Article:
O'Connor, DB orcid.org/0000-0003-4117-4093, Branley-Bell, D, Green, JA et al. (3 more authors) (2021) Resilience and vulnerability factors influence the cortisol awakening response in individuals vulnerable to suicide. Journal of Psychiatric Research, 142. pp. 312-320. ISSN 0022-3956

https://doi.org/10.1016/j.jpsychires.2021.08.006

Resilience and Vulnerability Factors Influence the Cortisol Awakening Response in Individuals Vulnerable to Suicide

Accepted

Journal of Psychiatric Research

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Running head: Resilience and vulnerability, cortisol and suicide

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ABSTRACT

Suicide is a global health issue. Dysregulated hypothalamic-pituitary-adrenal (HPA) axis activity, as measured by cortisol levels, has been identified as one potential risk factor. Evidence is emerging to suggest that different psychological factors may be associated with increased resilience and vulnerability in this context. The current study investigated whether trait resilience, social support, socially prescribed perfectionism, trait worry and trait impulsivity influenced the cortisol awakening response (CAR) over a 7-day study in individuals vulnerable to suicide. 142 participants with a history of suicidal attempt or ideation (suicide vulnerability group; n = 95) and with no suicide risk history (control group; n = 47) were recruited. Participants completed baseline questionnaires before commencing a 7-day study where they provided cortisol samples immediately upon waking, at 15 mins, 30 mins and 45 mins on 7 consecutive days. Higher worry, socially prescribed perfectionism and impulsivity, lower resilience and social support were found in the suicide vulnerability group compared to the control group. Lower levels of resilience, higher levels of socially prescribed perfectionism, worry and impulsivity were associated with significantly lower total CAR. Suicide group membership was also found to have an indirect effect on total CAR via trait worry. The current findings show for the first time, that these well-known psychological risk factors for suicide are associated with smaller total cortisol awakening responses. Researchers ought to elucidate the precise causal mechanisms linking these traits, CAR and suicide risk in order to develop interventions to help build resilience in vulnerable populations.

Keywords: resilience, perfectionism, impulsivity, worry, stress, allostatic load, cortisol awakening response

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INTRODUCTION

Suicide is a major global health issue (WHO, 2014). Close to 800,000 people die by suicide each year worldwide and there are 25 million nonfatal suicide attempts annually (Centers for Disease Control and Prevention [CDC], 2016; WHO, 2019). As a consequence, understanding, predicting and preventing suicide has been the focus of enormous scientific effort (O'Connor & Nock, 2014; van Heeringen & Mann, 2014). A myriad of psychological, social, psychiatric and neurobiological factors have been found to be associated with suicide risk and vulnerability (O'Connor & Kirtley, 2018; O'Connor & Nock, 2014; van Heeringen & Mann, 2014; van Orden et al., 2010). One avenue of recent investigation has focussed attention on the role of the hypothalamic-pituitary-adrenal (HPA) axis and the stress response system (Giletta et al., 2015; Melhem et al., 2016; 2017; McGirr et al., 2010; O'Connor et al., 2016; 2017; 2020a). Specifically, researchers have begun to explore HPA axis functioning following acute laboratory stressors in vulnerable and non-vulnerable groups, as well as recently the relationships between naturally fluctuating cortisol levels and suicide behavior (e.g., Giletta et al., 2015; Melhem et al., 2016, O'Connor et al., 2017; 2020a).

The key aim of the laboratory-based stress studies has been to examine whether cortisol reactivity to stress can differentiate individuals who have a history of suicide attempt or ideation compared to individuals who have no such history (e.g., McGirr et al., 2010; Melhem et al., 2016; O'Connor et al., 2017). For example, McGirr et al. (2010) showed that a sample of first-degree relatives of individuals who had died by suicide exhibited a blunted (i.e., lower) cortisol response to stress compared to matched controls. Two more recent laboratory-based cortisol studies have also found evidence of blunted HPA axis activity in individuals with a history of suicide compared to controls (Melhem et al., 2016; O'Connor et al., 2017). Taken together the evidence is converging to indicate that the HPA axis, as indexed by cortisol reactivity to stress, is dysregulated in individuals vulnerable to suicide. Surprisingly, only limited research has examined relations between suicide risk and other components of HPA function, such as the cortisol awakening response (CAR). The CAR is

defined as the rapid increase in cortisol levels following morning awakening (Clow et al., 2010) and has been found to be influenced by chronic stress, trauma and a range of other negative psychosocial variables – all factors frequently implicated in increased suicide risk (Boggero et al., 2017; Chida & Steptoe, 2009; Clow et al., 2010; Gartland et al., 2014; O'Connor et al., 2013; O'Connor, Thayer & Vedhara, 2021).

One study that has investigated the association between suicide vulnerability and the CAR (as well as the diurnal cortisol slope) is a recent study by O'Connor et al. (2020a). The results showed that participants who had a history of suicide attempt or ideation had a significantly lower total CAR compared to control participants over 7 days. This study also found that childhood trauma was significantly associated with lower total CAR. The authors argue that these findings suggest that the experience of childhood trauma may predispose individuals to vulnerability to suicide in adulthood by leading to diminished HPA axis activity during awakening and during stress. A considerable body of research has accumulated to suggest that repeated activation of the HPA axis leads to dysregulation (Miller et al., 2007; McEwen, 1998; O'Connor et al., 2021). This is known as allostatic load (McEwen, 1998), whereby, if the HPA axis is repeatedly activated (e.g., by chronic stress or exposure to childhood trauma), the immune, cardiovascular and endocrine systems are potentially exposed to excessive demands that over time can lead to dysregulation of these systems (Miller et al., 2007; McEwen, 1998; O'Connor et al., 2021).

In the broader suicide literature, leading models such as the Integrated Motivational-Volitional Model (IMV; Branley-Bell et al., 2019; O'Connor, 2011; O'Connor and Kirtley, 2018) of suicidal behavior have identified numerous other psychological vulnerability factors (e.g., trait perfectionism, trait impulsivity, social support). For example, it is well established that levels of socially prescribed perfectionism – holding excessive beliefs and expectations that significant others have high standards for you – are often significantly higher in individuals who have previously attempted to end their own lives (Smith et al., 2018; O'Connor, 2007). Similarly, trait impulsivity has been found to be an important variable in helping to explain why some individuals are more likely to act on their suicidal thoughts and attempt suicide than other individuals (O'Connor & Nock, 2016). The absence of social support (i.e., social isolation) has also been implicated in numerous models and

studies of suicidal behaviour (e.g., Haw and Hawton, 2011; O'Connor and Kirtley, 2018). However, how these more established *vulnerability* factors may be associated with HPA axis dysregulation, in particular the CAR, together with identifying resilience factors that may help protect against dysregulation, remains under researched.

The IMV model (O'Connor, 2011; O'Connor and Kirtley, 2018) of suicidal behavior provides a theoretical basis for examining the factors associated with the development of suicidal ideation and the transition from ideation to suicide attempts. It integrates predominant factors from existing psychosocial models including Williams' arrested flight model (Williams and Williams, 2001), the diathesis-stress hypothesis (Schotte and Clum, 1987), and the theory of planned behavior (Ajzen, 1991). The IMV model conceptualises suicide as a behavior that results from a complex interplay of factors; and provides a detailed map of the pathway from ideation to behavior, through defeat and entrapment (Branley-Bell et al., 2019). The diathesis-stress component of the IMV model recognizes that individual vulnerabilities confer elevated risk for developing suicidal ideation when activated by the presence of stressors. Examples of these vulnerabilities are personality characteristics, such as high socially prescribed perfectionism and socio-economic deprivation (O'Connor & Nock, 2014).

The IMV model proposes that the central predictor of a suicide attempt is an individual's intention to engage in suicidal behavior. Feelings of defeat/humiliation trigger feelings of entrapment, which in turn predicts intention (i.e., ideation) as an escape from intense psychological distress. Throughout this process, there are stage-specific moderators that facilitate or prevent progress to the next stage, with threat-to-self moderators (e.g., trait worry, rumination processes) and motivational moderators (e.g. trait resilience, social support) predicting ideation, and volitional moderators (e.g., trait impulsivity) governing enactment. As outlined earlier, relatively few, if any studies have explored the relationship between these key established vulnerability and resilience factors, and HPA axis functioning in naturalistic settings or have investigated in the same study whether this range of factors are different in suicide vulnerable individuals.

Using data from the recent O'Connor et al. (2020a) study that included individuals with a suicide risk history (suicide vulnerability group) alongside individuals with no suicide risk history (control group), the current investigation aimed:

1. To test whether resilience factors' scores (trait resilience and social support) were lower and vulnerability factors' scores (trait worry, socially prescribed perfectionism, trait impulsivity) higher in individuals vulnerable to suicide compared to controls.
2. To examine the effects of resilience and vulnerability factors on the cortisol awakening response in individuals vulnerable to suicide.
3. To test whether there were indirect effects of suicide vulnerability group membership on cortisol awakening response via the resilience and vulnerability factors.

METHODS

Design and Participants

One hundred and fifty-four participants were recruited to a suicide attempt (n=53), a suicidal ideation but no attempt (n=52) and a control group (n=49) based upon responses given in the Self-Injurious Thoughts and Behaviors Interview (SITBI; Nock et al., 2007) and the Beck Scale for Suicide Ideation (Beck et al., 1988). Following screening of the cortisol data, 12 participants' data were unable to be included (see Treatment of cortisol data, in supplementary materials). The statistical analysis was conducted on 142 participants (control group = 47, ideation group = 46, attempt group = 49; see Table 1 for baseline characteristics and demographics and Table 2 for descriptive statistics for the main study variables). Participants were aged between 18-63 years of age (M = 27.74 years, SD = 9.27 years) and 73.4% identified as Caucasian. The sample consisted of 105 (68.1%) females, 49 (31.9%) males. Consistent with O'Connor et al. (2020a), participants were categorised into a suicide vulnerability group (the attempt and the ideation groups combined) and a non-suicide vulnerability group (control group). Combining the groups allowed us to analyse the data from the entire sample and ensured we captured a good range of scores on the resilience and vulnerability measures. Moreover, preliminary analyses showed that the attempt and ideation groups did not differ in terms of total CAR ($p=0.37$) but differed from the control group (ps <0.01). Participants were recruited to the

study in response to a local advertising campaign on websites (e.g., Gumtree, Twitter), via posters, flyers and emails. As outlined in O'Connor et al. (2020a), the current study was not planned using a conventional power analysis. Instead it was designed to ensure good reliability of the main cortisol measures, in particular, the CAR. It has been recommended that when assessing the CAR to sample each individual on at least 6 days (e.g., Stalder et al., 2016). Therefore, informed by our previous work (n=64 sampled over 4 days; Gartland et al., 2014) and based on our experience of recruiting vulnerable populations (such as individuals at risk of suicide), as well as by statistical considerations for detecting cross-level interactions in multi-level models (Snijders & Bosker, 1999), a sample size of 150-154 participants were recruited to the current study.

Eligible participants were required to be at least 18 years old and to understand English. Participants were allocated to the suicide vulnerability group if they reported attempting to take their own life in the past (lifetime) or if they reported having thoughts of ending their life in the past 12 months. Participants were recruited to a control group if they reported no lifetime history of suicide attempt or ideation (and did not report any current psychiatric or psychological conditions). Participants were excluded from the study if they were taking steroid-based medication, antibiotics or anti-inflammatories, were pregnant (or had recently been pregnant) or had used recreational drugs in the last month or if they had a neuroendocrine or chronic pain condition. Six participants reported using prescribed medications in the control group (e.g., hormonal contraceptives) and 17 and 22 participants in the ideation and attempt groups, respectively (e.g., antidepressants). In the attempt group, 14 participants reported an attempt within the previous 12 months and 35 participants reported an attempt more than 12 months ago. The current study was approved by the Research Ethics Committee of the School of Psychology, University of Leeds and the US Department of Defense Human Research Protections Office. Participants received £40 for completing both laboratory visits (£30 for the first visit, and £10 for the second visit). Given the vulnerable nature of some of the participants and sensitive aspects of the study, all participants were provided with a list of relevant online, telephone and in-person support resources and were reminded to contact their general practitioner (or the emergency services) if they felt at risk at any stage. If any participant presented to the research team as being at immediate risk, with their consent, we would contact their general

practitioner, emergency services and/or their next of kin (as appropriate). Participants could withdraw from the study at any time.

Questionnaire measures

Resilience factors

Trait resilience: The Brief Resilience Scale (Smith et al., 2008) was used to measure the ability to bounce back or recover from stress. This is a 10-item measure with each item answered on a scale of 0 (not true at all) to 4 (true nearly all of the time), and summed to give an overall score. Items included "Able to adapt to change" and "Can stay focussed under pressure". The Cronbach's alpha in the current sample was 0.89.

Social Support: The ENRICHD Social Support Inventory (ESSI; Mitchell et al., 2003) was used to measure social support. The ESSI is a 7-item measure that assesses the main attributes of social support: emotional, instrumental, informational, and appraisal. It is scored from 1 (none of the time) to 5 (all of the time), and then summed to produce an overall score. Items included "Is there someone available to you whom you can count on to listen to you when you need to talk?" and "Is there someone available to give you good advice about a problem?" The Cronbach's alpha in the current sample was 0.88.

Vulnerability factors

Trait worry: The Penn State Worry Questionnaire (PSWQ; Meyer, Miller, Metzger and Borkovec, 1990) was used to assess trait worry. The PSWQ is a 16 item self-report instrument which assesses trait tendency to worry and have perseverative cognitions. Items are directed at measuring the excessiveness, duration and uncontrollability of worry (e.g., "My worries overwhelm me", "As soon as I finish one task, I start to worry about everything else I have to do"). The Cronbach's alpha in the current sample was 0.94.

Socially prescribed perfectionism: The socially prescribed perfectionism sub-scale from the Multidimensional Perfectionism Scale (MPS; Hewitt and Flett, 1991) was used. This subscale has 15-items scored from 1 (disagree) to 7 (agree). Items included "I find it difficult to meet others'

expectations of me", "I feel that people are too demanding of me". The MPS is a widely used measure to assess the multidimensional aspects of perfectionism, however, in order to reduce participant burden and because we were particularly interested in socially prescribed perfectionism, only this subscale was administered. This approach has been used in numerous previous studies and it has been found to be reliable and valid (e.g., Branley-Bell et al., 2019; Dhingra et al., 2015). The Cronbach's alpha in the current sample was 0.90.

Trait impulsivity: The Barrett Impulsiveness Scale (BIS, Patton, Stanford and Barratt, 1995) was used to measure impulsivity. The scale consists of 30 items measured on a 4-point scale from "Rarely/Never" to "Almost Always/Always". Items included "I do things without thinking." and "I act on the spur of the moment." High scores equate to higher levels of impulsivity. The Cronbach's alpha in the current sample was .86.

Cortisol measurements

Cortisol samples were collected from saliva using Salivettes (Sarstedt, UK) 8 times a day for 7 days (56 samples per participant), however, the current analyses have focussed only on the samples taken immediately upon waking (when still in bed), +15 mins after waking, +30 mins, and +45 mins. The treatment of the cortisol data has been described in detail in O'Connor et al. (2020a, p. 97), therefore, a fuller description is provided in the supplementary materials.

Cortisol awakening response (CAR). The total daily cortisol concentrations post-awakening (total CAR) were calculated using the Area Under the Curve with respect to ground (AUC_G) for the saliva samples collected immediately upon waking (0), at 15, 30 and 45 min following established procedures (Gartland et al., 2014; Pruessner et al., 2003). The CAR can be operationalised in a number of different ways (e.g., as Area Under the Curve with respect to increase (AUCi)). We elected to use this measure because it has been employed in comparable studies investigating the effects of chronic stress and cortisol (e.g., Chida & Steptoe, 2009) and we wanted to focus on a single measure of cortisol awakening to reduce the number of statistical tests performed relating to our primary outcome.

Procedure

On arrival at the university, each participant provided written consent and completed the Self-Injurious Thoughts & Behaviors Interview (SITBI) with the researcher. Following the SITBI and risk assessment, participants completed a questionnaire pack that included demographic questions and a range of psychological measures. When in the laboratory, participants were instructed how to take cortisol salivary samples (and given a study procedure booklet to take home) and provided with the kit containing everything they would need to take the required samples over the following 7 days. In order to improve adherence to the cortisol sampling protocol and the accuracy of the assessment of the cortisol awakening response, participants also received an accelerometer (GeneActiv) device to wear on the wrist (of their non-dominant hand) at all times for the following week. In particular, participants were aware that the research team were monitoring their wake and sleep times using the GeneActiv device.

Starting the following day, for 7 consecutive days, participants completed a paper diary to record when each cortisol sample was due and the time the sample was taken (amongst other daily measures not relevant to the current study). On their second visit to the laboratory (i.e., a mutually convenient time soon after day 7), participants returned their cortisol samples, accelerometer and their saliva sampling diary and were then debriefed by the researcher.

Data analysis

The analysis was conducted in three blocks. First, Multivariate Analysis of Variance (MANOVA) was used to investigate whether there was a main effect of suicide vulnerability group on resilience (trait resilience and social support) and vulnerability (trait worry, socially prescribed perfectionism, trait impulsivity) factor scores. Next Pearson's Product Moment correlations were used to explore the associations between the resilience and vulnerability factors in the entire sample.

In the second block, multi-level modelling using HLM 7 (Raudenbush et al., 2011) was utilised to test the effects of resilience and vulnerability factors on the total CAR levels over the 7 day study. These data were considered to have a two-level hierarchical structure, Level 1 being the within-person variation (e.g., Total CAR) and Level 2 being the between-person variability (e.g., trait resilience, socially prescribed perfectionism, trait impulsivity, suicide vulnerability group). Note that

suicide vulnerability group was entered into the models alongside each separate vulnerability/resilience factor in order to test whether any observed effects where independent of group status. In analyses involving cortisol, it is conventional to control for age, gender, body mass index (BMI), medication usage (i.e., reported using prescribed medication or not) and smoking status. These variables were treated as covariates and entered into all of the HLM models. To ensure transparency about the inclusion of covariates, it has been recommended to report statistical results without and with covariates (see Simmons, Nelson and Simonsohn, 2011). Therefore, in order to strengthen the robustness of the current results, we present the main models first without any covariates and then with the covariates. The Level 2 dichotomous variables (e.g., gender, medication usage, smoking status, suicide vulnerability group) were uncentered and Level 2 continuous variables were grand mean centered (e.g., trait resilience, socially prescribed perfectionism, age, BMI). Note that the results of preliminary analyses showed that psychiatric diagnosis was not associated with any of the main study outcomes and it did not account for any of the observed effects.

The general form of the cross-level (main effect) HLM model for total CAR with trait resilience entered as the vulnerability factor, controlling for covariates, is expressed by the following equation:

$$\text{Total CAR} = \beta_{00} + \beta_{01}\,(\text{age}) + \beta_{02}\,(\text{gender}) + \beta_{03}\,(\text{BMI}) + \beta_{04}\,(\text{medication}) + \beta_{05}\,(\text{Smoking}) + \beta_{06}\,(\text{suicide vulnerability group}) + \beta_{06}\,(\text{trait resilience})\; r_0 + \varepsilon$$

Multilevel mediation analysis using MPlus Version 8 (Muthén & Muthén, 1998–2017) was performed to test whether the effects of suicide vulnerability group on total CAR were mediated by the trait resilience and vulnerability factors. The same control variables were also entered into the MPlus models.

RESULTS

Descriptive statistics for the main study variables are presented in Table 2. The mean levels of cortisol throughout the day were within acceptable normal ranges (Aardal and Holm, 1995; O'Connor

et al., 2009) and the mean daily cortisol levels were higher in the non-suicide vulnerable group compared to the suicide vulnerable group in the morning.

In terms of resilience and vulnerability factors, individuals in the suicide vulnerability group scored significantly lower on trait resilience and social support but higher on trait worry, socially prescribed perfectionism and trait impulsivity compared to individuals in the non-vulnerability group, $F(5, 148)=13.04$, $p < 0.001$.

Associations between resilience and vulnerability factors

Preliminary Pearson's correlations showed that the resilience and vulnerability factors were modestly associated with each other and the range extended from $r = 0.319$ (between trait resilience and social support) to $r = -0.530$ (between trait resilience and trait worry) (see Supplementary materials Table 1). With one exception, all correlation coefficients were less than $r = 0.36$ indicating little or no evidence of multicollinearity and suggesting good divergence between the constructs.

Initial model: Effects of suicide vulnerability group on cortisol awakening response levels over 7 days

An initial HLM model was run with only suicide vulnerability group entered as the single predictor of total CAR levels. The results showed that there was a significant main effect of vulnerability group on total CAR levels in the unadjusted ($\beta = -0.269$, $p<.001$) and adjusted model ($\beta = -0.283$, $p=0.002$) confirming that individuals in the suicide vulnerability group exhibited lower CAR levels compared to individuals in the control group.

Effects of resilience and vulnerability factors on cortisol awakening response levels over 7 days

Next the HLM models were run separately for each of the vulnerability/resilience factors and the findings for each model are presented in Table 3. The results showed there was a main effect of trait resilience on total CAR levels in the unadjusted ($\beta = 0.146$, $p=0.015$) and adjusted model ($\beta = 0.121$, $p=0.038$), indicating that individuals with lower trait resilience exhibited smaller cortisol awakening responses (Figure 1, upper panel). The second resilience factor, social support, was not significantly associated with total CAR in the unadjusted model ($\beta = -0.006$ $p=0.379$) or adjusted

model (β =-0.003 p=0.657). As predicted, there was a main effect of trait worry on total CAR levels in the unadjusted (β = -0.009, p=0.003) and adjusted model (β = -0.008, p=0.012), indicating that individuals with higher trait worry exhibited smaller cortisol awakening responses (Figure 1, lower panel). Next the main effect of socially prescribed perfectionism was examined and it was found to be significantly negatively associated with total CAR levels in the unadjusted (β = -0.005, p=0.023) and adjusted model (β = -0.004, p=0.035), indicating that individuals with higher socially prescribed perfectionism had smaller cortisol awakening responses (Figure 2, upper panel). Finally, the analysis found there was a significant main effect of trait impulsivity on total CAR levels in the unadjusted (β = -0.009, p=0.010) and adjusted model (β = -0.007, p=0.044) indicating that individuals with higher trait impulsivity scores had smaller cortisol awakening responses (Figure 2, lower panel).

Indirect effects of suicide vulnerability group membership on total CAR via trait resilience and vulnerability factors

Finally, using multilevel mediation analysis, we investigated whether the effects of suicide vulnerability group membership on total CAR was mediated via the trait resilience and vulnerability factors. In these analyses, suicide vulnerability group (at Level 2) and total CAR (at Level 1) were the X and Y variables, respectively, and each of the trait resilience and vulnerability factors (at Level 2) acted as the mediators (M variables) in separate analyses. The analysis showed that there was an indirect effect of suicide vulnerability group on total CAR levels through trait worry (estimate = -0.056, p =.035; see Figure 3). There were also direct effects of suicide vulnerability group (estimate = -0.232, p = .006) and trait worry (estimate = -0.008, p = .009) on total CAR levels, respectively. No other significant indirect effects were found.

DISCUSSION

There is a converging body of evidence demonstrating that dysregulation of the HPA axis is associated with suicidal behavior (Melhem et al., 2016; 2017; O'Connor et al, 2020b). There is also recent evidence, from O'Connor et al. (2020a), showing that suicide vulnerability is associated with a significantly lower total CAR. In this context, the major challenge for researchers has been to

understand the factors that may contribute to, and protect against, HPA axis dysfunction. In the current investigation, we identified for the first time in a 7 day study, a number of key vulnerability and resilience factors that are associated with one important aspect of HPA axis function. Specifically, we found that lower levels of trait resilience and higher levels of socially prescribed perfectionism, trait worry and impulsivity were significantly associated with lower total CAR. In addition, we also found that the effects of suicide vulnerability group on total CAR were mediated through trait worry.

These findings are important as they show that a range of established suicide vulnerability and resilience factors may not only increase risk of suicide behaviour by influencing the pathway from ideation to behavior, through defeat and entrapment, as per the IMV model, but also by influencing HPA axis activity. As outlined earlier, the IMV model proposes that trait worry (a threat-to-self moderator), trait resilience (a motivational moderator) and trait impulsivity (a volitional moderator) play key roles in facilitating or preventing progress from suicide ideation to action while recognising socially prescribed perfectionism as a background trait that confers elevated risk for developing suicidal ideation when activated by the presence of stressors. However, the current results suggest that these traits may also influence suicide vulnerability by contributing to the development dysregulation of the HPA axis. An important next step is to understand how HPA axis dysregulation can contribute to suicide vulnerability. One potential mechanism may be that diminished HPA axis functioning is associated with impaired executive functioning. For example, McGirr et al. (2010) showed that a sample of first-degree relatives of those who died by suicide exhibited a blunted cortisol response to stress and they also displayed evidence of impairment in aspects of executive function. Another recent study has shown that a smaller CAR is associated with increased stress-related brain activity in the perigenual anterior cingulate cortex – an area of the brain that is linked with the pathophysiology of environment risk (e.g., childhood trauma) and stress-related mental illnesses (Boehringer et al., 2015). Future research ought to attempt to establish the mechanisms of action that link HPA axis activity to increased suicide risk.

Our finding that higher levels of trait resilience were associated with a lower total CAR is noteworthy as a great deal of previous resilience research has focussed explicitly on mental health outcomes (Hu, Zhang & Wang, 2015). For example, a meta-analysis of 60 studies found that trait resilience appears to be predictive of mental health, with low trait resilience associated with negative indicators of mental health and high trait resilience associated with positive indicators of mental health (Hu, Zhang & Wang, 2015). Some evidence suggests a buffering effect of resilience on suicidal ideation in military personnel (Youssef et al., 2013), those who misuse alcohol and illegal drugs, and prisoners (Roy, Carli & Sarchiapone, 2011), but its effect on suicide attempts or deaths by suicide remains largely unknown. Moreover, there are few, if any studies that have investigated the relationship between trait resilience, CAR and suicide vulnerability and there is evidence emerging highlighting that understanding "psychological resilience" in the context of suicide is complex and it should be viewed as a multidimensional and not an unidimensional construct (e.g., Chmitorz et al., 2018; Harris et al., 2019). It remains important to ascertain which aspects of trait resilience help protect the HPA axis from dysregulation and whether these same components also impact on mental health outcomes.

A considerable amount of previous research has shown that high levels of socially prescribed perfectionism, trait impulsivity and trait worry are important in understanding and predicting suicidal behavior, and as outlined earlier, these variables are implicated in a number of dominant models of suicide behavior (e.g., the IMV model, see also O'Connor & Nock, 2014). For example, it is well established that socially prescribed perfectionism – holding excessive beliefs and expectations that significant others have high standards for you – plays a key role in the aetiology of suicidal behavior (Smith et al., 2018; O'Connor, 2007). Research suggests that the social dimensions of perfectionism increase suicide risk by promoting a sense of social disconnection (Roxborough et al., 2012). In particular, it has been suggested that perfectionistic beliefs can also interact with other factors (e.g., negative life events, adversity, and cognitions) to impede recovery from a suicidal episode or increase risk of further suicidal ideation and/or self-harm (e.g., O'Connor, 2007). It has also been suggested that the negative effects of socially prescribed perfectionism on suicide risk may be mediated via high levels of ruminative response tendencies (O'Connor, O'Connor & Marshall, 2007). Therefore, our

finding showing that high levels of socially prescribed perfectionism are associated with lower cortisol awakening responses is novel, but not surprising, as it is consistent with the broader literature.

We also found that higher levels of trait impulsivity were associated with lower total CAR. Impulsivity has been shown to be a candidate variable in understanding who may be at greater risk of acting on suicidal thoughts and attempting suicide (O'Connor & Nock, 2016). However, it is important to acknowledge that there has been debate about the extent to which suicides are always impulsive acts that have not been pre-planned (e.g., Smith et al., 2009). This debate notwithstanding, at the behavioral level, trait impulsivity is characterised by poor planning, premature responding without considering the consequences of one's actions, taking risks and an inability to delay gratification. Impulsivity tends to lead to the underestimation of potential consequences of one's actions and has been shown to be associated with suicide risk (Brezo, Paris, & Turecki, 2006; Gvion & Apter, 2011). Nevertheless, it is important for further work, using behavior/laboratory-based methods and self-report measures, to establish whether each of these components of trait impulsivity influences the CAR equally.

The findings of the current study also highlighted the importance of trait worry in the context of suicide risk – it was found to be associated with lower total CAR *and* to mediate the relationship between suicide vulnerability group membership and total CAR. The relationship between the related construct, rumination, has received a reasonable amount of empirical attention (Rogers & Joiner, 2017), with results showing that higher levels of rumination are associated with suicide ideation and attempt. However, surprisingly, less work has explored the role that trait worry plays in suicide vulnerability. The current findings show that trait worry can directly influence cortisol awakening responses but that it also plays a contributory role in explaining the relationship between suicide vulnerability group membership and lower total CAR group, such that, suicide vulnerability group has an indirect effect on smaller cortisol awakening responses through trait worry. Taken together, the novel contribution of these findings is that they show, for the first time, that these well-known psychological risk factors may also increase vulnerability to suicide by directly affecting aspects of HPA axis activity as well as by influencing cognitive and behavioral processes relating to suicide. An important next step would be to investigate the effectiveness of established psychological

interventions to help reduce worry, perfectionistic thinking and impulsivity while building resilience in vulnerable populations (e.g., Joyce et al., 2018; McCarrick et al., 2021)

The current study design does not allow us to elucidate the precise potential causal relationship between these four traits (resilience, socially prescribed perfectionism, worry & impulsivity) and lower total cortisol awakening responses. However, it is likely that stress-related mechanisms play a key causal role over time linking resilience, socially prescribed perfectionism, worry and impulsivity with diminished cortisol secretory activity. A recent meta-analysis found that stressful life events were associated with 37% higher odds of subsequently reporting suicidal ideation and behaviors combined (Howarth et al., 2020). Moreover, individuals who have lower levels of resilience and higher levels of socially prescribed perfectionism, worry and impulsivity are likely to encounter a greater number of stressors, to react more negatively, and be less well equipped to cope with stress (cf., Bolger and Zuckerman, 1995; Walker et al., 2011). Therefore, as outlined earlier, over time this excessive activation of the stress response system may cause the HPA axis to become less responsive leading to dysregulation and allostatic load (McEwen, 1998; 2000; Miller et al., 2007; O'Connor, Thayer & Vedhara, 2021). However, what is certain is that the exact mechanisms linking these trait variables remain unknown and there is a paucity of empirical studies that have explored the effects of trait resilience, socially prescribed perfectionism, worry and impulsivity on CAR and suicide. Researchers ought to attempt to replicate and build upon the current findings and remember that traits are not stable and they change as a function of life events and trauma, and so, future studies should assess traits at multiple time points using longitudinal panel designs over time (Ferguson & Lievens, 2017; Ferguson, Zhao & Smillie, 2020).

The relationship between age and total CAR was not a central focus of the current study; instead age was included as a covariate in the analyses. Nevertheless, it is worth noting that the results showed a positive relationship between age and total CAR indicating that larger cortisol awakening responses were observed in older participants. This is consistent with another sizable study of adults that also found a positive relationship in men but not in women (Almeida, Piazza, & Stawski, 2009). In contrast, a different study that included a broad age range found no relationship between age and CAR in men or women (Wust et al., 2000). There is also a growing body of research that has been

exploring the relationship between age, the CAR and aspects of cognition and executive functioning (e.g., Evans et al., 2012; Law et al., 2020). Future research ought to also consider how the CAR changes over the life course and explore how these changes may interact with changes in the suicide vulnerability and resilience factors investigated in the current study.

There are some limitations to the current study that require further comment. First, the sample size could be considered small compared to large scale, epidemiological studies of suicide. However, in terms of experimental research in this area, this sample size is relatively large and also includes all the strengths of adopting a within-participants, daily diary design (e.g., multiple observations, using each participant as their own control etc.). Second, we are fully aware that the current study did not include an objective test of participant adherence to the cortisol sampling protocol such as electronic (time stamped) containers for Salivettes. Unfortunately, these containers are costly and including them for every sample collected was prohibitively expensive given the large number of samples per participant (n=56). However, in order to address this issue, we included a number of methodological features that are likely to have substantially reduced protocol adherence problems (e.g., participants wore an accelerometer to record wake time, we explained that the experimenters could identify protocol non-adherence in the sampling, we ensured that participants kept diaries and received reminders). Third, participants were excluded from the study based upon self-reports (e.g., if they were currently taking steroid-based medication, antibiotics or anti-inflammatories etc.), therefore, we cannot be certain that all participants met our precise inclusion and exclusion criteria. Fourth, the current study did not collect data on whether participants in the suicide vulnerability group who may have had a psychological or psychiatric diagnosis were fully remitted or not at the time of study participation. Future studies ought to give due consideration to this issue when considering data collection. Fifth, the study only focussed on the socially prescribed perfectionism subscale from the Multidimensional Perfectionism Scale; therefore, further research might usefully consider measuring other dimensions of perfectionism (e.g., self-oriented perfectionism; other-oriented perfectionism).

In conclusion, the current findings show for the first time, that lower trait resilience, higher socially prescribed perfectionism, trait worry and trait impulsivity - well-known psychological risk

factors for suicide – are associated with smaller cortisol awakening responses. Suicide group membership was also found to have an indirect effect on total CAR via trait worry. Researchers ought to elucidate the precise causal mechanisms linking these traits, CAR and suicide risk in order to develop interventions to help build resilience in vulnerable populations.

Authors' contributions

All authors contributed equally

Acknowledgements

This research was supported in part by a research award from the US Department of Defense (Award No. W81XWH-12-1-0007). Opinions, interpretations, conclusions and recommendations are those of the authors and are not necessarily endorsed by the funder. The funder had no role in the writing of the manuscript.

Conflict of interest

None

Ethical standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

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Table 1. Baseline characteristics for participants in non-suicide and suicide vulnerable groups (n = 142)

Characteristic	Non-suicide vulnerable group (n=47)	Suicide vulnerable group (n=95)
Age (SD)	25.74 (6.8)	29.00 (10.28)
Sex (% female)	33 (70.2)	66 (69.5)
Current psychiatric/psychological diagnosis*		
Depression	0	24
Anxiety	0	11
Bipolar disorder	0	1
Post-traumatic stress disorder	0	2
Number of lifetime attempts+		1 attempt = 24 2 attempts = 8 3 attempts = 7 4 attempts = 2 ≥ 5 attempts = 8
Method in most recent attempt+		
Own prescription drugs		30
Illicit drugs (not rx)		1
Over-counter drugs		8
Firearm		1
Immolation		1
Hanging		4
Sharp object		1
Auto exhaust		1
Train/car		1
Drowning		1
Family history of suicide (%)	4 (8.5)	21 (22.1)
Prescribed medications (%)	6 (12.8)	39 (41.0)

* = Participants were asked to provide details of any current diagnosed medical conditions; physical and/or psychiatric/psychological; + = From Self-Injurious Thoughts and Behaviors Interview

Table 2. Descriptive statistics (means and standard deviations) for main study variables in non-suicide vulnerable and suicide vulnerability groups (n = 142)

	Non-suicide vulnerable group (n=47)		Suicide vulnerable group (n=95)	
	M	***SD***	***M***	***SD***
Within-persons (Level1) variables				
Cortisol variables				
Waking (00 min) (nmol/L)	8.35	3.84	7.34	3.76
15 min (nmol/L)	9.87	4.09	8.86	4.26
30 min (nmol/L)	11.46	4.62	9.83	4.61
45 min (nmol/L)	11.23	5.13	9.09	4.50
Total CAR (nmol/L)	31.12	10.63	26.90	11.15
Between-person (Level 2) variables				
Trait resilience	2.84	0.64	2.10	0.76
Social support	24.49	4.43	18.90	6.13
Trait worry	52.18	14.67	59.69	14.41
Social perfectionism	52.67	14.75	62.90	17.50
Trait impulsivity	31.78	8.86	39.87	13.11

Note: Total CAR = Total cortisol awakening response calculated using area under the curve with respect to ground; Social perfectionism = socially prescribed perfectionism

Table 3. Effects of resilience and vulnerability factors on total cortisol awakening response (Total CAR) across 7 days

	Unadjusted				*Adjusted for covariates*			
		Coeff	**SE**	***P* value**		**Coeff**	**SE**	***P* value**
Initial model								
Intercept	β_{00}	3.180	0.112	<0.001	β_{00}	3.174	0.184	<0.001
Vulnerability group	β_{01}	-0.269	0.076	<0.001	β_{01}	-0.283	0.088	0.002
Age	β_{02}	--	--	--	β_{03}	0.015	0.003	<0.001
Gender	β_{03}	--	--	--	β_{04}	0.029	0.101	0.770
BMI	β_{04}	--	--	--	β_{05}	-0.013	0.008	0.107
Medication status	β_{05}	--	--	--	β_{06}	0.054	0.087	0.499
Smoker status	β_{06}	--	--	--	β_{07}	-0.198	0.123	0.110
Intercept	β_{00}	2.987	0.174	<0.001	β_{00}	3.00	0.231	<0.001
Vulnerability group	β_{01}	-0.157	0.101	0.123	β_{01}	-0.194	0.102	0.060
Trait resilience	β_{02}	0.146	0.059	0.015	β_{02}	0.121	0.058	0.038
Age	β_{03}	--	--	--	β_{03}	0.014	0.004	0.002
Gender	β_{04}	--	--	--	β_{04}	0.038	0.088	0.665
BMI	β_{05}	--	--	--	β_{05}	-0.012	0.008	0.126
Medication status	β_{06}	--	--	--	β_{06}	0.063	0.092	0.494
Smoker status	β_{07}	--	--	--	β_{07}	-0.183	0.103	0.078
Intercept	β_{00}	3.247	0.171	<0.001	β_{00}	3.213	0.219	<0.001
Vulnerability group	β_{01}	-0.311	0.099	0.002	β_{01}	-0.303	0.100	0.003
Social support	β_{02}	-0.006	0.007	0.379	β_{02}	-0.003	0.007	0.657
Age	β_{03}	--	--	--	β_{03}	0.016	0.005	0.001
Gender	β_{04}	--	--	--	β_{04}	0.027	0.089	0.758
BMI	β_{05}	--	--	--	β_{05}	-0.013	0.008	0.111
Medication status	β_{06}	--	--	--	β_{06}	-0.037	0.093	0.689
Smoker status	β_{07}	--	--	--	β_{07}	-0.193	0.105	0.067
Intercept	β_{00}	3.090	0.117	<0.001	β_{00}	2.963	0.220	<0.001
Vulnerability group	β_{01}	-0.218	0.075	0.004	β_{01}	-0.228	0.085	0.008
Trait worry	β_{02}	-0.009	0.003	0.003	β_{02}	-0.008	0.003	0.012
Age	β_{03}	--	--	--	β_{03}	0.014	0.004	<0.001
Gender	β_{04}	--	--	--	β_{04}	0.095	0.113	0.402
BMI	β_{05}	--	--	--	β_{05}	-0.013	0.008	0.095
Medication status	β_{06}	--	--	--	β_{06}	0.075	0.088	0.397
Smoker Status	β_{07}	--	--	--	β_{07}	-0.201	0.118	0.092
Intercept	β_{00}	3.113	0.116	<0.001	β_{00}	3.080	0.196	<0.001
Vulnerability group	β_{01}	-0.231	0.076	0.003	β_{01}	-0.251	0.086	0.004
Social perfectionism	β_{02}	-0.005	0.002	0.023	β_{02}	-0.004	0.002	0.035
Age	β_{03}	--	--	--	β_{03}	0.016	0.004	<0.001
Gender	β_{04}	--	--	--	β_{04}	0.052	0.104	0.614
BMI	β_{05}	--	--	--	β_{05}	-0.012	0.008	0.153
Medication status	β_{06}	--	--	--	β_{06}	0.037	0.087	0.667
Smoking status	β_{07}	--	--	--	β_{07}	-0.179	0.119	0.136
Intercept	β_{00}	3.074	0.159	<0.001	β_{00}	3.074	0.111	<0.001
Vulnerability group	β_{01}	-0.209	0.092	0.025	β_{01}	-0.245	0.094	0.010
Trait impulsivity	β_{02}	-0.009	0.003	0.010	β_{02}	-0.007	0.003	0.044
Age	β_{03}	--	--	--	β_{03}	0.015	0.004	0.001
Gender	β_{04}	--	--	--	β_{04}	0.045	0.088	0.604
BMI	β_{05}	--	--	--	β_{05}	-0.009	0.008	0.228
Medication status	β_{06}	--	--	--	β_{06}	0.055	0.092	0.551
Smoker status	β_{07}	--	--	--	β_{07}	-0.159	0.104	0.129

Note: CAR is measured using area under the curve with respect to ground (AUCg), Social perfectionism = socially prescribed perfectionism

Figure 1: Effects of trait resilience (upper panel) and trait worry (lower panel) on total cortisol awakening response across 7 days (n=142; error bars represent SEM)

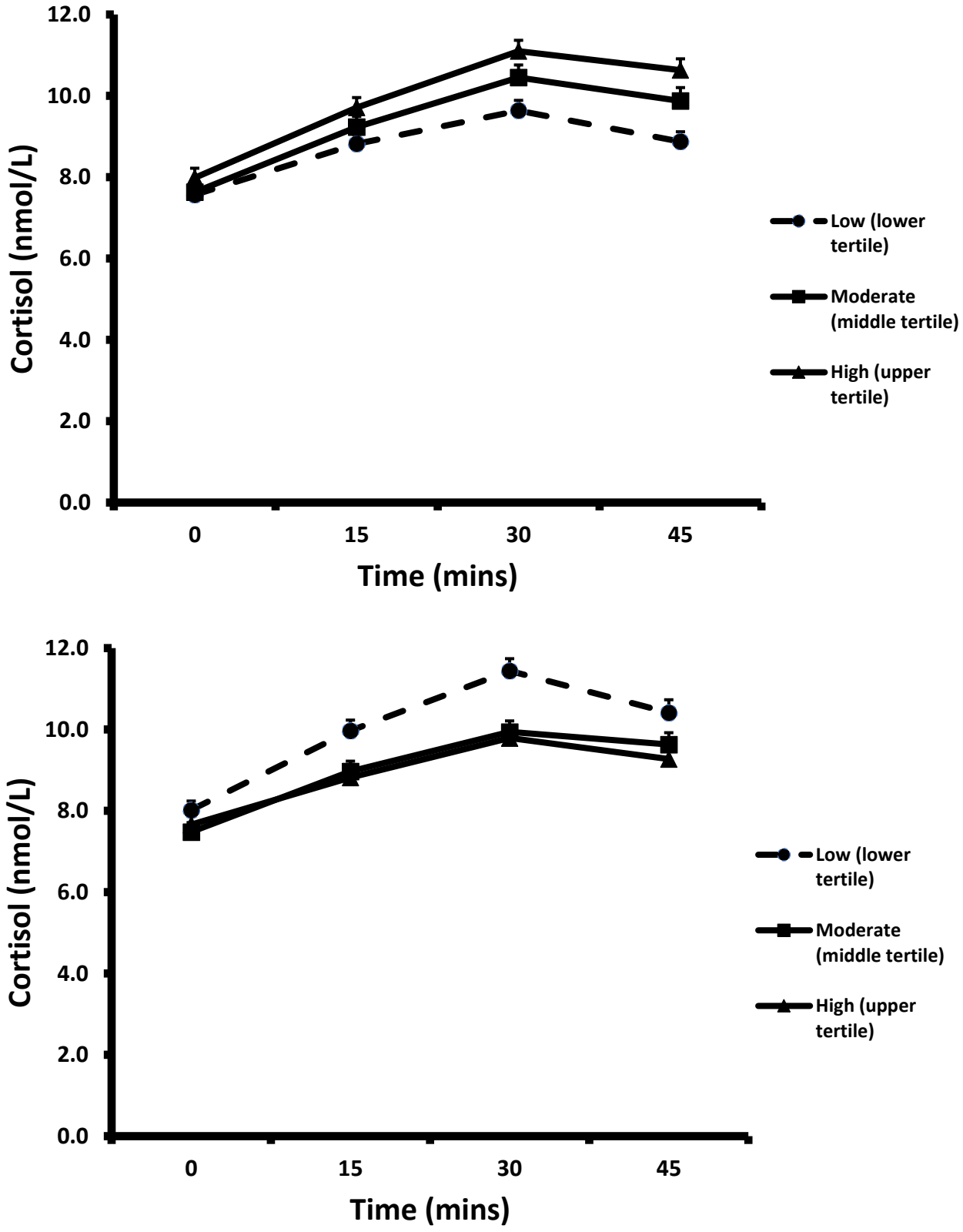

Figure 2: Effects of socially prescribed perfectionism (upper panel) and trait impulsivity (lower panel) on total cortisol awakening response across 7 days (n=142; error bars represent SEM)

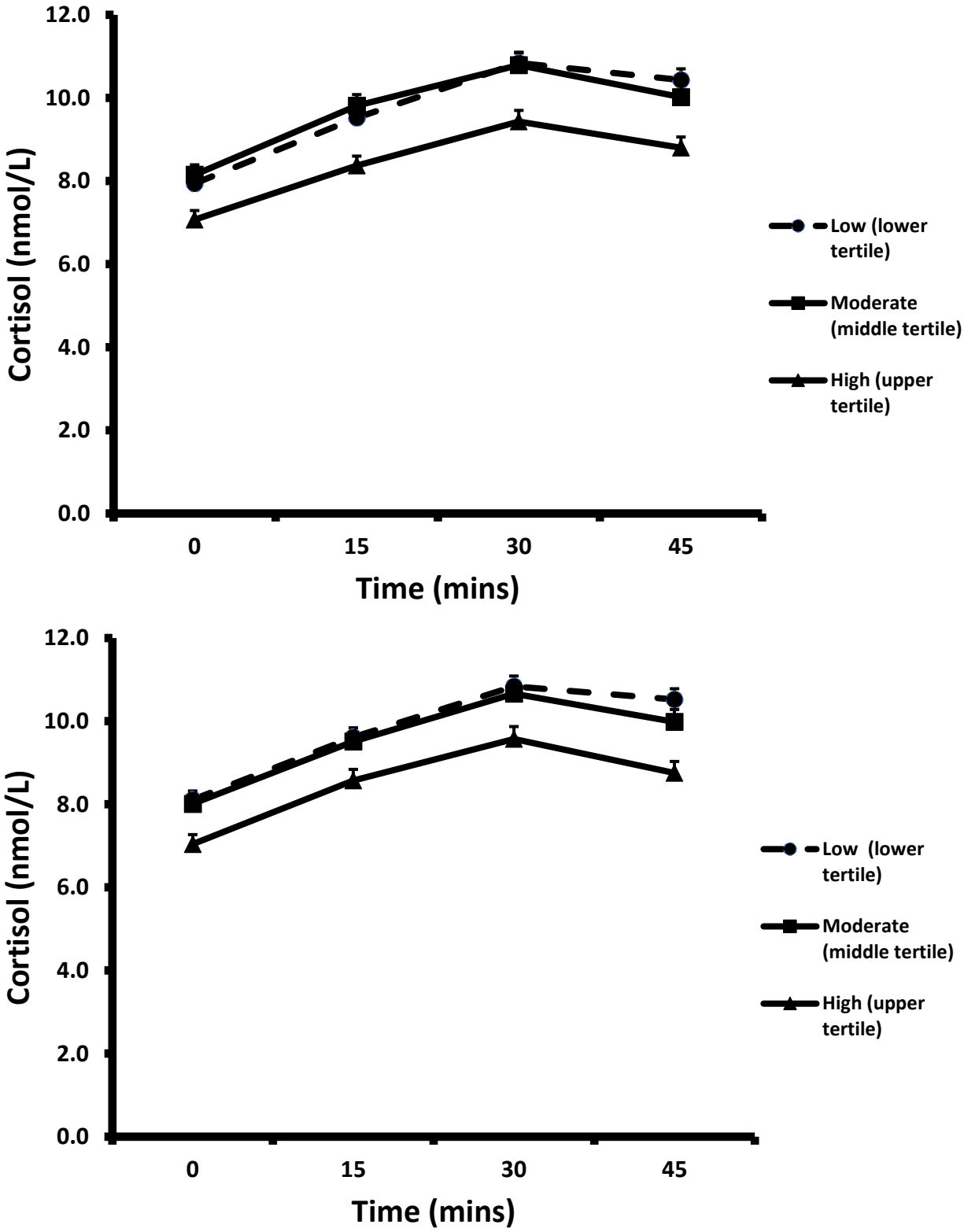

Figure 3: Indirect effect of suicide vulnerability group on total cortisol awakening response (CAR) levels via trait worry