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Impairments in Executive Functioning in Patients with Comorbid Substance Use and Personality Disorders: A Systematic Review

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ABSTRACT

Objective: The purpose of this systematic review was to examine the evidence for impaired executive functioning in patients diagnosed with a dual pathology of personality disorder (PD) and substance use disorder, and to identify whether differences exist in comparison to those with a single diagnosis. **Methods:** A systematic search was conducted to identify studies using measures of executive functioning in patients with PD-substance use disorder dual pathology. Sixteen studies were selected. **Results:** The results indicate that dual pathology patients with Cluster C personality disorder do not differ from controls, and that the presence of dual pathology does not influence the updating domain of executive functioning. The findings were inconclusive with regard to dual pathology patients with Cluster B personality disorders. Whilst the various studies consistently show that these patients show worse performance than the control groups, here are contradictory results with regard to whether Cluster B personality disorders add more alterations in executive functioning to those that already appear in substance use disorder. **Conclusions:** The results suggest the need for further research that more adequately controls variables such as time in treatment, medication, and sample size, whilst there is also a need to employ longitudinal designs that include more patients from Clusters A and C.



KEYWORDS


Dual pathology; substance use disorder; personality disorder; executive function; systematic review

The comorbidity of substance use disorder and other mental disorders has been widely documented (Fenton et al., 2012; Fernández-Calderón et al., 2015; Grant et al., 2016; Rosenthal et al., 2012). Personality disorders (PD) are among the most prevalent of the comorbid disorders, with rates reported to exceed 50% for antisocial personality disorder (APD) and borderline personality disorder (BPD; Trull et al., 2010, 2018; Vergés et al., 2014). The comorbidity between substance use disorder and PD has been associated with serious consequences for patients and those around them (Cavicchioli et al., 2019; Kienast et al., 2014; Langås et al., 2011). In comparison with those diagnosed with a single disorder, the clinical course of the disease has been described as being more severe in those individuals for whom both disorders are present (Fenton et al., 2012; Newton-Howes & Foulds, 2018), with more severe functional

impairment (Lozano et al., 2017; Newton-Howes & Gordon, 2017), as well as increased hospitalizations (Beckwith et al., 2014) and more severe psychiatric symptoms (Thornton et al., 2012).

To date, various models have been proposed to explain this comorbidity, and there does not seem to be a single etiopathogenesis (Skodol et al., 2011; Trull et al., 2018); rather, interactions between genetic and environmental factors have been proposed. Different studies have confirmed the genetic relationships between substance use disorder and PD (Distel et al., 2012; Few et al., 2014; Gillespie et al., 2018; Long et al., 2017), whilst others have highlighted their similarities in terms of emotional instability and disinhibition (Bornovalova et al., 2005; Kotov et al., 2010, 2017; Massey et al., 2018; Winsper et al., 2016; Yücel & Lubman, 2007). Brain circuits have also been identified as being involved in both types of disorders

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(Belcher et al., 2014; Conrod & Nikolaou, 2016). In this regard, evaluation through neuropsychological tests has detected common alterations in executive functions that include a reduced ability to inhibit responses (Garcia-Villamizar et al., 2017; Lev-Ran et al., 2012; Panenka et al., 2013; Spronk et al., 2013), alterations in working memory (Baliouisis, 2014; Garcia-Villamizar et al., 2017; Panenka et al., 2013; Stavro et al., 2013) and poor performance in both decision making and sensitivity to future consequences (Baldacchino et al., 2012; LeGris et al., 2012; Lev-Ran et al., 2012). Similarly, alterations in impulsivity in patients with PD have been associated with an increase in substance-associated risk behaviors (Thompson et al., 2017; Tull et al., 2011). These common cognitive impairments have led some authors to emphasize the need for an assessment to determine their importance in the development and maintenance of associated disorders (Bruijnen et al., 2019).

The results of the above studies indicate common elements between substance use disorder and PD patients. However, the comparison between patients with dual pathology (substance use disorder–PD) versus those with a single disorder has been rather less studied. In this regard, some studies have found worse executive functioning in people diagnosed with substance use disorder–PD compared to those with a single diagnosis in areas such as decision-making, updating, and inhibition (Albein-Urios, Martinez-Gonzalez, Lozano, et al., 2014; Coffey et al., 2011; Dom et al., 2006b; Malloy et al., 1990; Rubio et al., 2007). However, other studies have found no differences in executive functioning between people diagnosed with substance use disorder or PD alone and substance use disorder–PD in terms of inhibition (Dom et al., 2006a), cognitive flexibility (Malloy et al., 1990), or decision-making (Sargeant et al., 2012; Verdejo-Garcia et al., 2017). This apparent discrepancy in the literature could be due to methodological differences between the studies, such as the characteristics of the sample or the instruments used (Bornovalova et al., 2005; Maraz et al., 2016). However, the negative impact and clinical difficulty shown by dual pathology patients could be taken to indicate a different pattern of cognitive functioning in these patients. For example, some studies have demonstrated how decision-making is altered in patients with BPD (Lawrence et al., 2010; Paret et al., 2017) and this executive function has been related to lack of therapeutic adherence and relapse in patients with substance use disorder (Domínguez-Salas et al., 2016; Paret et al., 2017). Although deficits in neurocognitive

functioning are one of the most studied risk factors for treatment adherence and relapse (Klein, 2020), the results are inconclusive (Adinoff et al., 2016).

To date, no reviews have been done that cover the literature comparing executive functioning of patients with substance use disorders–PD to those with a single disorder. Therefore, the aim of the present study was to conduct a systematic review of the empirical literature to determine whether patients with substance use disorder–PD show different patterns of executive functioning compared with patients with only substance use disorder or PD.

Method

Literature search and selection of studies

The systematic review was conducted through the PubMed and PsycInfo databases and was completed in March 2020 following the PRISMA guidelines (Moher et al., 2009). The PRISMA checklist is available as [Supplemental Table 1](#). Initially, the search was conducted on the “title” and “abstract” fields including the words are listed in [Table 1](#). A complete example of the search strategy is available as [supplementary material](#) (see [Supplemental Table 2](#)). In order to further refine the search, the following inclusion criteria were established: (1) the participants had to be in treatment for substance use; (2) the patients had to be diagnosed according to Diagnostic and Statistical Manual of Mental Disorders (DSM) or International Classification of Diseases (ICD) diagnostic criteria; (3) the studies had to include at least one group of patients with dual pathology PD–substance use disorder, plus a comparative group: substance use disorder only, PD only, or healthy controls; (4) the evaluation of the patients had to include the assessment of some form of executive functioning according to the proposal of Fernández-Serrano, Pérez-García, and Verdejo-García (Fernandez-Serrano et al., 2011) and using quantitative measures such as mean differences.

The flow chart of the search process is shown in [Figure 1](#). As can be observed, the combinations of the different keywords revealed a total of 599 studies. After excluding duplicate articles ($n = 104$), the titles and abstracts of the remaining 493 papers were reviewed. The review of the abstracts led to the exclusion of 457 articles, which did not meet the inclusion criteria. Subsequently, the full text of the 34 selected studies was evaluated, excluding 20 articles for the following reasons: the neuropsychological assessments were not considered to measure executive functions

Table 1. Terms Used in the Literature Search.

Related to drug consumption	Related to measures of executive functioning	Related to mental disorders
Cocaine	Decision making	Dual pathology
Heroin	Cognitive	Personality disorder*
Opiate	Exec* function*	Comorb*
Alcohol	Neurop*	Dual diagnos*
Methamphetamine	Neurocog*	Axis II
Cannabis	Impulsiv*	Antisocial personality disorder
Marijuana		Avoidant personality disorder
MDMA		Borderline personality disorder
Ecstasy		Narcissistic personality disorder
Polydrug		Obsessive–compulsive personality disorder
Polysubstance		Schizotypal personality disorder
Drug dependence		Schizoid personality disorder
Substance dependence		Paranoid personality disorder
Substance use disorder		
Substance use		

Note. MDMA = 3,4-Methylenedioxymethamphetamine; * = wildcard character.

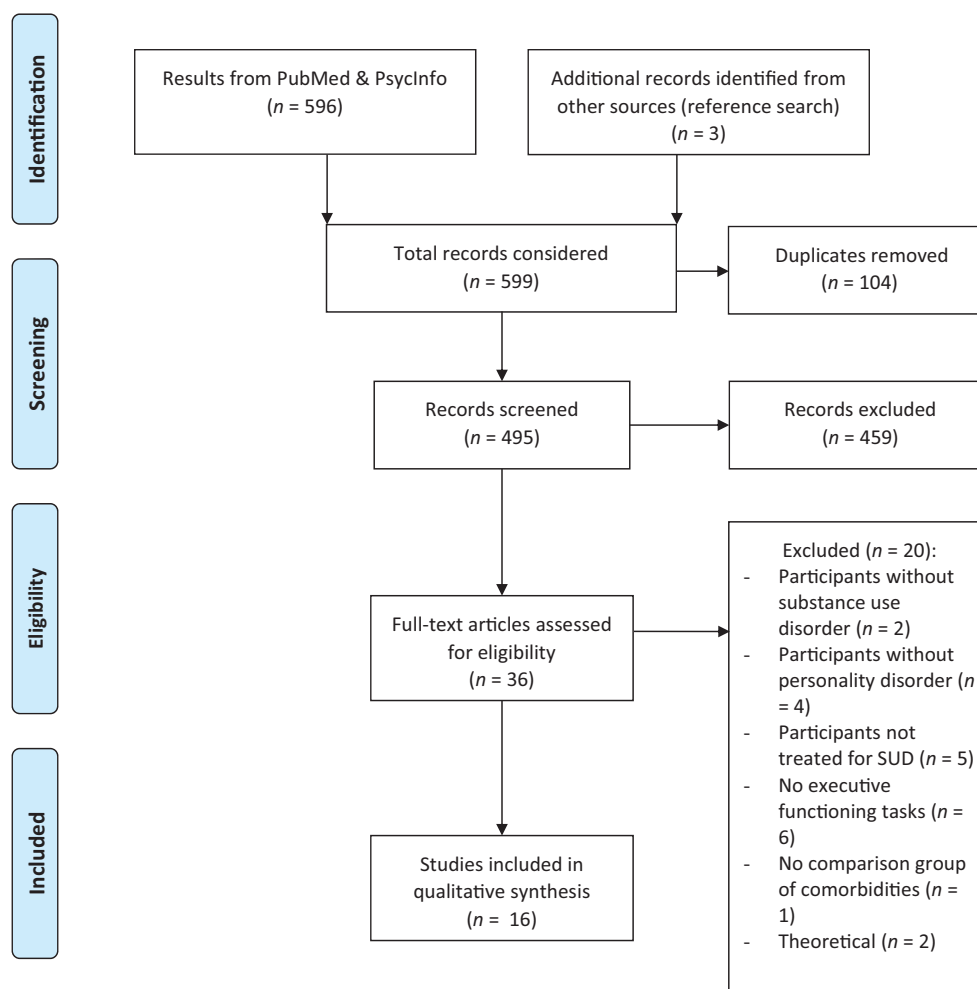


Figure 1. Flow diagram according to PRISMA guidelines.

according to the inclusion criteria ($n = 6$); they did not specify the criteria used to diagnose substance use disorder ($n = 2$) or personality disorder ($n = 4$); the

sample of participants were not in treatment ($n = 5$); they did not have comparison groups ($n = 1$); or they were not empirical studies ($n = 2$).

Table 2. Description of the Studies (n = 16).

Study	Country	Sample Size	Substance evaluated	Personality disorder	Gender	Age (years) [mean (SD)]	Treatment method	Abstinence	Neuropsychological tasks
Malloy et al. (1989)	USA	182 146 AUD 36 AUD-APD	Alcohol	Antisocial Personality Disorder	AUD: NA AUD-APD: 99% males; mean age 32.1 years (7.3)	AUD: 40.2 (12.7) AUD-APD: 32.1 (7.3)	Outpatient treatment	>21 days	1. Digit-symbol Substitution Test 2. Block Design Test 3. Category Test 4. Tactual Performance Test 5. Trail Making Test (Part B)
Malloy et al. (1990)	USA	60 30 AUD 30 AUD-APD	Alcohol	Antisocial Personality Disorder	1% males	32 (NA)	Outpatient treatment	>21 days	1. Digit-symbol Substitution Test 2. Block Design Test 3. Category Test 4. Tactual Performance Test 5. Trail Making Test (Part B)
Moeller et al. (2002)	USA	74 30 CUD 19 CUD-APD 25 GC	Cocaine	Antisocial Personality Disorder	CUD: 87% males CUD-APD: 79% males	CUD: 36.5 (1.41) CUD-APD: 34.0 (1.77)	Residential & outpatient treatment	ND	1. Delayed reward task
Dom et al. (2006 a)	Belgium	133 38 AUD 23 AUD-B 19 AUD-A/C 53 GC	Alcohol	Cluster A, B & C	AUD: 74% males AUD-B: 65% males AUD-A/C: 74% males GC: 49% males	AUD: 43 (11) AUD-B: 40 (7) AUD-A/C: 41 (11) GC: 41 (11)	Residential treatment	4-5 weeks	1. Iowa Gambling Task (IGT)
Dom et al. (2006a, 2006b)	Belgium	62 40 AUD 22 AUD-B	Alcohol	Cluster B	71% males	42.1 (9.5)	Residential treatment	>3 weeks	1. Go-No/Go task 2. Color and word test (STROOP) 3. Delay Discounting Task (DDT)
Rubio et al. (2007)	Spain	343 178 AUD 29 AUD-BPD 40 AUD-APD 96 GC	Alcohol	Cluster B: Borderline Personality Disorder Antisocial Personality Disorder	AUD: 100% males AUD-BPD: 100% males AUD-APD: 100% males GC: NA	AUD: 41.4 (8.1) AUD-BPD: 37.0 (7.2) AUD-APD: 38.0 (6.5) GC: 38.9 (6.8)	Residential & outpatient treatment	4-6 weeks	1. Stop Signal Task 2. Delay Discounting Task (DDT)
Coffey et al. (2011)	USA	79 19 BPD 32 BPD-substance use disorder 28 GC	NA	Borderline Personality Disorder	BPD: 26% males BPD-substance use disorder: 25% males GC: 7% males	BPD: 32.84 (10.85) BPD-substance use disorder: 37.34 (9.14) GC: 33.46 (12.94)	Residential treatment	>4 days	1. Delay Discounting Task (DDT) 2. Stop Signal Task
Sargeant et al. (2012)	USA	117 77 substance use disorder 40 substance use disorder-APD	Substance use disorder	Antisocial Personality Disorder	Substance use disorder: 70.7% males substance use disorder-APD: 59.5% males	Substance use disorder: 41.8 (8.9) substance use disorder-APD: 41.9% (8.9)	Residential treatment	NA	1. Delay-Discounting Questionnaire (DDQ)

Mellentin et al. (2013)	Denmark	63 30 substance use disorder 16 substance use disorder-APD 17 GC	Substance use disorder	Antisocial Personality Disorder	76% males	Substance use disorder/ substance use disorder-APD: 35.1 (8.2) GC: 36.7 (10.6)	NA	1. Iowa Gambling Task (IGT)
Albein-Urios et al. (2013)	Spain	110 44 CUD 32 CUD-B 34 GC	Cocaine	Cluster B	NA	CUD: 31.28 (6.5) CUD-B: 33.13 (7.7) GC: 30.5 (4.3)	>15 days	1. Letter and number sequence tests 2. N-back task 3. Color and word tests (STROOP) 4. Category Test
Albein-Urios, Martínez-González, Lozano, et al. (2014)	Spain	107 36 CUD 22 CUD-B 15 CUD-C 34 GC	Cocaine	Cluster B & C	CUD: 94.4% males CUD-B: 63.7% males CUD-C: 100% males GC: 94.4% males	CUD: 32.09 (6.3) CUD-B: 33.43 (7.2) CUD-C: 33.57 (5.8) GC: 30.5 (4.39)	>15 days	1. Letter and number sequence tests 2. N-back task 3. Color and word tests (STROOP) 4. Category Test
Albein-Urios, Pilatti, et al. (2014)	Spain	96 32 CUD 38 CUD-B 26 GD	Cocaine	Cluster B	NA	Age range 18–50 years	>15 days	1. Delay-Discounting Questionnaire (DDQ) 2. D2 cancellation test
Albein-Urios, Martínez-González, Lozano-Rojas, et al. (2014)	Spain	152 32 CUD 23 CUD-B 15 CUD-C 14 GD 36 GC	Cocaine	Cluster B & C	NA	Age range 19–52 years	>15 days	1. Delay-Discounting Questionnaire (DDQ) 2. D2 cancellation test
Moody et al. (2016)	USA	327 166 substance use disorder 44 substance use disorder-TD 35 substance use disorder-APD 22 substance use disorder-MDD-APD 60 GC	Substance use disorder	Antisocial Personality Disorder	Substance use disorder: 75.9% males substance use disorder-MDD: 81.8% males substance use disorder-APD: 77.1% males substance use disorder-MDD-APD: 86.4% males GC: 61.7% males	Substance use disorder: 43.05 (10.35) substance use disorder-MDD: 45.61 (9.71) substance use disorder-APD: 40.57 (9.91) substance use disorder-MDD-APD: 43.00 (11.04) GC: 35.15 (13.48)	NA	1. Delay Discounting Task (DDT)
Maraz et al. (2016)	Hungary	345 101 AUD 23 substance use disorder 36 BPD 49 AUD-BPD 25 substance use disorder-BPD 111 GC	Alcohol substance use disorder	Borderline Personality Disorder	AUD: 81.2% males substance use disorder: 56.5% males BPD: 11.1% males BPD-AUD: 62.5% males BPD-substance use disorder: 60% males GC: 39.6% males	AUD: 48.3 (9.5) substance use disorder: 31.4 (10.0) BPD: 30.6 (10.8) BPD-AUD: 40.1 (8.9) BPD-substance use disorder: 29.5 (10.2) GC: 36.6 (11.0)	>24h	1. Delay Discounting Task (DDT)

(Continued)

Table 2. Continued.

Study	Country	Sample Size	Substance evaluated	Personality disorder	Gender	Age (years) [mean (SD)]	Treatment method	Abstinence	Neuropsychological tasks
Verdejo-García et al. (2017)	Spain	62 19 CUD 24 CUD-PD 19 GC	Cocaine	Cluster B & C	CUD: 94.7% males CUD-TP: 83.3% males GC: 94.7% males	CUD: 35.42 (6.38) CUD-PD: 33.21 (7.00) GC: 30.84 (4.13)	Outpatient treatment	>15 days	1. fMRI task: Ultimatum Game (UG)

Note. CUD = group diagnosed with cocaine use disorder without comorbidity; CUD-B = group diagnosed with cocaine use disorder and Cluster B personality disorder; CUD-C = group diagnosed with cocaine use disorder and Cluster C personality disorder; CUD-APD = group diagnosed with cocaine use disorder and antisocial personality disorder; CUD-PD = group diagnosed with cocaine use disorder and personality disorder; SD = standard deviation; GC = group control; AUD = group diagnosed with alcohol use disorder without comorbidity; AUD-A/C = group diagnosed with alcohol use disorder and Cluster A and C personality disorders; AUD-B = group diagnosed with alcohol use disorder and Cluster B personality disorder; AUD-BZD = group diagnosed with alcohol use disorder and benzodiazepine use disorder; AUD-BZD-PD = group diagnosed with alcohol use disorder, benzodiazepine use disorder, and personality disorder; AUD-APD = group diagnosed with alcohol use disorder and antisocial personality disorder; AUD-PD = group diagnosed with alcohol use disorder and personality disorder; AUD-BPD = group diagnosed with alcohol use disorder and borderline personality disorder; NA = not available; substance use disorder = group diagnosed with substance use disorder without comorbidity; substance use disorder-APD = group diagnosed with substance use disorder and antisocial personality disorder; substance use disorder-MDD = group diagnosed with both substance use disorder and depression; substance use disorder-MDD-APD = group diagnosed with substance use disorder, depression, and antisocial personality disorder; substance use disorder-BPD = group diagnosed with substance use disorder and borderline personality disorder; GD = group diagnosed with pathological gambling disorder without comorbidity; BPD = group diagnosed with borderline personality disorder without comorbidity; MDD = group diagnosed with major depressive disorder.

Moreover, two studies identified in the references of the reviewed articles were included. A total of 16 studies were included in the review.

Classification of tests used to measure executive functioning

To categorize the tests of executive functioning, we decided to use the classification system established by Fernandez-Serrano et al. (2011). This classification provides a definition of each neuropsychological domain, along with a list of the most commonly used tests for measuring them. This classification considers the following domains of executive functioning: updating, cognitive flexibility, inhibition, decision-making, planning, organization, and sequencing.

Results

Description of the studies

Table 2 describes the characteristics of the 16 selected studies. Most of these ($n = 10$) were conducted in Europe (Spain, Belgium, Hungary, and Denmark), while the remaining six were conducted in the United States. The period of publication of these studies is from 1989 to 2017. With respect to the substance for which treatment was needed, six of the studies included patients with cocaine-related problems, and five studies included patients with alcohol-related problems. However, almost one third of the studies ($n = 5$) do not specify the particular substances for which the participants were being treated, instead using the category “substance use disorder.” Most studies ($n = 11$) assessed patients with Cluster B personality disorders, while the remaining studies included patients diagnosed with personality disorders from Clusters C and A.

The total sample size of the reviewed studies ranged from 60 (Malloy et al., 1990) to 345 (Maraz et al., 2016). Group size ranged from 14 (Albein-Urios, Martinez-González, Lozano, et al., 2014) to 178 (Rubio et al., 2007). In most studies ($n = 10$) the patients were treated on an outpatient basis and in four studies the patients received residential treatment ($n = 4$), while two studies evaluated patients that received both treatment modalities. With regard to abstinence prior to neuropsychological assessment, these periods ranged from 2 days to 6 weeks, with a period of longer than 15 days in most of the studies reviewed ($n = 10$). Four studies did not provide data on the period of abstinence prior to assessment. All of the studies employed a cross-sectional design.

Table 3. Main Results and/or Conclusions of the Selected Studies Organized According to Domains.

Domain	Substance	Personality disorder	Sample size	Study	Main results and/or conclusions
Updated	Alcohol	Antisocial Personality Disorder	182	Malloy et al. (1989)	No statistically significant differences were found between the groups with and without dual pathology on the Category Test
			146 AUD 36 AUD-APD 60		
	Cocaine	Cluster B & C	30 AUD 30 AUD-APD	Malloy et al. (1990)	No statistically significant differences were found between the groups with and without dual pathology on the Category Test
			107		
			36 CUD 22 CUD-B 15 CUD-C 34 GC		
Working Memory	Cocaine	Cluster B & C	110	Albein-Urios et al. (2013)	No statistically significant differences were found between the groups with and without dual pathology on the Category Test. The control group showed better performance than the dual-pathology patients with Cluster B personality disorder ($d = 0.89$) and those with cocaine use disorder only ($d = 0.59$)
			44 CUD		
			32 CUD-B		
			34 GC		
			107		
Cognitive Flexibility Changing Criterion	Alcohol	Antisocial Personality Disorder	36 CUD	Albein-Urios, Martinez-Gonzalez, Lozano, et al. (2014)	No statistically significant differences were found in performance on the letter and number sequence test between groups with and without dual pathology or between Cluster B and C patients. The group of cocaine users without dual pathology and the cocaine users with Cluster C personality disorder showed greater deficits in working memory compared with the control group ($d = 1.0$ and $d = 1.1$, respectively)
			22 CUD-B		
			15 CUD-C		
			34 GC		
			110		
Inhibition Impulsive Action	Alcohol	Cluster B	44 CUD	Albein-Urios et al. (2013)	The groups with and without dual pathology did not differ in terms of their performance on the letter-number sequence test. The control group differed significantly from the group with dual pathology ($d = 0.88$) and the group of cocaine dependent patients without dual pathology ($d = 1.06$)
			32 CUD-B		
			34 GC		
			110		
			44 CUD		
Cognitive Flexibility Changing Criterion	Alcohol	Antisocial Personality Disorder	182	Malloy et al. (1989)	The dual pathology group showed poorer performance than the non-dual group on the symbol and digit test ($F = 8.06, 1/179$ df, $p < .01$), but no significant differences were found on the Trail Making Test (Part B) or the tactical performance test
			146 AUD		
			36 AUD-APD		
			60		
			30 AUD		
Inhibition Impulsive Action	Alcohol	Cluster B	30 AUD-APD	Malloy et al. (1990)	No statistically significant differences were found between the groups on either the symbol and digit test or the tactical performance test, but the APD group showed poorer performance on the Trail Making Test ($t = 2.01, p < .05$)
			62		
			40 AUD		
			22 AUD-B		
			343		
Inhibition Impulsive Action	Alcohol	Cluster B	178 AUD	Dom et al. (2006a, 2006b)	No statistically significant differences were found between the groups with and without dual pathology in the color and word test (Stroop). However, the dual pathology group showed significantly lower inhibitory control in comparison with the alcohol group without dual pathology in the Go-No/Go task ($F = 4.062, p < .05$)
			29 AUD-BPD		
			40 AUD-APD		
			96 GC		
			343		
Inhibition Impulsive Action	Alcohol	Cluster B	178 AUD	Rubio et al. (2007)	Using the Stop-signal task, the groups with dual antisocial and borderline pathology showed greater deficits in inhibition compared with the control group and the alcohol group without pathology ($F = 6.68; df = 34,1, p = .001$)
			29 AUD-BPD		
			40 AUD-APD		
			96 GC		
			343		

(Continued)

Table 3. Continued.

Domain	Substance	Personality disorder	Sample size	Study	Main results and/or conclusions
Impulsive Choice	Cocaine	Cluster B & C	96	Albein-Urios, Piliatti, et al. (2014)	No significant differences were found on the response inhibition tests (Stroop and D2 cancellation test) between the groups with and without dual pathology
			32 CUD		
	Substance use disorder (NA)	Cluster B	38 CUD-B	Albein-Urios, Martinez-Gonzalez, Lozano, et al. (2014)	There were no statistically significant differences between the dual-pathology groups and the group without comorbidity, or between the two dual-pathology groups. The cocaine-dependent group with Cluster B personality disorder showed poorer behavioral inhibition compared with controls, on both the Stroop test ($d = 0.7$) and the D2 cancellation test ($d = 1.0$) The group with dual pathology had significantly performed significantly worse on the task in comparison with the group of cocaine users, on both the Stroop test ($d = 0.5$) and the D2 cancellation test ($d = 0.79$). The groups with and without dual pathology showed greater deficits in response inhibition when compared with the control group (D2, $d = 1.05$; Stroop, $d = 0.79$)
			26 GD		
			107		
			36 CUD		
			22 CUD-B		
			15 CUD-C		
			34 GC		
			110		
44 CUD					
Impulsive Choice	Substance use disorder (NA)	Borderline Personality Disorder	42 CUD-B	Coffey et al. (2011)	No statistically significant differences were found between the two groups with BPD.
			34 GC		
	Alcohol	Cluster B	79	Dom et al. (2006a, 2006b)	The two groups with BPD showed poorer behavioral inhibition than the control group on the Stop-signal task (BPD versus GC: $d = 1.26$; BPD-substance use disorder versus GC: $d = 0.90$) The ability to delay rewards did not differ between the two groups ($F = 0.285$)
			19 BPD		
			32 BPD-substance use disorder		
			28 GC		
			62		
			40 AUD		
			22 AUD-B		
			343		
178 AUD					
Impulsive Choice	Cocaine	Cluster B & C	29 AUD-BPD	Rubio et al. (2007)	Statistically significant differences were found between all groups, with the deterioration being greatest among patients with antisocial personality disorder, followed by the borderline disorder group, the alcohol use group without Cluster B disorder, and finally the control group ($F = 11.31$)
			40 AUD-APD		
	Substance use disorder	Antisocial Personality Disorder	96 GC	Albein-Urios, Martinez-Gonzalez, Lozano-Rojas, et al. (2014)	No significant differences were observed between the cocaine groups with and without comorbidity, or between these groups and the control group
			152		
			32 CUD		
			23 CUD-B		
			15 CUD-C		
			14 GD		
			36 GC		
			74		
30 CUD					
Impulsive Choice	Substance use disorder	Antisocial Personality Disorder	19 CUD-APD	Moeller et al. (2002)	No statistically significant differences were found between the two groups with substance use disorder. Regardless of the presence of antisocial personality disorder, cocaine-dependent subjects showed more impulsive behavior during the tasks compared with the control group ($F = 3.64$)
			25 GC		
	Substance use disorder	Antisocial Personality Disorder	327	Moody et al. (2016)	People with APD and substance use disorder, and people with MDD, APD and substance use disorder discounted future rewards significantly more than substance users without comorbid psychopathology ($d = 0.412$ and $d = 0.964$, respectively). All groups with substance use disorder exhibited significantly more impulsive behavior than healthy controls
			166 substance use disorder		
			44 substance use disorder-MDD		
			35 substance use disorder-APD		
			22 substance use disorder-		
			MDD-APD		
			60 GC		

Decision-making	Alcohol	Cluster A, B & C	117 substance use disorder	Sargeant et al. (2012)	For this domain, no statistically significant differences were found between the groups with and without dual pathology
			40 substance use disorder-APD		
			345		
Planning, organizing, and sequencing	Alcohol	Antisocial Personality Disorder	101 AUD	Maraz et al. (2016)	The group with alcohol use disorder plus BPD showed greater delay discounting impulsivity than the group with alcohol use disorder alone ($p < .05$).
			23 substance use disorder		There were statistically significant differences between the control group and the groups with BPD plus substance use disorder ($d=0.86$), and BPD plus alcohol use disorder ($d = 0.61$).
			36 BPD		No statistically significant differences were found between the rest of the groups
			49 AUD-BPD		
			25 substance use disorder-BPD		
			111 GC		
			79	Coffey et al. (2011)	The dual pathology group showed greater inability to delay reward compared with the control group ($d = 0.66$). However, no significant differences were found between the rest of the groups
			19 BPD		
			32 BPD-substance use disorder		
			28 GC		
Decision-making	Alcohol	Cluster A, B & C	133	Dom et al. (2006a)	The group of alcohol users with Cluster B personality disorder showed the poorest performance on the IGT compared with the alcohol users with Cluster A or C personality disorder, and the alcohol group without dual pathology, $F(2, 79)=3.230$; $p = .045$.
			38 AUD		Regardless of the presence of personality disorder, the alcohol drinking groups with and without dual pathology showed more impulsive decision-making compared with the control group
			23 AUD-B		No significant group differences were found for either the Ultimatum Game task or for brain activation. The cocaine group with dual pathology showed less connectivity of the brain regions involved in the emotional processing of the task
			19 AUD-A/C	Verdejo-García et al. (2017)	The presence of antisocial personality disorder was not associated with poorer IGT performance in participants with substance use disorder.
			53 GC		Greater impairment on task performance was found in the groups with and without dual pathology in comparison with the control group ($d = 1.01$ and $d = 1.43$, respectively)
			62		
			19 CUD		
			24 CUD-PD	Mellentin et al. (2013)	The results revealed no differences between the groups with and without antisocial personality disorder
			19 GC		
			30 substance use disorder		
Planning, organizing, and sequencing	Alcohol	Antisocial Personality Disorder	16 substance use disorder-APD	Malloy et al. (1989)	The group of patients with dual pathology showed significantly worse performance compared with the group without dual pathology, $t(58)=1.97$
			17 GC		
			182		
			146 AUD		
Planning, organizing, and sequencing	Alcohol	Antisocial Personality Disorder	36 AUD-APD	Malloy et al. (1990)	The group of patients with dual pathology showed significantly worse performance compared with the group without dual pathology, $t(58)=1.97$
			60		
			30 AUD		
			30 AUD-APD		

Note. CUD = group diagnosed with cocaine use disorder without comorbidity; CUD-B = group diagnosed with cocaine use disorder and Cluster B personality disorder; CUD-C = group diagnosed with cocaine use disorder and Cluster C personality disorder; CUD-APD = group diagnosed with cocaine use disorder and antisocial personality disorder; CUD-PD = group diagnosed with cocaine use disorder and personality disorder; SD = standard deviation; GC = group control; AUD = group diagnosed with alcohol use disorder without comorbidity; AUD-A/C = group diagnosed with alcohol use disorder and Cluster A and C personality disorders; AUD-B = group diagnosed with alcohol use disorder and Cluster B personality disorder; AUD-BZD = group diagnosed with alcohol use disorder and benzodiazepine use disorder; AUD-BZD-PD = group diagnosed with alcohol use disorder, benzodiazepine use disorder, and personality disorder; AUD-APD = group diagnosed with alcohol use disorder and antisocial personality disorder; AUD-PD = group diagnosed with alcohol use disorder and personality disorder; AUD-BPD = group diagnosed with alcohol use disorder and borderline personality disorder; NA = not available; substance use disorder: group diagnosed with substance use disorder without comorbidity; substance use disorder-APD = group diagnosed with substance use disorder and antisocial personality disorder; substance use disorder-MDD = group diagnosed with both substance use disorder and depression; substance use disorder-MDD-APD = group diagnosed with substance use disorder, depression, and antisocial personality disorder; substance use disorder-BPD = group diagnosed with substance use disorder and borderline personality disorder; GD = group diagnosed with pathological gambling disorder without comorbidity; BPD = group diagnosed with borderline personality disorder without comorbidity.

Comparisons for the cognitive updating domain

This cognitive domain, updating, has been studied in four articles, none of which report differences between groups with and without dual pathology, or between dual pathologies with different personality disorders. Two of the studies exclusively analyzed analogical reasoning in patients with alcohol use disorder (AUD) and found no differences between the comorbid group diagnosed with APD, and the group without comorbidity (Malloy et al., 1989, 1990). Two other studies concluded that, regardless of the presence of Cluster B or C personality disorder, patients with cocaine use disorder (CUD) performed worse on both analogical reasoning and working memory tasks when compared with controls (Albein-Urios et al., 2013; Albein-Urios, Martinez-Gonzalez, Lozano-Rojas, et al., 2014).

Comparisons for the cognitive flexibility domain

Two studies investigated the performance on cognitive flexibility tasks of AUD patients with and without APD using the subtests Trail Making Test, Digit and Symbol Test, and the tactual performance test from the Brain Age Quotient (BAQ) Battery. One of the studies found that the dual pathology group showed worse performance on the Trail Making Test (Malloy et al., 1990) whilst another found that this group performed worse on the Digit and Symbol Test (Malloy et al., 1989), with no differences on the rest of the tests.

Comparisons for the cognitive inhibition domain

For the inhibition domain, mixed results are found when comparing substance use disorder–PD and substance use disorder patients. Most papers ($n = 11$) compare results in the inhibition domain in patients with Cluster B personality disorder. Three studies have used different tasks to measure the construct (Table 3).

Seven papers addressed impulsive action. In three of these, patients diagnosed with substance use disorder–PD from Cluster B showed greater deficits compared with patients with AUD (Dom et al., 2006a; Rubio et al., 2007) and CUD (Albein-Urios et al., 2013). Four others found no such differences in studies with CUD (Albein-Urios, Martinez-Gonzalez, Lozano-Rojas, et al., 2014; Albein-Urios, Pilatti, et al., 2014; Coffey et al., 2011; Dom et al., 2006a). In comparison with the control group, four articles report that patients with dual pathology in Cluster B had worse outcomes than patients with AUD (Rubio et al., 2007), CUD (Albein-Urios et al., 2013; Albein-Urios, Martinez-Gonzalez, Lozano-Rojas, et al., 2014), and

substance use disorder (Coffey et al., 2011). Of these, the two studies that analyzed the differences between non-dual pathology drug users and controls also found that the former showed more deficits (Albein-Urios et al., 2013; Coffey et al., 2011).

With regard to impulsive choice, there are eight studies reporting discrepant results when comparing the performance of dual pathology patients with Cluster B personality disorder with substance use disorder-only patients. While three of these studies found worse performance in the groups with dual pathology Cluster B in alcohol (Rubio et al., 2007) or other substance use disorder (Maraz et al., 2016; Moody et al., 2016), five other studies did find these differences in either alcohol (Dom et al., 2006a), cocaine (Albein-Urios, Martinez-González, Lozano, et al., 2014; Moeller et al., 2002), or other substance use disorder (Coffey et al., 2011; Sargeant et al., 2012). However, five studies compared control groups with dual pathology Cluster B patients, and all reported performance in the latter groups regardless of whether they used alcohol (Rubio et al., 2007), cocaine (Moeller et al., 2002), or other substances (Coffey et al., 2011; Maraz et al., 2016; Moody et al., 2016). When analyzing the differences between the control group and the non-dual pathology groups, three studies also found these same differences (Moeller et al., 2002; Moody et al., 2016; Rubio et al., 2007), while two others did not (Coffey et al., 2011; Maraz et al., 2016).

Three studies also included dual pathology with Cluster C personality disorders in patients with cocaine or alcohol use disorders. These studies found no difference between patients with and without dual pathology (Albein-Urios, Martinez-Gonzalez, Lozano-Rojas, et al., 2014; Albein-Urios, Martinez-González, Lozano, et al., 2014; Albein-Urios, Pilatti, et al., 2014), whilst the latter groups did not differ from the control group (Albein-Urios, Pilatti, et al., 2014).

Comparisons for the decision-making domain

Three studies included tests to evaluate the decision-making domain. One of these studies found that patients with AUD and PD from Cluster B presented more alterations in performance on the Iowa Gambling Task (IGT) than those from Clusters A and C, and those with AUD only (Dom et al., 2006b). However, a study with CUD patients using the Ultimatum Game (Verdejo-Garcia et al., 2017) and another with substance use disorder patients using the IGT (Mellentin et al., 2013) found no differences between patients with and without dual pathology.

However, the two studies using the IGT found differences between patients with substance use disorder and the control group regardless of whether dual pathology was present (Dom et al., 2006b; Mellentin et al., 2013), whilst the study using the Ultimatum Game did not find such differences (Verdejo-Garcia et al., 2017).

Comparisons for the cognitive planning/organizing/sequencing domain

With regard to this domain, two studies were found, both in patients with AUD and APD. Whilst in one of the studies the dual pathology group showed significantly worse performance than the group with AUD only (Malloy et al., 1990), the other reported that the two groups behaved similarly (Malloy et al., 1989).

Discussion

The aim of this paper was to systematically review the evidence for deficits in the executive functioning of patients diagnosed with comorbid substance use and personality disorder. The results reveal that patients with dual pathology with a Cluster C personality disorder do not differ from controls, and the presence of dual pathology does not influence cognitive updating. However, the findings are inconclusive with regard to dual pathology patients with Cluster B personality disorder. Whilst the various studies consistently show that these patients present worse performance than the control groups, it is unclear as to whether Cluster B personality disorder adds more alterations in executive functions to those already observed in substance use disorder. Overall, the evidence available about the role of executive function in substance use disorder-PD is limited. The present review highlights the need to homogenize assessment instruments in executive functioning, as well as to increase the research efforts in this area and include more studies with patients from Cluster C and especially from Cluster A, since it was identified as an area for future development.

The analysis of executive functions reveals that it is in the updating domain where it is most clearly observed that the comorbidity of personality disorders with substance use disorder is not associated with a major alteration. However, for the remaining domains, discrepancies in the findings were found. Such discrepancies are observed exclusively in studies of personality disorders belonging to Cluster B, and

never to those of Clusters A or C. Impulsivity and other executive function disorders are a central feature of APD (Ogilvie et al., 2011) and BPD (McClure et al., 2016). Therefore, it is not surprising that dual pathology patients with Cluster B personality disorders are those that show the greatest alterations. In this regard, it could be hypothesized that PDs belonging to Cluster B interact with substance use disorder, increasing the pathology related to executive functions, and causing greater difficulties in impulse control and appropriate decision making. However, the discrepancies between the results of the different studies suggest that there is no conclusive support for this hypothesis. Furthermore, the results are mixed, even among studies conducted with patients diagnosed with the same substance use disorder and using the same neuropsychological tests.

These discrepant findings do not appear in studies with patients from Cluster C. It is likely that this type of PD does not have such clear executive components. Some authors have proposed that in patients with dual pathology with disorders characterized by avoidance (such as those in Cluster C), the presence of substance use disorder could be associated with a lower tendency toward rigidity and sensation-seeking (Duijkers et al., 2016). The fact that Cluster C groups do not usually present as many differences with respect to controls as Cluster B and non-dual controls could mean that the presence of these PDs decreases the impulsive tendencies that are usually associated with substance use disorder. That is, it is possible that the presence of dual pathology with Cluster B personality disorders does not increase the impulsivity of substance use disorder patients but, rather, the presence of dual pathology with Cluster C personality disorders decreases such impulsivity. However, it should be noted that few studies include patients from this cluster, so it is not possible to confirm this hypothesis. For this same reason, it is also not possible to draw any clear conclusions on comorbidity with Cluster A personality disorders.

However, the results show that dual pathology patients with Cluster B personality disorders present more alterations in their executive functions compared with healthy controls, particularly in the domains of updating, inhibition, and decision making. In studies with patients in treatment for AUD or CUD (Fernandez-Serrano et al., 2011), these alterations appear in the absence of comorbidity, in addition to functional and structural alterations in frontal lobe neuroimaging (Bühler & Mann, 2011; Goldstein & Volkow, 2011). Therefore, the differences with respect

to control groups could be linked to addiction-related factors. Further, in many PD without comorbidity (schizotypal, borderline, antisocial, narcissistic, and obsessive–compulsive), alterations in executive functions (Garcia-Villamisar et al., 2017) and in neuroimaging (Ma et al., 2016) have also been found, but there are almost no data on the rest of the disorders. It is possible that in some cases of dual pathology such as schizotypal, obsessive–compulsive, antisocial, narcissistic, and borderline, both conditions interfere with executive functions, and in the remaining cases (schizoid, paranoid, avoidant, dependent, and histrionic) the difference observed in comparison with healthy controls are more related to substance use disorder. These results are also consistent with the daily difficulties faced by dual pathology patients in terms of decision making, inhibition of problematic behaviors, planning, and behavioral flexibility.

The results of this work have clinical implications for the treatment of dual pathology patients. There is abundant evidence to suggest that poor executive functioning is related to unfavorable treatment outcomes in addiction, including a higher rate of relapse and abandonment (Domínguez-Salas et al., 2016; Stevens et al., 2014). This implies that improving executive functioning should be one of the aims of intervention programs, and, in fact, cognitive training has been observed to improve the effectiveness of treatments (Holmes et al., 2014; Shoptaw, 2014). Therefore, this aspect of the intervention would be of special relevance for both non-dual patients and for those with comorbid personality disorders from Clusters A or B, but it would be less important for those of Cluster C, since this group does not appear to present alterations in executive functioning.

However, it should be noted that all of these studies have been conducted using the DSM-IV or DSM-5 Section II categorical classification for PDs that include among their criteria some behaviors related to executive functioning, such as impulsivity. This diagnostic system has been shown to have a number of limitations (Widiger & Samuel, 2005), which could be, at least in part, responsible for some of the discrepant results found in the literature. Thus, it could be more productive to explore the relationship between executive functions and the alternative diagnostic model of PD in Section III of the DSM-5. This model is dimensional rather than categorical and is based on the measurement of pathological personality traits that include 25 facets configured in five domains (Krueger & Markon, 2014; Krueger et al., 2012). Different scores on these domains and facets are associated with

the presence of different PDs (Samuel & Widiger, 2008; Saulsman & Page, 2004), so that while APD includes several other facets of the antagonistic domain, schizotypal disorder includes facets of the psychotic domain. It is likely that some of the facets that make up the different PDs will be associated with alterations in executive functions, whilst others will not (Arnevik et al., 2019). Therefore, it could be interesting to directly study the relationships between executive functions and the different facets and domains that make up the PDs.

With regard to the limitations found in this review, it is worth noting the heterogeneity of the findings reported in the various studies. This could be attributed to methodological differences between the studies, where different tasks have been employed to evaluate the same construct. Also, there were important differences in the methodological quality of the selected studies. Sample sizes varied from 60 to 345 participants, and the description of potential bias in participant flow (including recruitment, withdrawals, and dropout) was incomplete or even absent in several cases. Only one study (Dom, 2006a) included a CONSORT flowchart. The groups of interest were partially matched at best in most studies, and differences in relevant confounders such as sociodemographic variables, IQ, severity of psychiatric pathologies, and use of other drugs were reported in different studies, which should make us cautious when interpreting the differences found (or their absence). Moreover, the periods of abstinence were not the same for all studies, and four studies did not even supply such information, which could affect the results found. Finally, the sample sizes in many of the studies were relatively modest, particularly in the dual pathology groups, which could limit the possibility of generalizing the results. Also, the small number of participants in certain subgroups could explain by itself some of the negative results due to limited statistical power. Adopting clear sample size calculation strategies (Pye et al., 2016) would improve the research practice in the field.

Based on the most salient conclusions of this review, we believe that future studies in this area could benefit from using the standardized protocol for assessing executive functioning proposed by Dickinson, Berra, and Coombes (Dickinson et al., 2017). These authors point out the importance of taking into account the following aspects when evaluating executive functioning: (a) parameters of symptom remission; (b) pharmacotherapy and condition of psychiatric comorbidity; (c) definition of executive

function; and (d) neuropsychological tests of executive function.

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