Rassegna

Psychosocial interventions in stimulant use disorders: a systematic review and qualitative synthesis of randomized controlled trials

Interventi psicosociali nei disturbi da uso di psicostimolanti: una revisione sistematica e sintesi qualitativa di studi clinici randomizzati

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SUMMARY. Stimulant use disorders are highly prevalent with a large burden of disease. Most clinical guidelines recommend psychosocial interventions, but there are no clear hierarchies or indications. Moreover, these interventions have been reported unevenly in the literature. Identifying the most suitable treatment for each patient therefore represents a major challenge. In this review, we describe all psychosocial interventions for stimulant use disorders investigated in randomized controlled trials – including contingency management, cognitive behavioral interventions, community reinforcement approach, 12-step program, meditation-based interventions and physical exercise, supportive expressive psychodynamic therapy, interpersonal psychotherapy, family therapy, motivational interviewing, drug counseling –, and we synthesize the main findings of these studies. Similarities and differences between treatments are highlighted, suggesting that distinct psychosocial interventions can be relevant for certain patients' groups but not for others. Conversely, several interventions can be equally effective in similar clinical contexts, suggesting that a shared element such as therapeutic alliance is key. Finally, combined approaches emerge as a viable option for people with complex needs. Future studies will need to benchmark psychosocial interventions in stimulant use disorders and ascertain markers of response with a view to individualized treatment.

KEY WORDS: Stimulant use disorders, psychosocial interventions, cocaine, systematic review, amphetamine.

RIASSUNTO. I disturbi da uso di stimolanti sono altamente prevalenti e hanno gravi ripercussioni nei pazienti a livello medico, psicologico e sociale. La maggior parte delle linee-guida cliniche raccomanda l'uso di interventi psicosociali per il trattamento, ma le indicazioni sono generiche e non si riferiscono a quali interventi psicosociali si debbano preferire. Inoltre, gli interventi sono stati riportati in modo non uniforme in letteratura. Identificare il trattamento più adatto da offrire per un singolo paziente rappresenta una grande sfida. In questa revisione sistematica, descriviamo tutti gli interventi psicosociali che sono stati studiati in studi clinici randomizzati per i disturbi da uso di psicostimolanti e sintetizziamo i principali risultati di questi studi. Evidenziamo anche le somiglianze e le differenze tra i trattamenti, suggerendo che distinti interventi psicosociali possono essere rilevanti per alcuni gruppi di pazienti ma non per altri. Al contrario, diversi interventi possono essere ugualmente efficaci in contesti clinici simili. Infine, gli approcci combinati emergono come un'opzione praticabile, soprattutto in caso di diagnosi doppia. Gli studi futuri dovranno valutare i marcatori di risposta in vista di un trattamento individualizzato.

PAROLE CHIAVE: disturbi da uso di psicostimolanti, interventi psicosociali, cocaina, amfetamina, revisione sistematica.

INTRODUCTION

Stimulants are a class of psychoactive substances that excite the nervous system through complex interactions with monoamine transporters and neurotransmitters[1]. Cocaine and amphetamines are the most commonly abused stimulants, with an annual prevalence of 0.38% and 1.20% respectively in those aged 15-64 years[2]. Stimulant use disorders are characterized by the sustained use of these substances leading to substantial impairment and distress[3]. Common symptoms include craving for stimulants, failure to control use, continued use despite interference with major obligations or

social functioning, use of greater amount over time, development of tolerance, spending a great deal of time to obtain and use stimulants, and withdrawal symptoms that occur after stopping or reducing use. These patients are at increased mortality risk and suffer from several comorbidities including psychosis and other mental illnesses, neurological disorders, cardiovascular dysfunctions, sexually-transmitted diseases, and blood-borne viral infections[4]. Moreover, the impact on society is large because of the association between stimulants use and offending[5].

Recent data suggest that people affected by stimulant use disorders are increasingly seeking out treatment[2]. Usually these patients do not require inpatient care because withdrawal syndromes are not severe or complex, and most can be safely treated in outpatient programs. Psychiatric and psychological management is advocated as the best evidence-based option for these patients and aims to:

- motivate the patient to change;
- establish and maintain a therapeutic alliance with the patient;
- assess the patient's safety and clinical status;
- manage the patient's intoxication and withdrawal state;
- develop and facilitate the patient's adherence to a treatment plan;
- prevent the patient's relapse;
- educate the patient about substance use disorders;
- reduce the morbidity and sequelae of substance use disorders.

Clinical guidelines recommend psychosocial interventions as the treatments of choice for all stimulant use disorders[6-9], and there is no evidence of differential effect for any psychosocial intervention in the management of patients using distinct stimulants[10]. The development and assessment of psychosocial interventions for substance use disorders has been a priority of the National Institute on Drug Abuse for over 20 years[11]. However, a key limitation of studies investigating psychosocial interventions is that even well designed randomized controlled trials are subject to biases that can falsely increase the likelihood of a positive outcome[12-14]. A recent systematic review and meta-analysis provided encouraging results on the efficacy and acceptability of all types of psychosocial interventions for stimulant use disorders[15]; however, this study did not compare qualitatively the various treatments.

In this paper, we performed a systematic review and qualitative synthesis of all psychosocial interventions assessed in randomized controlled trials. Our aim is to provide clinicians with a comprehensive description of all the available psychosocial interventions for stimulant use disorders and report the most recent evidence-base for them.

METHODS

Literature search

We performed an extensive computer literature search of peer-reviewed articles about psychosocial interventions in stimulant use disorders on the following databases: Cochrane Drugs and Alcohol Group Register of Trials, Medline, Embase, CINAHL, ISI Web of Science, PsycINFO. The search strategy is available as appendix 1 in the supplementary material. We added a hand-search of the reference list of retrieved articles. All searches included non-english literature.

Study selection

We included all randomized controlled trials comparing psychosocial interventions, either alone or in combination with pharmacological therapy, against no-treatment, waiting list, or any other psychosocial treatment. We only accepted studies performed in adults (>18 years old) with a diagnosis of stimulant use disorder according to the Diagnostic and Statistical Manual of Mental Disorders (DSM) -III, -IV or -5 or the International Classification of Diseases (ICD) -9 or -10.

We excluded review articles, editorials, letters, comments, conference proceedings, case reports, and case series; studies dated before 1990 if the system used for the diagnosis did not use operationalized criteria, but only disease names with no diagnostic criteria (i.e. ICD-9); trials lacking a control group.

Three authors (FDC, GLDA, MC) independently reviewed the titles and abstracts of the articles retrieved, applying the inclusion and exclusion criteria; then, they examined the full-texts to confirm the studies' eligibility for inclusion. Disagreements were resolved by consensus.

Data extraction

We designed and used a structured template to ensure consistency and we systematically appraised each study. Data extracted embraced characteristics of the studies (i.e. first author, publication year, journal), of the participants (i.e. mean age, diagnosis), and of the interventions (i.e. types of treatment, comparisons, duration of treatment, duration of follow-up).

Qualitative synthesis

Two authors (CC, RDG) retrieved the manuals for each psychosocial intervention included and summarized the key principles. Then, they integrated these data with the main findings from all the randomized controlled trials previously selected. Risks of bias in the included studies were assessed using the tool described in the Cochrane Collaboration Handbook as a reference guide, which pays particular attention to random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data and selective reporting[16]. This tool allows a rating of "low", "unclear" or "high" risk of bias.

RESULTS

Our computer-based search retrieved 6 728 records. After removing 2 660 duplicates, further 4 068 articles were excluded because they did not meet the required criteria, leaving 108 full-text articles included. Further six studies were added from trial registries and one additional article was retrieved from hand-search. A total of 115 articles correspon-

ding to 91 randomized controlled trials (RCTs) were finally included in this review (see figure 1 in the supplementary material).

The characteristics of the studies included is reported in Table 1, while in Table 2 we summarized the main differential elements of the psychosocial therapies included. A risk of bias summary is available as Table 3 in the supplementary material, while the references of all the included RCTs are listed in the Appendix 2 in the supplementary material.

Overall, contingency management (CM) was investigated in 45/91 studies (49%), cognitive behavioral interventions in 32/91 studies (35%), community reinforcement approach (CRA) in 9/91 studies (10%), 12-step program (12SP) in 8/91 studies (9%), meditation-based interventions (MbI) and physical exercise (PhE) in 6/91 studies (7%), supportive expressive psychodynamic therapy (SEPT) in 3/91 studies (3%), interpersonal psychotherapy (IPT) in 3/91 studies (3%), family therapy (FT) in 3/91 studies (3%), motivational interviewing (MI) in 11/91 studies (12%), drug counselling (DC) in 10/91 studies (11%). It should be noted that some studies examined numerous or combined interventions at the same time (see Table 1).

Contingency management (CM)

Theoretical background

Contingency management (CM) is a behavioral intervention that emphasizes the positive reinforcement of healthy behaviors, whereby addicted patients are incentivized with rewards for providing drug-free urine samples[17]. It differs from non-contingent reward where patients are remunerated irrespective of the results of the urine drugs screening. Similarly to drugs, CM applies positive reinforcers to abstinent behavior and immediately conveys relief and satisfaction. The purpose is to promote abstinence and improve the welfare of an often-deprived population.

Trials

A wealth of studies examined CM in stimulant use disorders.

a) *Cash rewards*

There is little research on CM using cash rewards, which showed that a cash-based CM combined with bupropion[18] or topiramate[19] improved outcomes in cocaine users compared to non-contingent rewards, regardless of the use of medication.

b) *Voucher rewards*

Since cash rewards may be spent on substances, most CM approaches offered vouchers instead. Voucher-CM was not inferior to cash-CM in improving cocaine abstinence and treatment attendance, regardless of the high or low value of the rewards[20,21]. Cocaine and crack cocaine users responded to voucher-based CM with increased acceptability and abstinence rates[22] and reduced craving[23]. The use of CM coupons of escalating value was associated with sustained cocaine and opiate abstinence in a population of methadone-maintained patients[24,25]. Conversely,

Rawson et al.[26] and Menza et al.[27] reported an improvement in short-term outcomes that was not maintained at follow-up, while Umbricht et al.[28] did not show any difference in abstinence between voucher-based CM and non-contingent rewards.

c) *Prize rewards*

Stakeholders underlined that the cost of vouchers paid by the health system can be high on a large scale; therefore, another approach consisted of awarding prizes and lottery tickets attracting numerous low-value and limited high-value rewards. Petry et al.[29] showed that voucher and prize CM were equally effective in cocaine-using methadone patients, and prize-based incentives improved abstinence outcomes[30] and psychiatric comorbidities[31,32]. Low-cost prizes can increase abstinence[33-35], but higher-magnitude prizes proved better on the long term[36,37]. Longer periods of prize-CM promoted longer durations of abstinence[38] and increased post-exposure prophylaxis in men who have sex with men using methamphetamine[39]. However, some studies showed that prize-based CM did not significantly improved abstinence in stimulant use disorders, but it did in opioid[40] and alcohol use[41].

d) *Other rewards*

Addicted patients may struggle with failing the lottery draw or can be inadvertently fed into a gambling addiction; hence some alternative CM strategies were devised. In case of stimulant- and opioid-use comorbidity, buprenorphine doses were provided as CM rewards, resulting in increased abstinence at follow-up compared to CM vouchers[42,43] used an employment-based reinforcement that proved effective in long-term abstinence, but another study showed low engagement with a similar approach[44].

Cognitive behavioral interventions

Theoretical background

Cognitive behavioral interventions are based on cognitivism and behaviorism paradigms. Cognitivism assumes that mental disorders are triggered by unhealthy beliefs[45,46]: thoughts such as "I need to escape", "I cannot deal with this unless I am high", and "I deserve to get high considering what I am going through" are commonly noted to precede stimulants use[47]. Behaviorism maintains that most human traits and actions are learned[48], therefore stimulants use can be considered a learned behavior[47]. Cognitive behavioral interventions aim to modify cognitions and behaviors that lead to substance misuse. Trials in stimulant use disorders included cognitive behavioral therapy (CBT), gay-specific cognitive behavioral therapy (G-CBT), and relapse prevention (RP).

a) *Cognitive behavioural therapy (CBT)*

Theoretical background

CBT for stimulant use disorders is a short-term psychotherapy divided into functional analysis and coping-skills training[47].

Functional analysis is based on the antecedents, behavior, and consequences model[46]. Initially, patient and therapist ex-

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Table 1. Table of included studies.

Study	Participants	Gender (males%)	Mean Age (yrs)	Diagnosis	Interventions (n)	Duration of intervention (wks)	Follow-up (wks)
Glasner-Edwards, 2017	63	71.4%	45.3	Cocaine dependence (DSM-IV) or methamphetamine dependece (DSM-IV)	1. Voucher based CM plus MbI (31) 2. Voucher based CM plus TAU (health education control) (32)	8	12
Pirnia, 2017	100	100%	NA	Self-reported cocaine dependence; at least one month history of cocaine avoidance	1. Cash based CM (25) 2. Cash based CM + Topiramate (25) 3. Topiramate (25) 4. Placebo control (25)	12	NA
Trivedi, 2017	302	60%	39.0	Stimulants abuse or dependence (DSM-IV-TR)	1. Exercise (152) 2. Health education (150)	36	NA
Carrico, 2016	138	0%	27 (median; IQR: 23-13)	Amphetamine-like-using female entertainment and sex workers	1. CBT (NR) 2. CBT plus cash based CM (NR)	12	NA
Carroll, 2016	99	72.7%	39.3	Cocaine dependence (DSM-IV)	1. CBT with disulfiram (28) 2. CBT without disulfiram (26) 3. CBT plus cash-based CM with disulfiram (23) 4. CBT plus cash-based CM without disulfiram (22)	12	48
De La Garza, 2016	24	76%	44.7	Cigarette smokers with concurrent cocaine use	1. CBT plus Rew (7) 2. CBT plus Rew plus Physical Exercise (running) (10) 3. CBT plus Rew plus Physical Exercise (walking) (7)	4	NA
Miguel, 2016	55	85.7%	35.3	Crack-cocaine dependence (DSM-IV)	1. TAU (32) 2. Voucher based CM (33)	12	24
Pirnia, 2016	50	100%	NA	Self-reported physical dependency to cocaine; at least three months history of cocaine avoidance	1. TAU (25) 2. Voucher based CM (25)	12	NA
Zhu, 2016	60	100%	40	Sedentary, stimulant abusers	1. Tai Chi (30) 2. TAU (recreational activities) (30)	12	NA
Agarwal, 2015	24	76%	48.2	Crack-cocaine users diagnosed with HIV	1. Yoga meditation (12) 2. No intervention (12)	8	16

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Table 1. Table of included studies.

Study	Participants	Gender (males%)	Mean Age (yrs)	Diagnosis	Interventions (n)	Duration of intervention (wks)	Follow-up (wks)
Landovitz, 2015	140	10.6%	36.8	Stimulant-using men who have sex with men (MSM)	1. CM (70) 2. Rew (70)	8	24
Petry, 2015	240	50.4%	40.3	Cocaine dependent (DSM-IV) patients on methadone maintenance	1. TAU (standard methadone maintenance) (57) 2. Cash-based low magnitude prize CM (58) 3. Cash-based high magnitude prize CM (62) 4. Voucher-based high magnitude prize CM (63)	12	24
Rawson, 2015	135	80%	31.7	Methamphetamine dependence (DSM-IV)	1. TAU (Health education) (66) 2. Physical exercise (69)	8	32
Tait, 2015 160	160	75.6%	22.3	Methamphetamine abusers	1. Brief CBT plus MI (81) 2. TAU (waitlist) (79)	BI	24
Carroll, 2014	101	40%	42	Cocaine dependence (DSM-IV)	1. TAU (standard methadone maintenance) (54) 2. CBT (computer-based training for CBT, CBT4CBT) plus methadone maintenance (47)	8	52
Festinger, 2014	222	69%	37.2	Cocaine dependence (DSM-IV)	1. Voucher-based CM (71) 2. Cash-based CM (73) 3. Rew (78)	12	NA
Gonçalves, 2014	46	84.1%	31.8	Cocaine dependence (DSM-IV)	1. Motivational Chess (26) 2. TAU (active control) (20)	4	NA
Norberg, 2014	174	65%	23.6	Ecstasy users	1. MI (E Check-up) (89) 2. TAU (Education control group) (85)	BI	24
Petitjean, 2014	60	80.1%	34.5	Cocaine dependence (DSM-IV)	1. CBT plus prize based CM (29) 2. CBT (31)	24	52
Polcin, 2014	217	50.69%	38.4	Methamphetamine dependence (DSM-IV)	1. 9-session Intensive motivational interviewing (IMI) (111) 2. Single standard session of MI (SMI) + 8 nutrition education sessions (106)	9	52

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Study	Participants	Gender (males%)	Mean Age (yrs)	Diagnosis	Interventions (n)	Duration of intervention (wks)	Follow-up (wks)
Umbricht, 2014	171	52%	41.5	Cocaine dependent (DSM-IV-TR) in methadone maintained patients	1. Voucher-based CM plus topiramate and methadone maintenance (40) 2. Voucher-based Rew plus topiramate and methadone maintenance (45) 3. Voucher-based CM plus placebo and methadone maintenance (39) 4. Voucher-based Rew plus placebo and methadone maintenance (47)	12	NA
Chen, 2013	56	56.1%	45.2	Cocaine dependence (DSM-IV)	1. TAU (intensive outpatient program, IOP) (37) 2. TAU plus IMEA (ear acupuncture and integrative meditation) (35)	12	NA
Donovan, 2013	471	41.2%	47.1	Stimulants use or dependence (DSM-IV)	1. TAU (237) 2. 12-step (234)	8	24
Dursteler-MacFarland, 2013	62	64.5%	36	Cocaine, eroin dependent (DSM-IV) Diacetylmorphine (DAM) maintained patients	1. Group CBT with methylphenidate (15) 2. Group CBT with placebo (17) 3. TAU with methylphenidate (15) 4. TAU with placebo (15)	12	NA
Hagedorn, 2013	139	98.59%	50	Stimulant dependent veterans diagnosed with alcohol dependence only (n=191) or stimulant dependence (n=139). Only data of stimulant dependents reported	1. Voucher based CM (71) 2. TAU (68)	8	52
McDonell, 2013	176	34.6%	42.7	Stimulants (amphetamines, cocaine) dependence (MINI); concurrent schizophrenia or schizoaffective disorder or bipolar disorder or recurrent major depressive disorder	1. Prize based CM (91) 2. Rew (85)	12	24
McKay, 2013a	321	76%	43.2	Cocaine dependence (DSM-IV)	1. TAU (108) 2. TMC (106) 3. TMC plus Rew (107)	104	NA
McKay, 2013b	152	77%	42.8	Cocaine dependence (DSM-IV)	1. TAU (78) 2. Brief continuing care sessions (TMC or in-person sessions) (74)	52	NA
Petry, 2013	19	58%	41.7	Cocaine dependent (DSM-IV) patients with severe and persistent mental health disorder	1. Prize Based CM(10) 2.TAU (9)	8	NA

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Study	Participants	Gender (males%)	Mean Age (yrs)	Diagnosis	Interventions (n)	Duration of intervention (wks)	Follow-up (wks)
Roll, 2013	118	55%	32	Methamphetamine dependence (DSM-IV)	1. Matrix Model (n= 29) 2. Matrix Model plus 1 month prize CM (30) 3. Matrix Model plus 2 months prize (30) 4. Matrix Model plus 4 months prize (29)	16	52
Secades Villa, 2013	118	85.5%	31.2	Cocaine dependence (DSM-IV)	1. CRA plus voucher based CM (50) 2. CRA (68)	24	NA
Carroll, 2012	112	59%	38.3	Cocaine dependent (DSM-IV) patients on methadone maintenance, or patients self-referred or referred by clinician as cocaine users, not on methadone maintenance	1. TAU with disulfiram (30) 2. TAU with placebo (26) 3. 12-step with disulfiram (29) 4. 12-step with placebo (27)	12	60
Petry, 2012a	130	53.4%	36.7	Cocaine dependent (DSM-IV) patients on methadone maintenance	1. TAU (59) 2. Prize based CM (71)	12	36
Petry, 2012b	442	44.5%	36.8	Cocaine dependence (DSM-IV)	1. TAU, cocaine negative patients at baseline (108) 2. Prize based CM, cocaine negative patients at baseline (118) 3. Rew, cocaine negative patients at baseline (107) 4. TAU, cocaine positive patients at baseline (34) 5. Low magnitude prize based CM, cocaine positive patients at baseline (35) 6. High magnitude prize based CM, cocaine positive patients at baseline (40)	12	36
Suvanchot, 2012	200	NR	25	Amphetamine use; co-occurrent psychological problems	1. MI plus Brief CBT (100) 2. No intervention (100)	BI	24
Garcia-Fernandez, 2011	58	87.9%	30	Cocaine dependence (DSM-IV)	1. CRA plus prize based CM (29) 2. CRA (29)	24	48
Ingersoll, 2011	54	46.29%	45	Crack cocaine use and HIV with <90% highly active antiretroviral therapy (HAART) adherence	1. MI plus feedback and skills building (MI+) (28) 2. Video information plus debriefing (Video+) (28)	8	24
Schottenfeld, 2011	145	0%	31.1	Cocaine dependent (DSM-IV) women who were either pregnant or had custody of a young child	1. CRA plus voucher based CM (36) 2. TSF plus voucher based CM (37) 3. CRA plus Rew (35) 4. TSF plus Rew (37)	24	52

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Table 1. Table of included studies.

Study	Participants	Gender (males%)	Mean Age (yrs)	Diagnosis	Interventions (n)	Duration of intervention (wks)	Follow-up (wks)
Van Horn, 2011	195	75%	43.6	Cocaine dependence	1. TMC (95) 2. TMC plus Rew (100)	52	NA
McKay, 2010	100	42%	41.0	Cocaine dependence (DSM-IV)	1. TAU (Intensive Outpatient Program, IOP) (25) 2. TAU (IOP) plus RP (24) 3. TAU (IOP) plus voucher based CM (26) 4. TAU (IOP) plus RP plus voucher based CM (25)	20	76
Menza, 2010	127	34.6%	39	Methamphetamine user men who have sex with men (MSM)	1. Voucher based CM (70) 2. TAU (57)	12	24
Smout, 2010	104	60%	34.9	Methamphetamine Use or Dependence (MINI)	1. CBT (53) 2. MbI (Acceptance and Commitment Therapy, ACT) (51)	12	24
DeFulio, 2009	51	33%	43	Cocaine dependence (DSM-IV)	1. Employment only (24) 2. Employment based CM (27)	24	52
Stein, 2009	198	61.6%	38.1	Cocaine use or dependence	1. MI (97) 2. No intervention (101)	BI	24
Milby, 2008	206	74.5%	40	Cocaine dependent (DSM-IV), homeless patients	1. Vocational training, work and contingent housing based CM (103) 2. Vocational training, work and contingent housing based CM plus CBT day treatment (103)	24	76
Preston, 2008	67	57.75%	39.7	Cocaine user, physical opiates dependent patients	1. Prize based CM (opiate-cocaine use depending CM) with methadone (38) 2. Prize based CM (cocaine use depending CM) with methadone (29)	17	25
Sanchez Hervas, 2008	82	86.3%	31.4	Cocaine dependence (DSM-IV)	1. CRA (47) 2. TAU (35)	24	52
Shoptaw, 2008	128	100%	37	Gay or bisexual men with stimulant abuse	1. Gay-specific CBT (64) 2. TAU (Gay social support therapy) (64)	16	52
Garcia-Rodriguez, 2007	96	90%	29	Cocaine dependence (DSM-IV)	1. CRA plus low voucher based CM (15) 2. CRA plus high voucher based CM (29) 3. TAU (52)	24	48
Ghitza, 2007	116	56%	37	Heroin and cocaine users on methadone maintenance	1. Prize based CM (76) 2. Rew (40)	12	24
McKee, 2007	74	73%	35	Cocaine dependence (DSM-IV)	1. Brief CBT plus MI (38) 2. Brief CBT (36)	7	16
Mitcheson, 2007	29	65.5%	40	Crack cocaine dependent patients on methadone maintenance	1. MI (17) 2. Information leaflets (12)	BI	12

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Table 1. Table of included studies.

Study	Participants	Gender (males%)	Mean Age (yrs)	Diagnosis	Interventions (n)	Duration of intervention (wks)	Follow-up (wks)
Petry, 2007	74	43.2%	41.6	Cocaine dependent patients (DSM-IV) on methadone maintenance	1. TAU with methadone (19) 2. Voucher based CM with methadone (27) 3. Prize and voucher based CM with methadone (30)	12	36
Srisurapanont, 2007	48	89.5%	16.9	14-19 years old, methamphetamine dependent (DSM-IV) patients	1. TAU (health education) (24) 2. MI (24)	BI	8
Knealing, 2006	47	10.6%	36.6	Cocaine dependence (DSM-IV)	1. Employment based CM (22) 2. TAU (25)	36	64
Marsden, 2006	342	66.3%	18.4	Stimulants use	1. MI plus information leaflets (166) 2. Information leaflets (176)	BI	24
Peirce, 2006	402	55.8%	42	Stimulants dependent patients on methadone maintenance	1. Prize based CM (204) 2. TAU (198)	12	24
Poling, 2006	106	69.8%	34.6	Cocaine use and opiate dependence (DSM-IV)	1. CBT plus cash based CM with buporion (27) 2. CBT plus cash based CM with placebo (25) 3. CBT plus Rew with bupoprion (30) 4. CBT plus Rew with placebo (24)	25	NA
Rawson, 2006	177	76%	NA	Stimulant dependence (DSM-IV)	1. CBT (58) 2. CBT plus voucher-based CM (59) 3. Voucher-based CM (60)	16	52
Baker, 2005	214	62.6%	30.2	Regular users of amphetamines	1. Brief CBT (2 sessions) (74)	BI	24
Petry, 2005a	415	44.6%	35.8	Stimulants use or dependence (DSM-IV)	1. Prize based CM (223) 2. TAU (222)	12	24
Petry, 2005b	77	27%	40	Cocaine dependence (DSM-IV) in methadone maintenance	1. CM with methadone (40) 2. TAU with methadone (37)	12	24
Rawson, 2005	978	45%	32.8	Methamphetamine dependence (DSM-IV)	1. TAU (NR) 2. Matrix Model (NR)	16	52

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Table 1. Table of included studies.

Study	Participants	Gender (males%)	Mean Age (yrs)	Diagnosis	Interventions (n)	Duration of intervention (wks)	Follow-up (wks)
Shoptaw, 2005	162	100%	37	Gay and Bisexual with Methamphetamine dependence (DSM-IV)	1. CBT (40) 2. Voucher based CM (42) 3. CBT plus voucher based CM (40) 4. Gay-specific CBT (40)	16	52
Weiss, 2005	487	76.8%	33.9	Cocaine dependence (DSM-IV)	1. TAU (NR) 2. 12-step (NR) 3. SEPT (NR) 4. CBT (NR)	24	NA
Carroll, 2004	121	74%	34.6	Cocaine dependence (DSM-IV)	1. CBT with disulfiram (30) 2. CBT with placebo (30) 3. IPT with disulfiram (30) 4. IPT with placebo (31)	12	NA
Epstein, 2003	286	57%	39	Cocaine abusers in methadone maintenance	1. CBT plus voucher based Rew (methadone maintenance) (48) 2. CBT plus voucher based CM (methadone maintenance) (49) 3. Voucher based CM (methadone maintenance) (47) 4. Voucher based Rew (methadone maintenance) (49)	12	52
Higgins, 2003	100	59%	34	Cocaine dependence (DSM-III-R)	1. CRA plus voucher based CM (49) 2. Voucher based CM (51)	24	104
Covi, 2002	68	88.2%	34	Cocaine and other substances dependence (DSM-III-R)	1. CBT (once every two weeks) (21) 2. CBT (once a week) (21) 3. CBT (twice a week) (26)	12	52
Petry, 2002	42	28.6%	38.5	Concurrent cocaine and opioid dependence (DSM-IV)	1. TAU (23) 2. Low prize CM (19)	12	24
Rawson, 2002	108	55%	43.6	Cocaine dependence (DSM-IV) patients on methadone maintenance	1. TAU (27) 2. CBT (28) 3. Voucher based CM (27) 4. CBT plus voucher based CM (26)	16	104
Baker, 2001	64	62%	32	Regular use of amphetamines	1. Brief CBT (RP Brief) and self-help booklet on reducing amphetamine use and related harms (32) 2. Self-help booklet only (32)	BI	24
Higgins, 2000	70	73%	30.4	Cocaine dependence (DSM-III-R)	1. CRA plus voucher based CM (36) 2. CRA plus Rew (34)	24	52

(continued)

Psychosocial interventions in stimulant use disorders

Table 1. Table of included studies.

Study	Participants	Gender (males%)	Mean Age (yrs)	Diagnosis	Interventions (n)	Duration of intervention (wks)	Follow-up (wks)
Crits-Cristoph, 1999	487	76.8%	33.9	Cocaine dependence (DSM-IV)	1. CBT (119) 2. SEPT (124) 3. 12-step (121) 4. TAU (Group Drug Counseling) (123)	36	48
Carroll, 1998	122	73%	30.8	Cocaine dependence with comorbid Alcohol dependence or abuse (DSM-III-R)	1. CBT (19) 2. CBT with disulfiram (27) 3. 12-step alone (n=25) 4. 12-step with disulfiram (25) 5. TAU with disulfiram (27)	12	NA
Gottheil, 1998	447	NA	NA	Cocaine dependence (DSM-III-R)	1. Intensive program (150) 2. Individual counseling (146) 3. Individual counseling plus group sessions (151)	12	36
Kirby, 1998	90	67%	31.7	Cocaine dependence (DSM-III-R)	1. CBT plus voucher based CM (44) 2. CBT (46)	12	NA
Maude-Griffin, 1998	128	98.4%	NA	Cocaine dependence (DSM-III-R)	1. CBT (59) 2. 12-step (69)	12	26
Silverman, 1998	59	66%	37.8	Cocaine use (DSM-III)	1. Voucher based CM (20) 2. Voucher based CM with Start-up bonus (20) 3. Rew (19)	12	20
McKay, 1997	98	100%	40	Cocaine dependence (DSM III-R)	1. TAU (52) 2. RP (46)	24	NA
Monti, 1997	128	69%	28.4	Cocaine use or dependence (DSM-III-R)	1. CBT (rural site) (44) 2. CBT (urban site) (16) 3. TAU (rural site) (51) 4. TAU (urban site) (17)	1-3	12
Schmitz, 1997	32	50%	34.9	Cocaine dependence (DSM-III-R)	1. Group CBT (16) 2. Individual CBT (16)	8	24
Weinstein, 1997	423	NA	NA	Cocaine dependence (DSM-III-R)	1. Intensive outpatient treatment (SE-INT) (137) 2. Outpatient individual therapy (SE-IND) (144) 3. Individual therapy + a weekly group (SE-IND-GRP) (142)	12	36

(continued)

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Table 1. Table of included studies.

Study	Participants	Gender (males%)	Mean Age (yrs)	Diagnosis	Interventions (n)	Duration of intervention (wks)	Follow-up (wks)
Silverman, 1996	37	NA	36.05	Cocaine use or dependence (DSM-III-R)	1. Voucher based CM (19) 2. Rew (18)	12	16
Carroll, 1994	110	63%	28.8	Cocaine use or dependence (DSM-III-R)	1. CBT with desipramine hydrochloride (29) 2. CBT with placebo (29) 3. TAU with desipramine hydrochloride (25) 4. TAU with placebo (27)	12	NA
Higgins, 1994	40	67.5%	31.3	Cocaine dependence (DSM-III-R)	1. CRA plus voucher CM (20) 2. CRA (20) For subjects who met also criteria for alcohol dependence/abuse (41%) was offered Disulfiram (~ 250 mg/day).	24	52
Hoffman, 1994 Hoffman, 1996	303	68%	32	Cocaine users from an outpatient treatment program	1. TAU (standard group therapy) (50) 2. IPT plus standard group therapy (53) 3. IPT plus FT plus standard group therapy (50) 4. Intensive Group Therapy (50) 5. IPT plus Individual Psycho- therapy (51) 6. IPT plus FT plus Individual Psycho-therapy (49)	16	52
Wells, 1994	110	64%	29.4	Cocaine use or dependence	1. CBT (RP) (48) 2. 12-step (62)	12	24
Higgins, 1993	38	89%	29.3	Cocaine dependence (DSM-III-R)	1. CRA plus voucher based CM (19) 2. 12-step plus Rew (19) To subjects who also met criteria for alcohol dependence/abuse it was offered Disulfiram (~250 mg/day)	24	52
Carroll, 1991	42	74%	27	Cocaine use or dependence (DSM-III)	1. CBT (RP) (21) 2. IPT (21)	12	NA
Kang, 1991	168	86%	NA	Cocaine use or dependence (DSM-III-R)	1. FT (n=NR) 2. TAU (individual therapy) (n=NR) 3. TAU (group therapy) (n=NR)	24-52	NA

Legend: BI: brief intervention; CBT: cognitive behavioural therapy; CM: contingency management; CRA: community reinforcement approach; FT: family therapy; FU: follow-up; IPT: interpersonal therapy; MbI: mindfulness based intervention; MI: motivational interviewing; NA: not assessed; NR: not reported; Rew: non-contingent rewards; RP: relapse prevention; SEPT: Supportive-Expressive Psychodynamic Therapy; SUD: stimulant use disorder; TAU: treatment as usual; TMC: telephone monitoring and counselling; TSF: twelve-step facilitation.

Psychosocial interventions in stimulant use disorders

Table 2. Differential elements of psychosocial therapies included.

Therapy	Elements of therapy	Duration	Target population
Cognitive behavioural coping skill treatment (CBT)	– Functional analysis of substance use: history, when it occurs, triggers, frequency, intensity, motivation and resources about change – Coping skills training: role play to adopt new different strategies (positive modelling), systematic analysis of the short and long term consequences of substance use (operant conditioning), to increase awareness, avoidance of high-risk situations (classical conditioning)	12 to 16 sessions, usually over 12 weeks	Individuals with psychostimulant addiction
Gay specific cognitive behavioural therapy (GCBT)	– Functional analysis of substance use and coping skills training – Specific HIV prevention	48 sessions in 16 weeks or 24 sessions in 8 weeks	Individuals homosexual or bisexual with methamphetamine use
Relapse prevention (RP)	– Specific interventions: to identify and cope with high-risk situations, enhance self-efficacy, to eliminate positive myths and placebo effect assumptions about the drug, lapse management – Global interventions: to reduce stressful lifestyle, promote "positive addictions", to cope with craving	12 weeks	Individuals who have received, or are receiving, treatment for addictive behavior problems. RP can be used to foster initial abstinence or as a maintenance strategy
Community reinforcement approach (CRA)	– To identify and address causes of drug abuse to more complex relational and psychiatric problems – Functional analysis – Coping skill training – Eventually vouchers with urinalysis monitoring two-three times a week – Eventually meetings outside the office	24 weeks, twice weekly counselling sessions for the first 12 weeks, then once weekly	Cocaine use, 18 years or older, living within a reasonable distance of the clinic, due to the intensive nature of the intervention
Contingency management	– Positive reinforcement of positive behaviours and attitudes – Using objective measures such as urinalysis – Giving prizes: vouchers, lottery tickets, methadone doses (in case of comorbidity with opioid addiction) – No relationship with a therapist	Not specified	Individuals with psychostimulants addiction. May not be appropriate for people with problematic gambling.
Supportive-expressive psychodynamic therapy	– To develop awareness of personal hopes or needs from a relationship (wish), personal expectations and experiences from others (Response from Others - RO), and personal reaction to this response (Response from Self - RS) – To be aware of how repetitive patterns are related to past relationship with the caregivers, and to the present as triggers for craving – To work with transference and countertransference	6-month active phase and 3-month booster phase, During the first 3 months sessions are held twice per week, during the next 3 months sessions are held weekly, during the booster phase 1 session is held each month	Individuals with psychostimulants addiction, who can achieve initial abstinence
Interpersonal psychotherapy	– To develop the need to stop using cocaine and to abandon the ambivalence about the substance – Comparison between the negative and positive effects of drug abuse – To recreate the thoughts and emotions that precede the use of cocaine – To manage the impulsiveness – Analysis of interpersonal problems that have caused and maintained drug abuse and – Identify new functional solutions in preference of cocaine use	12-16 sessions	Individuals with psychostimulants addiction, who feel the abuse is secondary to interpersonal problems
Family therapy	– To focus on relationships in the family system rather than the drug and the patient themselves – To redefine the addiction and its functions at the family life cycle actual stage – To restructure the system to maximise the potential in each member – To work on family's boundaries – To work on present and past – To identify repetitive family patterns	5 months	Individuals with psychostimulants addiction who feel the addiction stems from and is maintained by family patterns
The 12-step program	– Based on self-help group – Spiritual and pragmatic vision embraced in twelve steps: acceptance of being addicted and surrender to a "higher Power"	Not specified	Individuals who desire to stop using cocaine and all other mind-altering substances

(continued)

(continued) - **Table 2.**

Therapy	Elements of therapy	Duration	Target Population
Mindfulness based stress reduction (MBSR)	– Body scan, sitting meditation and hatha yoga practice – To develop greater attention to internal and external experiences as they occur moment by moment – To adopt non-judgement of, and openness to, current experience, instead of trying to modify or suppress it – Promote detachment and lower reactivity to stimuli that lead to relapse, as opposed to complete avoidance of them	8 weeks program comprised of weekly two and a half hour sessions, a one day retreat and daily homework (about 45 minutes)	Individuals with psychostimulant addiction who can renounce to traditional talking based therapy
Mindfulness based relapse prevention (MBRP)	– Integration of relapse prevention and mindfulness practice – To develop awareness and acceptance of thoughts, feelings, and sensations – To utilize these mindfulness skills as an effective coping strategy in the face of high-risk situations	8 weeks program	Individuals with psychostimulant addiction who can renounce to traditional talking based therapy
Motivational interviewing	– Manage the patient's ambivalence about change – Reflective listening, understanding and empathy – Highlight discrepancies between the client's current situation and their hopes for the future, – To allow them to identify their own motivation – Enhancing motivation	2-4 sessions	Initial tool in individuals with psychostimulant use who feel poorly motivated
Individual counselling	– Focuses on the present, with short-term and behavioural goals related to the symptoms of substance abuse – Support to achieve and maintain abstinence – Recognising and avoiding triggers, – Enhancing motivation, – Developing new and more effective coping strategies – Using objective measures such as urinalysis	36 sessions over 6 months	Cocaine addicts with the exception of opiates if methadone maintenance is to be used
Group drug counselling	– Phase one: psycho-educational group of 12 standard sessions to improve knowledge about addiction and the recovery process. – Phase two: problem solving	34 sessions (once a week)	Early and middle stages of recovery from addiction, preferred in combination with an individual treatment

plore the features of historical drug use. They move next at analyzing maladaptive behavioral patterns including timing, frequency, and intensity of misuse, as well as any environmental, psychological, or somatic trigger for craving. Finally, emerging personal and interpersonal resources, motivation for change, and future goals are discussed.

Coping-skills training works on basic learning mechanisms that led to stimulants use in the first place, such as modeling[49,50], classical conditioning[51], and operant conditioning[52]. Modeling theory suggests that people learn new behaviors by watching and then imitating others, so patients exposed to negative models of drug use within their family or peer group will shape their behavior accordingly and develop an addiction. On this basis, CBT aims to replace that negative model with a positive one conveyed by the therapist; also, new skills such as rejecting an offer of drugs and managing relationships with peer users are presented through role-play in a therapeutic setting and then routinely practiced by patients. Classical conditioning occurs when an unconditioned stimulus is paired with another conditioned stimulus, producing a conditioned response; thus, the recurrent use of stimulants (i.e. the unconditioned stimulus) can be associated with places, times, money, and other triggers (i.e. the conditioned stimuli) that will elicit craving for substances (i.e. the conditioned response). Here, CBT is used for increasing awareness of these unhelpful mechanisms and facilitate the avoidance of high-risk situations. Operant conditioning requires active involvement of the subject because future behavior relies on the consequences of past behavior; in stimu-

lant use disorders, the intake of cocaine and amphetamines is reinforced by its most desired consequences such as increased energy and efficiency, euphoria, grandiosity, and disinhibition. A CBT approach encourages patients to examine the short- and long-term outcomes of stimulant use, which turn out to be negative in most cases (i.e. a negative reinforcement); moreover, the therapist can redirect patient's behavior to other pleasant endeavors such as hobbies, work, and relationships (i.e. positive reinforcement).

Trials

Many trials assessed CBT in stimulant use disorders. CBT was associated with improved outcomes in cocaine[53], crack cocaine[54], and methadone-maintained cocaine users[26] with lasting effects. Even non-intensive CBT delivered fortnightly over 12 weeks was effective in cocaine use[55], and Baker et al.[56,57] obtained comparable results with a brief CBT intervention plus psychoeducation via self-help booklets in amphetamine users. A CBT strategy focusing on the negative effects of misuse significantly reduced craving for the substance in methamphetamine[58] and cocaine users[59]. Carroll[47] and Carroll et al.[11] showed that combined CBT and disulfiram was effective in cocaine use disorder irrespective of concurrent alcohol misuse. In contrast, one study reported that CBT was less effective than counseling in reducing days of cocaine use and drug-related problems[60], whilst another compared CBT with other interventions, but no abstinence outcomes were reported for it[61]. As CBT can be resource-consuming, some researchers attempted strategies for in-

creasing availability. Group CBT failed to show any difference against usual treatment[62]. A preliminary study by Keoleian et al.[63] used a CBT-based text-messaging intervention for methamphetamine users that showed high feasibility and acceptability. Carroll et al.[64], delivered a computer-based CBT to cocaine users on methadone, reporting easy accessibility and increased abstinence with lasting effects. Finally, another study used a self-guided web-based intervention based on CBT and motivational interviewing principles over 6 months via a free-to-access site for amphetamine users, but this failed to show improvement in drug use and engagement remained low[65].

b) *Gay-specific cognitive behavioral therapy (G-CBT)*

Trials

Cognitive behavioral interventions can be targeted to specific populations: G-CBT was adapted for men who have sex with men affected by methamphetamine dependence by Shoptaw et al.[66,67]. In addition to standard cognitive-behavioral principles, G-CBT considered cultural aspects of methamphetamine use by men who have sex with men including triggers such as circuit parties and sex clubs, and obtained significant and sustained improvements in both drug use and prevention of HIV.

c) *Relapse prevention (RP)*

Theoretical background

Once abstinence is achieved, cognitive behavioral interventions aim to prevent further relapses. The RP model views relapse as secondary to difficulty in coping with immediate determinants (i.e. negative emotional states, relational problems, social pressures, lapses) and to covert antecedents (i.e. life-style, urges and craving)[68]. Through RP work, patients learn to identify high-risk situations such as lapses that are associated with guilt and other negative emotions, eventually leading to relapses. Lapse management uses cognitive restructuring to recognize lapses and relapses not as failures but opportunities to learn from mistakes. RP interventions also focus on the antecedents and aim to reduce stressful lifestyle factors by eliminating all items associated with stimulants use and promoting "positive addictions" such as meditation, relaxation training, and other recreational activities.

Trials

RP reduced cocaine and other drugs use post-treatment[69], and it was more effective in those whose drug use was the most severe[70-72]. Group and individual approaches showed comparable results[73]. However, McKay et al.[74] stressed that RP was useful only after abstinence was fully achieved.

d) *Cognitive behavioural interventions plus CM*

Trials

Cognitive behavioral interventions are often combined with CM with a view of increasing the engagement with therapy. CBT plus CM increased abstinence in cocaine users[75], especially when rewards were arranged in conjunction with therapeutic progress[76]. Also, combining RP with CM improved outcomes in cocaine users who had achieved initial abstinence[77]. Rawson et al.[26,78] reported superior short- and long-term outcomes for CBT and CM respectively, but no additive effect was observed. On the contrary, combined CBT and CM obtained significantly better outcomes than CBT or CM alone in cocaine[79,80] and methamphetamine users[67]. Milby et al.[81] studied a population of homeless cocaine users and showed that the combination of a housing- and employment-based CM with cognitive behavioral interventions lead to more durable abstinence. A preliminary study by Carrico et al.[82] highlighted the feasibility of CBT plus CM in a high-risk population of Cambodian female sex workers using amphetamines who live in a resource-limited area.

Community reinforcement approach (CRA)

Theoretical background

The community reinforcement approach (CRA) is a multilayered intensive intervention delivered over 24 weeks and adapted to treat cocaine and amphetamines addiction[83]. It teaches drug avoidance skills, encourages lifestyle changes, gives relationship counseling, and addresses comorbid substance use and psychiatric disorders. As in CBT, it involves functional analysis and coping-skills training. Social, familial, recreational, and vocational reinforcers are largely used, providing a comprehensive and supportive structure to treatment.

a) *CRA alone*

Trials

Only one trial used CRA alone, showing better retention and abstinence rates, and improvements in addiction severity scores after 24 weeks of treatment[84].

b) *CRA plus CM*

Trials

Incentives such as vouchers and out-of-treatment sessions (e.g. meetings outside the office hours) are frequently added to improve treatment compliance. Numerous studies by Higgins et al.[17,85-87], García-Rodríguez et al.[88], García-Fernández et al.[89,90] showed that CRA plus CM was effective, had increased retention rates, and improved psychosocial outcomes in cocaine users, although this was not demonstrated at follow-ups longer than 6-12 months after the end of treatment. These findings were confirmed in cocaine users of any socioeconomic status[91]. However, another study failed to show any superiority of CRA when added to CM[92].

12-step program (12-SP)

Theoretical background

The 12-step program (12-SP) was originally designed for alcoholism[93] and then adjusted to several other substance use disorders including cocaine and amphetamines. Contrarily to other treatments, it considers addiction as a chronic illness that can be controlled, but never cured. It is largely based on spiritual and relational principles applied to a fellowship of peers associated by the willingness to fight addic-

tion. All members share a transcendent yet pragmatic vision embraced in twelve steps (see box 1 in the supplementary material), including the acceptance of being addicted and the surrender to a "higher Power", often but not necessarily interpreted as God. The self-help group reduces social isolation and conveys support and empathy from people facing similar problems, all in complete anonymity. However, complex group dynamics pose frequent challenges, especially because most members are not trained to work on this aspect. Moreover, group therapies normally do not allow enough time to address deeper individual experiences. A 12-step facilitation therapy was therefore developed with the aim to improve participation and involvement in the 12-SP[94]. This is a structured, individual, and time-limited intervention delivered by a trained psychotherapist.

a) *12-SP alone*

Trials

Trials of 12-SP and 12-step facilitation in stimulant use disorders achieved modest[95] or mixed[96] results. Two studies showed that 12-SP and cognitive behavioral interventions were equally effective in patients addicted to cocaine and alcohol[69,97]. Maude-Griffin et al.[54] obtained opposite results but highlighted a potential benefit from 12-SP in the specific subgroup of African American with strong religious beliefs.

b) *12-SP plus other interventions*

Trials

Few studies on combined interventions are reported in literature. The effectiveness of 12-SP plus counseling in cocaine use disorder was supported by Weiss et al.[61], who reported that active participation predicted less cocaine use. Higgins et al.[85] compared 12-SP plus non-contingent reward with CRA plus CM, but the former resulted in worse outcomes. However, when CM was combined with either 12-SP or CRA, no difference between treatments was found[92].

Meditation-based interventions (MbI) and physical exercise (PhE)

Meditation-based interventions (MbI) and physical exercise (PhE) share several theoretical underpinnings and therefore are reported together.

a) *Meditation-based interventions (MbI)*

Theoretical background

Meditation refers to a broad variety of practices including body scan, yoga, and mindfulness meditation, whereby individuals train their minds to pay greater attention to internal and external experiences as they occur[98,99]. It is not designed to suppress dysfunctional behaviors, but encourages the adoption of a non-judgmental approach to stressful experiences, leading to detachment and lower reactivity to stimuli associated with relapse and reduced distress. It can be delivered in group and then self-applied, so the overall cost is low. The engagement with MbI can vary as some patients may have a positive attitude towards it, but others may be reluctant to abandon traditional talking-based therapies.

Trials

MbI for stimulant use disorders were examined in 3 trials. Smout et al.[100] devised a modified version of the acceptance and commitment therapy[101,102], integrating aspects of mindfulness training and behavioral therapy and consisting of weekly 60-minute individual sessions for 12 weeks. This was tested on a sample of methamphetamine users and showed results comparable to those of a CBT intervention of the same intensity. Chen et al.[103] used a different MbI to treat cocaine addiction, which involved adjusting the breath to near-resonant frequency, regulating the mind with inward attention and guided imagery, and ear acupressure. This treatment was confirmed to increase abstinence and to reduce craving and anxiety when compared to usual treatment. Yoga meditation was used on a population of crack cocaine users with comorbid HIV, showing high feasibility and acceptability as well as modest improvements in measures of quality of life[104]. Finally, a recent trial developed a Mindfulness Based Relapse Prevention and used it in addition to CM for patients with stimulant use disorders, showing declining stimulant use among those with comorbid depressive and anxiety disorders[105].

b) *Physical exercise (PhE)*

Theoretical background

PhE is an intervention that is thought to impact directly on stimulant use and mediates important health-related outcomes such as withdrawal symptoms, mood, sleep, cognitive function, and quality of life[106].

Trials

A few studies recently assessed various PhE interventions in stimulant use disorders. Zhu et al.[107] used tai-chi, a traditional Chinese sport classified as a moderate exercise, on amphetamine users, reporting significant improvements on all domains of a quality of life for drug addiction questionnaire. Rawson et al.[108] showed that a structured PhE program and health education for methamphetamine users decreased substance use among lower severity patients and significantly reduced comorbid depressive symptoms. However, walking and running, in addition to a baseline intervention of CBT and rewards including cash and sport equipment, improved the fitness of cigarette-smoker patients with concurrent cocaine use disorder, but did not significantly improved abstinence and craving from cocaine[109]. Likewise, a recent study failed to show any significant difference in abstinence rates between PhE and health education[110].

Supportive-expressive psychodynamic therapy (SEPT)

Theoretical background

All psychodynamic approaches derive from Freud's psychoanalytic model; amongst these, supportive-expressive psychodynamic therapy (SEPT) is the only evidence-based

for stimulant use disorders[111]. This psychotherapy was adapted for cocaine misuse by Mark and Luborsky[112]. It uses a "core conflictive relationship theme" based on the patients' hopes and needs from relationships (i.e. wish), the reactions elicited from others and their experience of them (i.e. response from others), and their own reactions to the latter (i.e. response from self). According to this model, people who misuse cocaine often are or anticipate being criticized, rejected, mistreated, controlled, and humiliated (response from others). Consequently, they feel ashamed, guilty, helpless, suspicious, and angry (response from self). Cocaine is used as a means for regulating their pain, but this makes their targets (wish) difficult to recognize because of the effects of addiction. They refuse to take responsibility for their negative actions and are unable to consider the needs of others, which further reinforces cocaine use. The therapist supports the patient in viewing this aspect as another response from self and promotes the expression of deeper wishes such as being accepted, understood, loved, and independent. Patients become progressively more conscious of the three components of the core conflictive relationship theme, whereby they appreciate how their past and present relationships are linked to their cravings and relapses. As in all psychodynamic therapies, the analysis of transference and countertransference is framed within the approach.

Trials

Trials on SEPT for stimulant use disorders are scarce and only addressed cocaine misuse. A multimodal intervention based on the principles above determined significant improvements in drug use and psychological functioning[113]. However, another study reported worse outcomes for cocaine users treated with SEPT compared to counseling[60] although a following analysis suggested that SEPT can be particularly effective to those patients who can achieve initial abstinence. Weiss et al.[61] described the use of SEPT amongst other interventions, but no results about this therapy were reported.

Interpersonal psychotherapy (IPT)

Theoretical background

Interpersonal psychotherapy (IPT) maintains that psychiatric disorders are caused and sustained by disturbances in interpersonal functioning[114]. Rounsaville et al.[115] adapted IPT for ambulatory cocaine users and set two goals for therapy: reduction or cessation of cocaine use, and improvement in interpersonal functioning. Initially, patient and therapist agree a contract where the former recognizes the necessity of abstinence and abandons any ambivalence about the substance, whilst the latter can support in decision-making by comparing the negative and positive effects of drug misuse. Patients are prompted to recreate those thoughts and emotions preceding cocaine use and discuss strategies for managing their impulsiveness and avoiding social contexts that can be triggers. Attendance to self-help groups is encouraged to replace the addiction to drugs with engagement in group relationships. Usually, further work is required to achieve better interpersonal relationships, because patients often see

drugs as having an important role in navigating interpersonal problems; for instance, cocaine is used when facing disputes, transitions, shortfalls, and grieves and to become more sociable, friendly, self-confident, and sexually disinhibited. Therapist and patient investigate these issues and try to identify alternative coping mechanisms instead of cocaine use. IPT is often considered a comprehensive approach to substance use disorders because it focuses on both drug misuse and interpersonal functioning; however, if the misuse is not directly linked to interpersonal problems, the applicability of IPT is poor.

Trials

Only 2 studies tested IPT in cocaine use disorder. Carroll et al.[70] delivered weekly IPT sessions of 50-60 minutes for 12 weeks and reported significantly improved abstinence compared to CBT in the most severe users. However, a following trial by the same authors disconfirmed this result[11].

Family Therapy (FT)

Theoretical background

Family therapy (FT) poses emphasis on the relationships within the family system, including those who live in the household or are closely related, rather than the drug or the individual patient[116]. Firstly, addiction is reviewed in the context of the current family situation; for instance, an adolescent using cocaine can shift parental attention from a latent marital conflict to his drug problem, therefore preserving a degree of stability in the family. This assumes that family systems naturally reach a homeostatic state that may inadvertently maintain maladaptive patterns of behavior. The patient's self and family blend in, producing separation anxiety and fear to grow, so that the whole family system is trapped at a developmental stage. The therapist's task is to stimulate a restructuring of the system to maximize the potential of each family member. Enmeshment and disengagement are additional therapeutic avenues where family members can establish or loosen boundaries as appropriate[117]. Patients are encouraged to draw a genogram of their family history for at least three previous generations; then, they are supported to identify recurrent maladaptive family patterns and develop an understanding of how these can be linked to their behavior, including drug misuse[118].

Trials

There are few trials using FT specifically in stimulant use disorders. Hoffman et al.[119] included an unstructured supportive FT in their study, where they combined several psychosocial interventions for treating a sample of cocaine users; however, no specific data for each treatment were provided. Kang et al.[120] used weekly sessions of FT in a similar population, but no beneficial effect was observed. Both Hoffman et al.[119] and Kang et al.[120] used an unstructured supportive type of FT. On the contrary, Slesnick and Zhang[121] developed a more structured ecologically-based FT (EBFT), which is a 12-session family system therapy, based on a social ecological theoretical perspective[122]. Slesnick and Zhang[121]

showed that EBFT is associated with a quicker decline in cocaine use in mothers using substances.

Motivational interviewing (MI)

Theoretical background

Motivational interviewing (MI) is an evolution of Rogers' person-centered counseling[123] integrated with cognitive and behavioral strategies[124], which argues that poor motivation and resistance contribute significantly to adverse outcomes in drug users. MI is a brief intervention, usually delivered in 2-4 sessions, aiming to manage the patient's ambivalence about change through reflective listening, understanding, and empathy. Contrarily to other cognitive behavioral interventions, direct challenging is avoided as it could elicit defiance at this stage. Instead, discrepancies between the patients' situation and their hopes for the future are highlighted, leading to a constructive discussion where the therapist shows patience and optimism and provides constant support in self-efficacy. Eventually, patients become more capable of identifying and enhance their motivation and readiness to change.

a) *MI alone*

Trials

There are several studies on MI for stimulant use disorders. Two articles reported that a single session of MI, either alone or in combination with written health risk information, did not prove beneficial in respectively crack cocaine users on methadone maintenance[125] and in a heterogeneous population of stimulant users[126]. Stein et al.[127] compared 4-session MI to an assessment control and concluded that the former was better at reducing days of cocaine use amongst the heaviest community-based users. Polcin et al.[128] delivered an unusually intensive 9-session intervention to patients with methamphetamine dependence, reporting a reduction in drug use and alleviated co-occurring psychiatric problems. Computerized versus in-person MI were compared with a view of further increasing the availability of this brief intervention, but no reduction in stimulants use was elicited regardless of treatment[129].

b) *MI plus other interventions*

Trials

MI is frequently combined with other brief interventions. Srisurapanont et al.[130] assessed MI and health education in young students with methamphetamine dependence, reporting short-term benefits such as fewer days of drug use. The same combination was also trialed in a sample of crack cocaine users with comorbid HIV and poor adherence to antiretroviral therapy, showing improved compliance with treatment and fewer drug problems[131]. A single 50-minute session known as motivational enhancement therapy[132] combining MI with personalized feedback about a preliminary assessment and health education, showed improved outcomes when used on ecstasy users[133]. Goncalves et al.[134] integrated MI with chess playing and showed that this can be an effective intervention in improving executive functions, associated with abstinence outcomes, in a population of cocaine users.

Other 2 studies combined brief CBT with MI respectively for cocaine and amphetamine users, but results on abstinence outcomes were either inconclusive[135] or not reported[136].

Drug counseling (DC)

Theoretical background

Individual drug counseling (IDC) for stimulant use disorders is largely inspired by 12-SP principles, seeing addiction as a disease damaging the person physically, mentally, and spiritually[137]. It is a semi-structured, time-limited intervention of 36 sessions over 6 months, which focuses on the present and sets short-term goals. Initially, patients need to accept having an addiction, seeing this as a disease, and aiming to abstinence. Then, they learn to recognize and avoid triggers, develop new coping strategies, and use objective measures of abstinence such as urinalysis. Finally, the counselor supports them to enhance their motivation and promotes lifestyle changes to prevent relapse and maintain recovery as a lifelong process. Drug counseling can also be delivered in groups (GDC) and it usually involves two phases[138]. The first 12 sessions consist of a structured psychoeducational group to improve knowledge about addiction and learn about the recovery process; a second phase between sessions 12-36 educates on problem-solving techniques. As for any group therapy, it should offer a warm atmosphere, where each member can express opinions, problems, feelings and support; however, domination by an individual or isolation are common pitfalls. Both IDC and GDC usually encourage additional participation to 12-SP groups such as cocaine or amphetamine anonymous.

Trials

IDC and GDC are very commonly used in stimulant use disorders, although many available trials employed it as a baseline intervention[29,54] or in conjunction with several other treatments[139] without providing specific outcomes data. Gottheil et al.[140] compared IDC, IDC plus GDC, and an intensive outpatient program for cocaine users, reporting improvements in drug use and severity of associated problems for all three interventions with no significant differences between treatments. Crits-Christoph et al.[60] showed that a combination of intensive IDC and GDC was superior to psychodynamic and cognitive behavioral approaches in reducing days of cocaine use and drug-related problems. Weiss et al.[61] reported that IDC was beneficial in cocaine users both in improving drug outcomes and in promoting participation to 12-SP sessions. Rawson et al.[141] used a complex and intensive "matrix model" that combined 4 sessions of IDC, 16 weeks of twice-weekly group CBT, 12 sessions of family education groups, 4 sessions of social support groups, encouragement to attend 12-SP, and weekly testing for alcohol and stimulants on a large sample of methamphetamine users, showing significant improvements during the treatment phase that were not maintained on the longer-term. Other studies used telephone monitoring and adaptive counseling on cocaine users and showed that, when vouchers are used as rewards, engagement with therapy increased and abstinence outcomes improved[141-143].

DISCUSSION AND CONCLUSIONS

In this article, we systematically reviewed and qualitatively synthesized all psychosocial interventions studied in randomized controlled trials. Currently, this is the most complete review available on this subject.

There are several theoretical differences between therapies. Cognitive and behavioral models predominate in randomized controlled trials, possibly because they are more likely to rely on standardized delivery protocols. CM, cognitive behavioral interventions, and CRA see addiction as deriving from dysfunctional thoughts and maladaptive learned behaviors, which they aim to modify through cognitive and behavioral techniques such as functional analysis, coping-skills training, and operant conditioning, with or without the addition of social support. The 12-SP acknowledges these issues, though does not address them in a systematic fashion, but adds a spiritual element that promotes acceptance of the disease. Similarly, MbI and PhE include practices focusing on understanding, modulating, and exerting inner bodily and spiritual energies and external experiences as a mean to reach acceptance and change. Relationships are central to the formulation of stimulant use disorders for SEPT, IPT, and FT, which differ because of their emphasis on the study of transference and countertransference, interpersonal functioning, and family systems respectively. Finally, MI and DC are classic counseling approaches because they refuse to assign a "sick role", encouraging the development of immediate modifications of attitude and behavior.

Moreover, practical differences can affect the choice of treatment. Some therapies are manualized and consistently available in the public health sector or via charities (e.g. CBT, 12-SP), whereas others are based on common theoretical principles but are not standardized (e.g. RP, SEPT), and therefore it is difficult to produce evidence to promote their diffusion. Clinicians and patients should discuss the pragmatic aspects of treatment delivery beforehand, because psychosocial interventions may vary in terms of intensity (e.g. low in DC, high in cognitive behavioral interventions), duration (e.g. brief in cognitive behavioral interventions, extended in SEPT and DC, lifelong in 12-SP), modality (e.g. IDC vs GDC or 12-SP), and media (e.g. face-to-face in most psychotherapies, very limited contact in CM, online or telephone in DC).

The group of patients suffering from stimulant use disorders is heterogeneous. Several authors highlighted how specific psychosocial interventions may work best for particular subgroups of stimulant users or for a particular phase of the disorder, and indeed empirical research suggested that psychosocial treatment should be tailored to patients' individuality and context[144,145]. Further research should address the need for more precise treatments, whereby evidence-based interventions can be personalized to the individual characteristics of people misusing substances[146]. In the absence of reliable predictors of response to different therapies, a better understanding of the underpinnings of psychosocial interventions in stimulant use disorders will aid clinical judgment.

Likewise, interventions for stimulant use disorders are diverse, but they generally involve a therapeutic relationship between patient and therapist, with CM being the only exception. Considering all the theoretical and practical differences between psychosocial interventions, the "equivalence paradox" argues that a shared therapeutic alliance is essential for successful treatment of mental illness[147], a concept which could hold true for stimulant use disorders.

Some studies tested a range of combined treatments and there is evidence that the combination of diverse approaches, especially CM with other interventions, is feasible and leads to better outcomes in patients with several needs[148]. This review provide clarity around the similarities and differences between psychosocial interventions and therefore represent a useful framework for clinicians to conceive combined interventions that are clinically meaningful and likely to provide additive or synergistic effects.

This review has several limitations. We only included psychosocial interventions investigated in randomized controlled trials leading to published articles, so it is conceivable that some treatments are not reported because no randomized controlled trials assessed them or, if so, they were not published. Although the search algorithm allowed a methodical analysis of the literature, the presentation of findings is narrative and we did not quantitatively analyze clinical outcome measures such as acceptability and efficacy, for which we refer to other studies[15].

In conclusion, our study shows that numerous psychosocial interventions are available for the treatment of stimulant use disorders. Different interventions should be offered, either alone or in combination, according to patients' circumstances and needs. Additional evidence from primary and secondary research is required to characterize profile of differential response to treatment and compare psychosocial interventions, therefore providing useful guidance for clinicians and patients.

Conflict of interests: the authors declare no conflict of interests.

Take home messages

- Psychosocial interventions are a heterogeneous group of treatments with the best evidence-base for stimulant use disorders, but the indications for each intervention are unclear.

- Contingency management, cognitive behavioral interventions, community reinforcement approach, 12-step program, meditation-based interventions and physical exercise, supportive expressive psychodynamic therapy, interpersonal psychotherapy, family therapy, motivational interviewing, and drug counseling have been assessed in randomized controlled trials for the treatment of stimulant use disorders.

- A range of theoretical and practical factors distinguishes between interventions and different treatments are preferable in specific clinical groups according to patients' individual characteristics.

- An effective therapeutic alliance is a commonly shared feature potentially explaining why different interventions are equally beneficial within the same clinical contexts.

- Interventions can be combined to achieve better results in complex patients with multiple needs.

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