framework may be overly reductionistic and not adequately considerate of the principle of multifinality, which holds that identical biological predispositions can be expressed in markedly different ways. In the current paper, we focus on the topic of suicidal behavior to illustrate how basic biobehavioral constructs from the RDoC framework that are generally relevant to psychopathology (i.e., transdiagnostic) can help inform our understanding of specific clinical problems. In doing so, we highlight

an ontogenetic process perspective (Patrick and Hajcak, 2016; see also Durbin and Hicks, 2014), which views clinical problems as outcomes of general transdiagnostic liabilities that contribute, in concert with developmental transitions and experiential factors, to the emergence of specific problem-promoting processes.

The RDoC initiative encourages a focus on specific clinical-problem phenomena that can be characterized dimensionally (e.g., anhedonic mood, sleep disturbance, ruminative thinking) in place of diagnostic categories that are defined using arbitrary criteria, clouded by issues of comorbidity, and not easily relatable to biological systems and processes (Kozak and Cuthbert, 2016). Suicidal behavior is a distinct clinical problem that can be conceptualized in dimensional terms. Lethal suicide attempts, while rare, have antecedents that are far more common: In the vast majority of cases, the presence of suicidal

* Correspondence to: Department of Psychology, Florida State University, Tallahassee, FL 32306, United States.
E-mail addresses: buchman@psy.fsu.edu (J.M. Buchman-Schmitt), cpatrick@psy.fsu.edu (C.J. Patrick).

<http://dx.doi.org/10.1016/j.jad.2016.09.050>

Received 23 April 2016; Received in revised form 27 September 2016; Accepted 30 September 2016

Available online xxxxx

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ideation, progressing to active intent and planning, precedes active attempts to take one's life (Van Orden et al., 2012). Thus, suicidality can be viewed as a continuum ranging from passive ideation about death, to active suicidal desire, to general planning for suicide, to specific preparations for taking one's life, to non-lethal or lethal suicide attempts (Drum et al., 2009). Systematic research has identified a number of proximal and distal risk factors for suicidal behavior (Nock and Kessler, 2006). While proximal risk factors aid in detecting individuals at imminent risk for suicidal behavior, knowledge of distal risk factors enhances our ability to identify persons at risk for suicide in the longer term. Thus, an approach that focuses on general biobehavioral tendencies that predispose individuals to develop specific suicidogenic states across time is likely to be crucial for identifying high-risk candidates for suicide prevention programs before permanently damaging or lethal self-harm occurs.

1.1. Dispositional Factors in Suicidality

Considerable evidence points to a role for dispositional risk factors in suicidal behavior. Specifically, family studies indicate increased risk for suicidal tendencies among relatives of suicide completers even after controlling for the presence of shared psychiatric disorders (Brent and Mann, 2005). Similarly, twin and adoption studies have documented an appreciable contribution of genetic influences to suicidal behavior (Brent and Mann, 2005; Bondy et al., 2006; Statham et al., 1998). When suicidality is defined to include behavioral antecedents such as ideation, plans, and attempts, heritability estimates range from 30% to 50% (Brezo et al., 2008), with estimates even higher for death by suicide in comparison to estimates for ideation and non-fatal attempts (Mann et al., 2009).

Recent research on risk for suicidal behavior has focused on two specific constructs from the RDoC matrix system, framed in trait-dispositional terms (Yancey et al., 2016): acute threat or “fear,” from the Negative Valence Systems domain, and response inhibition, from the Cognitive Systems domain. Framed in dispositional terms—i.e., as threat sensitivity (THT) and weak inhibitory control (or disinhibition; DIS)—these constructs connect to personality trait variables known to predict suicide proneness. THT relates to the broad personality dimension of negative emotionality (NE) or neuroticism, which has been conceptualized as reflecting sensitivity to aversive events and experiences (Tellegen, 1985). However, THT is narrower in scope than NE, referring specifically to proneness to react with defensive (fear) activation to immediately threatening stimuli or situations (Kramer et al., 2012; Patrick and Bernat, 2010)—and can be operationalized using psychological scales combined with physiological response measures (Vaidyanathan et al., 2009; Yancey et al., 2016). DIS relates to the personality dimension of constraint versus impulsiveness, theorized to involve variations in regulatory control or executive function (Barkley, 1997; Rothbart et al., 2003). When assessed as scores on the common factor underlying externalizing problems and impulsive traits, DIS shows reliable associations with brain measures of cognitive-attentional processing (Nelson et al., 2011; Yancey et al., 2013) and task-behavioral measures of executive control (Young et al., 2009).

Recent research demonstrates that elevations on THT and DIS are associated with increased suicide risk in clinic, military, and general community samples. Venables et al. (2015) found in two large samples ($N_s=1078$ and 3855) that these biobehavioral traits each related uniquely to suicide risk, accounting for separate portions of variance in a composite measure of suicidality, and also interactively, such that individuals high on both traits showed the highest risk for suicidal behavior. Moreover, in line with RDoC's emphasis on multi-domain assessment, Venables et al. (2016) demonstrated in a separate follow-up sample ($N=444$) that “psychoneurometric” operationalizations of THT and DIS that incorporated neurophysiological indicators together with self-report measures also evidenced unique as well as interactive

relations with suicide risk.

These findings suggest that the presence of both traits may confer a distinct liability to suicide and affiliated psychological processes. These findings also dovetail with research showing high rates of suicidal behavior in individuals with borderline personality disorder, a condition that includes impulsive-aggressive tendencies along with high negative affectivity (Brown et al., 2002). However, THT and DIS are known to increase risk for clinical problems of many different types (Nelson et al., 2016; Venables et al., in press), and the mechanisms by which these traits contribute specifically to risk for suicidal behavior remain unclear. To clarify possible mediating mechanisms, we turn to a prominent model of suicidal behavior: the interpersonal theory of suicide (ITS; Joiner, 2005; Van Orden et al., 2010).

1.2. Theoretical Model of Suicide Processes

The ITS model posits that suicidal ideation arises when an individual's need for social connectedness is blocked or impeded (*thwarted belongingness*) and the individual feels overly reliant/demanding on others (*perceived burdensomeness*). Furthermore, the model specifies that suicidal ideation is likely to progress toward active desire for death as these interpersonal states persist, and hopelessness mounts that they will continue across time (Van Orden et al., 2010). Additionally, the model posits a third process, *capability for suicide* (or acquired capability; Van Orden et al., 2010), that contributes critically to the progression from ideation to enactment. This capability factor is theorized to involve fearlessness about death (i.e., nullification or suppression of the instinctual fear of dying) along with increased tolerance for pain (Ribeiro et al., 2014), and is presumed to arise from influences separate from those that engender thwarted belongingness and perceived burdensomeness. When it occurs together with these two interpersonal states (especially when persistent), the presence of capability opens the door to suicidal action. That is, it contributes in a synergistic, interactive manner to suicidal action (Van Orden et al., 2010).

The ITS model has been a prominent focus of research since it was proposed and considerable support has emerged for its major tenets (Ribeiro and Joiner, 2009). The model is process-oriented and specific to suicide. It conceives of hopelessness arising from persistent feelings of social estrangement and overreliance on others along with reduced fear of death as combining to form a distinct suicidogenic state. As such, the ITS model provides a potentially valuable point of reference for clarifying how biobehavioral dispositions corresponding to RDoC constructs contribute to this devastating clinical problem.

1.3. Current study aims and hypotheses

The present study sought to extend prior work documenting replicable predictive relations for RDoC trait constructs of THT and DIS with suicidal behavior (Venables et al., 2015, 2016) by examining whether the basis of these associations lies in the effects of these traits on specific promotive processes that are psychologically more proximal to suicidal behavior. Our broader aim was to illustrate an ontogenetic process approach to RDoC-oriented research (Patrick and Hajcak, 2016), in which the contributions of broad biobehavioral liabilities to distinct clinical outcomes are clarified by investigating how they interface with specific problem-promoting processes.

More specifically, we undertook analyses of data for the two RDoC traits of interest (THT, DIS) along with measures of the three ITS process constructs (thwarted belongingness, perceived burdensomeness, capability for suicide) in a sample prescreened to provide overrepresentation of suicidal tendencies ranging from ideation to actual attempts. We used standard correlational techniques (simple r_s , multiple regression) to investigate relations of traits and ITS processes with each other, and in turn with suicidality. In addition, we utilized mediational analyses to test our major *a priori* hypotheses—namely,

that the RDoC trait variables would account for variance in suicidality as a function of their associations with the processes of the ITS model (i.e., that the ITS process variables would mediate observed relationships for THT and DIS with suicidality).

Our specific study hypotheses were as follows:

- (1) Consistent with prior research findings, the ITS process variables and the two target traits (THT, DIS) would each show significant associations with suicidality. As processes theorized to directly promote suicidal ideation and action, scores on the ITS constructs were expected to strongly predict scores on an index of suicidal tendencies. The two trait variables, reflecting general liabilities less proximal to suicidal behavior, were expected to predict suicidality to a more moderate degree.
- (2) The two trait variables were each predicted to relate to the ITS processes of thwarted belongingness and perceived burdensomeness. THT was expected to relate to these processes because it includes a component of social timidity/anxiousness (Kramer et al., 2012) and is associated with avoidant tendencies and feelings of dependence (Nelson et al., 2016; Patrick and Bernat, 2010). Associations for DIS were predicted because high-DIS individuals act in impulsive/irresponsible ways that strain relationships and tend to be demanding/needily. The two traits were expected to relate less, if at all, to capability for suicide, because this ITS process is theorized to arise mainly from experiential factors (Van Orden et al., 2010).
- (3) We predicted that observed relationships of the two traits with suicidality would be completely accounted for (i.e., fully mediated by) their associations as predicted above with the ITS process variables—in particular, thwarted belongingness and perceived burdensomeness.

2. Method

2.1. Participants

Participants were 105 undergraduates (58.1% female; M age=19.3 years, range=18–35) recruited through an elective screening survey administered to introductory psychology classes at a large public university in Florida. Procedures for the study were reviewed and approved by the Institutional Review Board at Florida State University and informed consent was obtained from all participants prior to testing.

To enhance sample representation of participants exhibiting suicidal tendencies, individuals who endorsed a history of suicide attempts and/or suicide ideation in the screening survey were prioritized for recruitment. Participants were also required to be: (1) at least 18 years of age, (2) able to speak and read English fluently, and (3) non-smoking. We excluded smokers due to the potential influence of tobacco use on pain tolerance (Mercer and Holder, 1997; Murray and Hagan, 1973), as assessed in the manner described below. In addition, we asked all participants to abstain from pain suppressants for a minimum of eight hours and caffeine and sugary foods for a minimum of one hour prior to participation (Mercer and Holder, 1997; Pomerleau et al., 1984). The racial and ethnic composition of the study sample was: 79% Caucasian, 7% African American, 3% Asian, 1% American Indian or Alaska Native, and 4% other, with 6% declining to respond; 22% of participants identified as being of Hispanic, Latino, or Spanish origin.

As intended, the recruitment strategy resulted in overrepresentation of individuals reporting a history of suicidal tendencies. Approximately 43% of participants ($n=45$) endorsed one or more suicide-related items among those included in the composite index of suicidality described below, 19% ($n=20$) endorsed engaging in planning and/or preparations for a suicide attempt, and 15.2% ($n=16$) reported one or more past attempts. One-third of participants ($n=35$) reported

current suicidal symptoms of at least one of these types.

2.2. Procedures and measures

2.2.1. Procedures

Following informed written consent, participants completed questionnaires as described below. Testing was performed individually, with questionnaires completed in pencil-and-paper format. Afterward, participants underwent a pressure-pain (algometer) assessment, as described below. All participants received course credit as compensation for completion of testing.

2.2.2. Measures

2.2.2.1. Trait measures: threat sensitivity (THT) and weak response inhibition (DIS). The two trait constructs of interest, threat sensitivity (THT) and weak inhibitory control (or disinhibition; DIS), were assessed using scales employed in Study 1 of Venables et al. (2015). The THT scale was a 19-item measure of dispositional fear/fearlessness (“boldness”; Patrick, 2010; Drislane et al., 2014), with each item answered on a 4-point scale and coded such that higher scale scores reflected greater fearful tendencies; scores on this THT scale correlate very highly ($\sim .8$) with scores on the general factor of a structural model of the fear/fearlessness domain (Kramer et al., 2012). The alpha reliability for this scale in the current sample was .83. Females scored somewhat higher than males, but not significantly so, $t(97) = 1.89, p = .06$.

The scale measure of DIS was the General Disinhibition scale from the brief-form Externalizing Spectrum Inventory (ESI-BF; Patrick et al., 2013a). This scale comprises 20 items indexing weak self-control, impulsiveness, irresponsibility, impatience and boredom proneness, mistrust, and thievery—each answered on a 4-point scale, with responses coded such that higher scale scores reflect greater disinhibitory tendencies. Scores on this scale correlate very highly ($r > .9$) with scores on the general factor of the full-form ESI (Krueger et al., 2007). The alpha reliability coefficient for this 20-item DIS scale in the current sample was .81. Females scored significantly lower on this scale than males, $t(97) = -3.06, p < .005$.

2.2.2.2. Interpersonal Theory of Suicide (ITS) constructs: thwarted belongingness, perceived burdensomeness, and capability for suicide. Thwarted belongingness and perceived burdensomeness were measured using the Interpersonal Needs Questionnaire (INQ; Van Orden et al., 2012), an inventory that assesses these two process constructs through scales of 9 and 6 items, respectively. Participants are asked to rate the items of the INQ based on how they have been feeling recently; thus, the inventory yields current-state indices of thwarted belongingness and perceived burdensomeness as opposed to trait-level indices. Items are answered using a 7-point scale, and coded such that higher scores reflect greater feelings of thwarted belongingness and burdensomeness. Research supports the two-factor structure of the INQ and identifies thwarted belongingness and perceived burdensomeness as correlated but distinct constructs, showing differential associations with external criterion measures (Van Orden et al., 2012). The two scales demonstrated good internal consistencies within the current sample ($\alpha = .91$ and $.94$). Females and males did not differ significantly in either thwarted belongingness or perceived burdensomeness, $t_s(97) = -1.95$ and $.16$, respectively, $p_s = .054$ and $.16$.

In line with recent ITS-model research (Ribeiro et al., 2014), and consistent with RDoC's recommendation that constructs be indexed if possible using different modes ('units') of measurement, the third ITS construct, capability for suicide, was assessed as a unit-weighted composite of two measures: a scale measure of comfort with the idea of death, and a behavioral measure of tolerance for physical pain. The

scale measure was the 7-item Fearlessness About Death (FAD) scale (Ribeiro et al., 2014), which assesses level of comfort with death and the pain associated with it.¹ Items (e.g., “I am not afraid at all to die.”; “The pain involved in dying frightens me.”) are answered using a 5-point scale, with responses coded such that higher scores reflect greater comfort with death and capability for suicidal action. Internal consistency in the current sample was .85. Scores on this scale were higher for males than females, $t(97)=-3.45, p < .005$.

The behavioral, pain-tolerance measure was obtained using a pressure-algometer procedure (Somedic, Solletuna, Sweden Type II brand), which assesses the level of pressure an individual is able to withstand – applied via a blunt-tipped rod positioned on the dorsal side of his/her dominant hand, midway between the knuckles of the middle and index fingers. The pain assessment consisted of two trials in which pressure was applied in gradual increments (of 50 kPa/s) until the participant said “stop,” indicating that he/she had reached pain tolerance. Research supports the use of the pressure algometer as a reliable index of pain tolerance (Pollatos et al., 2012). The pressure levels reached by participants correlated quite highly across the two trials ($r=.73$), and thus were averaged to form the pain tolerance score.

The index of capability for suicide used in the analyses reported below was computed by averaging standardized scores for the FAD scale and the pain-tolerance assessment. Five participants who completed questionnaires did not undergo the pain tolerance assessment, and thus analyses of the capability for suicide variable used a reduced sample of 100 participants.

2.2.2.3. Suicidality. In line with our aim of measuring suicidality along a continuum from passive and active suicidal ideation to planning and suicide attempts, the criterion measure of suicidality consisted of a factor-analytically derived composite of scores for five variables: (1) an index of passive ideation consisting of the average score for eight items from the Suicide Cognition Scale (SCS; Ellis and Rufino, 2015) assessing desire to escape psychological pain, perception of oneself as not deserving to live, and thoughts about suicide; (2) an item from the Depressive Symptom Inventory-Suicide Subscale (DSI-SS; Metalsky and Joiner, 1997) that indexes active suicidal ideation (i.e., impulses toward suicidal behavior); (3) an item from the Beck Depression Inventory-II (BDI-II; Beck et al., 1996) that indexes resolve to attempt suicide; (4) another item from the DSI-SS that indexes level of planning for a suicide attempt; and (5) an item from the prescreening inventory indexing number of historic suicide attempts. Items from the SCS, DSI-SS, and BDI pertaining to suicidal ideation and intent/planning were assessed within a current time frame (i.e., two weeks ago to present), whereas the prescreening attempt item covered all past instances. The internal consistency of the five items used to form the suicidality composite was .81.

Scores for these five variables were subjected to a principal axis factor analysis, which revealed a single common factor (largest eigenvalue=2.42; all others ≤ 1.00), interpretable as a dimensional index of suicidal tendencies. Scores on this common factor (computed via the regression method) were used as the criterion measure of suicidality in all analyses. Females and males did not differ in scores on this suicidality factor, $t(97)=.45, p=.64$.

Our quantification of suicidality as a behavioral continuum accords with the continuous-dimensional approach to assessment advocated by RDoC (Kozak and Cuthbert, 2016; Morris and Cuthbert, 2012). This approach is also advantageous in that it incorporates past along with current suicidal symptoms, and combines narrower indicators into a more reliable aggregate score. Regarding the first of these points,

¹ The items comprising the FAD scale are a subset of the 20-item Acquired Capability for Suicide Scale (ACSS; Van Orden et al., 2008), an inventory designed to index fearlessness about death along with exposure to painful and provocative life events and perceived tolerance for pain.

lifetime history of attempts is commonly assessed when evaluating current risk for suicide (Chu et al., 2015) because research has shown that prior suicidal behavior is predictive of risk for future death by suicide (Brown et al., 2000).

2.2.3. Data analyses

Correlations and multiple regression analyses were used to test for predictive relations of the two trait variables (THT, DIS) with the ITS processes (thwarted belongingness, perceived burdensomeness, capability for suicide) and the criterion measure of suicidality. In addition, we undertook mediational analyses of two types: (1) single mediator analyses testing whether individual ITS constructs that qualified as mediators (i.e., by showing significant r s both with the trait and suicidality) accounted for trait/suicidality associations, and (2) multiple mediator models testing for effects of all qualifying ITS constructs as mediators of trait/suicidality relationships.

To test for mediation, we performed bias-corrected bootstrapped confidence interval (CI) tests of indirect effects using the INDIRECT macro within SPSS (Preacher and Hayes, 2008). Specifically, 1000 bootstrap re-samples were used to evaluate the indirect effect of each trait variable on suicidality, via the ITS constructs that qualified as potential mediators. This method is advantageous in that it increases statistical power in comparison to more traditional tests of indirect effects (MacKinnon et al., 2002). In each analysis, THT or DIS served as the independent variable, and suicidality served as the dependent variable. In this context, it bears noting that the cross-sectional nature of the current study precluded determination of the causal directionality of observed associations.

3. Results

Table 1 shows zero-order correlations among (a) the two trait variables (THT, DIS), (b) the three ITS process constructs as indexed by the INQ (thwarted belongingness, perceived burdensomeness) and the FAD-scale/pain-tolerance composite (capability for suicide), and (c) the suicidality criterion measure. The first two subsections of the Results section present further information about relationships, respectively, for the three ITS constructs with suicidality, and the two trait variables with suicidality and the ITS constructs. The third subsection reports results from analyses testing for mediation of trait/suicidality associations by the ITS process constructs.

3.1. Associations of ITS constructs with suicidality

Regarding associations between ITS constructs and suicidality, thwarted belongingness, perceived burdensomeness, and capability for suicide (FAD/pain-tolerance composite) showed significant positive associations as expected with suicidality at the zero-order level (see

Table 1
Zero-order correlations among study variables.

Study variables	1	2	3	4	5	6	7
1. THT	–						
2. DIS	-.04	–					
3. Thwarted Belongingness	.47**	.29**	–				
4. Perceived Burdensomeness	.26**	.19*	.47**	–			
5. Capability for Suicide	-.13	.05	.11	-.09	–		
6. Suicidality	.38**	.21*	.62**	.41**	.23*	–	
7. Age	-.08	.09	.04	.09	.19	-.02	–

Note. $N=105$ for all r s except those involving capability for suicide, for which $N=100$. Capability for suicide is computed as the mean of standardized scores for the Fearlessness About Death (FAD) scale and the pain tolerance task. Suicidality reflects scores on the common factor underlying five indicators of suicidal behavior. THT=threat sensitivity; DIS=weak inhibitory control.

** $p < .01$.

* $p < .05$.

Table 1). When thwarted belongingness, perceived burdensomeness, and capability for suicide were entered together in a regression model with suicidality as the outcome variable, the overall model was significant: $F(3, 96)=24.89, p < .001$. All three process variables demonstrated unique predictive relations with suicidality: thwarted belongingness, $\beta=.52, p < .001$; perceived burdensomeness, $\beta=.18, p < .05$; and capability for suicide (FAD), $\beta=.19, p < .05$. Consistent with their hypothesized proximity to suicidality, the omnibus prediction coefficient for this model including all three ITS variables was high, $R=.66 (R^2=.44)$.

Regarding the role of capability for suicide, the ITS (as noted at the outset) posits that capability for suicide should contribute most strongly to suicidality at high levels of the two interpersonal processes (i.e., at which salient suicidal ideation/intent is likely to be present). In view of this, we tested for effects of capability for suicide in combination with (i.e., in interaction with) thwarted belongingness and perceived burdensomeness in predicting increased suicidality. This was done by computing an interaction term consisting of the product of the mean-centered score for the capability for suicide variable (i.e., FAD/pain-tolerance composite) with the mean-centered score for one or the other INQ score variable. The interaction product-term for capability for suicide with thwarted belongingness showed a significant, positive correlation with suicidality at the zero-order level ($r=.57, p < .001$). Moreover, when this interaction product-term was entered into a regression model after including thwarted belongingness, perceived burdensomeness, and capability for suicide, the overall model remained significant ($F[4,99]=30.76, p < .001$), and the interaction term contributed to prediction over and above the three ITS process variables ($\beta=.40, p < .001$; $\Delta R^2=.13, p < .001$). Similarly, the interaction term for capability for suicide with perceived burdensomeness showed a positive association with suicidality at the zero-order level ($r=.51, p < .01$). When this interaction product-term was entered into a regression model after including scores for the three ITS processes, the overall model was again significant ($F[4,100]=24.27, p < .001$), with the interaction term contributing to prediction over and above the individual ITS variables ($\beta=.64, p < .001$; $\Delta R^2=.13, p < .001$).²

3.2. Associations of trait dispositions with suicidality and ITS constructs

Both THT and DIS showed robust positive associations with suicidality at the zero-order level (Table 1). In line with prior published work (Venables et al., 2015), we entered the two traits together into a regression model, along with a product term reflecting their interaction, as predictors of suicidality. The overall model was significant, $F(4, 100)=9.38, p < .001$, adjusted $R^2=.20$. THT and DIS each evidenced robust positive associations with suicidality in this model ($\beta s=.39$ and $.22, ps < .001/.05$), with the THT by DIS interaction term showing a weaker, nonsignificant positive relationship ($\beta=.12, p=.16$). The omnibus prediction coefficient for this regression model was moderate, $R=.46 (R^2=.21; \Delta R^2=.01, p=.21)$.

As for relationships of THT and DIS with the ITS constructs, both THT and DIS demonstrated significant positive relationships with thwarted belongingness and perceived burdensomeness at the zero-order level, which were related in turn to suicidality as noted above; additionally, THT and DIS each showed significant independent associations with each of these suicide-promoting processes when

included together as predictors in regression models ($\beta s=.48$ and $.30$, respectively, for thwarted belongingness, and $.26$ and $.20$ for perceived burdensomeness, all $ps < .05$). Notably, neither THT nor DIS was correlated with capability for suicide (FAD/pain-tolerance composite) at the zero-order level. However, THT showed a robust positive correlation with the capability for suicide by thwarted belongingness interaction term ($r=.32, p=.001$; corresponding r for DIS $=.11, ns$). Neither THT nor DIS showed a significant association with the interaction of capability for suicide with perceived burdensomeness (r for each trait $=.11$), though this interaction term as noted earlier did show a predictive association with suicidality.

3.3. Mediation analyses

3.3.1. Single mediator tests

Three process variables qualified as potential mediators of the observed relationship of THT with suicidality (i.e., by showing significant associations with both predictor and criterion): thwarted belongingness, perceived burdensomeness, and the interaction term for capability for suicide (FAD and pain tolerance) with thwarted belongingness. Accordingly, we conducted individual mediation tests for these three process variables. The test of the indirect effect for thwarted belongingness was found to be significant (95% confidence interval [CI]=.65, 3.12), with the C' path coefficient emerging as nonsignificant ($\beta=.12, p > .10$)—indicating full mediation of the relationship between THT and suicidality by this process variable. The indirect effect test for perceived burdensomeness was likewise significant (CI=.11, 1.42), but in this case the C' path coefficient remained significant ($\beta=.30, p < .001$)—indicating only partial mediation of the relationship between THT and suicidality by this variable. The mediation test for the capability for suicide (FAD and pain tolerance) by thwarted belongingness interaction term was also significant (CI=.04, 2.20), and again the C' path coefficient remained significant ($\beta=.23, p < .01$), indicating partial mediation.

In the case of DIS, both thwarted belongingness and perceived burdensomeness qualified as potential mediators, but the interaction term for capability for suicide (FAD and pain tolerance) by thwarted belongingness did not (i.e., because it did not correlate significantly with DIS). Thus, we conducted individual mediation tests for thwarted belongingness and perceived burdensomeness only. Both indirect effect tests yielded significant outcomes (CIs=.39, 2.93 and $.11, 1.32$, respectively), with the C' path coefficient emerging as nonsignificant in each case ($\beta s=.04$ and $.14, ps > .10$)—indicating full mediation of the relationship between DIS and suicidality by both thwarted belongingness and perceived burdensomeness.³

3.3.2. Multiple mediator tests

As thwarted belongingness, perceived burdensomeness, and the interaction between capability for suicide (FAD) and thwarted belongingness were found to mediate the relationship between THT and suicidal behavior, the three ITS variables were evaluated together in a joint model to determine the unique mediating role of each, controlling for the others. As depicted in Fig. 1, the direct path between THT and suicide was no longer significant after accounting for indirect paths via

² One bivariate outlier was identified in the association of perceived burdensomeness with capability for suicide. To rule out an impact of this outlier on the results, we re-ran the regression analysis incorporating the interaction term for these two ITS variables with the outlier removed. The pattern of results remained the same, with the overall regression model remaining significant ($F[4,98]=30.39, p < .001$), and the interaction term contributing to prediction of suicidality over and above the individual ITS variables ($\beta=.61, p < .001$; $\Delta R^2=.11, p < .001$).

³ To evaluate the directional specificity of these mediational effects, we re-ran the above-described analyses with the ITS process variables (thwarted belongingness, perceived burdensomeness) serving as the independent variables, the trait variables (THT and DIS) as the mediators, and suicidality as the dependent variable. Neither THT (95% CI: $-.002, .007$) nor DIS (95% CI: $-.0001, .011$) mediated the relationship between thwarted belongingness and suicidality, and DIS did not significantly mediate the relationship between perceived burdensomeness and suicidality (95% CI: $-.002, .02$). Evidence was found for a mediating effect of THT on the association between perceived burdensomeness and suicidality (95% CI: $.004, .034$); however, consistent with the idea of ITS processes being more proximal to suicidality than traits, the lower bound of the CI for this effect (.004) was much closer to zero than the CI for the mediating effect of perceived burdensomeness on the THT/suicidality association (.11).

these three mediators ($\beta=.04$), and the model indicated distinct mediating effects for each of the three variables: thwarted belongingness ($CI=.37, 2.02$); perceived burdensomeness ($CI=.04, .88$); and interaction between capability for suicide (FAD/pain-tolerance composite) and thwarted belongingness ($CI=.09, 2.21$).⁴

For the relationship between DIS and suicide, single mediator effects were evident for both thwarted belongingness and perceived burdensomeness, so the relative contributions of these two variables to this relationship were evaluated in a joint model. As depicted in Fig. 2, the direct path between DIS and suicide was no longer significant after accounting for indirect paths via these two mediators ($\beta=.03$), with the model revealing significant mediation for thwarted belongingness ($CI=.29, 2.57$) and a nonsignificant trend toward mediation ($p < .10$) for perceived burdensomeness (95% $CI=-.03, .80$; 90% $CI=.01, .70$).

4. Discussion

The RDoC matrix framework was formulated to improve and help coordinate research on mental health problems by encouraging a systematic focus on core biobehavioral processes studied across multiple units of analysis (measurement domains). Critics have raised concerns about RDoC's overemphasis on biological concepts/measures and its disregard for the principle of multifinality – and questioned whether the pathophysiology of complex clinical problems can be understood in terms of simple, biologically-oriented constructs. In the current work, we propose an ontogenetic process perspective (Patrick and Hajcak, 2016; see also Durbin and Hicks, 2014) as one means for addressing these concerns. This conceptual approach views clinical problems as outcomes of transdiagnostic liabilities that contribute, through interplay with developmental shifts and experiential influences, to the emergence of specific problem-promoting processes. Using suicidal behavior as an example, we show that basic trait dispositions corresponding to constructs from the RDoC matrix predict suicidal tendencies through their associations with psychological processes theorized to directly impel suicidal ideation and action.

4.1. Biobehavioral traits and suicide-promoting processes

An important aspect of the current study was its effectiveness in replicating major findings from prior research, necessary for undertaking mediational analyses to extend what is known from prior work. Consistent with extensive data pertaining to the ITS model of suicidal behavior, we found that constructs of thwarted belongingness, perceived burdensomeness, and capability for suicide each contributed uniquely and significantly to prediction of a dimensional index of suicidality, encompassing tendencies ranging from passive ideation through to actual attempts. Moreover, and also consistent with tenets of the ITS model, capability for suicide interacted with the other two constructs of the model in predicting suicidality, over and above its individual-level contribution. The implication is that decreased fear of death and pain associated with dying contributes to suicidal tendencies especially when coupled with salient feelings of estrangement from others and concerns about overreliance on their support.

Importantly, the current study also replicated prior work (Venables et al., 2015, 2016) showing that traits corresponding to RDoC constructs of acute threat (THT) and weak response inhibition (DIS) are each uniquely predictive of suicidal tendencies. In line with the idea that traits are more distally related to suicidal behavior than ITS processes, the prediction coefficient for the two traits together ($R=.46$)

⁴ We also re-ran this analysis with capability for suicide (FAD/pain tolerance composite) included, to test for a unique mediating effect of this variable per se. The confidence interval for this variable crossed zero, indicating no significant mediation, with effects for the other variables remaining significant: thwarted belongingness ($CI=.32, 1.80$); perceived burdensomeness ($CI=.07, .95$); capability for suicide by thwarted belongingness interaction term ($CI=.02, 1.74$).

was appreciably lower than the coefficient for the ITS variables combined ($R=.66$, increasing to $.75$ when interaction terms involving capability for suicide were added as predictors). Notably, a trend toward a distinct predictive contribution for the interaction of the two traits was also evident, but this effect did not reach significance. However, the magnitude of the association for this interaction was consistent with that reported in much larger samples where it emerged as significant (Venables et al., 2015, 2016; $Ns=3855/1078$ and 444 , respectively), suggesting that the current study was underpowered for detecting this effect.

The replicability of the foregoing findings fulfilled conditions for

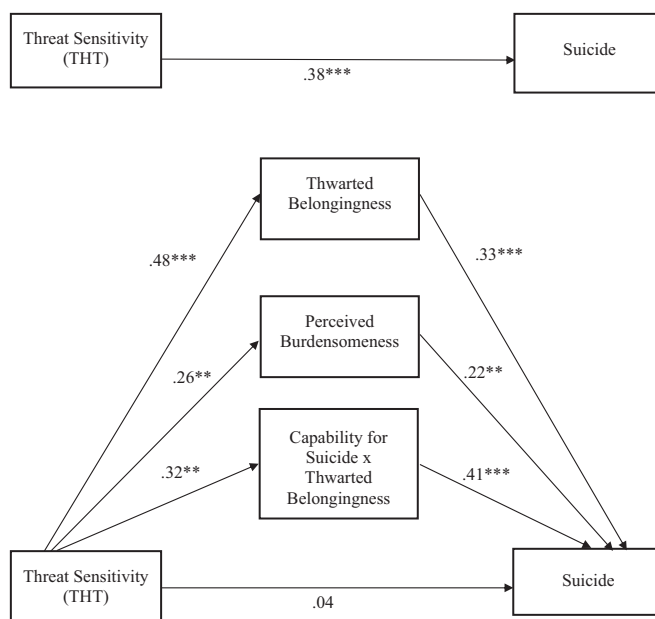


Fig. 1. Multiple mediator model evaluating contributions of (a) thwarted belongingness, (b) perceived burdensomeness, and (c) interaction of thwarted belongingness with capability for suicide (=average of Fearless About Death and pain tolerance) to the relationship between weak inhibitory control (DIS) and suicidal behavior; coefficients for upper and lower paths between DIS and suicidal behavior reflect associations between these variables before and after accounting for effects of the three mediators. ** $p < .01$, * $p < .05$.

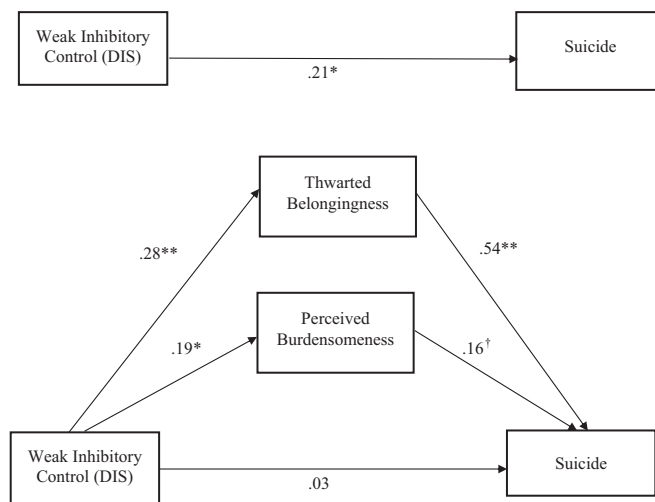


Fig. 2. Multiple mediator model evaluating contributions of (a) thwarted belongingness and (b) perceived burdensomeness to the relationship between weak inhibitory control (DIS) and suicidal behavior; coefficients for upper and lower paths between DIS and suicidal behavior reflect associations between these variables before and after accounting for effects of the two mediators. ** $p < .01$, * $p < .05$, † $p < .10$.

mediational analyses directed at evaluating the role of ITS processes in mediating predictive relations for THT and DIS with suicidality. Results from the mediational analyses demonstrated, consistent with *a priori* hypotheses, mediating roles for thwarted belongingness and burdensomeness in the associations for both traits. Additionally, a unique role was found for the *interaction* between belongingness and capability for suicide in mediating the observed relationship for THT specifically. Notably, and also consistent with hypothesis, the ITS processes in concert fully mediated relationships for each of the trait variables with suicidality. Although caution is warranted in interpreting these findings given study limitations as described below, the observed effects have intriguing implications for understanding the origins and development of suicidal tendencies.

4.2. Implications for understanding of suicidal behavior

The current results are interesting to consider in light of prior work demonstrating associations for THT and DIS with clinical problems of various other types besides suicidal behavior – THT with phobic conditions and anxious-fearful personality disorders in particular, and depressive conditions to some extent, and DIS with antisocial and substance-related problems, impulsive-erratic personality disorders, and depressive conditions to some degree as well (Nelson et al., 2016; Patrick and Bernat, 2010; Patrick et al., 2013b, 2012). Importantly, THT and DIS maintain associations with problems of these various types, and with suicidality as well, when operationalized using physiological response indicators together with psychological scale indicators (Patrick et al., 2013b; Yancey et al., 2016; Venables et al., 2016) – and these associations are traceable mainly to genetic influences (Venables et al., *in press*). These findings, together with developmental evidence for fear/fearlessness and inhibitory control as early-emerging temperament dimensions (Durbin et al., 2007; Kochanska, 1997; Rothbart et al., 2003), provide support for the idea that THT and DIS represent core biobehavioral liabilities for multiple forms of psychopathology.

What, then, determines the specific expressions these general trait liabilities take in terms of clinical outcomes? From an ontogenetic process perspective, these liability factors intersect across time with other shaping influences that give rise to distinct psychological (neuro-cognitive/affective) states characteristic of particular problems—such as phobic fear, obsessive or depressive rumination, social estrangement, or substance-related expectancies/urges. As regards suicide, findings from the current study, though tentative given its cross-sectional design, are consistent with the idea that THT and DIS contribute to suicidal tendencies by facilitating the emergence of pathological processes more proximal to suicide, as specified by the ITS model.

Existing data regarding the psychological correlates of THT and DIS suggest mechanisms by which they may contribute to the emergence of distinct suicide-promoting processes. THT includes a component of interpersonal timidity (Kramer et al., 2012) that likely contributes in a direct way to social disengagement (thwarted belongingness). Consistent with this, THT shows strong predictive relations with symptoms of adult social phobia and avoidant personality (Nelson et al., 2016; Patrick et al., 2012; Yancey et al., 2016), and when operationalized as fearless temperament in young children predicts the emergence of later social anxiousness and avoidance (Durbin et al., 2007; Moser et al., 2015; Schwartz et al., 2003). Given the well-established role that thwarted belongingness plays in suicidal ideation, it is plausible to suppose that social disengagement related to high THT contributes to the emergence of thoughts pertaining to non-being or non-existence. More speculatively, high THT may also contribute to the experience of perceived burdensomeness by fostering dependency (Patrick et al., 2012) on family members and other ‘safe’ persons for tangible resources and social support.

The relationship of DIS with suicidality was also found to be

mediated by thwarted belongingness and perceived burdensomeness, although the mediating role of burdensomeness appeared weaker than that of belongingness. In considering how DIS interfaces with these ITS processes, it is notable that DIS was uncorrelated with THT in the current sample (cf. Nelson et al., 2016; Venables et al., 2015). The implication is that high DIS contributes to these ITS processes in different ways than THT. Consistent with this view, regression analyses confirmed that DIS contributed separately from THT to prediction of thwarted belongingness and burdensomeness, and also suicidality. Whereas THT involves fearful/avoidant tendencies, DIS entails reckless-impulsive tendencies that are problematic for—and in some cases, injurious to—other people. DIS is associated, for example, with early conduct problems, persistent aggression, law-breaking, and substance abuse—and in connection with these adverse behavior patterns, school failure, employment problems, and conflictual relationships. As such, it is not difficult to imagine how high DIS would contribute over time to feelings of estrangement from family and friends and a growing sense of overreliance on others for financial and personal support.

The other mediation effect we found, for the capability for suicide by thwarted belongingness interaction, was specific to the association of THT with suicidality. Of note, capability for suicide was quantified as a composite of self-reported fear about death (FAD scale) and behaviorally-assessed tolerance for pain (algometer task). Conceptually, this composite-score variable can be seen as occupying a position intermediate between the psychological-experiential and behavioral response domains (cf. Patrick et al., 2013b; Yancey et al., 2016). A further notable point is that the presence of capability is theorized to enhance risk for more severe suicidal tendencies (i.e., active planning and attempts; Joiner, 2005; Van Orden et al., 2010). Considered in this light, the finding that the capability by thwarted belongingness interaction term accounted partly for the observed association between THT and suicidality is particularly intriguing. It could indicate that feelings of thwarted belongingness engendered by social timidity/avoidance, and reduced fear of injury and death arising from other sources (e.g., painful accidents; witnessing injury or death of others; Van Orden et al., 2010), combine in a synergistic manner to augment suicide risk. Alternatively, repeated engagement in suicidal ideation associated with persistent social estrangement may instigate opponent processing (Solomon, 1980) that operates to dampen the distressing nature of suicide-related thoughts and foster comfort with the prospect of death (Joiner, 2005; Van Orden et al., 2010). As discussed more below, longitudinal follow-up studies will be needed to clarify the conditions/pathways by which high dispositional THT contributes to the distinct nexus of low belongingness and heightened capability that adds uniquely to risk for more severe degrees of suicidality.

4.3. Limitations and future directions

Some important limitations of the current study must be acknowledged. First, the study utilized a relatively small participant sample ($N \sim 100$), which as noted may have hindered our ability to detect certain effects—in particular, the previously reported finding of a contribution of the THT \times DIS interaction to prediction of suicidality (Venables et al., 2015, 2016). Future studies with larger sample sizes are needed to corroborate and further clarify these small, but theoretically meaningful, interactive effects. Additionally, participants in the current study consisted of undergraduate students rather than population-representative adults or clinic patients. Mitigating this concern somewhat: (1) participants were preselected to increase representation of suicidal tendencies, and a substantial portion of the sample reported some level of suicidality, with approximately 33% reporting current suicidal symptoms and 15% reporting a history of suicide attempts, and (2) relationships of traits and ITS processes with suicidality reported in previous work with clinical samples were successfully replicated in the current study. Nonetheless, follow-up studies employing larger, treat-

ment-seeking clinical samples varying more widely in age will be needed to establish whether ITS processes mediate trait/suicidality associations in the ways reported here. In particular, clinical samples are likely to include a higher proportion of individuals with severe, comorbid psychopathology, associated with higher levels of both THT and DIS and greater adverse life experiences. The relative contribution of DIS to suicidality, and the process variables found to mediate this contribution, may be more substantial in samples of this type.

Another key limitation of the study from the standpoint of RDoC is that trait dispositions, ITS processes, and suicidality were operationalized largely through self-report. The exception was the capability for suicide variable, which was quantified using self-report and behavioral response. However, the trait variables used as predictors in the current study were chosen specifically because of their correspondence to biobehavioral constructs from the RDoC matrix (i.e., acute threat, response inhibition), and because substantial background work demonstrates that these traits can be operationalized jointly using report and neurophysiological indicators, and still maintain their effectiveness in predicting clinical problems of various types including suicidality (Patrick et al., 2013b; Yancey et al., 2016; Venables et al., 2016, in press). Thus, the foundation exists for a more intensive RDoC-oriented investigation of suicidality in which both traits and ITS processes are quantified using indicators from different domains of measurement (units of analysis). Further research will be needed to establish effective cross-domain operationalizations of belongingness and burdensomeness constructs from the ITS model. Notably, some work has been done to index suicidal tendencies through implicit behavioral means (e.g., Nock et al., 2010).

A further important limitation of the current study is its cross-sectional nature. Without question, longitudinal studies involving assessments of trait dispositions, ITS process variables, and suicidal tendencies at earlier and later ages will be required to corroborate the current findings and establish that general trait liabilities in fact contribute causally to the emergence of more proximal suicide-promoting processes. Measurement of salient life events across differing time points will also be critical for establishing the specific nature of factors that shape trait liabilities in the direction of suicide-promoting states versus states more proximal to problems of other types. To the extent possible, it will be important to capitalize on existing longitudinal datasets that include variables of the types included in the current study. In some cases, it may be possible to estimate with reasonable effectiveness scores on relevant trait and process dimensions in longitudinal studies not specifically designed to investigate suicidality, but that include trait-dispositional, psychological-attitudinal, life-event, and clinical-problem measures of various types (see: Brislin et al., 2015; Smith et al., 2012).

Notwithstanding these limitations, the current study adds importantly to existing knowledge of influences contributing to one of the most severe and damaging expressions of psychological dysfunction—suicidal behavior. More broadly, it illustrates an ontogenetic process approach to the study of clinical problems that serves to address concerns that have been raised about the RDoC research framework. To understand and reduce the incidence of severe mental health problems, it will be necessary to identify core biobehavioral liabilities that place certain individuals at elevated risk for their occurrence, and—through analyses of relevant multi-domain data from cohort-sequential longitudinal studies—quantify and track developmental shifts in cognitive-affective functioning and impactful life events that promote the emergence and intensification of distinct psychological states associated with clinical problems of specific types (cf. Durbin and Hicks, 2014). By applying this investigative approach to suicide, it should become possible in the foreseeable future to identify individuals at maximal dispositional risk for this tragic outcome and, utilizing ongoing screening procedures akin to those currently used to test for incipient medical conditions, intervene at critical points to prevent the occurrence of lethal acts of self-harm and the lasting damage they

inflict on families, friends/associates, and society as a whole.

Acknowledgements

This work was supported by Grant W911NF-14-1-0027 from the U.S. Army, Grant T32 MH93311 from the National Institute of Mental Health, Grant 952090 from the National Science Foundation Graduate Research Fellowship, and Grant W81XWH-10-2-0181 from the Military Suicide Research Consortium, an effort supported by the Office of the Assistant Secretary of Defense for Health Affairs. The content of this paper is solely the responsibility of the authors and does not necessarily represent the official views of the U.S. Government, Department of Defense, Department of the Army, Department of Veterans Affairs, Military Suicide Research Consortium, or U.S. Recruiting Command. Funding sources had no role in the study design, in the collection, analysis and interpretation of data, in the writing of the report, or in the decision to submit the article for publication.

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