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Unhealthy Aggression: Intermittent Explosive Disorder and Adverse Physical Health Outcomes

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Objective: To examine the relationship between Intermittent Explosive Disorder (IED; a psychiatric diagnosis characterized by episodes of affective aggression) and adverse physical health outcomes. ***Design:*** A large epidemiological sample drawn from the Collaborative Psychiatric Epidemiological Surveys ($N = 10,366$), was used to compare participants with a lifetime diagnosis of IED ($n = 929$) to those without any history of IED ($n = 9,437$) on demographic variables (age, education, gender, race) common risk factors (smoking status, body mass index, substance use disorders, past accident or injury requiring treatment, major depression) and the presence of 12 adverse health outcomes. ***Main Outcome Measures:*** History of heart attacks, coronary heart disease, hypertension, stroke, lung disease, diabetes, cancer, arthritis, back/neck pain, ulcer, headaches, and other chronic pain. ***Results:*** Logistic regression analysis controlling for demographic and other risk factors indicated that IED was associated with 9 of the 12 adverse physical health outcomes (coronary heart disease, hypertension, stroke, diabetes, arthritis, back/neck pain, ulcer, headaches, and other chronic pain). Only cancer, heart attacks, and lung disease were not significantly related to IED. ***Conclusion:*** IED may be a risk factor for several significant adverse physical health outcomes.

Keywords: Intermittent Explosive Disorder, aggression, physical health, pain

Intermittent Explosive Disorder (IED) is a psychiatric diagnosis used to classify individuals who engage in repeated acts of affective (anger-based) aggression that are disproportionate to any provocation and not better accounted for by the effects of a substance, medical condition, or other psychological disorder (American Psychiatric Association [APA], 2000). IED is the only disorder in the *DSM–IV–TR* whose central feature is affective aggression. Though a part of the psychiatric nomenclature for more than 30 years (APA, 1980), IED has been an understudied disorder relative to other psychiatric disorders with similar prevalence rates and poor outcomes. Indeed, we are only beginning to appreciate the breadth, scope, and consequences of this disorder.

Though initially believed to be rare (APA, 2000), recent epidemiological studies indicate the prevalence of IED is about 4–7% (Coccaro, Posternak, & Zimmerman, 2005; Kessler et al., 2006; Ortega, Canino, & Alegria, 2008). Prototypically, IED tends to run a chronic course, lasting on average 12–20 years. Over this time, the IED patients will engage in ~55 acts of physical aggression, several of which require medical attention (Kessler et al., 2006; McElroy, Soutullo, Beckman, Taylor, & Keck, 1998). Not surprisingly, the limited research suggests that IED is associated with considerable social and occupational impairment that can include loss of work, relationship problems, and legal difficulties (McCloskey, Berman, Noblett, & Coccaro, 2006; McElroy et al., 1998). However, despite its relatively high prevalence and chronic course, the relationship between IED and physical health has yet to be examined.

Previous research has shown that psychiatric conditions, particularly those associated with negative mood states, are associated with physical health problems. Major depression is associated with a 1.5 to 2.0 relative risk for coronary heart disease (CHD) in healthy individuals and an even greater risk for cardiac morbidity and mortality among those with preexisting CHD (Blumenthal & Lett, 2005; Lett et al., 2004). Depression is also associated with increased risk of developing other negative health outcomes such as diabetes (Carnethon et al., 2007; Carnethon, Kinder, Fair, Stafford, & Fortmann, 2003), hypertension (Davidson, Jonas, Dixon, & Markovitz, 2000; Jonas, Franks, & Ingram, 1997), cerebrovascular accident [stroke] (Jonas & Mussolino, 2000; Liebetrau, Steen, & Skoog, 2008), and chronic pain (Currie & Wang, 2005). Among individuals who already have these health problems, comorbid depression is associated with increased functional impairment, symptom burden, and worsened prognosis (Lett et al., 2004; Whooley, 2006; Whooley et al., 2008). In contrast to depression, the potential adverse physical health outcomes associated with IED have not been systematically examined. However, research on

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constructs presumably associated with IED, such as anger and hostility, may provide insights into the association between IED and health problems.

Anger refers to an emotional experience (feeling angry) which can be assessed as either a current mood state or a general predisposition toward feeling angry (trait anger), with the latter more common in both aggression and health outcome research. Hostility refers to a trait-like tendency toward having suspicious, cynical, or resentful thoughts. Despite focusing on different domains (emotional vs. cognitive), hostility and anger are strongly related constructs (Buss & Perry, 1992). Furthermore, both are elevated among individuals with IED (McCloskey et al., 2006). A rich literature has examined the association between both anger and hostility and CHD dating back to research on Type A personality (of which hostility is one component) and CHD (Friedman & Rosenman, 1974). The majority of studies provide at least partial support for a relationship between both anger and hostility and CHD. Cross sectional studies of men (Meesters, Muris, & Backus, 1996), women (Lahad, Heckbert, Koepsell, Psaty, & Patrick, 1997), and low income African Americans (Grothe, Bodenlos, Whitehead, Olivier, & Brantley, 2008) show higher levels of hostility among individuals with CHD. Longitudinal studies show that hostility and anger predict CHD onset (Kawachi, Sparrow, Spiro, Vokonas, & Weiss, 1996; Niaura et al., 2002), recurrence (Chaput et al., 2002; Haas et al., 2005), and mortality (Matthews, Gump, Harris, Haney, & Barefoot, 2004), with anger possibly being more associated with CHD among normotensive patients (Williams et al., 2000). Meta-analyses of prospective CHD studies have likewise generally supported the contention that hostility is a risk factor for CHD (Hemingway & Marmot, 1999; Krantz & McCeney, 2002; Miller, Smith, Turner, Guijarro, & Hallet, 1996; Smith, 1992), though some of these findings have been contested (Petticrew, Gilbody, & Sheldon, 1999) and meta-analyses showing only modest support have also been published (Kuper, Marmot, & Hemingway, 2002; Myrtek, 2001). One issue is that the relationship between CHD and anger or hostility may be moderated by such demographic factors as culture (Ikeda, Iso, Kawachi, Inoue, & Tsugane, 2008), socioeconomic status (Grothe et al., 2008), or gender (Haas et al., 2005). It is also possible that the extent to which angry feelings and hostile thoughts lead to overt aggressive behaviors may play a role in the relationship between these variables and CHD.

The relationship between anger and hostility and negative health outcomes is not limited to CHD. Other studies have shown that anger and hostility are also associated with Type 2 diabetes (Golden et al., 2006), hypertension (Rutledge & Hogan, 2002), and stroke for young to middle-aged individuals (Arthur, 2002; Williams, Nieto, Sanford, Couper, & Tyroler, 2002). Chronic anger may also compromise lung functioning and accelerate the natural decrease in lung power that occurs with aging (Kubzansky et al., 2006; Lehrer, 2006).

Pain problems are also associated with an angry or hostile temperament. Individuals with a history of migraine or tension headaches have higher anger levels and poorer anger control (Materazzo, Cathcart, & Pritchard, 2000; Perozzo et al., 2005). Furthermore, anger levels predict headache activity among those with a history of headaches (Materazzo et al., 2000). Among chronic pain patients, high levels of hostility, anger, and anger suppression are associated with greater muscle tension, pain severity, and pain behaviors (Burns, Bruehl, & Quartana, 2006; Burns, Holly et al., 2008; Burns, Quartana et al., 2008).

In summary, research suggests that anger and hostility are associated with several adverse physical health outcomes. However, it is less clear if overt aggressive behavior is associated with poor health outcomes. Results of several studies indicate that aggressive tendencies are a risk factor for problems such as CHD (Siegman, Townsend, Civelek, & Blumenthal, 2000) and chronic pain (Bruehl, Chung, Burns, & Biridepalli, 2003). Other studies have reported that suppression of aggressive tendencies is a risk factor for health problems (Burns et al., 2006; Eng, Fitzmaurice, Kubzansky, Rimm, & Kawachi, 2003; Lahad et al., 1997). One limitation of these studies, however, is the use of self-ratings of aggressive disposition (items such as "Once in awhile I can't control the urge to strike another person"; Buss & Perry, 1992) rather than measures of actual aggressive behaviors. Examination of IED may be particularly important to better understanding the relationship between aggression and poor health outcomes because IED is an established disorder in the psychiatric nosology that requires the presence of repeated acts of aggressive behavior that are disproportionate to any existing provocation or stressor. Thus, IED serves as both a psychopathological diagnostic entity and as an exemplar of a life-history of clinically relevant impulsive aggressive behavior.

In the current study we examined the data from 10,366 individuals who completed interview assessments of psychiatric history (including IED) and physical health as a part of the Collaborative Psychiatric Epidemiological Surveys [CPES] (Alegria, Jackson, Kessler, & Takeuchi, 2003). We hypothesize that individuals diagnosed with IED will have a higher incidence of CHD, hypertension, stroke, and chronic pain than individuals without an IED diagnosis. We further hypothesize the relationship between IED and adverse health outcomes will persist after controlling for IED group differences in demographic variables and other risk factors (e.g., smoking, weight, substance use history, accidents, injuries, and major depression).

Method

Participants

Participants were interviewed as a part of the 2001–2003 Collaborative Psychiatric Epidemiological Surveys [CPES] (Allegria et al., 2003), which included data from the National Comorbidity Survey Replication (NCS-R), National Survey of American Life (NSAL), and the National Latino and Asian American Study (NLAAS). The total CPES sample consisted of 20,013 noninstitutionalized individuals aged 18 or over residing in the United States (see Heeringa et al., 2004, for a detailed description of the CPES sampling procedure). The CPES recruitment and consent procedures were approved by human subjects committees of Harvard Medical School (Boston) and the University of Michigan (Ann Arbor). The subsample used in the current study consisted of the 10,366 (4,521 men and 5,845 women) adults ages 18–65 (M = 42.25, SD = 16.04) for whom data on both lifetime IED status and health outcomes were available. Participants were categorized into mutually exclusive groups with a history of IED (n = 929) and without a diagnosis of IED (n = 9,437). Thus, the percentage of

participants with IED in this sample (9.1%) is slightly higher than found using the full NCS-R database (7.3%) (Kessler et al., 2006).

Self-Report Measures

The CPES surveys were derived from the World Mental Health Composite International Diagnostic Interview (WMH-CIDI; [Kessler & Ustun, 2004]). The WMH-CIDI was itself derived partly from the Diagnostic Interview Schedule and partly from an earlier version of the CIDI. The data were collected by the Survey Research Center (SRC) of the Institute for Social Research at the University of Michigan using computer assisted personal interviewing between 2001 and 2003.

IED status. Lifetime IED versus control was based on the CPES variable 07866, *DSM–IV* Intermittent Explosive Disorder (LifeT). Pilot data have shown strong concordance for the diagnosis of lifetime IED between the CPES interview and a semi-structured diagnostic interview by trained clinicians ($N = 50$; $\kappa = .76$) (Coccaro, McCloskey, & Lee, 2009).

Demographic variables. Participant data on items assessing participant age, gender, race, marital status, and education were obtained. The CPES 12 category race variable (RANCEST) was recoded to identify five racial/ethnic groups: Hispanic, non-Hispanic Asian, non-Hispanic African American, Non-Hispanic White, and "other." For marital status, two groups of unmarried individuals (never married and divorced/separated) were combined to create a single dichotomous variable of married or cohabiting versus not married and not cohabiting. Similarly, education was dichotomized into individuals with <4-year college degree versus those with a 4-year college degree (with or without postgraduate education).

Potential health risk variables. To assess and control for potential differences between IED and control groups on factors known to be associated with negative health outcomes, information was obtained on the participant's smoking status, Body Mass Index (BMI) classification (i.e., underweight [BMI < 18.5], healthy weight [BMI 18.5–24.99], overweight [BMI 25–29.99], obese Level I [BMI 30–34.99], obese Level 2 [BMI 35–39.99], and obese Level 3 [BMI ≥ 40]), history of alcohol abuse or dependence, history of other drug abuse or dependence, and previous accidents or injuries. Please note that the investigator extended the BMI classification from one decimal (e.g., healthy weight = BMI 18.5–24.9) to two decimals (e.g., healthy weight = BMI 18.5–24.99) to classify individuals with BMIs that placed them between classifications (see below). To assess previous injury, we used the item "in the past 12 months did you have an accident, injury or poisoning that required medical attention?" (injury requiring treatment). This is likely a conservative estimate of previous injuries and accidents as it only takes into account those injuries and accident that were severe enough to necessitate medical treatment and only accounts for injuries and accidents in the past year. Exercise was also assessed by averaging items that asked about the frequency of moderate exercise >30 min in the winter and in the summer.

Health outcomes. To assess physical health outcomes, we used a set of 12 items from the chronic conditions section of the CPES that assessed the proportions of individuals who experienced a disease (heart disease, lung disease, cancer, diabetes), conditions associated with a chronic health problem (stroke, heart attack, ulcer, hypertension) or chronic pain condition (arthritis, headaches, back/neck pain, other chronic pain).

Data Analysis

Dichotomous data were recoded to so that 0 represented the absence of a disorder or condition and 1 represented its presence. Obesity data were missing for 141 participants. For 95 of these participants, this was because the exact BMI was in between the BMI classifications in the initial dataset (which did not extend beyond one decimal place). In these situations, the BMI was calculated by the investigators using available height and weight data and the participant was placed in the appropriate BMI classification. IED and control groups were compared on demographic variables and putative risk factors using chi-square for categorical data and *t* tests for continuous data. The same method was used to assess the simple relationship between IED status and health outcomes. Finally, to assess the health risk associated with IED, independent of groups differences on other variables, a series of logistic regressions were used in which demographic variables (i.e., gender, race, age, education, marital status) and risk factors (i.e., smoking status, alcohol abuse and dependence, drug abuse and dependence, BMI, lifetime major depression, past year injury requiring treatment) were first entered into the logistic regression, followed by IED status.

Results

Preliminary Analyses

Demographic variables. IED participants ($M = 35.67$ years; $SD = 12.91$) were younger than their control ($M = 42.90$ years; $SD = 16.17$) counterparts, $t(10, 364) = 13.22$, $p < .001$. IED participants were more likely than controls to be male, unmarried, and not to have graduated college (see Table 1). IED and control groups also differed with respect to racial composition. Follow-up chi-square analyses showed that, relative to controls, the IED group had a higher proportion of White participants and a lower proportion of Asian, African American, and Hispanic participants (all ps $< .05$).

Risk factors. IED and control participants differed with respect to smoking history. Follow-up chi-square analyses showed that IED participants were more likely to be a current smoker and less likely to have never been a regular smoker than control participants (all ps $< .01$). IED participants were also more likely to have a history of both moderate (abuse) and severe (dependence) problems for both alcohol and other drugs. IED and control participants also differed in BMI such that, relative to a healthy BMI, a higher proportion of IED participants were obese, $\chi^2(1, 6507) = 16.39$ $p < .001$.

A smaller portion of participants (IED $n = 73$, control $n = 800$) reported on their exercise habits. Among those, IED ($M = 4.36$; $SD = 1.58$) and control ($M = 4.56$; $SD = 1.65$) participants did not differ in their frequency of moderate exercise, $t(871) = 1.12$, $p = .26$. Both groups exercised 30 min or more between once week and several times a month on average over the course of a year. Finally, IED participants were more likely to have an accident or injury requiring treatment in the past year though no participant (IED or control) reported an accident or injury requiring treatment

Table 1
Characteristics of Participants (N and %) as a Function of IED Status (N = 10,366)

	IED (n = 929)	Control (n = 9,437)	χ^2
Male gender	498 (53.6)	4023 (42.6)	41.43**
Married/cohabitating	530 (57.1)	5790 (61.4)	6.58*
College graduate	764 (82.2)	6936 (73.5)	33.83**
Race			121.16**
Asian	98 (10.5)	2080 (22.0)	
Hispanic	248 (26.7)	2836 (30.1)	
African-American	98 (10.5)	624 (6.6)	
White	446 (48.0)	3747 (39.7)	
Other	39 (4.2)	150 (1.6)	
Smoking status			135.72**
Current smoker	358 (38.5)	2070 (21.9)	
Ex-smoker	190 (20.5)	2068 (21.9)	
Nonsmoker	381 (41.0)	5299 (56.2)	
Lifetime drug abuse	203 (21.9)	625 (6.6)	266.87**
Lifetime drug dependence	92 (9.9)	225 (2.4)	161.28**
Lifetime alcohol abuse	294 (31.6)	1039 (11.0)	321.44**
Lifetime alcohol dependence	152 (16.4)	399 (4.2)	247.40**
BMI category[a]			25.57**
Underweight (BMI <18.5)	29 (3.1)	328 (3.5)	
Healthy (BMI 18.5–24.99)	339 (36.5)	3852 (41.0)	
Overweight (BMI 25–29.99)	291 (31.4)	3104 (33.0)	
Obese level 1 (BMI 30–34.99)	165 (17.8)	1345 (14.3)	
Obese level 2 (BMI 35–39.99)	56 (6.0)	478 (5.1)	
Obese level 3 (BMI 40+)	48 (5.2)	285 (3.0)	
Past year injury requiring treatment	114 (12.3)	718 (7.6)	24.89**
Lifetime major depression	301 (32.4)	1846 (19.6)	84.89**

[a] Data missing from 46 participants (1 IED and 45 non-IED).
* $p < .05$. ** $p < .001$.

in the past year that was a direct result of fighting. Not surprisingly, a greater proportion of IED participants had a life-history of depression compared to controls.

Health outcomes. There was a small amount of missing data for the different health outcomes (missing data: $n = 17$ arthritis, $n = 10$ ulcer, $n = 9$ CHD, $n = 7$ hypertension, $n = 7$ diabetes, $n = 6$ heart attack, $n = 3$ cancer, $n = 2$ lung disease, $n = 1$ back pain, $n = 1$ other chronic pain). As can be seen in Table 2, participants with IED were more likely to have a stroke and to have lung disease than controls. IED participants were also more likely to have most kinds of pain including ulcers, neck/back pain, headaches, and other chronic pain. Surprisingly, IED status was not associated with hypertension. IED was also unrelated to coronary heart disease or history of heart attacks, diabetes, cancer, or arthritis.

Regression analyses. To determine which health outcomes were associated with IED after controlling for demographic and other risk variables, a series of logistic regression analyses were performed using the different health outcomes as the dependent measures. With the exception of exercise habits (which did not show a group effect and for which only a small portion of participants responded) all previously identified demographic variables

Table 2
Health Outcomes as a Function of IED Status

	IED (N = 929)	Control (N = 9437)	χ^2
Heart attacks: *n* (%)	23 (2.5)	243 (2.6)	0.03
Heart disease: *n* (%)	46 (5.0)	489 (5.2)	0.10
Hypertension: *n* (%)	190 (20.5)	2025 (21.5)	0.53
Stroke: *n* (%)	27 (2.9)	177 (1.9)	4.66*
Lung disease: *n* (%)	24 (2.6)	154 (1.7)	4.28*
Diabetes: *n* (%)	67 (7.2)	724 (7.7)	0.26
Cancer: *n* (%)	38 (4.1)	426 (4.5)	0.36
Arthritis: *n* (%)	207 (22.3)	2179 (23.1)	0.32
Neck/back pain: *n* (%)	330 (35.5)	2469 (26.2)	37.56**
Headaches: *n* (%)	339 (36.5)	2199 (23.3)	79.57**
Ulcer: *n* (%)	120 (12.9)	840 (8.9)	16.24**
Other chronic pain: *n* (%)	124 (13.3)	912 (9.7)	12.75**

* $p < .05$. ** $p < .001$.

and health risk factors were entered into the regression in a single step, followed by IED status. Results (see Table 3) show that the presence of IED was unrelated to history of a heart attack ($p = .61$) or cancer ($p = .12$) and showed only a nonsignificant trend toward being associated with lung disease ($p < .09$). IED was significantly associated with all other negative health outcomes (heart disease, hypertension, stroke, diabetes, arthritis, neck/back pain, headaches, ulcer, and other chronic pain).

Among the variables controlled for in Step 1 of the model, increased age was the strongest predictor of poor health (Wald = 15.54 [headaches] to 1,370.78 [arthritis]; all ps $< .001$). Race was also a significant predictor across all health outcomes with being African American (relative to White) associated with an increased prevalence of hypertension, stroke, and diabetes, but reduced prevalence of neck/back pain, cancer, and ulcers (all ps $< .05$). Hispanic ethnicity (relative to non-Hispanic Whites) was associated with increased likelihood of heart disease, stroke, and diabetes, but a reduced prevalence of cancer, arthritis, neck/back pain, headaches, ulcers, and other chronic pain (all ps $< .05$). Women were more likely to have arthritis, neck/back pain, and headaches. Men were more likely to have a heart attack, heart disease, and hypertension. Individuals who did not finish college were more likely to suffer from stroke, lung disease, diabetes, arthritis, and headaches (all ps $< .05$). In terms of behavioral risk factors, obesity (relative to healthy weight) was associated with all negative health outcomes other than cancer, though mild obesity was not associated with lung disease or stroke. Smoking was associated with heart attacks, heart disease, stroke, lung disease, diabetes, cancer, arthritis, neck/back pain, headaches, ulcers, and other chronic pain. History of substance problems (alcohol or other drug abuse or dependence) was also associated with several adverse health outcomes including heart disease, lung disease, cancer, arthritis, neck/back pain, and other chronic pain. Recent history of accident or injury requiring treatment was associated with hypertension, ulcer, stroke, as well as most pain problems (arthritis, neck/back pain, headaches, and other chronic pain). Finally, depression was associated with a history of heart attack, lung disease, ulcers, and pain problems (arthritis, neck/back pain, headaches, and other chronic pain).

Discussion

We hypothesized that IED would be associated with several negative physical health outcomes and that this relationship would persist after controlling for demographic variables and risk factors. Our findings generally supported our hypothesis. Initial examination of the simple relationship between IED and health outcomes showed IED to be associated with stroke, lung disease, ulcers, and most forms of pain. After controlling for demographic variables and risk factors, IED showed a nonsignificant association with lung disease, but was also found to be associated with an increased prevalence of CHD, hypertension, diabetes, and arthritis. Thus, IED was associated with most of the negative health outcomes examined. The discrepancy between the initial findings and the results of the logistic regression appear to be accounted for largely by impact of age, as non-IED control participants were significantly older than IED participants and age was significantly associated with all of the aforementioned health outcomes.

The strongest findings for IED were with chronic pain. IED participants were more likely to suffer from headaches, chronic neck/back pain, and other chronic pain both before and after controlling for demographic and risk factors. This is consistent with the majority of research that suggests chronic pain patients have higher levels of anger, increased anger expression, and decreased aggression inhibition (Bruns & Disorbio, 2000; Carlsson, 1986) and argues against the notion that suppressed anger, rather than expressed anger is more common among headache sufferers (Nicholson, Gramling, Ong, & Buenaver, 2003). It is worthwhile to note that other studies have also found that tension headache sufferers have more anger and anger expression than healthy volunteers (Materazzo et al., 2000).

There are multiple pathways through which IED could interact with chronic pain. Chronic pain can make individuals feel more dysphoric, including more irritated and less tolerant to distress, which could increase the likelihood of aggression (Berkowitz, 1989). However, if aggressive behavior only occurs within the context of chronic pain an IED diagnosis cannot be assigned. It is also possible that the presence of IED makes one more vulnerable to develop chronic pain or headaches via an increased likelihood of

Table 3
Logistic Regression of IED Status on Health Outcomes After Controlling for Demographic Variables and Risk Factors (Including MDD)

Outcome	B	*SE* (B)	Wald	OR	95% CI
Heart attacks	0.12	.24	0.26	1.13	0.71–1.81
Heart disease	0.35	.17	4.07*	1.42	1.01–1.99
Hypertension	0.27	.10	7.40**	1.31	1.08–1.59
Stroke	0.70	.23	9.51**	2.01	1.29–3.14
Lung disease	0.42	.24	2.94	1.52	0.94–2.45
Diabetes	0.29	.15	3.88*	1.33	1.00–1.77
Cancer	0.29	.19	2.33	1.33	0.92–1.91
Arthritis	0.27	.10	7.86**	1.31	1.09–1.58
Neck/back pain	0.33	.08	17.02***	1.39	1.19–1.62
Headaches	0.49	.08	38.75***	1.64	1.40–1.91
Ulcer	0.31	.12	7.44**	1.36	1.09–1.69
Other chronic pain	0.23	.11	4.70*	1.27	1.02–1.58

* $p < .05$. ** $p < .01$. *** $p < .001$.

physical trauma. Individuals with IED report that 2–3 of their aggressive acts lead to hospitalization of themselves or their victim (Kessler et al., 2006) and other altercations that might not result in hospitalization (e.g., concussion, mild spinal damage) could lead to chronic pain if left untreated. It is also possible that IED is linked with chronic pain through dysregulation of a biologic process, such as the endogenous opioid system. Opioids and opioid receptors, which help to modulate pain are located in the anterior cingulate, an area that is also an important component of the circuit governing emotion regulation (Casey et al., 2000; Davidson, Putnam, & Larson, 2000). High levels of anger expression are associated with opioid dysfunction among chronic pain patients (Bruehl, Burns, Chung, & Quartana, 2008) and opioid challenge studies using naloxene show that diminished opioid functioning partially mediates the relationship between anger expression and chronic pain intensity (Bruehl et al., 2003). Moreover, administration of opioids has been shown to increase aggressive responding under controlled, laboratory conditions (Berman, Taylor, & Marged, 1993).

There was partial support for an association between IED and CHD. Though IED was not initially associated with either the presence of CHD or a history of heart attacks, after controlling for age and other risk factors IED emerged as a risk factor for CHD. Odds of a heart attack, though slightly higher, were not significantly associated with IED. This could be explained by the fact that our sample included individuals aged 18 to 65 years, but the mean age for a first heart attack is typically older than this (i.e., 66–70 years old; American Heart Association [AHA], 2005). This fact, especially in light of the group finding for CHD, suggests that the relatively young sample may have limited our ability to identify differences in heart attack prevalence between the IED and non-IED participants. Studies of older adults would clarify the relationship between IED and history of heart attacks.

Any relationship between IED and CHD is likely to be overdetermined. IED may facilitate CHD indirectly through the potentiation of risk factors associated with CHD. Participants with IED showed a higher incidence of several negative health behaviors linked to CHD. For example, individuals with IED were almost twice as likely to be smokers and had approximately a two- to fourfold increase in substance use disorders. These behaviors were statistically controlled for in this study but this does not make them any less likely to increase the risk of CHD and other negative health outcomes among IED participants. In addition, the health behaviors assessed in this study are clearly not exhaustive. Other behaviors associated with both impulsive behavior behaviors and adverse health outcomes, such as risky sexual behaviors, are worthy of future study.

Risk factors can also include other medical conditions. We found that hypertension and diabetes, known risk factors for CHD (Carneiro, 2004; Mensah, Brown, Croft, & Greenlund, 2005), were linked to IED. Relatedly, the increased intensity and frequency of exaggerated cardiovascular responses associated with anger and aggression (Lorber, 2004) can contribute to the development and progression of CHD (Smith & Ruiz, 2002; Treiber et al., 2003).

Psychosocial factors may also play a role in the relationship between IED and adverse health outcomes. Individuals with IED have increased interpersonal difficulties that can lead to decreased social support, higher levels of stress, and more impaired functioning (McElroy et al., 1998). Thus, individuals with IED may both demonstrate an exaggerated physiological response to situations they perceive as stressful and an increased tendency to see situations as stressful, but they might also encounter more objectively stressful situations. However, these suggestions all assume that IED is a risk factor for CHD. It is also possible that early symptoms of CHD pose a risk factor for IED by increasing irritability and aggressiveness.

Some previous research using individuals with low to moderate levels of anger and aggression found that anger expression was a protective factor for stroke (Eng et al., 2003). However, we found that pathological levels of aggression (i.e., IED status) are associated with increased likelihood of having a stroke. This is consistent with research showing high trait anger as a risk factor for stroke in adults 60 and younger (Arthur, 2002; Williams et al., 2002). IED status was also linked to hypertension and it is therefore possible that hypertension may contribute to the relationship of IED to both CHD and stroke.

IED was also associated with increased incidence of ulcers and (after controlling for other variables) arthritis. Ulcers and arthritis may be linked to IED through increased stress and reactivity to stress. Though stress is no longer thought to play a causal role in the development of ulcers, it may still be contributory (Wachirawat et al., 2003) as emotional stress has been shown to increase gastric acid secretions (Bresnick, Rask-Madsen, Hogan, Koss, & Isenberg, 1993). Individuals with IED tend to have more adverse life events and to be more distressed by them, suggesting they receive a higher "dose" of stress that may over time increase the likelihood of ulcers. Likewise, though there is little evidence suggesting stress causes arthritis (Li, Schiottz-Christensen, & Olsen, 2005), psychological stress appears to increase arthritic symptoms in both human and nonhuman animals (Seres, Stancikova, Svik, Krsova, & Jurcovicova, 2002; Smith & Zautra, 2002; Zautra et al., 2007). It is also possible that wear to the body associated with frequent physical fights that occur for many participants with IED may increase the likelihood of developing arthritis. But again, it is also possible that the increased pain and impairment caused by these physical conditions may increase ones irritability and reduce their capacity to use more adaptive (nonaggressive) coping responses to other stressors. Finally, we must consider the possibility that IED is associated with factors (e.g., neglect of physical health) that contribute to health problems in general.

Lung disease was initially more prevalent in the IED group, with only a trend level relationship remaining after controlling for demographic and other risk factors. This was not surprising in light of the fact that the greatest risk factor for lung disease is smoking and participant smoking status was one of the variables controlled. More work is needed to tease out the relationship between IED and lung disease. For example, it is possible that even among smokers, IED participants had a more extensive smoking history which directly contributed to the increased prevalence of lung disease. Alternately, there is some evidence to suggest that chronic increased levels of anger and hostility can result in decreased lung capacity and accelerate the natural lung decline associated with aging (Lehrer, 2006).

Neither cancer nor diabetes was more prevalent in IED as compared to control participants. However, after controlling for risk factors, diabetes (but not cancer) was significantly associated with IED. This is in contrast to previous research which found that an angry temperament initially was a risk factor for Type 2

diabetes, but was no longer significant after controlling for lifestyle variables and BMI (Golden et al., 2006). However, that study used an older sample and did not examine high levels of aggression. It is possible that chronic anger and aggressiveness can result in changes in insulin sensitivity via continual activation of the sympathetic nervous system (Wiesner, Bluher, Windgassen, & Paschke, 2003). However, this remains to be tested among individuals with IED.

This study has several strengths. We used a large epidemiological sample that received comprehensive structured assessment for psychiatric disorders (including IED) and relevant health outcomes. The study also controlled for several behavioral, demographic and psychological risk factors. However, there are also several aspects of the study that limit its generalizability. First, it should be emphasized that this was cross sectional study and not a prospective study. Therefore we can speak only to the extent that IED is associated with negative health outcomes. We can speculate as to the possible nature of this relationship, but we cannot make any definite statements as to whether IED is a causal factor for these outcomes. In addition, the data collection involved lay interviewers as opposed to clinical professionals, which may have impacted the accuracy of the IED and other psychiatric diagnoses. Furthermore, because the data collection method was not designed to assess the relationship between health outcomes and IED, more detailed assessments of the health outcomes (e.g., severity rating, physiological measures), risk factors (e.g., detailed eating and smoking and injury/accident history), and aggression (e.g., level of anger, hostility) were not fully assessed. To address these issues (e.g., the extent to which angry feelings, hostile thoughts and aggressive behaviors are independently associated with negative health outcomes) longitudinal studies specifically designed to assess the impact of aggression and IED on physical well-being are needed.

This study is the first to demonstrate that the presence of an IED diagnosis is associated with several major medical disease processes. If future studies establish a causal link between IED and these disease processes, interventions designed to reduce the expression of aggressive behavior may also be useful in reducing associated medical disease processes. Accordingly, aggression outcome studies should include assessments of health behaviors and medical outcomes, and not limit dependent measures to behaviors and costs directly tied to aggression.

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