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Consumed by a forbidden emotion: anger and aggression in patients with psychiatric disorders

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Citation

Bles, N. J. de. (2023, April 26). *Consumed by a forbidden emotion: anger and aggression in patients with psychiatric disorders*. Retrieved from <https://hdl.handle.net/1887/3594670>

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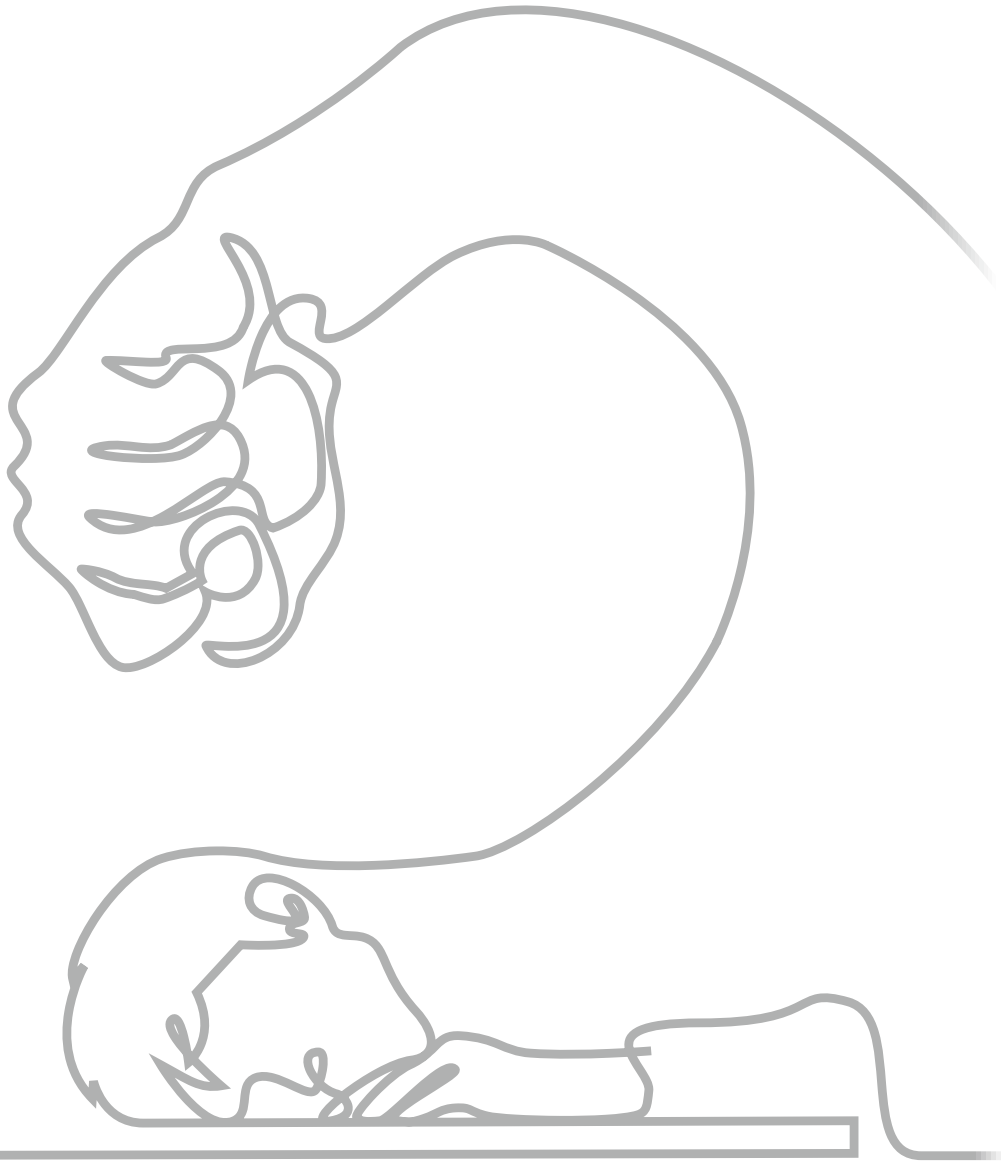
Note: To cite this publication please use the final published version (if applicable).



Published as: de Bles, N. J., Rius-Ottenheim, N., van Hemert, A. M., Pütz, L. E. H., van der Does, A. J. W., Penninx, B. W. J. H., & Giltay, E. J. (2019). Trait anger and anger attacks in relation to depressive and anxiety disorders. *Journal of Affective Disorders*, 259, 259-265.

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Trait anger and anger attacks in relation to depressive and anxiety disorders



Abstract

Background: Patients with various psychiatric disorders may suffer from feelings of anger, sometimes leading to maladaptive (e.g., aggressive) behaviours. We examined to what extent depressive and anxiety disorders, relevant clinical correlates, and sociodemographics determined the level of trait anger and the prevalence of recent anger attacks.

Methods: In the Netherlands Study of Depression and Anxiety (NESDA), the Spielberger Trait Anger Subscale and the Anger Attacks Questionnaire were analysed in patients with depressive ($n = 204$), anxiety ($n = 288$), comorbid ($n = 222$), and remitted disorders ($n = 1107$), as well as in healthy controls ($n = 470$) based on DSM-IV criteria.

Results: On average, participants were 46.2 years old ($SD = 13.1$) and 66.3% were female. Trait anger and anger attacks were most prevalent in the comorbid group ($M = 18.5$, $SD = 5.9$, and prevalence 22.1%), followed by anxiety disorder, depressive disorder, remitted disorder, and controls ($M = 12.7$; $SD = 2.9$, and prevalence 1.3%). Major depressive disorder, social phobia, panic disorder, and generalized anxiety disorder were most strongly associated to trait anger and anger attacks.

Limitations: Due to a cross-sectional design, it was not possible to provide evidence for temporal or causal relationships between anger and depressive and anxiety disorders.

Conclusions: Trait anger and anger attacks are linked to depressive and anxiety disorders, although the strength of the relationship differed among both anger constructs.

Introduction

Anger is a common emotion and ranges from mild irritation to fury. In mild forms, anger can be functional in threatening situations but becomes problematic if it occurs regularly or is very intense. High levels of anger may be associated with maladaptive behaviours, resulting in adverse health outcomes and poorer quality of life⁽¹⁻⁵⁾. Anger can also trigger aggression and violent behaviour^(6,7), and is related to lifetime suicidality⁽⁸⁾. Given the serious consequences for individuals and society, it is of importance to identify individuals most prone to high levels of anger.

To identify predictors of anger, we made the distinction between “trait anger” and “state anger.” Trait anger connotes an angry disposition: a proneness to experience feelings of anger. State anger refers to an emotional–physiological condition that occurs in response to an immediate stressor or threat^(9,10). If severe, such a state can develop into an anger attack: sudden spells of anger accompanied by symptoms of autonomic activation such as tachycardia, sweating, hot flashes, or tightness of the chest⁽¹¹⁾.

Several psychological constructs are closely linked to anger. Almost half of patients with major depressive disorder (MDD) have shown high levels of irritability^(12,13). Also, elevated levels of anger and hostility are often reported in depressed patients^(14,15). The prevalence of anger attacks ranged from 26% to 49% in individuals with MDD⁽¹⁶⁻²⁰⁾ and from 28% to 53% in patients with dysthymia^(4,21).

Patients with anxiety disorders also showed increased levels of anger; 29–32% experience anger attacks⁽²²⁾. Similarly, patients with generalized anxiety disorder (GAD), obsessive–compulsive disorder (OCD), social phobia (SP), and panic disorder (PD) experience higher levels of hostility and anger compared to controls⁽²³⁻²⁵⁾.

To summarize, the available literature on this topic indicates that anger is more prevalent in individuals with depression or anxiety. Yet, most previous studies used insufficiently validated instruments or used only a single item to measure irritability. To date, two large-scale population-based cohort studies have been conducted, including 5692⁽²⁶⁾ and 8841 participants⁽²⁷⁾ and a patient-based study included 3800 psychiatric outpatients⁽²⁸⁾. All three studies reported strong relationships with depressive and anxiety disorders—even after adjusting for demographics and comorbidity. However, anger was assessed through two⁽²⁸⁾ and four items⁽²⁷⁾ that were compiled from larger questionnaires (i.e., Schedule for Affective Disorders and Schizophrenia and the International Personality Disorder Examination respectively). Those items were originally part of a questionnaire measuring another construct. Hence, their

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validity to measure anger is unknown. In addition, existing research has not provided for a clear distinction between trait and state anger. Given that anger research is scarce, it is important to examine the construct and broader context of anger in order to understand this heterogeneous construct. While research suggests different patterns for anger experience and anger expression in relation to anxiety disorders⁽²⁶⁾, the same can be thought of for state and trait anger. Making a distinction between patients with an angry disposition as a constant factor embedded in personality, and patients that respond angrily to an immediate situation, is of clinical importance. This may enable patients and clinicians to more effectively target anger-related problems.

We aimed to investigate the prevalence of anger and its sociodemographic and clinical associations using validated trait anger and anger attack measures in a cohort that included patients without lifetime psychiatric disorders (“control subjects”), with current or remitted depressive and anxiety disorders, or comorbid depressive and anxiety disorders.

Methods

Participants

Participants stemmed from the Netherlands Study of Depression and Anxiety (NESDA), an ongoing longitudinal, multisite, naturalistic cohort study. At baseline, 2981 participants (18–65 years) were recruited from community care (19%), primary care (54%), and specialized mental health care (27%) in the Netherlands. The study included individuals without lifetime psychiatric disorders (“control subjects”), with current or remitted depressive and anxiety disorders, or comorbid depressive and anxiety disorders. Exclusion criteria included not speaking Dutch and having another primary clinical diagnosis (e.g., psychotic, obsessive–compulsive, bipolar, or severe addictive disorders). All participants gave written informed consent before enrolment, and the ethical committees of participating universities (VU University Medical Centre, Leiden University Medical Centre, and University Medical Centre Groningen) granted ethical approval. For a detailed description of NESDA⁽²⁹⁾.

Data on anger were gathered at the 4th wave at 4-year follow up between August 2008 and May 2011. Participants who completed this wave totalled 2402 (80.6%). Participants with missing data on one or both anger questionnaires ($n = 111$) were excluded, yielding 2291 participants for the current analyses. Participants with missing data at the 4-year follow-up had more severe depressive ($p < 0.001$) and anxiety (p 's < 0.05) symptoms compared to the sample included in this paper.

Measurements

Trait anger

We assessed trait anger using the Dutch adaptation of the Spielberger State–Trait Anger Scale (STAS; ^(30,31), which consists of two self-report questionnaires that measure state and trait anger. In the current study, we only administered the subscale for trait anger that measured individual differences in anger proneness as a personality trait. The trait anger scale consists of 10 items and is further divided into two sub scores: temperament (i.e., a general disposition for experiencing anger and eventually expressing it; Items 1, 2, 3, 5, and 6) and reaction (i.e., a general disposition for expressing anger, especially after provocation; Items 7, 8, and 10). Participants score each item on a 4-point Likert scale, ranging from 1 (*almost never*) to 4 (*almost always*), and total sum score ranges from 10 to 40. Items 4 and 9 (“I get annoyed quickly,” “I am quickly irritated,” respectively) measure the immediacy of an anger response ⁽³²⁾. Psychometric research showed good item correlations and high test–retest reliability ⁽³¹⁾. The internal consistency (i.e., Cronbach’s alpha) in our sample was 0.89.

Anger attacks

The Anger Attacks Questionnaire is a self-rating scale developed to assess the presence of distinct forms of anger attacks during the past 6 months ⁽³³⁾. Anger attacks are sudden spells of anger accompanied by symptoms of autonomic activation and are uncharacteristic actions that are inappropriate for a situation ⁽¹¹⁾. To identify a patient who is experiencing anger attacks, all of the following criteria needed to be met during the past 6 months: (1) irritability, (2) overreaction to minor annoyances, (3) inappropriate anger and rage directed at others, (4) incidence of at least one anger attack within the past month, and (5) occurrence of at least four out of the following 13 autonomic and/or behavioural features in at least one of the attacks: tachycardia, hot flashes, tightness of the chest, paraesthesia, dizziness, shortness of breath, sweating, trembling, panic, feeling out of control, feeling like attacking others, attacking physically or verbally, and throwing or destroying objects ⁽³⁴⁾.

Depressive and anxiety disorders

The Composite International Diagnostic Interview (CIDI; WHO version 2.1), a comprehensive, fully standardized diagnostic interview, was used to screen for depressive (i.e., MDD, dysthymia) and anxiety disorders (i.e., PD, SP, GAD, agoraphobia [AP]) based on criteria of the fourth edition of the Diagnostic and Statistical Manual of Mental

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Disorders (DSM-IV⁽³⁵⁾). Upon completing the CIDI, participants were categorized into one of five psychopathology groups: (1) healthy participants with no current or past history of psychiatric disorders ($n = 470$); (2) participants with a lifetime history of a depressive or anxiety disorder, but not in the preceding 6 months ($n = 1262$); (3) patients with a depressive ($n = 141$) or (4) anxiety disorder ($n = 263$) within their last 6 months; and (5) patients with comorbid depressive and anxiety disorders within their last 6 months ($n = 155$).

Symptom severity

Depression. The 30-item Inventory of Depressive Symptomatology (self-report version; IDS-SR) was used to measure severity of depressive symptoms during the last 7 days^(36,37). Patients scored items on a 4-point Likert scale (0–3), ranging from 0 to 84 points (only 28 of the 30 items are rated). A higher overall score on the IDS indicates more severe depression symptoms.

Anxiety. Anxiety was assessed using three severity scales. The self-report, 21-item Beck Anxiety Inventory (BAI) focuses on somatic symptoms of anxiety during the past week⁽³⁸⁾. Patients rated items on a 4-point Likert scale with total scores ranging from 0 to 63 points. The self-report, 15-item Fear Questionnaire (FQ;⁽³⁹⁾) assesses level of distress and avoidance of situations (i.e., AP, SP, and blood-injury phobia) using a 9-point Likert scale, with total scores ranging from 0 to 120. The 16-item, self-report Penn State Worry Questionnaire (PSWQ;⁽⁴⁰⁾) assesses pathological worry and general anxiety on a 5-point Likert scale. Although the original PSWQ includes 11 positively worded items and 5 negatively worded items, NESDA used the abbreviated 11-item version due to significantly stronger correlations and a higher internal consistency, with a Cronbach's alpha of 0.94 compared to a Cronbach's alpha of 0.90 for the original version⁽⁴¹⁾. The total score ranges from 11 to 55 points.

Covariates

Sociodemographic covariates were self-reported age, gender, level of education (in years), and any use of drugs in the past month. Body Mass Index (BMI) was calculated based on measured height and weight, and smoking status (current/not current) and lifetime DSM IV-based alcohol dependency and abuse were assessed using the CIDI.

Statistical analyses

Sociodemographic and clinical characteristics were summarized within the five groups of psychopathologies using descriptive statistics. Categorical variables were presented

as proportions and continuous variables as means with standard deviations (*SD*). An analysis of variance (ANOVA) compared the mean levels of the continuous variable trait anger, and chi-squared tests were used to compare the prevalence of the dichotomous variable anger attacks among psychopathology groups. In our study, we repeated the analyses and adjusted for sex, age, level of education, BMI, smoking, alcohol dependence/abuse, and drug use using analysis of covariance (ANCOVA) and multivariable logistic regression analyses. We used (stacked) bar plots to examine differences in prevalence rates among psychopathology groups. Therefore, we divided the total score of trait anger into high and low scores based on the 75th percentile scores of the total group—a score higher than P_{75} represented high trait anger.

We also performed multivariable linear and logistic regression analyses to examine the associations of trait anger and anger attacks, respectively, according to demographic characteristics and psychiatric disorders. These associations were first tested in an unadjusted model. Subsequently, we adjusted the full model according to sex, age, level of education, BMI, smoking status, alcohol dependency/abuse, drug use, dysthymia, MDD, SP, PD, AP, and GAD.

Four symptom severity scales (i.e., depression, anxiety, fear, and worry) were measured to explore which symptom was more strongly associated with trait anger and anger attacks. We plotted fully adjusted mean scores of these anger scores for the four severity scales. All statistical tests were based on continuous scores of severity scales. A two-tailed significance level of $p < 0.05$ was considered statistically significant. Analyses were performed using IBM SPSS statistical software (version 23, IBM Corp).

Results

Sample characteristics

The mean age of the participants ($N = 2291$) was 46.2 years ($SD = 13.1$), and 66.3% were female. As shown in Table 1, participants with a remitted or current disorder had significantly fewer years of education and a higher BMI, were more often smokers, and more often suffered from alcohol dependency/abuse than healthy controls. These participants also scored higher on depression and anxiety severity scales and used more psychotropic medication compared to healthy controls.

Prevalence of trait anger and anger attacks

Between-group differences were present for all anger measures (all p values < 0.001 ; see Table 2) that persisted in the adjusted models, ($F(4, 2113) = 70.15, p < 0.001$ for trait

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anger and $\chi^2(11) = 122.12, p < 0.001$ for anger attacks). Similarly, (adjusted) subscale scores of trait anger (i.e., “Temperament” and “Reaction”) differed significantly among the five groups. The adjusted odds of anger attacks were 21.4 times higher for patients with current comorbid anxiety and depression than for healthy controls.

Fig. 1 shows the differences in prevalence rates among psychopathology groups in (stacked) bar plots. Controls had the lowest prevalence of high trait anger (5.1%), whereas patients with comorbid disorders had the highest prevalence (43.7%). A significant trend was found for anger attacks over psychopathology groups; controls showed the lowest prevalence (1.3%) and patients with comorbid disorders showed the highest prevalence (22.1%). The distribution of having anger attacks and trait anger scores are presented in Fig. 1 of the Supplementary material.

Correlates of trait anger and anger attacks

Table 3 shows the result of linear regression analyses for trait anger according to demographic characteristics and psychiatric disorders. In the fully adjusted model, being male, ($\beta = -0.060, p = 0.004$), completing fewer years of education ($\beta = -0.047, p = 0.03$), depending on or abusing alcohol ($\beta = 0.090, p < 0.001$), and drug use ($\beta = 0.045, p = 0.04$) remained independently associated with trait anger. All psychiatric disorders were associated with higher trait anger scores in the (adjusted) model; MDD, SP, and GAD showed the strongest independent associations (β s $> 0.1, p < 0.001$).

For results of logistic regression analyses for anger attacks see Table 4. Younger age, fewer years of education, alcohol dependency/ abuse, drug use, depressive and anxiety disorders related significantly to anger attacks in the crude models. In the fully adjusted model, significance remained only for age ($OR = 0.81$), drug use ($OR = 2.41$), MDD ($OR = 1.62$), and anxiety disorders (i.e., SP $OR = 1.70$, PD $OR = 2.08$, GAD $OR = 3.61$), but not AP.

The adjusted mean values and OR s of trait anger and anger attacks in relation to symptom severity (i.e., IDS, PSWQ, BAI, and FQ) are presented in Fig. 2 of the Supplementary material. The mean values indicated a general pattern of linear associations (Supp. Fig. 2A, 2C, 2E, 2G). Adjusted OR s with 95% confidence intervals (CI) show that all severity scores had linear associations with trait anger and anger attacks, though of different strengths (Supp. Fig. 2B, 2D, 2F, 2H). The IDS and PSWQ showed the strongest associations for both trait anger and anger attacks.

Table 1. Baseline characteristics of the study sample ($N = 2291$) according to psychopathology groups

	Controls ($n = 470$)	Remitted anxiety and/ or depressive disorder† ($n = 1107$)	Current depressive disorder† ($n = 204$)	Current anxiety disorder† ($n = 288$)	Current comorbid anxiety and depressive disorder† ($n = 222$)
Sociodemographics:					
Male sex, no. (%)	193 (41.1%)	361 (32.6%)	54 (26.5%)	85 (29.5%)	80 (36.0%)
Age in years, mean (SD)	45.9 (14.6)	46.0 (12.9)	48.0 (12.3)	45.8 (12.9)	46.4 (11.9)
Education in years, mean (SD)	13.4 (3.3)	12.9 (3.2)	12.7 (3.4)	12.4 (3.5)	11.7 (3.3)
BMI, kg/m ² , mean (SD)	25.6 (4.8)	26.3 (4.8)	26.3 (5.1)	25.8 (4.8)	27.1 (6.2)
Smoking, no. (%)	97 (20.6%)	347 (31.3%)	67 (32.8%)	92 (32.1%)	88 (39.6%)
Lifetime alcohol dependency/abuse, no. (%)	17 (3.6%)	60 (5.4%)	22 (10.8%)	23 (8.0%)	32 (14.4%)
Any use of drug in past month, no (%)	19 (4.0%)	57 (5.1%)	8 (3.9%)	19 (6.6%)	13 (5.9%)
Clinical characteristics:					
<i>Severity measures</i>					
IDS-SR total score, mean (SD)	6.0 (5.0)	12.6 (8.4)	25.2 (11.6)	19.9 (10.0)	33.8 (11.8)
BAI total score, mean (SD)	2.7 (3.5)	6.2 (5.8)	11.2 (7.9)	12.9 (9.2)	19.7 (10.7)
PSWQ total score, mean (SD)	16.7 (6.8)	24.5 (9.6)	33.0 (10.1)	31.7 (10.0)	38.2 (9.1)
FQ total score, mean (SD)	7.7 (9.1)	14.1 (13.1)	23.3 (17.9)	30.2 (18.1)	39.7 (21.6)
<i>Medication use</i>					
Benzodiazepines, no. (%)	7 (1.5%)	88 (7.9%)	42 (20.6%)	48 (16.7%)	69 (31.1%)
SSRI, no. (%)	3 (0.6%)	157 (14.2%)	41 (20.1%)	54 (18.8%)	40 (18.0%)
TCA, no. (%)	1 (0.2%)	29 (2.6%)	10 (4.9%)	6 (2.1%)	13 (5.9%)
Other AD, no. (%)	2 (0.4%)	46 (4.2%)	21 (10.3%)	21 (7.3%)	34 (15.3%)

Note. BMI = Body Mass Index; IDS-SR = Inventory of Depressive Symptomatology, self-report; BAI = Beck Anxiety Inventory; PSWQ = Penn State Worry Questionnaire; FQ = Fear Questionnaire; SSRI = Selective Serotonin Reuptake Inhibitor; TCA = Tricyclic Antidepressant. Chi-square values have been computed for categorical variables, ANOVA for interval variables.

† Based on 6 months.

Table 2. Prevalence of trait anger and anger attacks according to psychopathology groups

Trait Anger	Controls (n = 470)	Remitted anxiety and/or depressive disorder† (n = 1107)	Current depressive disorder† (n = 204)	Current anxiety disorder† (n = 288)	Current comorbid anxiety and depressive disorder† (n = 222)	Test statistic	p value
Total score, crude	12.70 (0.13) ^a	15.13 (0.13) ^b	16.48 (0.35) ^c	16.72 (0.30) ^c	18.51 (0.39) ^d	F(4, 641) = 99.44	< 0.001
Total score, adjusted‡	12.72 (0.21) ^a	15.08 (0.14) ^b	16.39 (0.31) ^c	16.67 (0.26) ^c	18.21 (0.30) ^d	F(4, 2113) = 70.15	< 0.001
Temperament subscale ¹	5.56 (0.06) ^a	6.42 (0.07) ^b	7.00 (0.18) ^c	6.94 (0.15) ^c	7.91 (0.21) ^d	F(4, 633) = 60.10	< 0.001
Temperament subscale ¹ , adjusted‡	5.55 (0.11) ^a	6.38 (0.07) ^b	6.94 (0.16) ^c	6.87 (0.13) ^c	7.80 (0.15) ^d	F(4, 2102) = 41.56	< 0.001
Reaction subscale ²	4.17 (0.06) ^a	5.07 (0.05) ^b	5.38 (0.13) ^c	5.66 (0.12) ^c	6.05 (0.14) ^d	F(4, 644) = 66.89	< 0.001
Reaction subscale ² , adjusted‡	4.21 (0.08) ^a	5.06 (0.05) ^b	5.33 (0.12) ^c	5.67 (0.10) ^d	5.90 (0.12) ^d	F(4, 2107) = 48.66	< 0.001
Anger Attacks							
Total prevalence of anger attacks (%):	6 (1.3%) ^a	52 (4.7%) ^b	10 (4.9%) ^b	33 (11.5%) ^c	49 (22.1%) ^d	χ ² (4) = 127.23	< 0.001
Crude odds ratio (OR)	Ref. ^a	3.81 (1.63–8.94) ^b	3.99 (1.43–11.12) ^b	10.01 (4.14–24.20) ^c	21.90 (9.22–52.05) ^d	χ ² (4) = 104.75	< 0.001
Adjusted odds ratio (OR)‡	Ref. ^a	3.83 (1.62–9.03) ^b	3.36 (1.14–9.92) ^b	9.32 (3.79–22.88) ^b	21.44 (8.88–51.76) ^b	χ ² (11) = 122.12	< 0.001

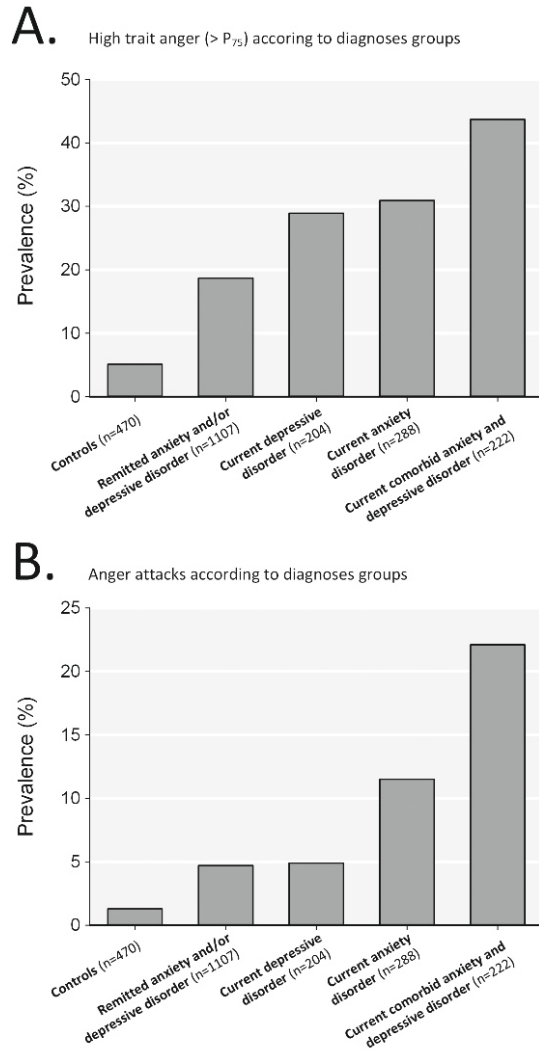
Note. Data are (adjusted) means (with standard errors in parentheses) or number of participants (with percentages in parentheses). Values in the same row with different superscript letters are significantly different, *p* < 0.05 (in post hoc comparisons).

¹Subscale consisting of items 1, 2, 3, 5, and 6.

²Subscale consisting of items 7, 8, and 10.

† Based on 6 months.

‡ Adjusted for sex, age, level of education, BMI, smoking, alcohol dependency/abuse, drug use.



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Fig. 1. Prevalence of trait anger and anger attacks according to psychopathology groups

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Table 3. Linear regression analyses predicting trait anger according to demographic characteristics and psychiatric disorders ($N = 2291$)

	Univariable		Full model†	
	β	p value	β	p value
Sociodemographics:				
Female sex	-0.083	< 0.001	-0.060	0.004
Age, in <i>SD</i> (standardized)	0.010	0.63	0.007	0.73
Education in <i>SD</i> (standardized)	-0.085	< 0.001	-0.047	0.03
BMI, in <i>SD</i> (standardized)	0.043	0.046	0.012	0.57
Smoking	0.060	0.004	0.006	0.77
Alcohol dependency/abuse	0.138	< 0.001	0.090	< 0.001
Any use of drug in past month	0.074	< 0.001	0.045	0.04
Mood disorders (6-month diagnoses)				
Dysthymia	0.190	< 0.001	0.053	0.02
MDD	0.206	< 0.001	0.111	< 0.001
Anxiety disorders (6-month diagnoses)				
Social Phobia	0.197	< 0.001	0.113	< 0.001
Panic Disorder	0.131	< 0.001	0.073	0.001
Agoraphobia	0.088	< 0.001	0.051	0.015
Generalized Anxiety Disorder	0.196	< 0.001	0.109	< 0.001

Note. Standardized beta-coefficients and accompanying p values by linear regression analyses.

†Model that includes all the independent variables in one multivariable regression model.

Discussion

In our study, trait anger and anger attacks were prevalent and associated with several depression and anxiety disorders. Our findings indicate that anger was most prevalent in participants with comorbid depressive and anxiety disorders—followed by anxiety-, depressive-, and remitted disorder—and that these participants exhibited a higher prevalence of anger than healthy controls.

Our finding that patients with a current disorder reported higher trait anger than controls supports prior population-based cohort studies^(26, 27) and one cohort of psychiatric outpatients⁽²⁸⁾. Likewise, recent anger attacks were more common in participants with a current disorder than healthy controls, which supports findings from two previous studies^(4, 42).

Participants with a remitted disorder still exhibited elevated levels of trait anger and recent anger attacks. This mirrors findings where recovered depressed

Table 4. Logistic regression analyses predicting anger attacks according to demographic characteristics and psychiatric disorders ($N = 2291$)

	Crude		Full model†	
	OR (95% CI)	<i>p</i> value	OR (95% CI)	<i>p</i> value
Sociodemographics				
Female sex	0.80 (0.57–1.12)	0.19	0.92 (0.63–1.35)	0.67
Age, in <i>SD</i> (standardized)	0.85 (0.72–1.00)	0.046	0.81 (0.67–0.98)	0.03
Education, in <i>SD</i> (standardized)	0.79 (0.67–0.94)	0.006	0.84 (0.70–1.02)	0.09
BMI, in <i>SD</i> (standardized)	1.14 (0.98–1.34)	0.10	1.08 (0.91–1.27)	0.39
Smoking	1.00 (0.70–1.44)	0.99	0.72 (0.47–1.10)	0.13
Alcohol dependency/abuse	2.62 (1.61–4.25)	< 0.001	1.43 (0.80–2.57)	0.23
Any use of drug in past month	2.24 (1.27–3.97)	0.005	2.41 (1.24–4.69)	0.01
Mood disorders (6-month diagnoses)				
Dysthymia	4.01 (2.55–6.29)	< 0.001	1.41 (0.80–2.50)	0.24
MDD	2.90 (2.03–4.14)	< 0.001	1.62 (1.04–2.51)	0.03
Anxiety disorders (6-month diagnoses)				
Social Phobia	3.06 (2.06–4.55)	< 0.001	1.70 (1.06–2.72)	0.03
Panic Disorder	3.16 (2.01–4.96)	< 0.001	2.08 (1.23–3.53)	0.01
Agoraphobia	2.20 (1.24–3.88)	0.007	1.60 (0.84–3.06)	0.15
Generalized Anxiety Disorder	7.13 (4.66–10.91)	< 0.001	3.61 (2.19–5.95)	< 0.001

Note. Odds ratios (OR), 95% confidence interval (CI), and accompanying *p* values by logistic regression analyses.

†Model that includes all the independent variables in one multivariable logistic regression model.

participants were more likely to report fear of anger expression and having experienced anger attacks compared to controls⁽⁴³⁾, which may be the result of residual symptoms or psychiatric disorders that were not assessed in this study. Higher levels of anger, however, may also indicate vulnerability to depressive and anxiety disorders.

We found the largest effect sizes in patients with comorbid depression and anxiety, which coincides with earlier findings in samples from the general population^(4,44). Considering specific disorders, MDD, SP, PD, and GAD most strongly associated with both trait anger and recent anger attacks. The strong association between anger and MDD and anxiety disorders supports previous research⁽²⁶⁻²⁸⁾.

In summary, our findings confirm that anger is highly prevalent in patients with MDD, SP, and GAD. Yet, trait anger and anger attacks may be easily overlooked or ignored by clinicians and patients themselves because they are not part of the core DSM-IV symptoms, and insight and self-consciousness of feelings of anger may be hampered. Addressing anger in therapy, however, might help clinicians to reduce

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conflicts or resistance to therapy⁽²⁶⁾. Even so, management of anger is a major public safety concern due to the relationship between anger and aggression⁽⁴⁵⁾. In recent years, research has increased regarding the treatment of anger in a clinical context (involving aggression–anticipation in psychiatric hospitals;⁽⁴⁶⁾ and in the effectiveness of therapies targeting anger. Cognitive behavioural therapy^(47,48) and psychopharmacological therapy like fluoxetine have received empirical support for reducing anger⁽⁴⁹⁻⁵¹⁾.

Interestingly, men reported higher levels of trait anger, which might be explained through neuroendocrine effects of testosterone and other androgens⁽⁵²⁾; however, previous large-scale studies^(27,28) found higher levels of anger in women. Similar to other studies, we found that individuals who were younger, who completed fewer years of education, who were dependent on or abused alcohol, and who used drugs the past month also reported higher levels of trait anger^(27,28,53,54).

Regarding symptom severity measures, we found that depressive and worry symptoms most strongly associated with trait anger and recent anger attacks, which is supported by previous studies^(24,55). These associations with anger might be explained by a common underlying factor, such as emotion dysregulation⁽⁵⁶⁻⁵⁸⁾. A key neural region involved in emotion regulation is the amygdala, which is part of the limbic system. Research has shown that the amygdala is hyperactive in anxious and depressed patients, as well as in individuals with heightened anger^(59,60).

We conducted our study within a large cohort study. In anger research, the use of two different anger measures is fairly unique; many previous studies reported on a single-item to a five-item measure of anger^(12,28,61) or used single instruments to measure anger^(32,44,62). Furthermore, the state of anger that can be studied in the form of anger expression (e.g., recent anger attacks) was not taken into account in one of the three previous cohort studies⁽²⁷⁾. The other cohort study took anger expression into account, but focused on the link with anxiety disorders⁽²⁶⁾.

Limitations of our study, however, must be addressed. First, our analyses had a cross-sectional design, so we cannot provide evidence for temporal or causal relationships between anger and depressive and anxiety disorders. Second, anger is a subjective measure based on self-report data, while there are some observation-based assessment tools for aggressive incidents, such as the Modified Overt Aggression Scale (MOAS;^(63,64) and the Staff Observation Aggression Scale-revised (SOAS-R;⁽⁶⁵⁾). Also, our sample was recruited in only one country while cultural differences might play a role in the expression of anger, making it less generalizable to other cultures⁽⁶⁶⁾. Lastly, according to the newest version of the DSM (DSM-V⁽⁶⁷⁾), there are several disorders in

which anger is a central feature, but that were either not included or not assessed in our study. One such example in which anger is a diagnostic criterion is post-traumatic stress disorder (PTSD) ⁽⁶⁸⁾, which patients were not included in NESDA. Several studies found high associations between PTSD and anger ^(69, 70). The intermittent explosive disorder (IED), a disorder that is characterized by impulsivity and aggression, was not assessed in NESDA. Previous studies found that patients with depression are at increased risk of IED ^(67, 71, 72) and that patients with Cluster B and C (especially borderline) personality disorder show higher levels of anger ^(28, 73, 74). Although anger attacks could be part of an IED, we define anger attacks by their internal affective and physical attributes rather than defining it by their external characteristics, which may result in smashing things or (threatening to) hitting someone.

In summary, the level of trait anger and the prevalence of recent anger attacks is higher in patients suffering from depressive and anxiety disorders than in healthy controls. Participants with a remitted disorder still had higher scores for both trait anger and anger attacks. Because anger is an adverse mood state related to numerous negative outcomes for patients, relatives, and society, it is important that clinicians enquire about feelings and attacks of anger and address this in their therapy of emotion regulation ^(62, 75). Temporal and causal relationships between anger and psychiatric disorders must be investigated further using longitudinal designs, which may have consequences for (psychotherapeutic) interventions targeting anger.

Funding

The funding source had no role in the design of this study, its execution, analyses, interpretation of the data, or decision to submit results.

CRedit authorship contribution statement

Nienke J. de Bles: Writing - original draft. Nathaly Rius Ottenheim: Supervision, Writing - review & editing. Albert M. van Hemert: Writing - review & editing. Laura E.H. Pütz: Writing - original draft. A.J. Willem van der Does: Writing - review & editing. Brenda W.J.H. Penninx: Writing - review & editing. Erik J. Giltay: Supervision, Writing - review & editing.

Data for reference

An a priori analysis plan for this study was approved by the principal investigator of NESDA and the NESDA board. Because of ethical and legal restrictions, data involving clinical participants are not included in the manuscript or made available in a public repository. However, subject to approval, data are available upon request from the NESDA Data Access Committee (nesda@ggzingeest.nl).

Declaration of Competing interest

A.J.W.D reports personal fees from Mitsubishi Tanabe Pharma Europe, outside the submitted work. All other authors declare that they have no conflicts of interest.

Acknowledgments

The infrastructure for the NESDA study (www.nesda.nl) is funded through the Geestkracht program of the Netherlands Organization for Health Research and Development (ZonMw, grant number 10-000- 1002) and financial contributions by participating universities and mental health care organizations (VU University Medical Center, GGZ inGeest, Leiden University Medical Center, Leiden University, GGZ Rivierduinen, University Medical Center Groningen, University of Groningen, Lentis, GGZ Friesland, GGZ Drenthe, Rob Giel Onderzoekscentrum).

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.jad.2019.08.023](https://doi.org/10.1016/j.jad.2019.08.023).

References

1. Abraham S, Shah NG, Diez Roux A, Hill-Briggs F, Seeman T, Szklo M, et al. Trait anger but not anxiety predicts incident type 2 diabetes: The Multi-Ethnic Study of Atherosclerosis (MESA). *Psychoneuroendocrinology*. 2015;60:105-13.
2. Chida Y, Steptoe A. The association of anger and hostility with future coronary heart disease: a meta-analytic review of prospective evidence. *Journal of the American College of Cardiology*. 2009;53(11):936-46.
3. Fraguas R, Iosifescu DV, Bankier B, Perlis R, Clementi-Craven N, Alpert J, et al. Major depressive disorder with anger attacks and cardiovascular risk factors. *International journal of psychiatry in medicine*. 2007;37(1):99-111.
4. Painuly N, Grover S, Gupta N, Mattoo SK. Prevalence of anger attacks in depressive and anxiety disorders: implications for their construct? *Psychiatry and clinical neurosciences*. 2011;65(2):165-74.
5. Painuly N, Sharan P, Mattoo SK. Antecedents, concomitants and consequences of anger attacks in depression. *Psychiatry research*. 2007;153(1):39-45.
6. McDermut W, Fuller JR, DiGiuseppe R, Chelminski I, Zimmerman M. Trait Anger and Axis I Disorders: Implications for REBT. *Journal of Rational-Emotive & Cognitive-Behavior Therapy*. 2009;27(2):121-35.
7. Owen JM. Transdiagnostic cognitive processes in high trait anger. *Clinical psychology review*. 2011;31(2):193-202.
8. Hawkins KA, Cogle JR. A test of the unique and interactive roles of anger experience and expression in suicidality: findings from a population-based study. *The Journal of nervous and mental disease*. 2013;201(11):959-63.
9. Deffenbacher JL, Oetting ER, Thwaites GA, Lynch RS, Baker DA, Stark RS, et al. State-trait anger theory and the utility of the trait anger scale. *J Couns Psychol*. 1996;43(2):131.
10. Spielberger CD, Krasner SS, Solomon EP. The Experience, Expression, and Control of Anger. In: Janisse MP, editor. *Individual Differences, Stress, and Health Psychology*. New York, NY: Springer New York; 1988. p. 89-108.
11. Fava M, Anderson K, Rosenbaum JF. "Anger attacks": possible variants of panic and major depressive disorders. *The American journal of psychiatry*. 1990;147(7):867-70.
12. Verhoeven FE, Booij L, Van der Wee NJ, Penninx BW, Van der Does AJ. Clinical and physiological correlates of irritability in depression: results from the Netherlands study of depression and anxiety. *Depression research and treatment*. 2011;2011:126895.
13. Fava M, Hwang I, Rush AJ, Sampson N, Walters EE, Kessler RC. The importance of irritability as a symptom of major depressive disorder: results from the National Comorbidity Survey Replication. *Molecular psychiatry*. 2010;15(8):856-67.
14. Fisher LB, Fava M, Doros GD, Alpert JE, Henry M, Huz I, et al. The Role of Anger/Hostility in Treatment-Resistant Depression: A Secondary Analysis From the ADAPT-A Study. *The Journal of nervous and mental disease*. 2015;203(10):762-8.
15. Riley WT, Treiber FA, Woods MG. Anger and hostility in depression. *The Journal of nervous and mental disease*. 1989;177(11):668-74.
16. Perlis RH, Smoller JW, Fava M, Rosenbaum JF, Nierenberg AA, Sachs GS. The prevalence and clinical correlates of anger attacks during depressive episodes in bipolar disorder. *Journal of affective disorders*. 2004;79(1-3):291-5.

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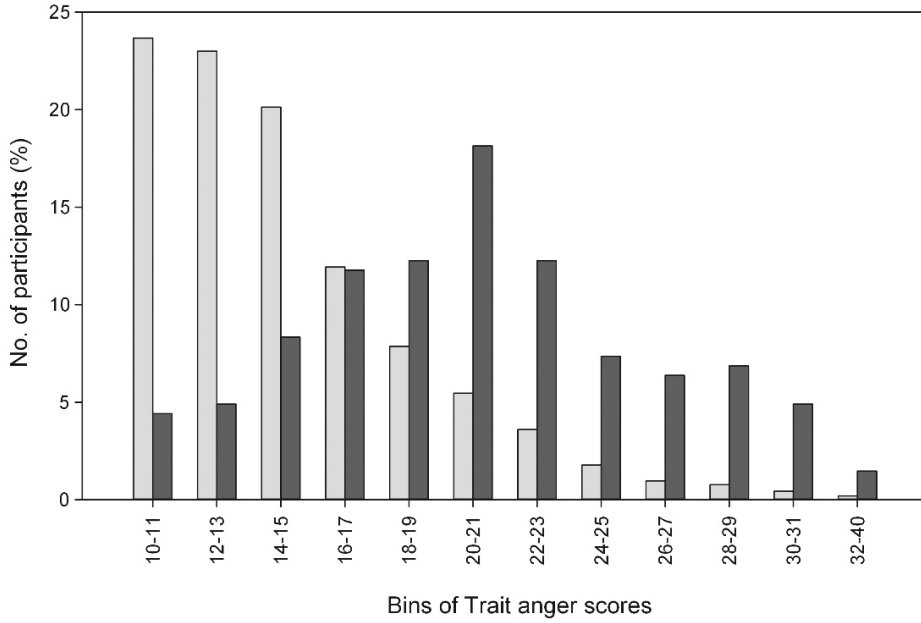
17. Sayar K, Guzelhan Y, Solmaz M, Ozer OA, Ozturk M, Acar B, et al. Anger attacks in depressed Turkish outpatients. *Annals of clinical psychiatry : official journal of the American Academy of Clinical Psychiatrists*. 2000;12(4):213-8.
18. Winkler D, Pjrek E, Kasper S. Anger attacks in depression--evidence for a male depressive syndrome. *Psychotherapy and psychosomatics*. 2005;74(5):303-7.
19. Winkler D, Pjrek E, Kindler J, Heiden A, Kasper S. Validation of a simplified definition of anger attacks. *Psychotherapy and psychosomatics*. 2006;75(2):103-6.
20. Fava M, Alpert J, Nierenberg AA, Ghaemi N, O'Sullivan R, Tedlow J, et al. Fluoxetine treatment of anger attacks: a replication study. *Annals of clinical psychiatry : official journal of the American Academy of Clinical Psychiatrists*. 1996;8(1):7-10.
21. Fava M, Nierenberg AA, Quitkin FM, Zisook S, Pearlstein T, Stone A, et al. A preliminary study on the efficacy of sertraline and imipramine on anger attacks in atypical depression and dysthymia. *Psychopharmacology bulletin*. 1997;33(1):101-3.
22. Gould RA, Ball S, Kaspi SP, Otto MW, Pollack MH, Shekhar A, et al. Prevalence and correlates of anger attacks: a two site study. *Journal of affective disorders*. 1996;39(1):31-8.
23. Deschenes SS, Dugas MJ, Fracalanza K, Koerner N. The role of anger in generalized anxiety disorder. *Cogn Behav Ther*. 2012;41(3):261-71.
24. Moscovitch DA, McCabe RE, Antony MM, Rocca L, Swinson RP. Anger experience and expression across the anxiety disorders. *Depression and anxiety*. 2008;25(2):107-13.
25. Fava GA, Grandi S, Rafanelli C, Saviotti FM, Ballin M, Pesarin F. Hostility and irritable mood in panic disorder with agoraphobia. *Journal of affective disorders*. 1993;29(4):213-7.
26. Hawkins KA, Coughle JR. Anger problems across the anxiety disorders: findings from a population-based study. *Depression and anxiety*. 2011;28(2):145-52.
27. Barrett EL, Mills KL, Teesson M. Mental health correlates of anger in the general population: Findings from the 2007 National Survey of Mental Health and Well-being. *Australian & New Zealand Journal of Psychiatry*. 2013;47(5):470-6.
28. Genovese T, Dalrymple K, Chelminski I, Zimmerman M. Subjective anger and overt aggression in psychiatric outpatients. *Compr Psychiatry*. 2017;73:23-30.
29. Penninx BWJH, Beekman ATF, Smit JH, Zitman FG, Nolen WA, Spinhoven P, et al. The Netherlands Study of Depression and Anxiety (NESDA): rationale, objectives and methods. *International Journal of Methods in Psychiatric Research*. 2008;17(3):121-40.
30. Spielberger CD. Preliminary Manual for the State-Trait Anger Scale (STAS). 1980.
31. Van der Ploeg HM, Defares PB, Spielberger CD. Handleiding bij de zelf-analyse vragenlijst ZAV. Een vragenlijst voor het meten van boosheid en woede, als toestand en als dispositie. Manual for the self-analysis questionnaire, a Dutch adaptation of the Spielberger State-Trait Anger Scale. Lisse: Swets & Zeitlinger; 1982.
32. Lubke GH, Ouwens KG, de Moor MH, Trull TJ, Boomsma DI. Population heterogeneity of trait anger and differential associations of trait anger facets with borderline personality features, neuroticism, depression, Attention Deficit Hyperactivity Disorder (ADHD), and alcohol problems. *Psychiatry research*. 2015;230(2):553-60.
33. Fava M, Rosenbaum JF, McCarthy M, Pava J, Steingard R, Bless E. Anger attacks in depressed outpatients and their response to fluoxetine. *Psychopharmacology bulletin*. 1991;27(3):275-9.

34. Fava MR, JF. Anger Attacks in Patients with Depression. *The Journal of clinical psychiatry*. 1999;60:21-4.
35. APA. Diagnostic and Statistical manual of mental disorders 4th edition (DSM-IV). Washington, DC: *British Library Cataloguing in Publication Data*. 1994.
36. Rush AG, CM; Basco, MR; Jarrett, RB; Trivedi, MH. The Inventory of Depressive Symptomatology (IDS): psychometric properties. *Psychological medicine*. 1996;26(3):477-86.
37. Rush AJ, Giles DE, Schlessner MA, Fulton CL, Weissenburger J, Burns C. The Inventory for Depressive Symptomatology (IDS): preliminary findings. *Psychiatry research*. 1986;18(1):65-87.
38. Beck AT, Epstein N, Brown G, Steer RA. An inventory for measuring clinical anxiety: psychometric properties. *Journal of consulting and clinical psychology*. 1988;56(6):893-7.
39. Marks IM, Mathews AM. Brief standard self-rating for phobic patients. *Behaviour research and therapy*. 1979;17(3):263-7.
40. Meyer TJ, Miller ML, Metzger RL, Borkovec TD. Development and validation of the penn state worry questionnaire. *Behaviour research and therapy*. 1990;28(6):487-95.
41. Fresco DM, Mennin DS, Heimberg RG, Turk CL. Using the Penn State Worry Questionnaire to identify individuals with generalized anxiety disorder: a receiver operating characteristic analysis. *Journal of behavior therapy and experimental psychiatry*. 2003;34(3-4):283-91.
42. Fava M, Rosenbaum JF, Pava JA, McCarthy MK, Steingard RJ, Bouffides E. Anger attacks in unipolar depression, Part 1: Clinical correlates and response to fluoxetine treatment. *The American journal of psychiatry*. 1993;150(8):1158-63.
43. Brody CL, Haaga DA, Kirk L, Solomon A. Experiences of anger in people who have recovered from depression and never-depressed people. *The Journal of nervous and mental disease*. 1999;187(7):400-5.
44. Judd LL, Schettler PJ, Coryell W, Akiskal HS, Fiedorowicz JG. Overt irritability/anger in unipolar major depressive episodes: past and current characteristics and implications for long-term course. *JAMA psychiatry*. 2013;70(11):1171-80.
45. Lee AH, DiGiuseppe R. Anger and aggression treatments: a review of meta-analyses. *Current Opinion in Psychology*. 2018;19:65-74.
46. Bowers L, Stewart D, Papadopoulos C, Dack C, Ross J, Khanom H, et al. Inpatient violence and aggression: a literature review. 2011.
47. Milkman HB, Wanberg KW. Cognitive-Behavioral Treatment: A review and discussion for corrections professionals.: Washington, DC: National Institute of Corrections; 2007.
48. Trupin EW, Stewart DG, Beach B, Boesky L. Effectiveness of a Dialectical Behaviour Therapy Program for Incarcerated Female Juvenile Offenders. *Child and Adolescent Mental Health*. 2002;7(3):121-7.
49. Capita LP, Chapman R, Murphy SE, Harvey CJ, James A, Cowen PJ, et al. A single dose of fluoxetine reduces neural limbic responses to anger in depressed adolescents. *Translational psychiatry*. 2019;9(1):30.
50. Choi-Kwon S, Han SW, Kwon SU, Kang DW, Choi JM, Kim JS. Fluoxetine treatment in poststroke depression, emotional incontinence, and anger proneness: a double-blind, placebo-controlled study. *Stroke*. 2006;37(1):156-61.

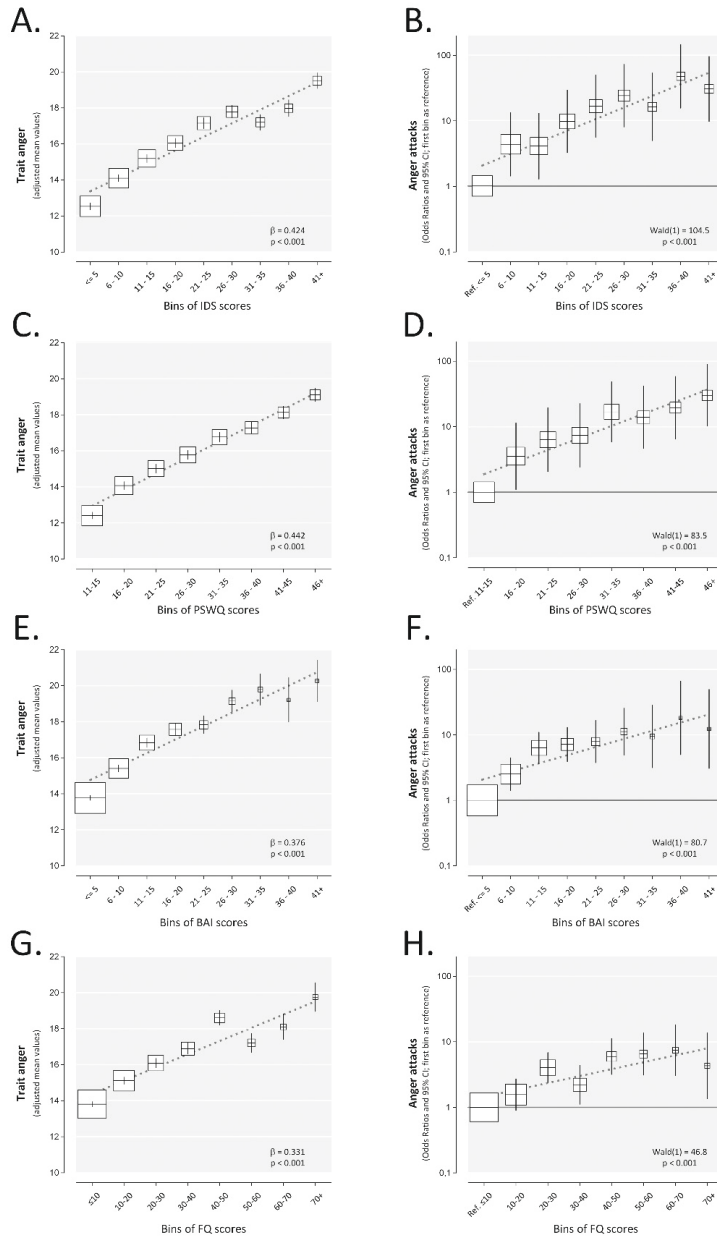
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51. Coccaro EF, Lee RJ, Kavoussi RJ. A double-blind, randomized, placebo-controlled trial of fluoxetine in patients with intermittent explosive disorder. *The Journal of clinical psychiatry*. 2009;70(5):653-62.
52. Batrinos ML. Testosterone and Aggressive Behavior in Man. *International Journal of Endocrinology and Metabolism*. 2012;10(3):563-8.
53. Giancola PR, Saucier DA, Gussler-Burkhardt NL. The effects of affective, behavioral, and cognitive components of trait anger on the alcohol-aggression relation. *Alcoholism, clinical and experimental research*. 2003;27(12):1944-54.
54. Sadikaj G, Moskowitz DS. Alcohol Consumption and Trait Anger Strengthen the Association Between Perceived Quarrelsomeness and Quarrelsome Behavior via Feeling Angry. *Alcoholism, clinical and experimental research*. 2018.
55. Fracalanza K, Koerner N, Deschênes SS, Dugas MJ. Intolerance of Uncertainty Mediates the Relation Between Generalized Anxiety Disorder Symptoms and Anger. *Cognitive Behaviour Therapy*. 2014;43(2):122-32.
56. Baker R, Holloway J, Thomas PW, Thomas S, Owens M. Emotional processing and panic. *Behaviour research and therapy*. 2004;42(11):1271-87.
57. Hawkins KA, Macatee RJ, Guthrie W, Cogle JR. Concurrent and Prospective Relations Between Distress Tolerance, Life Stressors, and Anger. *Cognitive Therapy and Research*. 2013;37(3):434-45.
58. Salters-Pedneault K, Roemer L, Tull MT, Rucker L, Mennin DS. Evidence of Broad Deficits in Emotion Regulation Associated with Chronic Worry and Generalized Anxiety Disorder. *Cognitive Therapy and Research*. 2006;30(4):469-80.
59. Sheline YI, Barch DM, Donnelly JM, Ollinger JM, Snyder AZ, Mintun MA. Increased amygdala response to masked emotional faces in depressed subjects resolves with antidepressant treatment: an fMRI study. *Biological psychiatry*. 2001;50(9):651-8.
60. Stein MB, Goldin PR, Sareen J, Zorrilla LTE, Brown GG. Increased Amygdala Activation to Angry and Contemptuous Faces in Generalized Social Phobia. *JAMA psychiatry*. 2002;59(11):1027-34.
61. Posternak MA, Zimmerman M. Anger and aggression in psychiatric outpatients. *The Journal of clinical psychiatry*. 2002;63(8):665-72.
62. Newman JL, Fuqua DR, Gray EA, Simpson DB. Gender Differences in the Relationship of Anger and Depression in a Clinical Sample. *Journal of Counseling & Development*. 2006;84(2):157-62.
63. Kay SR, Wolkenfeld F, Murrill LM. Profiles of aggression among psychiatric patients. I. Nature and prevalence. *The Journal of nervous and mental disease*. 1988;176(9):539-46.
64. Yudofsky SC, Silver JM, Jackson W, Endicott J, Williams D. The Overt Aggression Scale for the objective rating of verbal and physical aggression. *The American journal of psychiatry*. 1986;143(1):35-9.
65. Nijman HLI, Muris P, Merkelbach HLGJ, Palmstierna T, Wistedt B, Vos AM, et al. The staff observation aggression scale-revised (SOAS-R). *Aggressive behavior*. 1999;25(3):197-209.
66. Matsumoto D, Yoo SH, Chung J. The Expression of Anger Across Cultures. In: Potegal M, Stemmler G, Spielberger C, editors. *International Handbook of Anger: Constituent and Concomitant Biological, Psychological, and Social Processes*. New York, NY: Springer New York; 2010. p. 125-37.
67. APA. *Diagnostic and Statistical Manual of Mental Disorders, 5th ed*. Washington, DC: American Psychiatric Association; 2013.

68. Friedman MJ. Finalizing PTSD in DSM-5: getting here from there and where to go next. *Journal of traumatic stress*. 2013;26(5):548-56.
69. Orth U, Wieland E. Anger, hostility, and posttraumatic stress disorder in trauma-exposed adults: a meta-analysis. *Journal of consulting and clinical psychology*. 2006;74(4):698-706.
70. Taft CT, Creech SK, Murphy CM. Anger and aggression in PTSD. *Curr Opin Psychol*. 2017;14:67-71.
71. Coccaro EF. Intermittent explosive disorder as a disorder of impulsive aggression for DSM-5. *The American journal of psychiatry*. 2012;169(6):577-88.
72. Medeiros GC, Seger L, Grant JE, Tavares H. Major depressive disorder and depressive symptoms in intermittent explosive disorder. *Psychiatry research*. 2018;262:209-12.
73. Bertsch K, Krauch M, Roelofs K, Cackowski S, Herpertz SC, Volman I. Out of control? Acting out anger is associated with deficient prefrontal emotional action control in male patients with borderline personality disorder. *Neuropharmacology*. 2018:107463.
74. Mancke F, Herpertz SC, Bertsch K. Correlates of Aggression in Personality Disorders: an Update. *Current Psychiatry Reports*. 2018;20(8):53.
75. Weissman MM, Klerman GL, Paykel ES. Clinical evaluation of hostility in depression. *The American journal of psychiatry*. 1971;128(3):261-6.



Supplementary Fig. 1. Distribution of having anger attacks according to trait anger scores



Supplementary Fig. 2. Adjusted associations between trait anger and anger attacks and bins of the IDS (A and B), PSWQ (C and D), BAI (E and F), and FQ (G and H) scores in the overall sample. The size of each square is proportional to the number of participants in each bin. Error bars indicate standard errors. Standardized beta-coefficients, adjusted for sex, age, level of education, BMI, smoking, alcohol dependency/abuse, with their accompanying p values are given. Note: IDS = Inventory of Depressive Symptomatology; PSWQ = Penn State Worry Questionnaire; BAI = Beck Anxiety Inventory; FQ = Fear Questionnaire.