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Psychiatry Research

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

Separate and interactive contributions of weak inhibitory control and threat sensitivity to prediction of suicide risk



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ARTICLE INFO

Article history:

Received 21 July 2014

Received in revised form

23 December 2014

Accepted 6 January 2015

Available online 30 January 2015

Keywords:

Disinhibition

Weak response inhibition

Fear

Threat sensitivity

Suicide

ABSTRACT

Biobehavioral dispositions can serve as valuable referents for biologically oriented research on core processes with relevance to many psychiatric conditions. The present study examined two such dispositional variables—weak response inhibition (or disinhibition; INH[−]) and threat sensitivity (or fearfulness; THT⁺)—as predictors of the serious transdiagnostic problem of suicide risk in two samples: male and female outpatients from a U.S. clinic ($N=1078$), and a population-based male military cohort from Finland ($N=3855$). INH[−] and THT⁺ were operationalized through scores on scale measures of disinhibition and fear/fearlessness, known to be related to DSM-defined clinical conditions and brain biomarkers. Suicide risk was assessed by clinician ratings (clinic sample) and questionnaires (both samples). Across samples and alternative suicide indices, INH[−] and THT⁺ each contributed uniquely to prediction of suicide risk—beyond internalizing and externalizing problems in the case of the clinic sample where diagnostic data were available. Further, in both samples, INH[−] and THT⁺ interactively predicted suicide risk, with individuals scoring concurrently high on both dispositions exhibiting markedly augmented risk. Findings demonstrate that dispositional constructs of INH[−] and THT⁺ are predictive of suicide risk, and hold potential as referents for biological research on suicidal behavior.

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1. Introduction

Suicide is a socially devastating problem that calls for ongoing systematic investigation. In light of compelling evidence for heritable individual difference factors in suicidal behavior, research is needed to clarify how biobehavioral tendencies contribute to the emergence of distinct suicide-promoting processes (Van Orden et al., 2010). The current work addresses this need by demonstrating separate as well as interactive contributions of the biobehavioral constructs of weak inhibitory control and threat sensitivity, operationalized as externalizing proneness (disinhibition) and fear/fearlessness, to prediction of suicidal tendencies.

Although rare, lethal acts of self-harm have antecedents—in the form of ideation, planning, and attempts—that are far more common (Kessler et al., 1999). Thus, suicide risk can be conceptualized as a behavioral continuum ranging in severity from thoughts about death (e.g., “I wish this all would just end” or “I wish I was dead”) through contemplation of self-harm to planning and preparation to attempts. The importance of dispositional vulnerabilities in suicide risk is highlighted by family, twin, and adoption studies demonstrating heritability for suicidal behavior. When broadly defined to include suicidal ideation, plans, and attempts, heritability estimates range from 30% to 50% (Brezo et al., 2008). Notably, heritability estimates vary depending on the aspect of suicidality that is measured, with estimates for death by suicide consistently higher than those for ideation or non-fatal attempts (Brezo et al., 2008).

Evidence for a role of weak inhibitory control in suicidal behavior comes from research on impulsive-aggressive traits,

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which show robust predictive relations with suicidal ideation and behavior (Turecki, 2005) and have been characterized as a candidate endophenotype for suicide (Mann et al., 2009; Courtet et al., 2011). Evidence for a role of threat sensitivity in suicidality comes from research demonstrating positive relations of negative emotional tendencies with suicidal tendencies and clinical conditions associated with suicide (e.g., depressive and anxiety-related disorders; Brandes and Bienvenu, 2006). Negative emotional reactivity represents a pre-morbid vulnerability factor for depression (Kendler et al., 2003) and suicide (Khan et al., 2005), and constitutes the key dispositional variable linking internalizing disorders with suicidality. Notably, a diagnostic condition with high rates of suicidal behavior, borderline personality disorder (Sansone, 2004), reflects the conjunction of impulsive-aggressive tendencies and high negative affectivity. Older and newer studies point to reduced levels of the brain neurotransmitter serotonin as related to increased levels of both impulsivity and negative affectivity (Minzenberg and Siever, 2006; Seo et al., 2008), and in turn borderline personality tendencies (Gurvits et al., 2000) and risk for suicide (Joiner et al., 2005).

To further clarify the biological bases of suicide risk, it will be important to focus research attention on dispositional constructs akin to impulsivity and negative affectivity that connect more clearly to distinct neurobiological systems and can be related to core-suicide promoting processes (Van Orden et al., 2010). The National Institute of Mental Health's Research Domain Criteria (RDoC; Sanislow et al., 2010) framework provides an expert-consensus based listing of biobehavioral constructs to serve as targets for psychopathology research. Two such constructs are response inhibition, presumed to reflect variations in the functionality of executive control circuitry, and acute threat ("fear"), theorized to reflect variations in sensitivity of the brain's defensive system. In trait-dispositional terms, these constructs correspond to inhibitory control capacity and threat sensitivity.

The current work evaluated whether dispositional tendencies toward weak inhibitory control (INH−) and high threat sensitivity (THT+) would predict suicide risk in two large participant samples: (1) clinic outpatients from the U.S., and (2) young men reporting for military call-up in Finland. INH− was assessed using scale measures of trait disinhibition, or externalizing proneness, defined as the general propensity toward problems of impulse control (e.g., antisocial and substance use disorders; Krueger et al., 2007). In terms of biobehavioral correlates, disinhibition defined in this way predicts deficits in brain response to task stimuli in visual-motor paradigms (Yancey et al., 2013) and impaired behavioral performance on cognitive control tasks (Young et al., 2009). THT+ was assessed using scale measures of dispositional fear/fearlessness (or boldness; Patrick et al., 2012), defined in terms of reported fear in relation to specific stimuli, events, and contexts (Kramer et al., 2012). Scores on fear/fearlessness defined in this way are uncorrelated with disinhibitory-externalizing tendencies (Patrick et al., 2012), and show robust associations with DSM-defined phobic disorders and symptoms (Nelson et al., in press; Sellbom et al., 2012) and physiological defensive reactivity as indexed by aversive startle potentiation (Kramer et al., 2012; Vaidyanathan et al., 2012).

Operating from a process-oriented theory of suicidal behavior (Van Orden et al., 2010), which emphasizes a role for persisting negative affect in suicidal thoughts/desire and a role for impulsive risk-taking in the capacity for active self-harm, we hypothesized that weak inhibitory control (operationalized as disinhibition) and high threat sensitivity (operationalized as fear/fearlessness) would each contribute uniquely to increased suicide risk. In addition, we postulated that the co-occurrence of these two distinct suicide-promoting dispositions would exert a synergistic (i.e., interactive) effect on suicide-proneness. This hypothesis was based on the

markedly elevated rates of suicidality in borderline personality disorder, which entails elevations in both disinhibition and dispositional fear (Patrick et al., 2012), and evidence indicating that the co-occurrence of impulsivity and negative affectivity reflects a distinct neurobiological condition—entailing reduced serotonergic activity—that relates to high suicide risk.

2. Methods

2.1. Participants

2.1.1. Outpatient clinic sample

Outpatient participants were 1078 men and women who underwent psychological evaluations at a university psychology clinic from 2000 to 2010. The clinic serves both students and community residents presenting with clinical problems typical of a community mental health outpatient clinic. The mean age of the sample was 26.7 (S.D.=9.7); 55.2% were female. Most (77.6%) participants were treatment-seeking, with the remainder seen for psychological assessment only.

Patients provided informed written consent to participate and underwent an intake screening procedure assessing for psychological problems including suicide risk (Joiner et al., 1999) and psychopathology. Upon admission, patients were assigned to an individual therapist and underwent a diagnostic assessment that included a structured clinical interview assessing for DSM-IV disorders. Study procedures were approved by Florida State University's Review Board.

2.1.2. Finnish Army recruit sample

This sample consisted of adult men (born mainly in 1991) reporting for call-up to the Finnish military between September and November, 2009. The military call-up is a standard procedure for assessing suitability for military service that all Finnish male citizens undergo at age 18. To ensure a random population-representative sample of this designated age cohort, participants were selected across geographical areas of Finland, with emphasis on the most densely populated southern parts. The target sample included 4910 men attending the military call-up in these four military call-up districts. Altogether, 4324 men (88.1%) returned the questionnaires administered for the study.

At call-up, participants were given the option of completing a set of questionnaires. Participants were advised that this assessment was separate from the military call-up evaluation and was being conducted on a voluntary, research basis. To ensure anonymity, questionnaire responses were coded by number and returned in sealed envelopes. The questionnaire packet included a consent form that participants read and signed prior to completing measures. Data were obtained from 4309 males mainly aged 18 years; 454 (10.5%) of these did not to complete all questionnaire measures needed for current analyses, leading to a final sample size of 3855. The study was approved by the ethical committees of Turku University and Turku University Hospital, and authorized by the Finnish Defense Forces.

2.2. Measures

2.2.1. Weak inhibitory control and threat sensitivity

2.2.1.1. Minnesota Multiphasic Personality Inventory -2- Restructured Form (MMPI-2-RF).

The clinic sample completed the MMPI-2-RF, a 338 item global measure of personality and psychopathology with well-documented psychometric properties (Ben-Porath and Tellegen, 2008). Analyses focused on a subset of MMPI-2-RF Clinical and Specific Problems scales developed to index dispositional factors of impulsive-antisociality and fearless-dominance (Sellbom et al., 2012), corresponding to weak inhibitory control (INH−) and low versus high threat sensitivity (THT+) reversed; the validity of these factors as indicators of dispositional INH− and THT+ has been established in relation to various criterion measures (Sellbom et al., 2012). INH− was scored as a composite with strongest weightings for the Antisocial Behaviors and Hypomanic Activation clinical scales, and (with lesser weighting) Low Positive Emotionality. THT+ was scored as a composite with strongest weightings for the following scales: Multiple Specific Fears, Social Avoidance, Shyness, and Dysfunctional Negative Emotionality—coded such that higher scores reflected fearful-submissive tendencies.

2.2.1.2. Triarchic Psychopathy Measure (TriPM; Patrick, 2010).

The Finnish soldier sample was administered the TriPM, a 58-item measure that assesses for presence versus absence of inhibitory control (disinhibition), fear/fearlessness (boldness), and callous-aggressive tendencies (meanness). Current study analyses focused on two subscales: (1) Disinhibition (corresponding to INH−; 20 items), comprising items from the Externalizing Spectrum Inventory (Krueger et al., 2007; Venables and Patrick, 2012) that index tendencies toward impulsivity and unreliable behaviors; and (2) Boldness (19 items), which indexes low versus high fearfulness (cf. Kramer et al., 2012) in areas of social efficacy, affective experience (immunity versus susceptibility to stressors), and venturesomeness (preference versus avoidance of risk). The Boldness scale was reverse-coded to make higher scores indicative of

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