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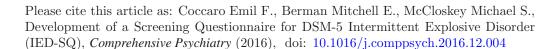
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Development of a Screening Questionnaire for DSM-5 Intermittent Explosive Disorder (IED-SQ)

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ABSTRACT

Objective. This study was designed to develop and test a screening approach to identify individuals with DSM-5 Intermittent Explosive Disorder (IED), a disorder of recurrent, problematic, impulsive aggression.

Methods. A screening approach to diagnose DSM-5 IED (IED-SQ) was developed by combining items related to life history of aggression and items related to the DSM-5 diagnostic criteria for IED. In Study 1, the IED-SQ was studied in 72 adult participants; 33 that met DSM-5 criteria for lifetime IED and 39 that did not. In Study 2, the IED-SQ was given to 740 undergraduates at a US university. Measures of aggression and anger expression and anger control were assessed in both studies.

Results. In Study 1, the IED-SQ demonstrated strong concordance with the best estimate diagnoses (Kappa = .80) for lifetime IED by DSM-5 criteria and good test-retest reliability (kappa = 0.71). In Study 2, the IED-SQ identified 4.3% of the undergraduate sample as meeting DSM-5 criteria for lifetime IED, a rate comparable to that in recent epidemiological studies. Participants identified as meeting DSM-5 criteria for lifetime IED, in both studies, had higher aggression scores, and higher anger expression, and lower anger control scores, compared to participants that did not meet DSM-5 criteria for lifetime IED.

<u>Conclusions</u>. These data suggest that the IED-SQ is a useful screening tool that can quickly identify the presence of IED by DSM-5 criteria in adults.

1.0 INTRODUCTION

Intermittent Explosive Disorder (IED), the sole DSM psychiatric diagnostic category for which recurrent acts of aggression are a cardinal symptom, was once thought to be quite rare [1]. However, community surveys report that IED, defined by DSM-IV, is a common psychiatric disorder, occurring in approximately 4-6% of the U.S. population [2]. In preparation for DSM-5, investigators developed Research Criteria (IED-R; [3], to correct several problems with the DSM-IV IED criteria set. Limitations in the DSM-IV criteria set included the lack of definition as to what qualified as "aggressive behavior", how often such aggressive behavior occurs and in what time frame, lack of a requirement that the aggressive acts be impulsive, or non-instrumental, in nature, lack of a distress and/or impairment requirement and, lack of clarity as to specific exclusion criteria. Later, IED-R criteria were modified further as Integrated Research Criteria for IED (IED-IR; [4-6]). While IED-R criteria stipulated that the core criterion for IED can be met by the presence of frequent (twice weekly for at least one month) verbal and/or non-destructive/nonassaultive aggressive outbursts, IED-IR stipulated that infrequent (three times a year), but physically destructive and/or assaultive aggressive outbursts, also met research criteria for IED, since these type of outbursts were included as A criteria symptoms in DSM-IV. IED-IR criteria were later adopted as DSM-5 criteria for IED with the exception that frequent verbal aggression and non-assaultive/non-destructive physical aggression are present for an average of twice weekly for three months (DSM-5) [7] instead of one month (IED-IR) [4-6]. In addition, the presence of frequent verbal aggression and nonassaultive/non-destructive physical aggression became the A₁ criteria while the presence

of infrequent but physically destructive and/or assaultive aggressive outbursts, became the A_2 criteria for IED by DSM-5.

In order to simplify the initial assessment of DSM-5 IED we developed a method to screen individuals for the presence of DSM-5 IED by conducting two studies. The first study compared the performance of an IED Screening Questionnaire (IED-SQ) with the standard clinical research assessment to identify DSM-5 IED. The second examined the ability of this IED-SQ to identify individuals with lifetime DSM-5 IED in a large group of general undergraduate students at a university.

We had three research aims designed to support the potential utility of screening for DSM-5 IED in adults. First, to demonstrate that the IED-SQ would have good psychometric characteristics and perform as well as an extensive clinical research assessment in identifying individuals with DSM-5 IED in a clinical research sample (Study 1); second, to demonstrate that participants identified as having DSM-5 IED by IED-SQ in Study 2, would display a similar pattern of scores on aggression, anger expression, and anger control assessments as individuals identified as DSM-5 IED in Study 1; and third, to demonstrate that the IED-SQ identifies individuals with DSM-5 IED in a non-clinical sample (Study 2) at a rate similar to that identified by structured interviews of individuals in a large community sample [2].

2.0 STUDY 1 - METHODS

- 2.1 <u>Participants</u>. Seventy-two individuals, included 36 men and 36 women, recruited as part of ongoing aggression studies, participated in Study 1. These participants were recruited though public service announcements seeking individuals with anger and aggression problems as well as seeking individuals without self-reported anger or aggression problems. More than half (61%) of participants had prior history of psychiatric treatment (36%) or of a behavioral disturbance for which mental health care should have been sought but was not (25%). The latter was based on whether the participant reported that the behavioral disturbance was associated with distress and/or impairment but that the participant did not seek mental health evaluation or care for that behavioral disturbance. The study was approved by the Institutional Review Board and informed consent was obtained from all participants.
- Diagnostic Assessment. Syndromal (formerly Axis I) and personality (formerly Axis II) disorder diagnoses were made according to DSM-5 criteria [7]. Research assessments using the Structured Clinical Interview for DSM Diagnoses (SCID) [8], Structured Interview for the Diagnosis of DSM Personality Disorder (SIDP) [9], and our own Intermittent Explosive Disorder Interview (IED-M) [10], were performed by individuals with masters or doctoral degrees in clinical psychology. Inter-rater reliability (kappa) for lifetime syndromal disorders by SCID were good to excellent and were as follows: IED-5 (IED-M; k = 0.82), mood (SCID; k = 0.85), anxiety (SCID; k = 0.79) substance use (SCID; k = 0.93) and personality disorder (SIDP; k = 0.83). Final diagnoses were assigned by best-estimate consensus procedures as previously described [11] and were performed "blind"

to IED-SQ data. Thirty-three participants met DSM-5 criteria for lifetime IED (23 also met for current IED) based on the best-estimate procedure. Lifetime diagnoses for the remaining participants were as follows: six for depressive disorder, one for anxiety disorder, seven for substance use disorder, two for eating disorder, and twelve for personality disorder.

2.3 Measures.

2.3.1. <u>Development of the IED Screening Questionnaire (IED-SQ)</u>. The development of a screening approach for the diagnosis of DSM-5 IED began with an examination of the relationship between IED and Life History of Aggression (LHA; [12]) data. The LHA is a widely used measure that quantitatively assesses one's life history of overt aggressive behavior (i.e., aggressive thoughts/urges are not counted) [13]. It is conducted as a semi-structured interview and consists of three subscales: a) Aggression (e.g., how many times have you had verbal arguments with others, broke something in anger, hit another person in anger); b) Consequences (e.g., how many times has your aggressive behavior led to discipline or other adverse consequence); and, c) Self-Directed Aggression including suicide attempts. Internal consistency for these subscales are very good for Aggression ($\alpha = 0.87$), acceptable for Consequences ($\alpha = 0.74$), and poor for Self-Directed Aggression ($\alpha = 0.48$). Inter-rater reliability is excellent for LHA Aggression ($\alpha = 0.94$) and very good for LHA Consequences ($\alpha = 0.88$); test-retest reliability for these two subscales is also good-to-excellent (Aggression: $\alpha = 0.80$). Consequences: $\alpha = 0.89$).

We chose to explore the utility of the first two subscales as an approach to screening for DSM-5 IED because each of these two subscales has good psychometric properties [12], DSM-5 IED is characterized by high levels of overt aggression and functional impairment/distress due to aggressive behavior [3,4], and participants with DSM-5 IED, in our research program, have significantly higher scores on both LHA subscales compared with healthy controls and compared with psychiatric controls (unpublished data). Examination of LHA data in 400 healthy individuals without personal (or family) history of psychiatric disorders revealed that LHA Aggression scores ≥ 12, and LHA Consequence scores > 4, were found only among the top 2.5% of the group (p = 0.05). Thus, we used these cutoff scores to represent abnormally high lifetime history of overt aggressive behavior and of consequences due to aggressive behavior. Applying both LHA cutoff scores in a group of 800 participants with various psychiatric disorders, in our research program, we found high specificity (90.5%) but low sensitivity (61.0%) for IED-5. Closer examination revealed that the low sensitivity was due to the fact that the LHA Consequence subscale assesses only the functional impairment of IED and not any of the other diagnostic criteria for DSM-5 IED.

Accordingly, we created a new seven-item set of questions, to be added to the five LHA Aggression items, to identify DSM-5 IED in adult research participants. These seven items included questions regarding: a) frequency of verbal / nondestructive aggression (A₁ Criteria) and offset of these behaviors (E Criteria), b) frequency of destructive/assaultive aggression (A₂ Criteria) and offset of these behaviors (E Criteria), c) proportionality of aggressive responses to the provocation (B Criteria), d) impulsive or

planned nature of aggressive outbursts (C Criteria), e) distress and/or impairment resulting from aggressive outbursts (D Criteria), f) exclusionary factors related to the presence of other psychiatric disorders (F_1 Criteria) and, g) exclusionary factors related to the behavioral influence of medication, or drugs of abuse, on aggressive outbursts (F_2 Criteria). Early in development, however, we discovered that aggressive individuals had substantial difficulty understanding the difference between an appropriate, compared with a disproportionate, behavioral response to social threat and aggressive individuals had difficulty disentangling the effects of multiple psychiatric disorders (though not regarding the effects of medications or drugs of abuse) in the association with their own aggressive behavior. Accordingly, items related to these two criteria (B and F_1) were dropped so that the IED-SQ would be composed of the five LHA Aggression items and the remaining five IED-Related items. The internal consistency of the LHA Aggression items in Study 1 participants was very good ($\alpha = 0.87$).

- 2.3.2. <u>Scoring the IED-SQ</u>. A lifetime diagnosis of DSM-5 IED was made when the respondent scored \geq 12 on the first five items (Part 1: LHA Aggression) and gave affirmative answers on items 1a, 2, 3, 4a/4, and 5a/5b (Part 2: IED-Related items).
- 2.3.3. <u>Aggression and Anger Assessments</u>. Trait aggression was assessed using the summary score of the Verbal Aggression, Physical Aggression, and Anger scales of the Buss-Perry Aggression Questionnaire [14]. The BPAQ has good psychometric properties [14] and this BPAQ variable had high internal consistency in Study 1 participants (BPAQ: $\alpha = .85$). Specific assessment of regarding the trait expression and control of aggression

when "angry or furious" was assessed with the State-Trait Anger Expression Inventory 2 - Anger Expression/Control Scales (STAXI-2 AX/AC) [15]. The two STAXI-2 Expression scales measure the tendency to engage in aggression against others or objects (Anger Expression-Out; AX-OUT: "I strike out at whatever infuriates me") or to express it passively without actively aggressing (Anger Expression-In; AX-IN: "I boil inside, but I don't show it"). The two STAXI-2 Control scales assess the frequency with which individuals use strategies to reduce their anger (Anger Control-In; AC-IN: "I try to soothe my angry feelings") and aggression (Anger Control-Out: AC-OUT: "I control my urge to express my angry feelings"). The STAXI-2 scales used in this study have good psychometric properties [15] and each had good internal consistency in Study 1 participants (AX-OUT: α = .88; AX-IN: α = .80; AX-OUT: α = .87; AX-IN: α = .88).

2.4 <u>Protocol</u>. Participants completed the diagnostic interview (and LHA Aggression) upon entering our research program; the five IED-Related items were completed on a separate day at least one, but typically weeks, apart (mean: 55.4 <u>+</u> 37.9 weeks).

2.5 STUDY 1 - RESULTS

2.5.1. <u>Participant Characteristics</u>. Study participants meeting, or not meeting, DSM-5 criteria for lifetime IED, by the best estimate process, differed in age and in years of education but not in distribution of sex or ethnicity. Accordingly, subsequent analyses were performed adjusting for these demographic variables. As expected, the DSM-5 IED participants had higher BDHI Aggression scores and STAXI-2 Anger Expression, and

lower STAXI-2 Anger Control, scores compared with participants that did not meet DSM-5 criteria for lifetime IED (Table 1).

2.5.2 <u>Properties of the IED-SQ</u>. The kappa coefficient for lifetime DSM-5 IED by best-estimate method, compared with that made through the IED-SQ was 0.80. The IED-SQ correctly identified 27 of the 33 (82% sensitivity) best-estimate method DSM-5 IED participants while excluding 38 of the 39 (97% specificity) individuals who did not meet DSM-5 criteria for lifetime IED by best-estimate method. Positive predictive power, negative predictive power, and overall accuracy for DSM-5 IED by IED-SQ were 0.96, 0.86, and 0.90, respectively. BDHI Aggression scores between the two DSM-5 IED groups did not differ as a function of whether the lifetime DSM-5 IED diagnosis was made by best-estimate (e.g., 63.7 ± 22.1) or by IED-SQ (65.1 ± 21.4). The kappa coefficient for test-retest reliability of the IED-SQ, after repeat administration in 56 subjects (6-12 months later), was 0.71.

2.6 STUDY 1 - DISCUSSION

The results of Study 1 suggest that the IED-SQ represents a valid and reliable screening approach for the DSM-5 diagnosis of IED. The IED-SQ showed strong agreement with expert best-estimate DSM-5 diagnosis of lifetime IED. In addition, aggression scores for participants with DSM-5 IED were the same regardless of whether participants met DSM-5 IED criteria by best-estimate or by the IED-SQ, indicating near identity for the two diagnostic approaches. More importantly, we found that sensitivity, specificity, as well as positive/negative predictive power and overall accuracy of the IED-SQ were excellent.

We also found that a DSM-5 diagnosis of lifetime IED on the IED-SQ was stable over a period of 6 to 12 months.

3.0 STUDY 2 - METHODS

The objective of Study 2 was to assess the utility of the IED-SQ as a screening tool in a larger second, non-clinical, university sample of participants and to compare the results with that from Study 1. This study was approved by the Institutional Review Board of the university and informed consent was obtained from all participants.

- 3.1. <u>Participants</u>. Seven hundred and forty-two undergraduate students at a South Eastern University in the United States (72%: Female, 53%: White, 44%: African-American, 3%: Other) with a mean age of 20.5 (SD: <u>+</u> 4.0) years, and 13.2 (SD: 1.1) years of education, participated in this study for class credit.
- 3.2 <u>Administration of the IED-SQ</u>. The IED-SQ in Study 2 was the same as that in Study 1 with the exception that LHA Aggression items were completed by questionnaire rather than by interview. This was done because it was impractical to administer the LHA Aggression items by interview to a large group of research participants at the same time and because we had found that LHA Aggression scores by interview or questionnaire are, statistically, the same. Specifically, in a group of 418 research participants in our program (298 with, and 138 without, lifetime history of psychiatric disorder) who completed the LHA Aggression items by interview and by questionnaire, within three months of each other (mean \pm sd: 2.0 \pm 2.6 weeks), we found nearly identical internal consistency

coefficients and means for the LHA Aggression items by interview (α = .88; 10.8 \pm 7.0) and questionnaire (α = .89; 10.6 \pm 6.7), as well as a very high intra-class correlation between the two scores (ICC = 0.91, p < 0.001). Internal consistency for the LHA Aggression items for the Study 2 participants was 0.72.

- 3.3 <u>Aggression and Anger Measures</u>. Aggression and anger measures were the same as in Study 1. Cronbach alphas for BPAQ Aggression and for the STAXI-2 Anger Expression/Control subscales were 0.85 (BPAQ), 0.80 (AX-OUT), 0.77 (AX-IN), 0.85 (AC-OUT), and 0.89 (AC-IN) for Study 2 participants.
- 3.4 *Protocol*. Participants completed the IED-SQ, BPAQ, and STAXI-2-AX/AC, as well as a brief demographic questionnaire, during a 1-hour group session.

3.4 STUDY 2 - RESULTS

- 3.4.1 <u>Participant Characteristics</u>. Participants identified as having lifetime DSM-5 IED by the IED-SQ differed from those not identified as DSM-5 IED by the IED-SQ in years of education but not in age or in distribution of sex. For comparability with Study 1, subsequent analyses were performed adjusting for all of these demographic variables.
- 3.4.2 <u>DSM-5 IED by IED-SQ</u>. Using the IED-SQ, a DSM-5 diagnosis of lifetime IED was assigned in 32 (4.3%) of the 742 participants.

3.4.1 Aggression and Anger Scores as a Function of IED-SQ Status. As in Study 1 (Table 1), BPAQ Aggression scores were higher in participants identified by IED-SQ has having lifetime DSM-5 IED compared with participants not identified as DSM-5 IED by IED-SQ. STAXI-2 Anger Expression and Anger Control Scores were also different as a function of DSM-5 IED groups with DSM-5 IED participants displaying an increased tendency to engage in aggression against others and less use of strategies to control such outbursts than the Non-DSM-5-IED participants. Participants identified as meeting DSM-5 criteria for IED did not differ from those not meeting DSM-5 criteria for IED in the extent to which they internalized anger or try to control internalized anger (Table 2).

3.5 STUDY 2 - DISCUSSION

The results from Study 2 suggest that the IED-SQ can be effective as a screening tool for the presence of DSM-5 IED in adult participants. In addition, the direction of group differences in BPAQ Aggression and STAXI-2 Anger Expression and Anger Control was the same for participants in both studies and the effect size for group differences in BPAQ Aggression, STAXI-2 Anger Expression-OUT, and in Anger Control-OUT for participants in both studies were comparable. This suggests that aggression and externally directed anger control are similarly quantified in participants identified as meeting DSM-5 criteria for lifetime IED by best-estimate and by the IED-SQ. Finally, while not a direct comparison with extant community studies, the proportion of individuals identified as meeting DSM-5 criteria for lifetime IED by the IED-SQ in Study 2 [4.3% (95% CI: 2.9-5.8%)] was comparable to the lifetime prevalence of DSM-5 IED [3.6% (95% CI: 3.2-

4.0%)] reported as part of a reanalysis of the National Comorbidity Study-Replication sample [16].

4.0 SUMMARY AND LIMITATIONS

In Study 1, the IED-SQ performed well in a mixed clinical sample of modest size. Additional validation research will benefit from larger clinical comparison groups with an even higher proportion of comorbid disorders associated with aggression, as we note that the rate of this comorbidity was lower in our subjects than in other studies. Limitations include, first, the relatively modest sample size of Study 1 and, second, the often lengthy period between initial clinical research interviews and completion of the IED-Related items. For example, the LHA assessment in Study 1 was performed during the initial diagnostic assessment while the data for the IED-Related items were collected at a later time limiting the screening approach to the identification of lifetime diagnoses of DSM-5 criteria for IED only. We have now added items to ascertain current vs. past status of IED (see Appendix) but specific data regarding such status were not available for these studies. Despite these limitations, the IED-SQ performed well even with the extended period of time between interview and questionnaire administration in Study 1. authors acknowledge the importance of also determining the predictive validity of diagnosing current IED by DSM-5 criteria and are currently conducting a study to assess the ability of IED-SQ to diagnose current DSM-5 IED in a mixed clinical sample. Finally, while the results of Study 1 suggest that a DSM-5 IED diagnosis by best-estimate, or by IED-SQ, are highly concordant (accuracy of 90%), a study of the receiver operating

characteristics of the IED-SQ in a general community sample will be helpful in fully assessing the diagnostic efficacy of the questionnaire version of the IED-SQ.

Study 2 supports the use of the IED-SQ in a non-clinical sample, especially in that the participants identified as meeting lifetime DSM-5 criteria for IED had similar patterns on aggression and anger measures as the DSM-5 IED participants of Study 1. The full IED-SQ form is presented in the Appendix. Limitations of Study 2 include, first, that this sample was obtained during one course at one university. Second, research interviews to ascertain the psychiatric diagnoses of these participants were not conducted and thus, sensitivity/specificity, and other screening performance parameters, of the IED-SQ could not be calculated. It is possible that the IED-SQ may have been more, or less, effective in detecting the presence of DSM-5 IED in this sample if more extensive assessment data were available. Third, undergraduate participants may yield invalid data, up to 10-15% in some cases, due to inadequate effort and random responding. Thus, inclusion of random responses may inflate correlations between any measures of deviance because nonrandom responses to such items tend to be infrequent in the general population. All this said, however, the IED-SQ identified a very similar proportion of DSM-5 IED participants in Study 2 as in a large community sample [4.3% vs. 3.6%, respectively; 16].

Finally, if the IED-SQ is shown to discriminate DSM-5 IED in subsequent studies in both clinical and community population samples, the IED-SQ may represent a quick and effective tool to identify those with recurrent, problematic, impulsive aggressive behavior. In the meantime, we proffer that the performance of the IED-SQ documented in this report supports the use of the IED-SQ in clinical research settings.

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CONFLICT OF INTEREST STATEMENT:

Dr. Coccaro reports being on the Scientific Advisory Board of Azevan Pharmaceuticals, Inc. and being a current recipient of a grant award from the NIMH. Drs. Berman and McCloskey report no conflicts of interest regarding this work.

Table 1

Characteristics of IED-5^a and Non-IED-5 Participants in Study 1

	Variable	IED-5	Non-IED-5	р
d			(N = 33)	(N = 39)
	Age	41.1 <u>+</u> 8.2	35.0 <u>+</u> 9.5	= 0.006 ^b
	Sex (% Female)	51	48	$= 0.813^{c}$
	Ethnicity (% W / AA / Other)	58 / 27 / 15	69 / 10 / 21	= 0.171 ^c
	Years of Education	14.8 <u>+</u> 2.3	15.9 <u>+</u> 2.5	= 0.046 ^b
	BPA Aggression 0.61	63.7 <u>+</u> 25.9	50.3 <u>+</u> 18.	$5 = 0.035^{d}$
	STAXI-2 AX OUT 1.24	22.6 <u>+</u> 6.4	14.7 <u>+</u> 4.	.4 < 0.001 ^d
	STAXI-2 AX IN 0.95	20.5 <u>+</u> 6.4	15.4 <u>+</u> 4.	.4 < 0.001 ^d
	STAXI-2 AC OUT 1.01	19.0 <u>+</u> 6.7	25.2 <u>+</u> 4.	5 < 0.001 ^d
	STAXI-2 AC IN 1.38	17.0 <u>+</u> 6.2	25.5 <u>+</u> 4.	2 < 0.001 ^d

<u>Notes</u>: a: Diagnosis by interview assessment followed by best-estimate (see text); b: t-test; c: Chi-Square; d: ANCOVA (covariates: age, sex, ethnicity, education); W: White, AA: African-American; BPAQ: Buss Perry Aggression Questionnaire; STAXI-2: State-Trait Anger Expression Inventory 2; STAXI-AX: Anger Expression, STAXI-AC: Anger Control.

 Table 2

 Characteristics of IED-5^a and Non-IED-5 Participants in

Study	2
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	Variable	IED-5 ^a	р	
d		C		
		(N = 31)	(N = 711)	
	Λ α. α.	24.4.2.2.4	20.4 . 4.0	0.242b
	Age	21.4 <u>+</u> 3.4	20.4 <u>+</u> 4.0	= 0.213 ^b
	Sex (% Female)	75	72	= 0.721 ^c
	Ethnicity (% W / AA / Other)	79 / 17 / 4	52 / 45 / 3	= 0.764 ^c
	Years of Education	13.6 <u>+</u> 1.2	13.2 <u>+</u> 1.1	$= 0.034^{b}$
	BPAQ Aggression	63.9 <u>+</u> 12.3	48.7 <u>+</u> 12.3	< 0.001 ^d
1.18	2			
	STAXI-2 AX OUT	21.0 <u>+</u> 4.5	16.9 <u>+</u> 4.5	< 0.001 ^d
	0.90			
	STAXI-2 AX IN	18.7 <u>+</u> 4.9	18.1 <u>+</u> 5.0	$= 0.537^{d}$
	0.12			
	STAXI-2 AC OUT	20.4 <u>+</u> 4.9	23.9 <u>+</u> 4.9	< 0.001 ^d
	0.71	_	_	
	STAXI-2 AC IN	21.1 <u>+</u> 5.3	23.0 <u>+</u> 5.2	$= 0.048^{d}$
	0.36	<u>-</u> •.•		

Notes: a: Diagnosis by IED-SQ (see text); b: t-test; c: Chi-Square; d: ANCOVA (covariates: age, sex, ethnicity, education); W: White, AA: African-American; BPAQ: Buss

Perry Aggression Questionnaire; STAXI-2: State-Trait Anger Expression Inventory 2; STAXI-AX: Anger Expression, STAXI-AC: Anger Control.

