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Interpersonal problems of cocaine dependent adults differ from those of a normative sample

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ABSTRACT

Our research examined patterns of interpersonal problems in patients with a primary diagnosis of cocaine dependence (CD), comparing them with those in a normative sample. We hypothesized that the patterns of individuals with CD would reveal constellations of interpersonal problems distinct from those of the sample, not only at baseline, but also at termination of treatment. Analysis was conducted on 402 CD patients from the training and the main trial phases of the National Institute on Drug Abuse Collaborative Cocaine Treatment Study. Responses to the Inventory for Interpersonal Problems were analyzed—from baseline, from month one, and at treatment termination—according to the Interpersonal Circumplex Model and were compared to the normative sample. The CD sample was described using four distinct subtypes, named according to their relative angular displacement at baseline and highest two subscale means: Cold and Socially Avoidant, Vindictive and Domineering, Overly Nurturant and Intrusive, Nonassertive and Exploitable. Each subtype remained distinct across treatment and consistently reported different types of interpersonal difficulties than the normative population at termination, consistent with the interpersonal pathoplasticity model. In all subtypes, overall interpersonal distress decreased over the course of treatment, to the extent that by treatment termination they were no more or less distressed than the normative sample. These findings have important clinical implications. The interpersonal challenges of patients struggling with addiction to cocaine warrant clinical attention, beyond mediating levels of distress.

Cocaine abuse is a persistent health problem worldwide. According to the World Drug Report 2019 (United Nations Office on Drugs and Crime 2019) stimulants comprise the second most widely used category of drugs globally, accounting for, at best estimate, 68 million users in 2017. Further, global production of cocaine reached an all-time high in 2017, with North America and Western and Central Europe as the two main markets. In North America, cocaine is the most commonly used form of stimulant, with a prevalence of 2.1%. In the US, an estimated 5.9 million people, 12 years old or older, used cocaine/crack in 2017, demonstrating an accelerating increase from the steady rise since 2011 (United Nations Office on Drugs and Crime 2019). Approximately 5%-6% percent of cocaine users become cocaine dependent (CD) within three years of first use. (Wagner and Anthony 2002). This substantial increase in the use of cocaine demonstrates the durability of cocaine use as a public health concern.

Sustained remission for CD is possible (e.g. Crits-Christoph et al. 1999). However, individuals with a comorbid diagnosis of personality disorder (PD)—often associated with CD (Skinstad and Swain 2001; Chen et al. 2011)—experience lower rates of remission (Lopez-Quintero **ARTICLE HISTORY**

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KEYWORDS

Interpersonal problems; interpersonal circumplex model; interpersonal pathoplasticity; cocaine dependence; cocaine addiction; clinical insight

et al. 2011). For example, in a cohort of people seeking treatment for CD, comorbid PD diagnosis has been as high at 79% (e.g. Kranzler et al. 1994). In the pilot of the National Institute on Drug Abuse (NIDA) Collaborative Cocaine Treatment Study, nearly 50% of patients with a primary diagnosis of CD were also diagnosed with at least one PD (Barber et al. 1996). Disentangling the causal relationship between PD and substance use disorders is difficult–and little research has explored the mechanisms by which characteristics of one's personality may impact one's cocaine use (Prisciandaro et al. 2011). The APA (2013) has stated that deficits in interpersonal functioning are a key factor in the poor remission rates in substance use disorders and personality disorders.

Research by Hulka et al. (2014) has identified interpersonal difficulties such as disturbances in social decisionmaking, reflective of deficits in prosocial behavior, as a vulnerability factor for CD. Additionally, Preller et al. (2014) found that cocaine users demonstrated significant social cognitive impairments. For example, compared to controls, both recreational and cocaine dependent users demonstrated less emotional empathy. Meanwhile, individuals with CD made a greater number of errors in a perspective taking task.

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b Supplemental data for this article can be accessed <u>here</u>.

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They concluded that interpersonal, or social functioning, is impaired in users of cocaine.

The empirical findings around the complex relationship between CD and interpersonal or social functioning can be theorized in terms of the pathoplasticity model. According to this model, patterns of interpersonal traits (e.g. disturbed prosocial behavior) are more than vulnerabilities to particular symptomology (e.g. drug seeking behaviors). Instead, an individual's modes of relating to others are inextricably linked to one's expression of psychiatric symptoms (e.g. Cain et al. 2012). Pathoplasticity of interpersonal traits can be defined as the mutually influencing non-etiological relationship between interpersonal traits and psychopathology (Klein et al. 1993; Widiger and Smith 2008; Przeworski et al. 2011). Although a group of people with the same psychiatric diagnosis may share a similar cluster of symptoms (e.g. CD), how those symptoms impact their daily lives, relationships, and behavior will be partially dependent on their interpersonal tendencies. For example, for someone who scores high on the trait 'Exploitable', CD may be intrinsically linked with romantic involvement with their drug dealer. In that context, reduction in cocaine use may not be sustainable, if interpersonal problems related to 'exploitability' are not addressed: Difficulties in saying, 'no', for example, or being too easily persuaded by others. In contrast, someone classified as 'Cold' might be less dependent on social relationships to ensure abstinence; in which case, a very intimate therapeutic bond might feel threatening, and become an obstacle to effective treatment.

Pathoplasticity of interpersonal traits offers a framework both for examining specific patterns that may be associated with CD and for potentially changing patterns of drug use over the course treatment. According to this model, the patterns of interpersonal traits (whether they are called 'social cognition deficits', 'tendencies', 'temperament', 'style', or 'comorbid disorders') are likely to continue to affect the CD individual's life choices and relationships, even after successful reduction in cocaine use. Clinically, this would explain the continued vulnerability to relapse even after successful treatment and it would point clinicians toward targeting interpersonal patterns, rather than solely CD symptoms, for CD treatment to be successful in the long-term.

The interpersonal circumplex model

One way of empirically conceptualizing interpersonal patterns and their pathoplasticity in CD patients is use of the Inventory of Interpersonal Problems (Horowitz et al. 1988), a self-report measure that adheres to the Interpersonal Circumplex Model (Leary 1996; Wiggins 1996). The interpersonal circumplex is defined by two axes (affiliation & dominance) which measure an individual's interpersonal motivations and behavioral tendencies. One axis runs on a continuum from 'warmth (friendliness or affiliation) to cold (hostility or distance)', while the other runs on a continuum from 'dominance (interpersonal assertion) to submission (passivity)'. Scores on these dimensions can be used to identify interpersonal patterns such as warm-dominant (affiliative and controlling), warm-submissive (affiliative and passive), cold-submissive (distant and passive), and cold-dominant (distant and demanding).

The Inventory of Interpersonal Problems-Circumplex (IIP-C; Alden et al. 1990; Horowitz et al. 2000) is the most widely used interpersonal circumplex measure (Gurtman and Lee 2009), and was constructed to assess the aspects of interpersonal functioning associated with personal distress or difficulty. The eight subscales of the IIP-C (Domineering, Intrusive, Overly Nurturing, Exploitable, Nonassertive, Socially Avoidant, Cold, and Vindictive) fall along the two axes of 'warm-cold' and 'dominance-submissive'. Distinct interpersonal patterns have been identified on the IIP-C among a variety of clinical populations, including different depressive disorders (e.g. Barrett and Barber 2007; Cain et al. 2012) and anxiety disorders, such as generalized anxiety disorder (e.g. Przeworski et al. 2011), post-traumatic stress disorder (e.g. Thomas et al. 2014) and panic disorder (e.g. Zilcha-Mano et al. 2015).

Interpersonal patterns specific to the patient's psychopathology are pertinent in psychological treatment, in narratives about other people in their lives, as well as in the relationship with the therapist. These interpersonal patterns are readily targeted by therapeutic intervention (Locke 2005), and can affect treatment outcome. For instance, anxious patients with an IIP-C 'warm and submissive' subtype reportedly had better therapy outcomes than those with a 'cold and dominant' subtype (Borkovec et al. 2002). Such findings highlight the value of the IIP-C in assessing interpersonal patterns in clinical contexts.

The present study

The present study builds on the National Institute on Drug Abuse (NIDA) Collaborative Cocaine Treatment Study, a multi-site, two-phase study (therapist training phase N = 261and the randomized control trial; RCT; N = 487) that examined the efficacy of four psychosocial treatments (cognitive therapy, supportive-expressive therapy, individual drug counseling-each with a group drug counseling component or group drug counseling alone) for patients with a primary diagnosis of CD (Crits-Christoph et al. 1997, 1999). CD outpatients were randomized to one of four six-month treatments in the main trial, and one of three six-month treatments in the pilot phase (group drug counseling was not included in the pilot phase of the trial). The main outcome was 'cocaine usage', captured by a composite score comprising the score on the Addiction Severity Index (ASI; McLellan et. al. 1992), number of days in the previous month on which cocaine was used), and the results of urinalysis. All treatment conditions demonstrated efficacy, although individual drug counseling plus group drug counseling yielded significantly greater clinical and statistical reduction of 'cocaine usage' than the other three treatment conditions in the main trial (Crits-Christoph et al. 1999).

The current study applies the Interpersonal Circumplex Model (Horowitz et al. 2000) to examine the patterns of interpersonal distress within this CD sample. Previous

studies of this trial, which included findings relevant to the IIP, demonstrated that CD patients experienced a significant overall decrease of interpersonal distress from baseline to the end of treatment not dependent on treatment condition (Crits-Christoph et al. 2001). Later, Crits-Christoph et al. (2007) elaborated with the report that interpersonal problems were not predictive of outcome within this sample. In consideration of the lack of relation between interpersonal problems and outcome, we addressed three further main questions: (a) whether CD patients show a distinct interpersonal profile on the IIP (Horowitz, et al. 1988); (b) whether this pattern of interpersonal problems of CD patients changes during treatment; (c) the differences between the CD patients' interpersonal profiles and a normative cohort's profile at baseline and termination. Previous research has linked CD with specific interpersonal traits, such as lower emotional empathy (Preller et al. 2014), less prosocial behavior (Hulka et al. 2014), and pronounced Machiavellian attitudes (Quednow 2017). Therefore, we expected patients with CD to show a distinct pattern of interpersonal problems within the 'cold and dominant' subtype at baseline. And we expected this interpersonal pattern to remain stable over the course of successful CD treatment and to be different from the normative sample.

Method

As described above, this study drew from archival data from the NIDA Collaborate Cocaine Treatment Study (Crits-Christoph et al. 1999). The study passed the Institutional Review Board of each of the five Northeastern United States sites at which it was conducted. Details about the original study have been published extensively elsewhere (e.g. Crits-Christoph et al. 1997, 1998, 1999, 2001).

Procedure

Participants were treatment-seeking adults, aged 18-60 years old, who had used cocaine within the last 30 days, and had a principal diagnosis of CD, as assessed by the fourth version of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV; American Psychiatric Association 1994). Exclusion criteria included: presence or history of bipolar disorders; psychotic symptoms; schizophrenia; organic brain syndrome; current diagnosis of opioid dependence or polysubstance abuse or dependence; current, active, suicide potential; medical contraindication; ongoing treatment with psychotropic medication; and homelessness. All patients were first screened by telephone for eligibility. Once determined eligible, all participants attended an initial orientation/assessment which included written informed consent procedures. Recruitment through randomization has been discussed in previous publications (for details, see Crits-Christoph et al. 1997, 1999).

Participants

The present analysis reports on archival data of a subsample of patients from both the training and the main trial phases of the NIDA Collaborative Cocaine Treatment Study (for details, see Crits-Christoph et al. 1997, 1999). As our goal was not only to assess baseline patterns of interpersonal problems, but to track changes in those patterns over time, we chose a listwise deletion of missing data in order to only include patients from each phase of the trial who had completed the Inventory of Interpersonal Problems (IIP; Horowitz et al. 1988) at three-time points (baseline, one month into treatment, and at month 6, at the end of active treatment) (N = 402). There were no significant differences found between those who had completed the IIP at all three time points and those who had not, in terms baseline demographics or cocaine usage. Additionally, there was no difference in the IIP subscales at baseline for those that did and did not complete the IIP at the additional two time points of interest. Further, the patients from the two phases of the RCT (pilot and main trial) did not differ from one another in regard to demographics, IIP subscales, or the composite score of 'cocaine usage' (outcome), and were therefore combined for this analysis.

The mean age of the participants was 34.25 (SD = 6.41, range 19-59) and males comprised 73% of the sample. Fiftysix percent were Caucasian, while 41% were African-American, and 1.5% Hispanic. Most patients (58.8%) were employed or in school at least part-time. Seventy-two percent of the patients lived alone. At the time of intake, the patients were using cocaine on average 11 days per month (SD = 7.86) and were spending over \$1177 a month (SD = \$1504.99) on cocaine. Over 75% ingested the drug through smoking crack/cocaine, while 17% inhaled the drug nasally, and less than 4% of the participants were IV users. Forty percent of the sample were diagnosed with at least one additional Axis I disorder and fewer than 30% were diagnosed with a co-morbid PD. Of the latter, 52% were diagnosed with Antisocial PD, 40% with PD-Not Otherwise Specified (which in the original study meant the patient met criteria for Antisocial PD, with the exception of a childhood diagnosis of Conduct Disorder), and 7% with other PDs.

Measures

The Inventory of Interpersonal Problems (IIP; Horowitz et al. 1988) is a 64 item self-report measure of the nature of interpersonal problems as well as the associated level of distress on a five-point scale ranging from 0 = Not at all to 5 = Extremely. The IIP has been used extensively in psychological research and has excellent psychometric properties, with Cronbach's alphas ranging from 0.76 to 0.88 for each subscale, and 0.96 for the IIP-C total score (Horowitz et al. 2000). Test-retest reliability coefficients are similarly high, ranging from r = 0.58 to 0.84 (Horowitz et. al. 2000). In our sample, the internal consistency of each IIP subscale at intake ranged from 0.72 to 0.90, and was 0.96 for the IIP total consistent with previous literature. At month one and at termination, the reliabilities increased somewhat, ranging from 0.84 to 0.94 for each subscale, and the total IIP Cronbach's α at termination was = 0.98.

Normative data

The present study used normative data in comparison to the clinical sample in order to expand on the understanding of differences in interpersonal problems of individuals with a primary diagnosis of CD from a community sample. The normative sample was derived from a community stratified sample demographically representative of the US population provided in the manual for the IIP-64 (Horowtiz et al. 2000). Each age group (18–24, 25–44, 45–64, and \geq 65) was comprised of 100 men and 100 women, creating an entire sample of N = 800, which included 400 men and women within the age range of 18–89.

Statistical analyses

Two types of analyses of the IIP data were used, the structural summary method and circular statistics. The structural summary method (Ansell and Pincus 2004; Wright et al. 2009) combines three aspects of the Interpersonal Circumplex Model: (a) the characteristic type of interpersonal problem (angular displacement); (b) the general level of interpersonal distress (elevation), and; (c) the measure of profile differentiation (amplitude). Goodness of fit of the model was determined by the variability of interpersonal problems as compared to theoretical expectations (R^2).

The circular statistics offer a set of parameters that are conceptually similar to their linear equivalents (i.e. mean, variance, and confidence intervals). These parameters each provide specific information regarding substantive theme and group homogeneity and allow for the statistical comparison of groups based on the geometry of the circular model—meaning that a lack of overlap between confidence intervals of the circular means demonstrates a significant difference between means.

When a homogenous interpersonal profile did not emerge from the CD sample (i.e. if $R^2 < 0.70$ and low amplitude), a cluster analysis was conducted in order to detect subtypes of distinct patterns of interpersonal problems within the sample. First, a hierarchical cluster analysis was conducted using Ward's minimum variance method (Ward 1963) in SPSS, which determined there was a distinct break in the agglomeration schedule. Ward's method minimizes total withincluster variance, using the squared Euclidean distance. Once subtypes of interpersonal patterns (clusters) were determined, discriminant cluster analyses, structural summaries, and circular statistics were then conducted to determine the characteristics, as well as whether the distinct subtypes of particular interpersonal patterns changed over time. We then compared each of the identified subtypes' interpersonal patterns to Horowitz's normative sample (Horowitz et al. 2000) to explore the comparative uniqueness of each one of the CD subtypes.

Analysis of variance (ANOVA) with Bonferroni *post hoc* correction, and chi-square analyses was conducted to identify potential differences between subtypes in terms of subscales on the IIP, demographics, treatment interventions, psychiatric severity, co-morbid personality diagnosis, and outcome.

Table 1		Structural	summary	for	the	whole	cd	sample	and	each	of	the	four
subtype	si	at each tin	ne point.										

	Angle	Amplitude	Elevation	R ²
Whole CD sample ($N = 402$)				
Baseline	138.40	0.08	0.38	0.81
Month 1	151.60	0.13	0.21	0.97
Month 6	147.00	0.18	-0.06	0.83
Cold/Socially avoidant-subtyp	e 1 ($N = 101$)			
Baseline	187.34	0.19	0.53	0.79
Month 1	179.39	0.09	0.15	0.99
Month 6	175.66	0.08	0.01	0.96
Vindictive/Domineering-subty	vpe 2 (N = 94)	1		
Baseline	110.03	0.29	0.27	0.99
Month 1	123.54	0.19	0.25	0.99
Month 6	126.25	0.14	0.14	0.99
Overly Nuturant/Intrusive-sub	type 3 ($N = 9$	4)		
Baseline	23.34	0.12	0.14	0.74
Month 1	39.77	0.03	0.04	0.62
Month 6	81.92	0.02	-0.13	0.85
Nonassertive/Exploitable-subt	xype 4 ($N = 11$	3)		
Baseline	292.14	0.13	0.54	0.99
Month 1	282.52	0.05	0.36	0.98
Month 6	267.11	0.01	-0.01	0.99

Note: Angle: circumplex location of the predominant interpersonal problem in degrees; Elevation: an index measure of interpersonal distress; Amplitude: a measure of profile differentiation; R²: interpersonal prototypicality.

Results

Comparison of our sample to Horowitz's normative sam**ple**. At baseline, patients in the CD sample (M = 67.79,SD = 37.23) were found to have significantly greater overall interpersonal distress, t(750) = 7.55, p < .0001, d = 0.46 CI [11.94, 20.64] than Horowitz's normative sample (M = 51.5,SD = 34.3; Horowitz et al. 2000), as well as significantly higher distress scores in each one of the eight IIP subscales (See Table 1 in the Supplemental section online for details). At month one, the IIP total score as well as each one of the IIP subscales (except the Exploitable and Overly Nurturing subscales) remained significantly higher for the CD sample compared with the normative sample. By month 6 the CD sample no longer differed from the normative sample in terms of overall interpersonal distress, however there remained differences in distress between the two samples within the subscales (Table 1 in the Supplemental section).

Structural summary. At pretreatment, the goodness of fit within the circumplex determined that the elevation and amplitude were interpretable (see Table 1 for all three time points). A homogenous profile of interpersonal problems was found with an angular displacement of 138° that evidenced a primarily Vindictive interpersonal style within this sample. At month 1, the same interpersonal profile was evident, though the angular displacement increased from a baseline of 138.4° to 151.6° , moving towards Cold, but remaining closer to Vindictive, and at month 6 it was 147.0° (see Figure 1 in the supplement for all three time points).

Subtypes within the CD sample

Distinct CD subtypes. Although a distinct profile was suggested by the prototypical R^2 of >0.80, the amplitude was 0.08 and much lower than expected considering the

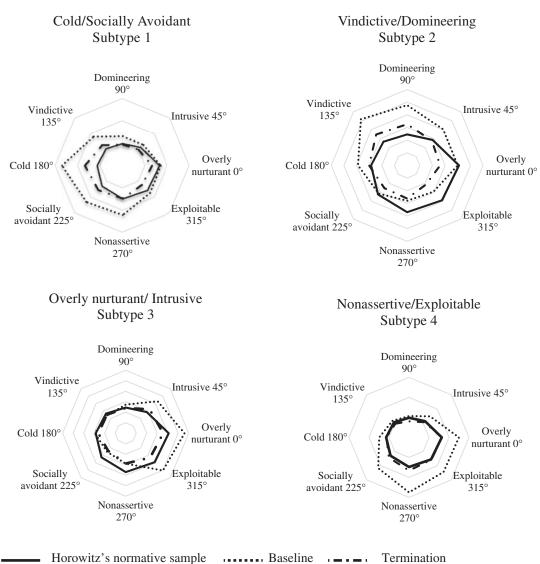


Figure 1. Four subtypes at baseline and termination as compared to Horowitz's normative sample.

observed R^2 . Wright et al. (2012) proposed a heuristic cutoff of >0.15 to indicate a sufficiently elevated (as defined by the elevation variable) or distinct profile (as defined by an amplitude variable). Amplitude measures the clear peaks and troughs of the data; low amplitude may point to the presence of more than one subtype (Ansell and Pincus 2004). Therefore, we conducted a cluster analysis to investigate the low amplitude and to determine if there was heterogeneity within the sample. A hierarchical cluster analysis using Ward's minimum variance method (Ward 1963) in SPSS, suggested the presence of four distinct clusters (subtypes). Based on a four-cluster membership, a multiple-discriminant analysis was performed to detect the pattern of IIP subscales that discriminate between the four subtypes. The discriminant cluster analysis determined that 87% of these groups were correctly classified, when predicted by the eight subscales of the IIP. Each of the three discriminant functions were statistically significant, $\Lambda = 0.19$, $\chi^2(24) = 648.38$, $p < .001; \quad \Lambda = 0.40, \quad \chi^2(24) = 364.49, \quad p < .001; \quad \Lambda = 0.77,$ $\chi^2(24) = 103.37$, p < .001. Importantly, and in line with the pathoplasticity model, the differences between the subtypes

could not be explained by demographic variables, such as gender, ethnicity, education, income, marriage status, or treatment type, such that there were no significant differences between subtypes in analyses of variance or Chi-square tests. Nor were there significant differences between the subtypes based on clinical characteristics such as co-morbid Axis I or Axis II psychopathology, symptom severity or outcome.

Structural summary. Next, each of the four subtypes determined at baseline was subjected to the structural summary method, at each treatment time point. We detected a distinct profile for the four independent subtypes, where two subtypes demonstrated an R^2 greater than or equal to 0.70, falling in the acceptable range, and two greater than 0.80 which indicates good fit (Zimmermann and Wright 2017; see Table 1). Each of the four subtypes was named according to their relative angular displacement at baseline, with consideration for the two subscales in which the highest mean for that subtype was demonstrated. The names and angular displacements are: Subtype 1, Cold/Socially Avoidant, $(n = 101) = 187^{\circ};$ Vindictive/Domineering, Subtype 2,

 $(n = 94) = 110^{\circ}$; Subtype 3, Overly Nurturing/Intrusive, $(n = 94) = 23^{\circ}$; and Subtype 4, Nonassertive/Exploitable $(n = 113) = 292^{\circ}$, (see Figure 1).

Using structural summary analyses, we showed that the subtypes classified at baseline remained or became more strongly distinct at termination, as evident in a strong R^2 for each group of 0.80 or greater (see Table 1; Figure 1). Due to the strong R^2 , the variables of angle, amplitude and elevation are interpretable. The four subtypes demonstrated a similar pattern in regards to amplitude and elevation, such that at baseline there were clear peaks and troughs in the data according to the amplitude scores, which became less distinct across treatment. Likewise, the elevation scores demonstrated significant interpersonal distress at baseline and month one for each group, with the exception of Subtype 3, Overly Nurturing/Intrusive. At month six no group remained in distress according to elevation scores (see Table 1).

Circular statistics of the four subtypes. We applied circular statistics to analyze the circumplex data (Wright et al. 2009) of the subtypes found. The circular means for the four subtypes over the three time points in the current analysis are provided in Table 2. No overlap was found for the four subtypes at any of the three time points (see Table 2). It is evident from the lack of overlap of the confidence intervals of the circular means that: (a) the four subtypes are distinct from one another at each time point, and that; (b) each subtype changed significantly over the course of treatment.

According to the structural summary method, which defines groups by their angular displacement, and the circular statistics, which provide confidence intervals that distinguish groups at baseline, these four groups presented widely across the circumplex, ranging from the Overly Nurturant octant, moving counter clockwise, to between the Exploitable and Nonassertive octant. By the sixth month, the spread between the four groups diminished considerably, such Nonassertive/Exploitable crossed to the interpersonally cold/distant side of the circumplex by treatment termination. Further, though Overly Nurturant/Intrusive remained shy of the cold side of the circumplex, this group made the largest move from warm to cold. Meanwhile, each group remained distinct from one another (see Figure 2).

Cold/Socially Avoidant-subtype 1. More specifically, at baseline the Cold/Socially Avoidant subtype was significantly different from Horowitz's normative sample. There was more overall distress; they were also significantly more distressed in the subscales of Domineering, Vindictive, Cold, Socially Avoidant and Nonassertive (see Table 3 for *t*-test results and effect sizes).

Over the course of treatment, the Cold/Socially Avoidant subtype demonstrated significant within-group decrease on the Domineering, Vindictive, Cold, Socially Avoidant, Nonassertive, Exploitable and Overly Nurturing subscales (see Table 4 for means, standard deviations and p values). At termination of treatment this subtype remained significantly different from Horowitz's normative sample on the subscales of Vindictive and Cold. Additionally, they became significantly less distressed than the normative cohort on the

 Table 2. Circular statistics for each of the four subtypes, at three time points.

Table 2. Circul	Table 2. Circular statistics for each of the four subtypes, at three time points.								
	Circular M	Circular variance	95% Circular Cls						
Cold/Socially av	voidant subtype 1	(n = 101)							
Baseline	182.44	34.73	189.21-175.66						
Month 1	166.73	55.36	177.53-155.94						
Month 6	165.05	48.47	174.55–155.55						
Vindictive/Dom	ineering subtype 2	(<i>n</i> = 94)							
Baseline	110.78	28.25	116.49-105.07						
Month 1	124.6	49.17	134.54-114.66						
Month 6	129.2	39	137.12-121.27						
Overly Nurturar	nt/Intrusive subtype	e 3 (<i>n</i> = 94)							
Baseline	34.16	55.84	45.45-22.88						
Month 1	63.65	69.93	77.79-49.51						
Month 6	103.98	64.06	116.93–91.03						
Nonassertive/Ex	ploitable subtype	4 (<i>n</i> = 113)							
Baseline	296.45	50.31	305.72-287.17						
Month 1	276.54	75	290.37-262.71						
Month 6	218.26	78.52	232.80-203.72						

Note: Lack of overlap in the CI (confidence intervals) indicates a significant difference.

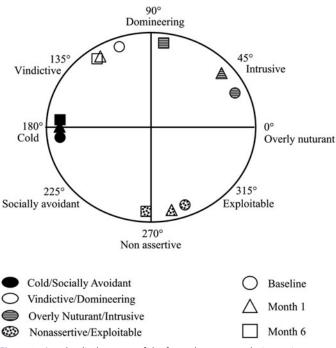


Figure 2. Angular displacement of the four subtypes at each time point.

subscales of Exploitable and Overly Nurturing, demonstrating a shift towards dominance.

In terms of movement of angular displacement over the course of treatment, this subtype moved away from the Socially Avoidant octant within the cold-submissive quadrant towards the Vindictive octant within the cold-dominant quadrant.

Vindictive/Domineering-subtype 2. At baseline, Vindictive/Domineering-Subtype 2, was significantly different from Horowitz's normative sample in total distress and in greater distress on the subscales Domineering, Vindictive, and Cold, while in less distress on the subscale of Exploitable. Within-group change over the course of treatment was demonstrated by a significant decrease in overall distress and in distress on the subscales of Domineering, Vindictive, Overly Nurturing and Intrusive. At treatment

Table 3. t-test Results and Effect Sizes for Differences Between Horowitz's Normative Sample and Each Subtype at Baseline and Termination.

	Cold/Socially Avoidant		Vindictive/D	omineering	Overly Nurt	urant/Intrusive	Nonassertive	e/Exploitable	
	Subt	ype 1	Subty	Subtype 2		Subtype 3		Subtype 4	
	t(899)	Cohen's d	t(891)	Cohen's d	t(891)	Cohen's d	t(910)	Cohen's a	
Total IIP score									
Baseline	6.45***	0.68	2.64*	0.29	1.43	0.16	6.95***	0.7	
Month 6	0.1	0.01	1.8	0.2	1.51	0.16	0.00	0	
Octants									
Domineering									
Baseline	3.20**	0.34	8.25***	0.9	1.04	0.11	0.822	0.08	
Month 6	0.41	0.04	2.89*	0.32	0.19	0.02	1.97*	0.18	
Vindictive									
Baseline	7.16***	0.76	8.76***	1	0.76	0.08	1.06	0.11	
Month 6	2.14*	0.23	2.76*	0.3	0.52	0.06	0.92	0.09	
Cold									
Baseline	12.12***	1.28	3.22**	0.35	0.25	0.03	2.97*	0.3	
Month 6	4.24***	0.45	0.49	0.05	0.78	0.09	0.17	0.02	
Socially avoidant									
Baseline	8.05***	0.85	1.9	0.21	2.44*	0.27	7.68***	0.77	
Month 6	1.93	0.2	2.27*	0.25	2.9*	0.32	1.1	0.11	
Nonassertive									
Baseline	5.43***	0.57	2.77	0.3	2.47*	0.3	10.27***	1.03	
Month 6	0.11	0.01	3.22**	0.35	2.42*	0.3	1.44	0.14	
Exploitable									
Baseline	1.42	0.15	3.33**	0.36	3.82***	0.42	8.25 ***	0.83	
Month 6	3.07*	0.32	6.17***	0.67	2.04*	0.22	0	0	
Overly nurturant									
Baseline	0.47	0.05	0.33	0.04	4.97***	0.54	7.75***	0.78	
Month 6	2.9*	0.31	5***	0.55	1.73	0.19	0	0	
Intrusive								-	
Baseline	1.59	0.17	0.22	0.02	5.46***	0.6	3.58**	0.36	
Month 6	1.37	0.14	0.32	0.03	1.34	0.15	0.61	0.06	

Note. ***p < .0001. **p < .001. *p < .05 denotes significant difference.

 Table 4. Within Subtype changes from Baseline to Month 6, including Means and Standard Deviations.

	Cold/Socially	avoidant	Vindictive/Do	omineering	Overly Nurtura	nt/Intrusive	Nonassertive/I	Exploitable
	Subtyp	e 1	Subtype 2		Subtype 3		Subtype 4	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Total IIP score								
Baseline	75.24	39.22	61.52	39.36	56.83	33.35	75.43	33.87
Month 6	51.89***	42.27	44.55 [*]	42.73	45.71	41.55	51.49***	41.5
Octants								
Domineering								
Baseline	6.56	5.06	9.53	6.9	5.45	4.63	5.33	4.35
Month 6	4.69*	4.68	6.51**	6.53	4.8	5.19	4	4.66
Vindictive								
Baseline	9.17	5.61	10.33	6.53	4.88	4.47	5.84	3.89
Month 6	6.46**	5.44	6.91**	6.67	5.01	5.32	4.83	5.08
Cold								
Baseline	13.51	7.53	7.77	5.88	5.86	5.04	7.44	5.01
Month 6	8.44***	7.61	6.02	6.63	5.21	6.00	5.59*	5.62
Socially Avoidant								
Baseline	11.45	6.26	6.33	5.36	5.01	4.64	10.89	5.7
Month 6	7.69***	6.79	5.09	5.73	4.72	5.64	7.14***	6.35
Nonassertive								
Baseline	10.97	7.18	5.57	5.58	5.79	4.67	13.75	6.5
Month 6	7.33**	7.01	5.23	6.8	5.78	6.35	8.29***	7.05
Exploitable								
Baseline	8.61	5.44	5.89	4.89	10.04	5.97	12.22	5.47
Month 6	6.06**	5.86	4.25	4.98	6.57***	6.02	7.92***	6.27
Overly nurturant	0.000	5100	1120		0107	0.02		0127
Baseline	8.46	5.15	8.00	5.9	11.21	5.99	12.48	5.44
Month 6	6.52*	5.95	5.22**	5.91	7.15***	6.16	8.2***	6.67
Intrusive	0.02	2.25	5.22	2.91		0.10	0.2	0.07
Baseline	6.5	4.56	8.07	5.33	8.61	5.45	7.44	5.09
Month 6	5	5.06	5.53**	5.01	6.45*	6.1	5.38**	5.17

Note. ****p < .0001. **p < .001. *p < .05. Denotes significant difference at Month 6 (termination) than from baseline.

termination, this subtype was no longer different from the normative cohort on the Cold subscale; however, they remained in significantly more distress on the Domineering and Vindictive subscale and in significantly less distress on the Exploitable subscale. Further, at termination this group developed a significant difference to the normative cohort characterized by less distress on the subscales of Socially Avoidant, Nonassertive, and Overly Nurturing that was not present at baseline.

In terms of angular displacement, this subtype moved away from the Domineering octant and towards the Vindictive octant, while remaining within the cold-dominant quadrant of the circumplex at baseline and termination.

Overly Nurturing/Intrusive-subtype 3. At baseline, Overly Nurturing/Intrusive-Subtype 3 was the only group not to be in more overall distress than the normative cohort. They were significantly more distressed on the subscales of Exploitable, Overly Nurturing, and Intrusive than the normative sample, while significantly less distressed on the subscales of Socially Avoidant and Nonassertive. There was no change in the Socially Avoidant and Nonassertive subscale, and at treatment termination they remained in significantly less distress than the normative sample. Between baseline and treatment termination this subtype became significantly less distressed on the Exploitable, Overly Nurturing and Intrusive subscales. As a result of these within group changes, at treatment termination, this subtype was no longer different from the normative sample on the Overly Nurturing and Intrusive subscales. Further, the direction of difference on the Exploitable subscale changed, in that at termination this group was significantly less distressed than the normative sample.

In terms of angular displacement, this group moved away from distress in the Overly-Nurturant and Intrusive octants within the friendly-dominant quadrant of the circumplex, to overlap with the confidence intervals of the baseline measure of the Vindictive/Domineering-Subtype 2 approaching the cold-dominant quadrant of the circumplex.

Nonassertive/Exploitable-subtype 4. At baseline, Nonassertive/Exploitable-Subtype 4 was significantly different from the normative sample in total distress and the subscales of Cold, Socially Avoidant, Nonassertive, Exploitable, Overly Nurturing, and Intrusive. Over the course of treatment, this subtype changed significantly in overall distress, and on each one of the subscales, such that they no longer were in more distress than the normative cohort. At treatment termination, the only subscale that significantly distinguished this subtype from the normative sample was Domineering, in that they were less distressed than the norms.

In terms of angular displacement, during treatment, this subtype moved from the friendly-submissive quadrant of the circumplex into the hostile-submissive quadrant. This movement towards the Cold octant placed three of the four groups on the cold half of the circumplex, and this group alone on the submissive side of the circumplex at treatment termination.

Discussion

Four distinct angular displacements emerged with unique interpersonal themes that characterize this CD sample. Each of the four subtypes differed from one another in patterns of interpersonal problems and from Horowitz's normative sample. These findings suggest that although the four groups were not different in terms of diagnosed personality psychopathology, there are unique interpersonal traits and therefore likely social deficits among individuals with CD that differ from a normative sample.

The four groups could not be differentiated in terms of abstinence from cocaine. This aligns with previous reports that neither psychiatric severity, nor antisocial personality traits were predictive of treatment outcome in the main trial from which this sample was derived (Crits-Christoph et al. 2007). Nonetheless, there are important clinical implications of these findings. The patients had a significant decrease in interpersonal distress, providing evidence that social problems can improve during treatment-however, social probat least sample, for this lems remained, when treatment ended.

While these four groups remained distinct at treatment termination, three of the four groups were positioned on the dominant half of the circumplex at treatment termination. Additionally, three of the four groups were positioned on the cold half of the circumplex in terms of their angular displacement at treatment termination. The four subtypes became more similar over time, all four moving towards cold on the affiliation axis. Clinically, this can be particularly important to keep in mind, considering the previously cited finding by Borkovec et al. (2002). They found that anxious patients within the 'Cold and Dominant' cohort had diminished therapy outcomes compared to those in the 'Warm and Submissive' subtype. People who score high on the Cold subscale report a deficit in feeling empathy and have difficulty with developing warm feelings towards others or maintaining commitments. These people generally do not feel socially obligated and strive for apparent freedom (Horowitz et al. 2000).

This lack of affiliation and empathy could be the result of habitual cocaine use. In fact, recent work has demonstrated that empathy worsened with increased cocaine usage, and decreased cocaine usage correlated with improved empathy (Vonmoos et al. 2019). It would be expected that family and friends diminish in importance in the eyes of the addicted individual. That being said, Quednow (2017) reported Machiavellianism to be a stable aspect of personality related more strongly to cocaine users than to controls. In a normative college sample, Dowgwillo and Pincus (2017) found Narcissism and Machiavellianism traits to be characterized by Domineering, Vindictive and Cold interpersonal problems. Taken together, it appears that coldness may be inherent in Machiavellianism, and perhaps a vulnerability factor for CD. Khantzian (1997), as well as Panksepp et al. (2002), has spoken to the strong desire for a feeling of autonomy in individuals who use cocaine, and the manner in which cocaine use bolsters a sense of self-sufficiency. Both groups report the reciprocal nature of using cocaine, which

perpetuates self-serving behavior (Khantzian 1997; Panksepp et al. 2002).

While all groups fell in the Cold quadrant, the first subtype, Cold/Socially Avoidant, was the only subtype to demonstrate significantly more distress on the Cold subscale at treatment termination. This subtype could be characterized by interpersonal coldness at the extreme end of the affiliation axis and in the mid-range of the submissive/dominance axis of the interpersonal circumplex model.

At baseline this subtype demonstrated significant distress on the subscale of Social Avoidance, endorsing difficulties when confronted with 'saying no to others,' being afraid of being taken advantage of, telling others when they feel angry, or feeling they are overly influenced by others compared to the normative sample. By the end of treatment, those concerns demonstrated a marked shift in that they became significantly less of a problem for this subtype than for the normative population. Perhaps this change was facilitated by a reduction in feeling vulnerable due to no longer being impaired while relating to others, or depending on others to score drugs. In treatment, though they were less fearful of others and of groups, they demonstrated an increased concern with trusting others. This finding is aligned with the stable Machiavellianism traits, reported by Quednow (2017), demonstrating a cynical view of others by cocaine users. It may be that being in a drug treatment group, or building a relationship with a therapist forced this subtype to address their social challenges. While abstinence may have reduced fears of vulnerability to being taken advantage of, dependence on others for coping support may have been unfamiliar, and stimulated the move from Socially Avoidant to Vindictive. Previous work by Vonmoos et al. (2019) has demonstrated that while social skills can improve with a reduction in cocaine use, CD patients retain smaller social network than controls. Stable cynical views of others may promote keeping networks small, and this group may feel stress in developing trusting relationships that ultimately may support longer term abstinence. It is possible that over a longer course of treatment this subtype might further develop meaningful and trusting relationships that allow movement towards warmth on the affiliation axis of the circumplex.

The second subtype we identified fit into the Vindictive/ Domineering quadrant of the interpersonal circumplex. Although they demonstrated a significant decrease in problems of the Domineering and Vindictive subscales, these areas remained significantly more problematic for the CD sample than the normative cohort. This profile is similar to the first subtype in their stable Machiavellian traits, although they demonstrate more dominance with less coldness, more closely aligned with earlier findings related to antisocial and narcissistic PD (Pincus and Wiggins 1990).

Pincus and Wiggins (1990) found a medium to large correlation between antisocial and narcissistic PD as captured by the Personality Adjective Checklist (PACL; Strack 1987) and the Dominant (r=0.59 and Vindictive (r=0.35) subscales. Similarly, they found a small to mid-size relation between the MMPI scales antisocial and narcissistic PD, and the IIP subscales of Dominance and Vindictive. In Dowgwillo and Pincus's (2017) study of the Dark Triad traits (Psychopath, Narcissistic, and Machiavellian) relation to the interpersonal circumplex, they found the Vindictive subscale of the IIP to be more strongly related to psychopathy than to Machiavellian traits.

Interestingly, in our sample, the first two groups, Cold/ Socially Avoidant and the Vindictive/Domineering subtypes, did not differ in terms of comorbid personality diagnosis-both were different from the normative sample at termination, in distress related to vindictiveness; however only the Vindictive/Domineering (Subtype 2) was different from the normative sample on the subscale of Dominance. This second subtype of patients may present as manipulative, authoritarian and vindictive, or perhaps overly critical or cold in order to protect their self-respect, self-worth and dignity. It may be inferred that they are less flexible in relationships, which potentially interferes with intimacy and developing relationships. These interpersonal traits may be related to the stable small social networks demonstrated by Vonmoos et al. (2019).

The third subtype we identified, the Overly Nurturing/ Intrusive subtype, was the least distressed at baseline compared to the other three subtypes, and did not differ from the normative sample in overall distress. This subtype was similarly leaning towards dominance on the dominance/submission axis but compared to the other three groups was characterized as warm on the affiliation axis. At baseline these individuals, self-described as sociable, friendly and outgoing, scored high on the Intrusive subscale. These individuals value the company of others and find it difficult to be alone. Individuals with histrionic PD and to a certain degree narcissistic PD reportedly score high on the Intrusive subscale (Horowitz et al. 2000). Although the PD comorbidity of our sample was comprised primarily of antisocial patients, this group may reflect the narcissistic and histrionic traits of cluster B membership, although we were not able to distinguish group membership by PD diagnosis. People who score high on the Overly Nurturing subscale value others, and tend to put other's needs before their own. In fact, there is evidence that people diagnosed with dependent PD tend to score high on this subscale (Horowitz et al. 2000). This warmth and the associated challenges significantly changed for this group between baseline and termination. Their interpersonal difficulties on the Intrusive and Overly Nurturing subscales became comparable to the normative sample. By treatment termination, this profile overlapped with the confidence intervals of the baseline of the Vindictive/Domineering group. They lost concern for difficulties related to affiliation, so much so that, by end of treatment, their baseline concern of being Exploitable-which had been greater than the normative cohort-were significantly less distressing for this group than for the normative group. This was unexpected, considering their cocaine use and that their response to any particular treatment condition did not differ from that of other subtypes.

For the Overly Nurturing and Intrusive subtype, the experience of treatment aligned them with the other two

groups. At baseline this subtype was distressed by being selfsacrificing and too accommodating, perhaps being too open, overly dependent and struggling to set limits with people who had cocaine, or other needed/desired resources. Over the course of treatment, they shifted to avoidance of and conflict with others, and reported struggling to take instructions from others. It is possible that, for this subtype of CD patients, their interpersonal problems were closely tied to their cocaine use, or that the treatment helped them not only to reduce cocaine use but also to gain interpersonal skills that then shifted distress around their interpersonal dependency. By the end of treatment, they were closer to their domineering counterparts, in that their angular displacement no longer centered between Overly Nurturant and Intrusive, but had moved adjacent to Domineering and Vindictive. This may suggest that Cold/Domineering interpersonal problems are related to an underlying vulnerability to CD. Similar to the stable Machiavellian traits of cocaine users found by (Quednow et al. 2017).

The fourth and final subtype, identified as Nonassertive/ Exploitable, remained, throughout treatment, the only group characterized by submissiveness on the dominance axis. While at baseline this group demonstrated similar warmth on the affiliation axis to group three, it moved to the cold side of the circumplex by treatment end. Nonassertive individuals are not prone to take initiative and likewise struggle to assert their opinion or maintain a stance in opposition to others. Like the Nonassertive/Exploitable subtype, individuals with dependent PD score high on this scale, as do people with avoidant PD (Pincus and Wiggins 1990). By the termination of treatment this subtype was the most similar to the normative sample, differing only in that they were significantly less distressed on the Dominant scale (even though they were similar to the normative sample on this subscale at baseline). It is striking that even for this groupwhose patterns of interpersonal problems most resemble the normative cohort-there was no evidence that they were less likely to have co-morbid PD or to demonstrate greater abstinence from cocaine usage.

Over the course of treatment, the angular displacement of this group moved from between the Exploitable and Nonassertive octants to lie between the Socially Avoidant and Nonassertive octants. This movement indicates that they sacrificed warmth, but may have gained some agency during treatment. This may be conceptualized as a complementary change on the IIP-C. The complementary relationship to the changes in all four profiles may suggest that people develop CD as a way to cope with interpersonal vulnerabilities. Once the drug is removed, their vulnerability is exposed, and they may need longer treatment to address the interpersonal patterns related to CD.

Previous studies addressing personality disorder and addiction were limited because they primarily focused on differences between CD patients with and without PD diagnosis. We contributed to the body of work that clarified the personality characteristics and social deficits that are specific to individuals with CD versus controls (e.g. Quednow et al. 2017; Vonmoos et al. 2019), beyond a secondary PD

diagnosis (e.g. Barber et al. 1996; Chen et al. 2011; Albein-Urios et al. 2014). The present study makes a potentially important contribution in that it identifies distinct CD subtypes that could not be explained by PD diagnosis. Further research on the dynamics of interpersonal problems and CD-and the role of social stress in vulnerability to substance dependence and relapse more generally-may indicate how CD treatments could be improved in the future (i.e. treating CD-related difficulties sequentially, by addressing drug use first and interpersonal difficulties later; Crits-Christoph et al. 2001). Crits-Christoph et al. (2001, 2003) proposed that it may take a prolonged period of abstinence to rebuild broken trust in relationships and to restore intimacy, as demonstrated in earlier studies by Carroll et al. (1995). By analyzing interpersonal problem change at the level of the IIP-C, we were able to identify intricacies of the changes during treatment that had not been evident, when looking at reduction in overall distress. By the end of treatment, none of the four subtypes demonstrated distress as reflected by an elevated total IIP score. Nor did any subtype demonstrate significantly different distress than the normative sample on the subscale of Intrusive. However, each subtype did show significant differences from a normative sample at the end of treatment on select subscales particular to their subtype membership. We did find that interpersonal change occurred in this sample during treatment-although with no apparent relationship to outcome or treatment condition at the point of termination.

Several study limitations warrant discussion. The effect sizes of the difference between the normative cohort and the CD sample varied-from small to moderate to large-at treatment termination, and should be considered accordingly. Additionally, our ability to definitively match our sample to the normative sample in term of age and gender was limited; it remains possible that age and gender could have impacted our findings. However, differences between our subtypes could not be accounted for by age or gender. Another concern is that our data were gathered twenty years ago, and may not represent the current CD population. However, there is little research to suggest that cocaine/crack addiction has lost its relevance. Cocaine use is on the rise as it was at the time of this clinical trial, and it remains a public health concern. The majority of our sample was white males, which according to the 2017 lifetime prevalence reports of cocaine use (SAMSHA 2017) is still the largest group of users, with black male crack users being the second largest group.

An additional limitation of the current sample is that it consisted of people who were seeking treatment, which means that the findings might be specific to those patients and not necessarily generalizable to other CD individuals who do not seek treatment. Additionally, as Crits-Christoph et al. (1999, 2001) have previously stated, the stringent nature of the inclusion criteria (no psychotropic medications, no polysubstance abuse or dependence) may have made this a relatively 'healthy' sample of CD patients and therefore non-representative of the CD population as a whole. That being said, recent important research investigating social and executive cognitive dysfunctions in cocaine-dependent samples from the Zurich Cocaine Cognition Study (ZuCo2St) have used similarly stringent criteria, with the exception of their sample being non-help seeking. The interpersonal problems of all four subtypes is consistent with earlier theory and research related to substance abuse (e.g. Khantzian 1997; Panksepp et al. 2002), as well as the findings of the ZuCo2St group (e.g. Hulka et al. 2014; Preller et al. 2014; Vonmoos et al. 2019). Perhaps the link between decrease in cocaine use and social difficulties can be partially explained by differences in treatment and non-treatment seeking groups. Future research could determine the representation of these four subtypes in samples of CD patients who were not seeking treatment, with a current sample that is by design matched to control for confounding variables. Such a study could establish the generalizability of these interpersonal subtypes within the CD population at large.

Future research should also address the lack of association of outcome to treatment modality. It was noteworthy that there was no difference in decrease in interpersonal distress for each subtype based on treatment modality. However, change in patterns of difficulties that occurred during treatment were specific for each group and remained significantly different from the normative sample for three of the four subtypes. It would be important to investigate if alternative treatments, targeting change in personality characteristics, might lower distress, and move the characteristic profiles more towards the normative sample—as well as facilitating similar gains in reduction in cocaine use.

Interpersonal problems may reflect vulnerability factors, may influence the manifestation of symptomatology, and may reflect treatment progress. In the case of CD, it is possible that effects of cocaine itself (or co-occurring drug-seeking behaviors) might result in interpersonal problems (Vonmoos et al. 2019), or that these problems are an indication of stable personality characteristics (Quednow et al. 2017) in individuals with CD. Future research that includes a measurement of interpersonal traits of CD patients *before* they developed CD is warranted, to elucidate the role of interpersonal difficulties in the development of CD, and changes in cocaine usage during treatment.

Our preliminary findings (a decrease in level of interpersonal distress and minimal change of interpersonal patterns following CD treatment), suggest that interpersonal problems reflect not only a vulnerability factor but also influence the manifestation of symptomology over time. The withingroup variation of interpersonal functioning of this CD sample suggests that understanding the interpersonal difficulties in this population is complex and should be attended to on an individual basis. Clinically, this means that when treating a CD patient, it is important to focus on the patient's interpersonal problems and possibly offer longer-term treatment. Although social problems can improve even during shortterm treatment, they are expected to continue to be present, to a certain degree, after treatment ends. Our findings highlight those patients with CD struggle with social deficits independent of diagnosed personality psychopathology and

abstinence from cocaine. Difficulties with coldness and cynicism within relationships continue for this population in periods of abstinence, and may be related to obstacles in sustaining strong social networks related to positive outcomes. Given that the level of interpersonal distress decreased, and that the interpersonal patterns themselves changed only minimally, following CD treatment, it might be suggested that interpersonal problems reflect a vulnerability factor that worsens with an increase in symptomology.

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Ethical statement

The present study analyzed archival data, that was collected during the pilot and main trial phase of the National Institute on Drug Abuse (NIDA) Collaborative Cocaine Treatment, which was conducted at five sites in the Northeast United States. The study passed the Institutional Review Board of each site, and all patients were first screenED by telephone for eligibility. Once determined eligible, all participants attended an initial orientation/assessment visit which included written informed consent procedures.

Author contributions

All authors (A, B, C, D, and E) contributed to the writing and editing of this manuscript.

Author A was involved in every aspect of the design, implementation of this study and wrote the first several drafts of this manuscript.

Authors A, B, D, and E were involved in the design of the study. Authors A, B, and D conducted the statistical analyses.

Author C conducted literature searches and wrote a revision of the introduction to the manuscript, as well as contributed to the editing of the entire manuscript.

Disclosure statement

No potential conflict of interest was reported by the authors.

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