



Substance use disorders: Relationship with intermittent explosive disorder and with aggression, anger, and impulsivity



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ABSTRACT

Background: A relationship between substance use and aggression has been noted for decades. While substance use appears to be associated with an increased risk of aggressive behavior, no study has yet reported on the pattern of comorbidity and temporal relationship between impulsive aggression (i.e., intermittent explosive disorder) and substance use disorders (SUD), specifically.

Methods: To specify these relationships, we examined DSM-5 diagnosis data from diagnostic interviews of 1355 adults who met one of five non-overlapping diagnostic subgroups: those with intermittent explosive disorder (IED; $n = 339$), those with SUD ($n = 136$), IED+SUD ($n = 280$), adults with psychiatric disorders but no SUD or IED ($n = 320$), and healthy Controls: HC, $n = 282$).

Results: Occurrence of lifetime SUD was elevated in IED vs. all Non-IED subjects (Odds Ratio: 3.61 [95% CI: 2.82–4.63]) and onset of IED preceded SUD in 80% of comorbid IED+SUD cases. Examination of the severity of impulsive aggression and SUD revealed that IED increased SUD severity but the presence of SUD did not increase severity of IED core features, including aggression, anger, or impulsivity.

Conclusions: Subjects with IED are at increased risk of developing substance use disorder, compared to those without IED. This suggests that history of recurrent, problematic, impulsive aggression is a risk factor for the later development of SUD rather than the reverse. Thus, effective treatment of impulsive aggression, before the onset of substance misuse, may prevent or delay the development of SUD in young individuals.

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1. Introduction

Intermittent Explosive Disorder (IED) is characterized by recurrent, problematic, impulsive aggressive behavior (American Psychiatric Association, 2013). While it was previously thought that the impulsive aggressive behavior in IED was due to the presence of other psychiatric disorders, data from an early study revealed that IED exists in pure form and is more prevalent than once thought (Feltous et al., 1991). Subsequent epidemiologic data from adults and adolescents indicate that the prevalence of IED is greater than 3–5% and that the age of onset of IED is earlier than that of most other psychiatric disorders (Kessler et al., 2006; McLaughlin et al., 2012). Accordingly, when impulsive aggressive

outbursts are not limited to episodes of another psychiatric or medical disorder, the diagnosis of IED may be made. In clinical samples, IED is typically co-morbid with other disorders such as depression, anxiety, and substance use, disorders (Coccaro, 2012). While we previously reported on comorbidity issues of IED with depressive and anxiety disorders (Coccaro, 2011; Coccaro et al., 1998), to our knowledge there are no published studies addressing the pattern of comorbidity and temporal aspects of IED and substance use disorders (SUDs). This is important because associative data suggests that substance use/misuse leads to aggressive behavior and that aggressive behavior, in those who use/misuse substances, should be considered secondary to substance use/misuse.

The relationship between aggressive behavior and SUDs has been addressed in the literature for many years. A variety of substances have been linked to an increase in the risk of aggressive behavior, notably, alcohol, cannabis, cocaine, and amphetamines

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(Beck et al., 2014; Boles and Miotto, 2003; Hoaken and Stewart, 2003). This statement belies the complexity of such comorbidity. One important issue concerns how aggression is defined. For example, there are at least two forms of aggressive behavior: a) aggressive behavior that is impulsive or reactive/defensive in nature (Barratt et al., 1997a; Cornell et al., 1996; Kockler et al., 2006; Stanford et al., 2003); and b) aggressive behavior that is pre-meditated and is typically associated with psychopathy (Barratt et al., 1997a; Coccaro et al., 2014; Cornell et al., 1996). The second important issue in understanding this comorbidity is the association between substance use and aggression. Substance use may influence aggressive behavior directly through disinhibitory effects of acute intoxication (McCloskey et al., 2009) or indirectly through social contexts, personality variables, or exposure to violence (Hoaken and Stewart, 2003). Conversely, it is also possible that problematic aggressive behavior increases the risk for substance use/misuse and/or that the two share a similar substrate as the two disorders share similar event related potential anomalies in electroencephalographic studies (Barratt et al., 1997b; Moeller et al., 2004). Accordingly, with the advent of the reliable and valid clinical diagnosis of IED, the categorical expression of impulsive aggression (Coccaro, 2012), it is timely to examine the relationship between IED and SUD.

In this study, we analyzed clinical research data from extensive diagnostic interviews conducted in the context of our larger clinical research program of impulsive aggression in order to examine the relationship between IED and SUD. Subjects with current SUD were not included in these studies because the current comorbid presence of SUD would compromise interpretation of the various psychobiological studies we were conducting. That said, a substantial number of our subjects had a lifetime history of SUD and this allowed us to examine the extent and nature of the comorbidity between IED and SUD, including patterns of aggression, anger, and impulsivity scores as a function of IED and SUD, as well as the relative ages of onset of IED and SUD in individuals with lifetime diagnoses of both disorders. The latter is particularly important because analysis of age of onset data can help elucidate which disorder appears first in comorbid cases. Based on the literature, and on research experience in working with individuals with recurrent, problematic, impulsive aggressive behavior (McCloskey et al., 2009), we hypothesized that: a) persons with current or past IED would have higher risk of lifetime SUDs compared with non-IED participants; b) persons with comorbid IED + SUD would show earlier age of onset of IED than SUD; c) persons with comorbid IED + SUD would exhibit greater severity of SUD but not the reverse; and, d) dimensional measures of aggression, anger, and impulsivity would be highest in both IED and in IED + SUD subjects compared with all other subjects.

2. Methods

2.1. Subjects

The sample was comprised of 1355 physically healthy adults systematically evaluated in regard to aggression, anger, impulsivity, and other behaviors as part of a clinical research program designed to study behavioral and biological correlates of impulsive aggressive, and other personality-related, behaviors in human subjects. Participants were recruited through public service announcements, newspaper, and other media, advertisements seeking out individuals who: a) reported psychosocial difficulty related to one or more syndromal (formerly Axis I) and/or personality (formerly Axis II), disorders or, b) had little evidence of psychopathology (i.e., healthy controls). All participants gave informed consent and signed the informed consent document approved by the University

of Chicago Institutional Review Board (IRB).

2.2. Diagnostic assessment

Syndromal and personality disorder diagnoses were made according to DSM-5 criteria (American Psychiatric Association, 2013). Diagnoses were made using information from: (a) the Structured Clinical Interview for DSM Diagnoses (SCID; First et al., 1995) for syndromal disorders and the Structured Interview for the Diagnosis of DSM Personality Disorder (Pfohl et al., 1997) for personality disorders; (b) clinical interview by a research psychiatrist; and, (c) review of all other available clinical data. The research diagnostic interviews were conducted by individuals with a masters or doctorate degree in clinical psychology. All diagnostic raters completed a rigorous training program that included lectures on DSM diagnoses and rating systems, videos of expert raters conducting SCID/SIDP interviews, and practice interviews and ratings until the raters were deemed reliable with the trainer. This process resulted in good to excellent inter-rater reliabilities (mean kappa of 0.84 ± 0.05 ; range: 0.79–0.93) across anxiety, mood, substance use (excluding nicotine), impulse control, and personality disorders. Final diagnoses were assigned by team best-estimate consensus procedures as previously described (Coccaro et al., 2014). All participants with a lifetime diagnosis of substance use disorder (SUD) met at least two DSM-5 criteria for SUD (with the exception of the criteria for craving which was not available for participants in this study). As in our previous studies, participants with a lifetime history of bipolar disorder, schizophrenia (or other psychotic disorder), or mental retardation were excluded from study, as were participants meeting DSM-5 criteria for a current SUD (i.e., participants with a life history of substance use were in a sustained remission of at least 1 year at time of study).

The sample was divided into five subgroups based on DSM-5 diagnosis: a) Healthy Controls (HC; $n = 282$): Participants with no evidence of current or past psychiatric disorder; b) Psychiatric Controls (PC; $n = 320$): Participants meeting criteria for a current or lifetime psychiatric disorder but not lifetime diagnosis of either IED or SUD; c) Substance Use Disorder (SUD; $n = 136$): Participants meeting DSM-5 criteria for at least one SUD lifetime but not IED; d) Intermittent Explosive Disorder (IED; $n = 339$): Participants meeting criteria for IED but not lifetime SUD; and, e) IED + SUD ($n = 280$): Participants meeting criteria for current or lifetime diagnosis of IED and a lifetime diagnosis of SUD. For participants with any psychiatric diagnosis ($n = 1073$), most (70.4%) reported: a) history of formal psychiatric evaluation and/or treatment (57.1%) or, b) history of behavioral disturbance during which the subject, or others, thought they should have sought mental health services but did not (13.3%). Table 1 displays the diagnostic data for each of the five study groups.

2.3. Measures of trait aggression, anger, impulsivity

Aggression was assessed with the Aggression score from the Life History of Aggression (LHA; Coccaro et al., 1997) assessment and with the Verbal and Physical Aggression scores from the Buss-Perry Aggression Questionnaire (BPAQ; Buss and Perry, 1992). The LHA assesses history of actual aggressive behavior and BPAQ and BPAQ assesses aggressive tendencies as a personality trait. Trait Anger was assessed with the State-Trait Anger and Expression of Anger Inventory (STAXI; Spielberger, 1996) and with the Anger score from the BPAQ. Impulsivity was assessed with the Barratt Impulsiveness Scale (BIS-11; Patton et al., 1995) and the Impulsivity Scale from the Eysenck Personality Questionnaire (EPQ-2; Eysenck and Eysenck, 1977). In addition, the Neuroticism, Psychoticism, and Extraversion scales, from the EPQ-1 (Eysenck and Eysenck, 1991), were

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