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Cognitive training and remediation interventions for substance use disorders: a Delphi consensus study

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Abstract

Aims: Substance use disorders (SUD) are associated with cognitive deficits that are not always addressed in current treatments, and this hampers recovery. Cognitive training and remediation interventions are well suited to fill the gap for managing cognitive deficits in SUD. We aimed to reach consensus on recommendations for developing and applying these interventions.

Design, Setting and Participants: We used a Delphi approach with two sequential phases: survey development and iterative surveying of experts. This was an on-line study. During survey development, we engaged a group of 15 experts from a working group of the International Society of Addiction Medicine (Steering Committee). During

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the surveying process, we engaged a larger pool of experts ($n = 54$) identified via recommendations from the Steering Committee and a systematic review.

Measurements: Survey with 67 items covering four key areas of intervention development: targets, intervention approaches, active ingredients and modes of delivery.

Findings: Across two iterative rounds (98% retention rate), the experts reached a consensus on 50 items including: (i) implicit biases, positive affect, arousal, executive functions and social processing as key targets of interventions; (ii) cognitive bias modification, contingency management, emotion regulation training and cognitive remediation as preferred approaches; (iii) practice, feedback, difficulty-titration, bias modification, goal-setting, strategy learning and meta-awareness as active ingredients; and (iv) both addiction treatment work-force and specialized neuropsychologists facilitating delivery, together with novel digital-based delivery modalities.

Conclusions: Expert recommendations on cognitive training and remediation for substance use disorders highlight the relevance of targeting implicit biases, reward, emotion regulation and higher-order cognitive skills via well-validated intervention approaches qualified with mechanistic techniques and flexible delivery options.

KEYWORDS

Cognitive remediation, cognitive training, Delphi method, interventions, neuroscience, treatment

INTRODUCTION

Substance use disorders (SUD) are associated with cognitive deficits that manifest during both active substance use and remission [1–3]. These deficits in executive functions, attention, memory, social processing and decision-making skills hinder everyday functioning in people with SUD [4–6]. Furthermore, cognitive deficits are associated with difficulties adhering to and benefitting from different SUD treatment programmes and settings [7, 8]. Current gold standard treatments for SUD focus upon substance use-related outcomes, such as drug use reduction or abstinence, often without consideration of cognitive deficits or with the assumption that cognition will recover following successful remission from substance use. However, cognitive deficits can persist even after long-term abstinence and contribute to relapse, reduced quality of life and difficulties reintegrating in society [9, 10]. Furthermore, cognitive deficits are potential obstacles for medication adherence [11] and successful implementation of cognitive behaviour therapies for those with mood, anxiety and trauma-related comorbidities [12].

Cognitive training and remediation interventions are a logical option to fill the current gap in managing cognitive deficits in SUD [13–15]. These interventions are purpose-built to restore or compensate for cognitive deficits, which may alleviate their impact on daily functioning and improve ability to benefit from SUD treatments, as suggested by demonstrated benefits in other mental health disorders [16]. Moreover, as some cognitive deficits, such as those impacting executive functions and decision-making, are not just correlates of SUD but also possibly a core psychopathological mechanism driving compulsive substance use [17, 18], cognitive training and remediation

have the potential to become treatments for SUD in and of themselves. Given this premise, it is surprising that this group of interventions have not yet permeated standard care for SUD. This probably relates to the heterogeneity among interventions and mixed quality of the existing literature [19]. There are numerous small pilot or proof-of-concept trials and comparatively fewer well-powered randomized trials, and there is a wide variety of intervention approaches, with few studies distilling the active ingredients that are purposely driving cognitive and behaviour change [20, 21]. Moreover, most cognitive training and remediation interventions applied in SUD were initially designed for people with other neurological and mental disorders, such as brain injury or schizophrenia, while there are few specific adaptations for people with SUD and addiction treatment programmes [22]. Altogether, there are currently very few high-quality, adequately powered and well-structured interventions for improving cognitive functions in SUD. At the same time, cognitive training and remediation for SUD is a growing research area, and both emerging studies and meta-analytical evidence suggests promising benefits for specific approaches [19, 23, 24].

Given the strong rationale for applying cognitive training and remediation interventions in SUD, while acknowledging the heterogeneity and lack of specificity of current approaches, we aimed to reach an expert consensus on recommendations for developing these interventions in the context of SUD. Specifically, we aimed to identify the best strategies for strengthening cognitive functions in people with SUD by surveying experts about the cognitive targets, therapeutic approaches, specific techniques and active mechanisms and modes of delivery of cognitive training, as well as remediation interventions likely to improve outcomes in the context of SUD treatment. To

achieve this, we used a Delphi approach [25, 26] to survey a pool of international experts in the field and reach a broad consensus via iterative consultation.

METHODS

Participants

We engaged two groups of experts during the study: (i) a steering committee (SC), namely, a small and collaborative group of researchers with well-established experience in the field of cognitive training and remediation in SUD who launched the project and inter-actively developed the initial survey; and (ii) a larger expert panel (EP) who represent the wider community of experts in the field and participated in the surveying. This approach is practical for the procedure of the Delphi study and ensures the quality of the consensus process [27, 28]. Both participants in the SC and EP are co-authors on this paper.

Steering Committee (SC)

Following a series of in-person and on-line meetings within the Neuroscience Interest Group of the International Society of Addiction Medicine (ISAM-NIG) regarding cognitive training and remediation interventions, we established a working group of 15 experts on the topic, which included (in alphabetical order): Jamie Berry, Alfonso Caracuel, Marc L. Copersino, Hamed Ekhtiari, Matt Field, Eric Garland, Valentina Lorenzetti, Leandro Malloy-Diniz, Victoria Manning, Ely M. Marceau, David L. Pennington, Tara Rezapour, Justin C. Strickland, Antonio Verdejo-García and Reinout Wiers (henceforth, the SC).

SC members outlined the scope and research questions of the Delphi study, which included four areas pertaining to cognitive training and remediation interventions for SUD: targets (i.e. cognitive processes that needed to be addressed), approaches (i.e. types of interventions), techniques/mechanisms (i.e. active ingredients of the interventions) and modes of delivery. Next, the SC designed the original Delphi survey via an interactive process of item development, followed by an iterative process until consensus was reached within the SC on the final set of items. All the comments and revisions during the survey design process were handled by two senior members (A.V. G. and H.E.). SC members also monitored and discussed the progress of the overall Delphi process during the subsequent rounds of the survey rating phase. Two assistants (A.K.Z. and E.G.) facilitated the process and managed all contacts and communications.

Expert Panel (EP)

Identification of the EP members was based on a systematic literature review. The review search was conducted on 31 July 2021 using PubMed and combining search terms and MeSH terms capturing

cognitive processes (e.g. inhibitory control) AND cognitive training and remediation interventions (e.g. computerized cognitive training) AND substance use (e.g. substance use/abuse/addict*, specific substances such as alcohol, cocaine, etc.). Eligibility criteria included: published in English; participants with SUD and/or hazardous patterns of substance use; testing the effects of a cognitive training and/or remediation intervention; including any type of comparator. This search yielded 108 cognitive training and remediation studies in SUD. The SC assistants screened the studies to identify key authors in the field to be invited to form the EP. The inclusion criteria regarding entering the EP were as follows: (a) appearing among the authors of at least two original publications in the systematic review database and (b) keeping the authorship position of first, last or corresponding of at least one of the papers. In addition, each of the SC members had the opportunity to nominate a maximum of two other candidates for the EP, based on their own knowledge and networks. The members of the SC were also part of the EP. Following identification of experts, we sent invitation e-mails to each person, with two reminders sent within 2-week intervals in the case of not responding.

Measures

The original Delphi survey included 67 items. The survey items were those identified by the SC as crucial to interrogate the best-suited set of targets (27 items), approaches (11 items), techniques (10 items) and modes of delivery (19 items) for interventions aimed at strengthening cognitive functions in the context of SUD treatment. The main structure of the questions was as follows: 'How important do you think [survey item here] is for strengthening cognitive function with the aim of improving the outcomes of addiction treatment?'. The items concerning intervention approaches included follow-up multiple choice subquestions for each intervention, in which we inquired about the best timing ['detoxification' (first 2 weeks after cessation/reduction of substance use), 'early remission' (first 3 months after cessation/reduction of substance use) or 'chronic phase' (more than 3 months after cessation/reduction of substance use)], frequency ('several times per day', 'several times per week', 'once per week' or 'monthly') and duration ('within 1 month', '1–3 months' or '4–12 months'). There was no obligation for the participants to answer all the questions.

Procedure

The Monash University Human Research Ethics Committee approved the study (reference: MUHREC #27242), and all participants provided informed consent. The study involved two sequential phases: (i) survey development and revision (conducted by the SC via e-mail) and (ii) survey rating (conducted by the EP via an on-line survey using Qualtrics software) (Figure 1). EP's responses to the Delphi survey were anonymous, and participants had the option of providing demographic and professional data via an independent survey that was not linked with their Delphi survey responses.

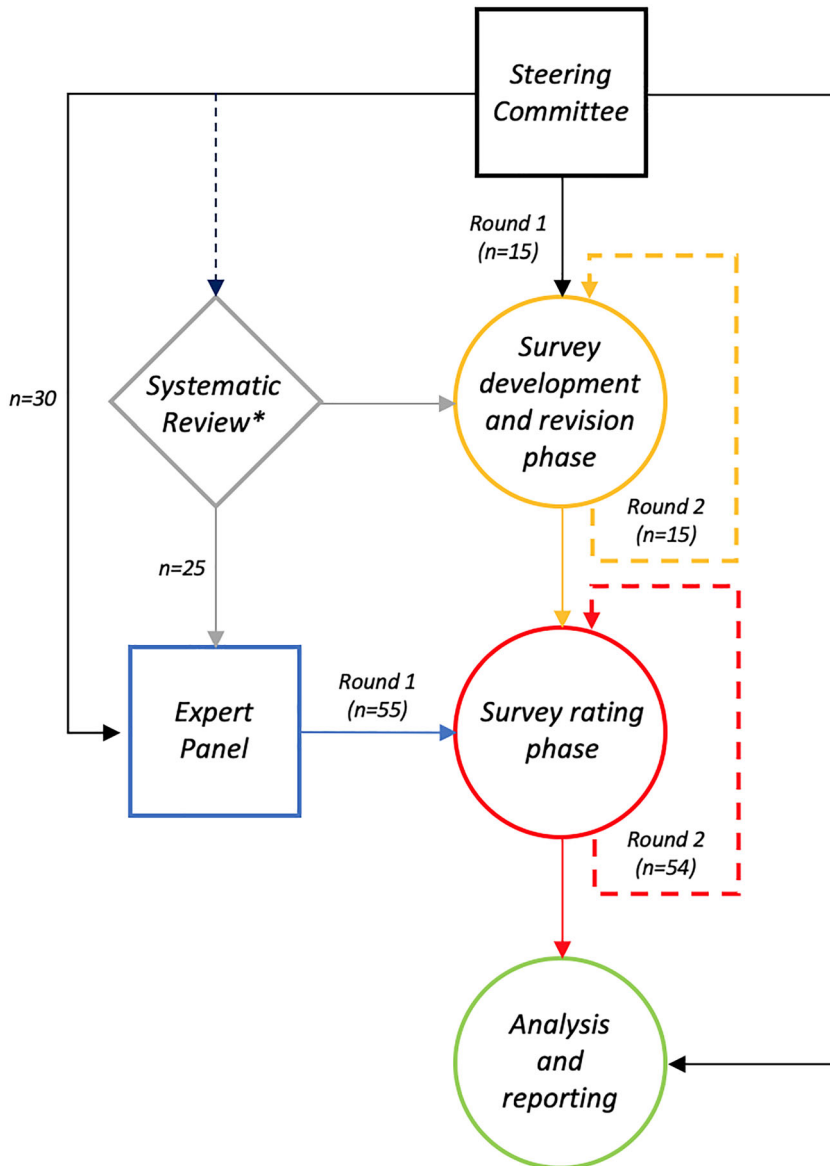


FIGURE 1 Schema of the study procedure. We had two groups of participants: the Steering Committee (in black) who designed the initial survey draft and participated in all phases of the study, and the Expert Panel (in blue) which includes the Steering Committee along with a broader group of experts in the field derived from a systematic review (in grey) and recommendations by the Steering Committee. The study comprised three main phases, including survey development/revision phase (in yellow), survey rating phase (in red), each happening in two discrete rounds based on reaching consensus and analysis and reporting phase (in green). The number of contributors from each source [i.e. Steering Committee (members or nominees) or Systematic Review] is displayed by 'n ='

Survey development/revision phase

SC members proposed items to survey the best-suited approaches for improving cognition among people with SUD in the context of SUD treatment, relying on their own experience and knowledge. Upon preparation of the initial draft, all the SC members were asked to add their comments on the survey as a whole and endorse the final version across two rounds of revisions [29]. The final survey was also pilot-tested by two senior members of the SC (H.E. and A.V.G.) to ensure the clarity and coherency of the questions.

A glossary of terms, which contained definitions on every item within the survey, was gathered based on comprehensive literature searches as well as consulting controlled vocabulary systems of bibliographic databases such as MeSH. This glossary received revisions and final approval by the SC.

Survey rating phase

During this phase, the EP rated the finalized version of the survey using their expertise and knowledge [30]. Participants used a 5-point Likert scale with the following options: 'not important', 'slightly important', 'moderately important', 'very important' and 'essential'. We also provided an 'unsure' option. The EP were also invited to suggest new items to be included in the survey using a textbox located at the end of each section (i.e. targets, approaches, techniques and modes of delivery); this feedback was optional. We also provided a study role-account e-mail, which the experts could use to request clarifications or technical support and to provide unsolicited qualitative feedback.

The consensus threshold was 70%, determined via summation of responses with a score of 'moderately important' and above [27, 28]. The procedure was iterative, with experts subsequently

surveyed until the greatest possible agreement was reached in a maximum of three rounds, notwithstanding that the same item could not be rated more than two times [25, 26]. The first round included the full set of survey items as agreed by the SC. The second round included: (i) items that reached > 50% but less than 70% agreement and (ii) new items suggested by the experts in the first round. The survey used in the second round also included, for each item, the proportion of agreement achieved during the first round; this information enabled experts to reflect upon their own responses in the context of those of the broader EP. We have included the two surveys (first and second rounds) as Supporting information.

To gauge the degree of diversity in the EP (including the SC) an independent survey, linked via de-identified alpha-numerical codes to ensure anonymity, collected socio-demographic and professional information from respondents. Specifically, we collected information regarding age, sex, highest academic degree, country of residence, primary affiliation, primary field of research (psychiatry, psychology, pharmacology, neuroscience, cognitive science, etc.), primary place of work (hospital, university, business, independent research institute, etc.), length of time spent in addiction medicine/science (years) and length of time spent in the field of cognitive rehabilitation in addiction treatment research (years).

Data analysis

We computed response percentages for each Delphi survey item and the degree of agreement from participants across the two iterations using IBM SPSS Statistics software version 25. In addition, for those items that were carried forward from the first to the second round, we calculated reliability statistics (Cronbach's alpha) to evaluate the temporal stability of ratings for each item.

RESULTS

Participants' characteristics

The EP identification process resulted in 86 potential candidates [45 based on the review (note that five potential participants identified by the review were already in the SC and one was uncontactable), 26 nominated by the SC and 15 were already members of the SC]. Of 86 original invitations, 59 (68.6%) people responded, 55 completed at least one item of the survey (64%) and 54 (62.7%) completed the full survey in the first iteration; the remaining four participants declined because of having moved away from the field ($n = 2$), conflict of interest ($n = 1$) or over-commitment ($n = 1$). Fifty-four (98%) participants completed the second and final iteration of the survey and formed the final expert panel. The expert panel comprised 45% female and 55% male respondents from geographical locations spanning Africa, the Americas, Asia, Australia, Europe and the Middle East. They had a median of 12.5 years of experience in

addiction neuroscience and a median of 10 years of experience in cognitive training and remediation in the context of SUD. They worked throughout university (80%) and clinical and hospital settings (20%) (Table 1). The EP included representatives from all the different scientific approaches surveyed, including cue-based therapies, computerized cognitive training, cognitive remediation, contingency management, emotion-related training (e.g. mindfulness and emotion regulation) and psychoeducation. Based on a descriptive analysis of public profiles (institutional websites, Google Scholar, ResearchGate), invitees who did not respond did not systematically differ from EP contributors regarding sex, location or scientific approaches.

Delphi survey results

Figure 2 displays the overall flow of the Delphi process, with the number of items from each category endorsed, discarded or carried forward during subsequent iterations. The experts reached consensus after the second round (i.e. 50 items endorsed by > 70% of experts), so a third round was not necessary. We achieved consensus once all the items had reached pre-established levels of agreement (endorsed) or disagreement (discarded), or had been rated by all experts at least twice without sufficient endorsement; these decisions were based on established processes used in previous Delphi studies [25, 26]. Item reliability across rounds showed adequate consistency (alpha range = 0.51–0.75). Figure 3 shows the pooled experts' responses (level of agreement) for each item across the two iterations.

Fifty items were endorsed by > 70% of the expert panel. Table 2 enumerates and provides definitions for each of the selected items, organized by category. Definitions were primarily sourced from the American Psychological Association's *Dictionary of Psychology* [31] and the National Institute of Mental Health's Research Domain Criteria (RDoC) constructs matrix [32], as well as from specialized literature on cognitive processes (i.e. targets) [33–38], intervention approaches [39–42], techniques/mechanisms [43–45] and modes of delivery [46–48]. In the following subsections, we summarize the results in terms of endorsed and discarded items organized by category.

Targets of intervention

The experts reached consensus on endorsing 21 cognitive processes that should be targeted by cognitive training and remediation interventions (Table 2). The selected processes fell into six higher-order systems; namely, cognitive biases, positive affect, arousal and regulatory systems, attention, executive functions and social processing. The experts discarded eight cognitive processes, including those categorized under perceptual, psychomotor and memory systems, as well as 'mentalizing', which is part of social systems.

TABLE 1 Participants' socio-demographics and professional characteristics

| Sample characteristic | Median | IQR | n | % |
|---|--------|-----|----|-------|
| Age (years) | 43.50 | 14 | 42 | |
| Length of time in addiction neuroscience (years) | 12.50 | 11 | 28 | |
| Length of time in cognitive interventions for addiction (years) | 10 | 5 | 29 | |
| Sex | | | | |
| Male | | | 23 | 54.76 |
| Female | | | 19 | 45.24 |
| Highest academic degree | | | | |
| Bachelors | | | 1 | 2.38 |
| Masters | | | 2 | 4.76 |
| PhD | | | 39 | 92.86 |
| Place of residence | | | | |
| Australasia | | | 8 | 19.51 |
| Africa | | | 1 | 2.44 |
| Europe | | | 18 | 43.90 |
| Asia | | | 1 | 2.44 |
| North America | | | 13 | 31.71 |
| Primary field | | | | |
| Addiction | | | 16 | 38.10 |
| Psychology | | | 7 | 16.67 |
| Behavioural science | | | 1 | 2.38 |
| Clinical psychology | | | 3 | 7.14 |
| Neuropsychology/clinical neuropsychology | | | 8 | 19.05 |
| Addiction and neuropsychology | | | 5 | 11.91 |
| Psychiatry | | | 2 | 4.76 |
| Primary placement | | | | |
| University | | | 34 | 80.95 |
| Hospital | | | 1 | 2.38 |
| University and hospital | | | 5 | 11.91 |
| Addiction Service | | | 2 | 4.76 |

Fifty-three participants were invited to answer the socio-demographic/professional survey independently from the Delphi survey, and 42 of them completed at least one question (i.e. data shown in the table).

IQR = interquartile range.

Intervention approaches

The experts reached consensus on endorsing four intervention approaches; namely, cognitive bias modification, contingency management, emotion regulation training and cognitive remediation (Table 2). The experts discarded six other approaches, including cue-exposure and aversive therapies, mindfulness and interoceptive trainings, computerized cognitive training and neuroscience-informed psychoeducation.

For the four interventions endorsed, the majority of experts recommended applying them during early remission (i.e. following detoxification and during the first 3 months after treatment or self-initiated behaviour change). In terms of frequency, the majority of experts suggested that cognitive bias modification and cognitive

remediation should be administered several times per week, whereas for contingency management and emotion regulation training results were more mixed, with preference towards once per week. In terms of duration, the majority of experts suggested that cognitive bias modification and emotion regulation training should be administered over 3 months, whereas experts suggested longer durations for cognitive remediation, and results for contingency management were inconclusive (Figure 4).

Mechanisms/techniques

The experts reached consensus on endorsing 10 different techniques that can be used to initiate and consolidate cognitive training and

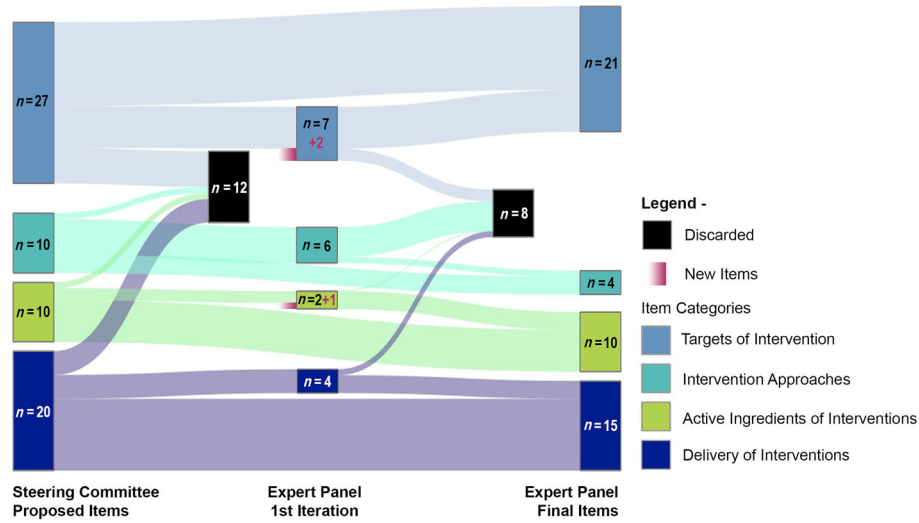


FIGURE 2 Diagram displaying the flow of the Delphi surveying process. It shows the number of items initially proposed by the Steering Committee for each of the four areas of interest (i.e. targets, intervention approaches, mechanisms or active ingredients and delivery) and how they were subsequently endorsed or discarded by the Expert Panel across two consecutive rounds. Left: the Steering Committee initially proposed 67 items; during the first iteration, the Expert Panel endorsed 36 items (continuous left-to-right flux) and discarded 12 items (black boxes). Middle: the remaining 19 items (which had reached more than 50% but less than 70% agreement in the first iteration) plus three newly proposed items (fading magenta) were carried forward to the second survey (n = 22 items). Right: during the second iteration, the Expert Panel endorsed 14 items and discarded eight items and thus reached consensus for 50 final items

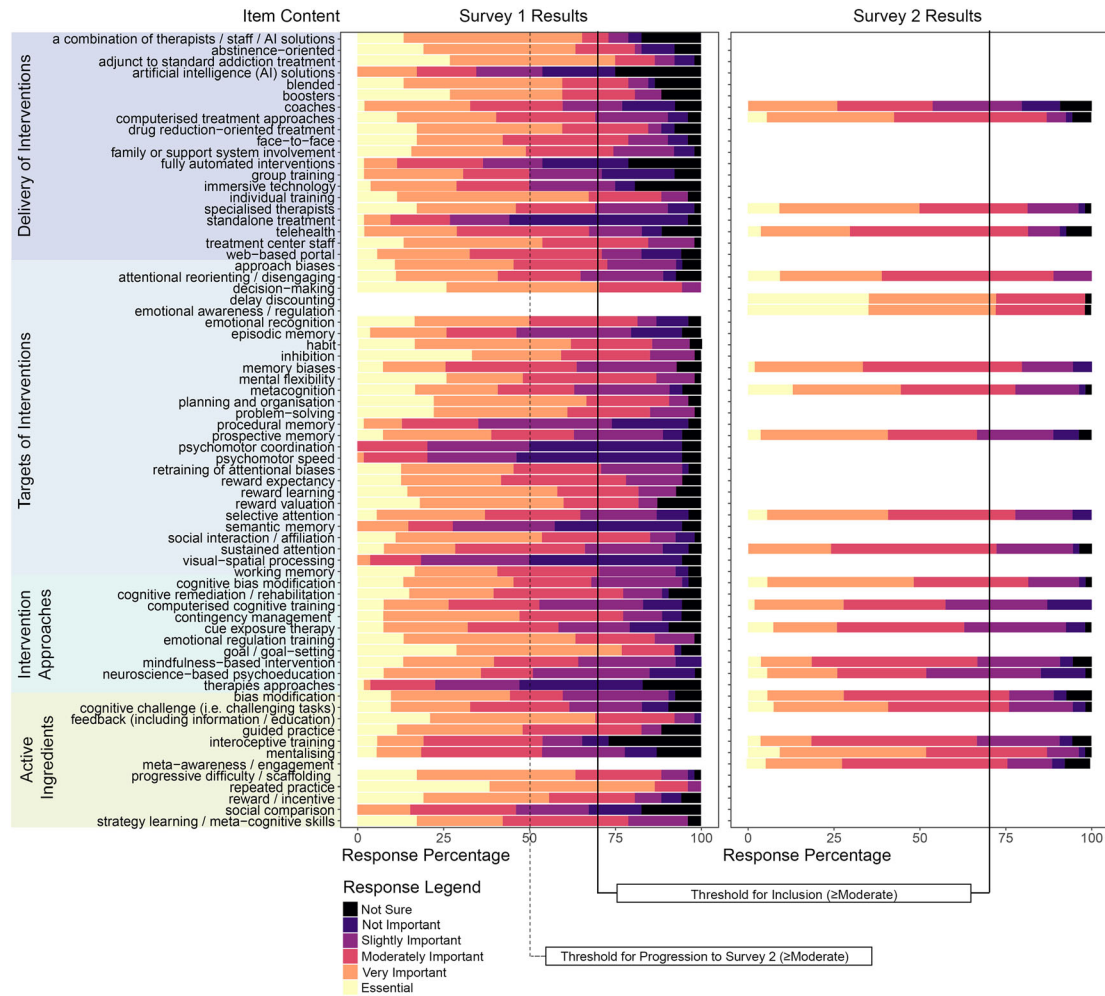


FIGURE 3 Expert panel participants' pooled responses to each survey item (i.e. response percentage for each of the Likert scale options), grouped by item category, across the first and second iterations of the Delphi survey

TABLE 2 Definitions of final selected items

| | Definitions |
|----------------------|---|
| Targets | |
| Biases | |
| Attentional | Elevated attention to stimuli with enhanced relevance for certain individuals |
| Approach | Automatic tendency to approach drug-related cues faster rather than avoiding them |
| Memory | Implicit associations held between substance-related cues and positive affective attributions |
| Positive affect | |
| Valuation | Processes by which the probability and benefits of a prospective outcome are computed by reference to external information, social context and/or prior experience. This computation is influenced by pre-existing biases, learning, memory, stimulus characteristics and deprivation states. Reward valuation may involve the assignment of incentive salience to stimuli |
| Expectancy | A state triggered by exposure to internal or external stimuli, experiences or contexts that predict the possibility of reward. Reward expectation can alter the experience of an outcome and can influence the use of cognitive resources |
| Learning | A process by which organisms acquire information about stimuli, actions and contexts that predict positive outcomes, and by which behaviour is modified when a novel reward occurs, or outcomes are better than expected. Reward learning is a type of reinforcement learning |
| Habit | A well-learned behaviour or automatic sequence of behaviours that is relatively situation-specific and over time has become motorically reflexive and independent of motivational or cognitive influence—that is, it is performed with little or no conscious intent. For example, the act of hair-twirling may eventually occur without the individual's conscious awareness |
| Discounting | The tendency to excessively discount the value of rewards when they are not immediately available |
| Attention | |
| Selective | Concentrating on certain stimuli in the environment and not on others, enabling important stimuli to be distinguished from peripheral or incidental ones |
| Disengaging | Shifting the focus of attention from one stimulus to another. Deficits in this process may involve difficulties to shift attention away from disorder-related cues |
| Sustained | Focusing on a task for an extended length of time |
| Executive functions | |
| Working memory | The short-term maintenance and manipulation of information necessary for performing complex cognitive tasks such as learning, reasoning and comprehension |
| Inhibition | The process of controlling one's impulses or prepotent responses to prevent inappropriate behaviours |
| Flexibility | The combination of various cognitive processes to adjust the course of thoughts or actions in response to changing situational demands. These changes occur without explicit instructions |
| Planning | The ability to organize cognitive behaviour in time and space. It is necessary in situations where a goal must be achieved through a series of intermediate steps, whereby each step does not necessarily lead directly towards that goal |
| Problem-solving | The process by which individuals attempt to overcome difficulties, achieve plans that move them from a starting situation to a desired goal or reach conclusions through the use of higher mental functions, such as reasoning and creative thinking |
| Decision-making | The cognitive process of choosing between two or more alternatives, ranging from the relatively clear-cut (e.g. ordering a meal at a restaurant) to the complex (e.g. selecting a mate) |
| Self and others | |
| Metacognition | Processes used to monitor and assess one's understanding and performance and recognizing one's own successful cognitive processing |
| Recognition | Identifying other humans' emotional states, mainly for basic emotions such as joy, sadness, surprise, anger, fear and disgust |
| Affiliation | Engagement in positive social interactions with other individuals. Affiliation is a behavioural consequence of social motivation and can manifest itself in social approach behaviours |
| Arousal/affect | |
| Awareness/regulation | The ability to accurately monitor and change emotional states as a function of context |

(Continues)

TABLE 2 (Continued)

| | Definitions |
|--|---|
| Approaches | |
| Cognitive bias modification (CBM) | A group of interventions that aim to retrain implicit biases towards drug-related cues. CBM approaches include retraining of drug-related attentional, approach and/or memory biases, as well as drug cue-related inhibitory control training |
| Contingency management | A set of interventions wherein immediate tangible incentives (e.g. a voucher, exchangeable for retail goods and services) are provided contingent upon objective evidence of behaviour change (e.g. negative urine drug test). In the context of cognitive training, contingency management has also been used to reinforce training gains (i.e. provide rewards contingent on objective evidence of training progress) |
| Cognitive remediation/rehabilitation | A therapeutic process targeting cognitive deficits to improve an individual's functioning in everyday life. This includes methods to train and restore cognitive functions and strategy learning techniques. Examples of specific cognitive remediation techniques are goal management training, episodic future thinking/implementation of intentions, spaced retrieval/memory reconsolidation and errorless learning |
| Emotional regulation training | Training patients to use adaptive emotion strategies and regulate maladaptive emotion strategies |
| Techniques | |
| Repeated practice | A learning strategy that involves 'doing something again and again in order to become better at it' |
| Guided practice | A transition practice that allows therapists to pull back and the clients to step forward through smooth movement from therapist- to client-centred learning |
| Feedback | Feedback is information provided by an agent (e.g. therapist, peer, book, parent, self and experience) regarding aspects of one's performance or understanding |
| Reward/incentive | Objects, events, situations or activities that attain positive motivational properties from internal brain processes |
| Progressive difficulty/scaffolding | Providing interventional material just beyond the difficulty level at which the recipient could benefit gradually in a stepwise manner over time |
| Bias modification | Practising tasks that require trainees to interact with substance-related cues and alternative reinforcers in a way that diminishes the salience of cues and enhances the salience of alternatives |
| Goal-setting | The development of an action plan designed to motivate and guide a person or group towards a goal |
| Metacognitive awareness/strategies | A range of mental strategies that involve the monitoring of one's cognition including planning and implementation of intentions, monitoring or awareness of comprehension and task performance and evaluation of the efficacy of monitoring processes and strategies to improve self-regulation |
| Meta-awareness/engagement with self-relevant stimuli | Promoting a state of deliberate attention towards the contents of conscious thought, serving as an appraisal of experiential consciousness |
| Delivery | |
| Therapeutic function | |
| Adjunct | Interventions provided as an add-on to existing treatment practice |
| Intended outcomes | |
| Abstinence-orientated | When the main goal of treatment is total cessation of substance use |
| Drug reduction | When the main goal of treatment is to minimize the negative consequences associated with substance use |
| Specifiers for delivery | |
| Individual training | When the intervention is delivered at the individual level (one-to-one) |
| Family/support system | When an individual participates in and has a relationship with members of their family or broader support system |
| Boosters | Additional therapy sessions held periodically (e.g. monthly, bi-annually and yearly) with the aim of 'refreshing' therapeutic components |
| Staff | |
| Specialized therapists | A licensed clinician with advanced training in brain function, cognition and behaviour (e.g. neuropsychologist and psychiatrist) who delivers and manages the cognitive training/remediation programme to ensure that the intervention's objectives are met effectively |
| Addiction treatment work-force | The clinical and peer support staff currently employed by addiction treatment services |
| Combination | Using both the current work-force and additional specialized therapists |

(Continues)

TABLE 2 (Continued)

| | Definitions |
|-----------------------------------|--|
| Interface | |
| Face-to-face | A direct encounter between two or more individuals |
| Fully automated | Interventions in which there is no therapist involved |
| Computerized treatment approaches | When interventions are delivered automatically via software which can work on computers, tablets, mobile phones or other digital devices |
| Web-based (portal) | Therapy provided through a computer or mobile device. This therapy may be delivered in separate, structured components (modules) based on themes relevant to the treatment goal(s) |
| Telehealth | The use of electronic information and telecommunications technologies to facilitate remote patient-treater interaction |
| Blended | Mixture of two or more of the modalities defined above; for example, face-to-face and computerized |

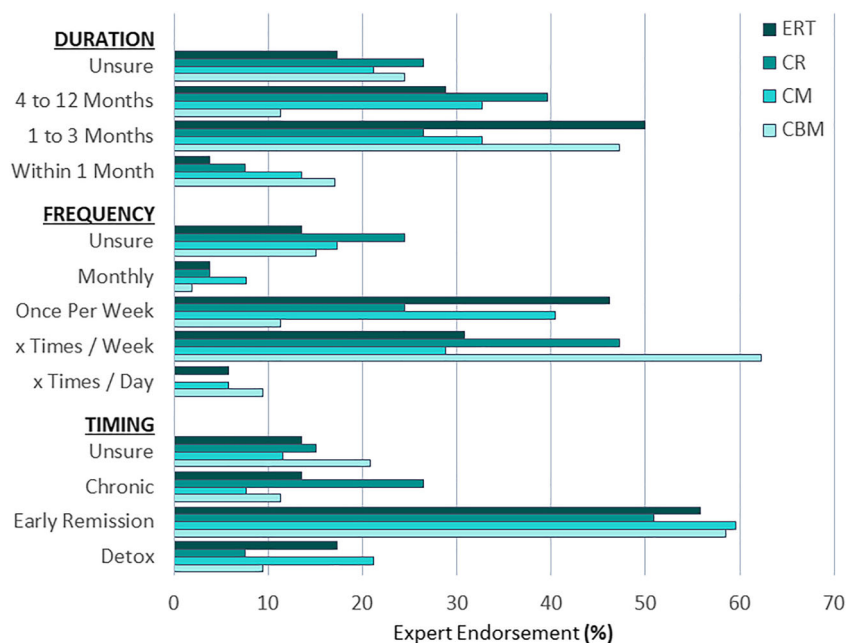


FIGURE 4 Expert panel participants' endorsement (percentage responses) of different options regarding timing, frequency and duration parameters for the selected intervention approaches. CBM = cognitive bias modification; CM = contingency management; CR = cognitive remediation; ERT = emotion regulation training

remediation approaches (Table 2). The selected techniques involved different forms of practice (guided and repeated), feedback (information and incentives), titration (progressive difficulty, cognitive challenge), bias modification, goal-setting, strategy learning and meta-awareness. Social comparison was the only discarded item.

Modes of delivery

The experts reached consensus on endorsing 15 different aspects of intervention delivery (Table 2), and agreed on considering cognitive training and remediation as an adjunct to best-practice interventions. Furthermore, we agreed that cognitive training and remediation could be applied as part of both abstinence-orientated and harm reduction treatment programmes. Regarding intervention context, the experts endorsed that cognitive training and remediation interventions should be individually delivered, leverage family support and include boosters to be administered after the active intervention phase. Regarding

providers, the experts endorsed involvement of both specialized therapists (e.g. clinical neuropsychologists) and the addiction treatment work-force, as well as combinations of therapists and artificial intelligence. Finally, the experts endorsed several different interfaces for cognitive training/remediation, such as face-to-face, telehealth, web portal, digital/computerized and fully automated, as well as blended approaches. The experts discarded five items, including consideration of cognitive training and remediation as a stand-alone intervention for addiction treatment, administration in group settings or using immersive technology and a primary involvement of coaches or artificial intelligence as providers.

DISCUSSION

This study successfully engaged a pool of 54 experts to provide a consensus on recommended targets, approaches, mechanisms and delivery of cognitive training and remediation interventions for SUD. The

experts agreed on endorsing 50 items across the four different categories (21 targets of intervention, four intervention approaches, 10 active ingredients of interventions and 15 aspects of delivery of interventions) and discarded 20 items (eight targets, six interventions, one mechanism and five aspects of delivery). In the following paragraphs, we discuss the logic and implications of each of these four areas of recommendations. Our interpretations are mainly based on contextualization of the experts' survey ratings and subsequent consensus (or lack of thereof) into the broader scientific literature on the topic. However, in some instances we also use insights gathered during the discussions of the SC and unsolicited qualitative feedback provided by the experts; for example, the level and quality of empirical evidence accrued for particular items was consistently mentioned as an important factor informing experts' responses.

The experts' selection of targets highlights the key role of cue-related biases, reward, emotion regulation, attention/executive functions and social processing in the core psychopathology and potential treatment of SUD [20, 49]. This set of processes partly overlaps with those proposed in the Addictions Neuroclinical Assessment (ANA) model (i.e. positive affect, negative affect, executive function) and with the results of a previous Delphi study into neuropsychological assessment for addiction [17, 18]. Our findings go beyond these existing frameworks by highlighting the importance of emotional awareness and regulation, implicit biases and social processing. Emotional awareness and regulation, which are higher-order (top-down) systems, were emphasized over the basic experience of negative affect, which was discarded for not being well suited for cognitive training and remediation interventions.

Implicit biases and social processes are now included in a hierarchical cognitive model of SUD that strongly aligns with the experts' view [50]. The selected set of targets also expands and qualifies the scope of previous work by pinpointing, for instance, different types of biases (i.e. approach, attention, memory) and both specific (i.e. working memory, inhibition) and complex (i.e. planning, problem-solving) aspects of executive functions. Discarded items (i.e. perceptual, motor and memory processes) are part of the cognitive deficits typically observed in people with SUD. In particular, they include perceptual and motor deficits in people with alcohol use disorders and memory deficits in those with stimulant use disorders [9]. However, discarded items have a relatively more tenuous relationship with clinical outcomes [7].

The experts endorsed only four (of the initial 10) intervention approaches. Importantly, there is almost perfect alignment between the endorsed interventions and the selected targets. Cognitive bias modification reduces cue-related biases, contingency management modifies reward processing, emotion regulation training targets emotional awareness and top-down regulation of emotions and cognitive remediation is the treatment of choice to address attention and executive function deficits in neurological populations [51]. There is no obvious match among selected interventions for social processing targets (i.e. emotion recognition, affiliation) which should be an area of future research, although emotion regulation training partly taps into these processes [52]. The selected interventions have also

demonstrated efficacy in the clinical trials literature. There is recent evidence from well-powered randomized controlled trials on the benefits of cognitive bias modification for alcohol abstinence and emotion regulation training for opioid use/misuse reduction [53, 54]. It should be noted, however, that [54] integrated mindfulness with emotion regulation training (i.e. reappraisal and savouring techniques); thus, the robust decrease in opioid misuse observed in this trial may be a function of synergistic interactions between mindfulness and emotion regulation training, as previously proposed [55]. Regarding contingency management, there is a solid evidence base supporting its efficacy for stimulant and opioid use disorders [56, 57]. Although most contingency management trials stemmed from a behavioural economic perspective, rather than being neuroscience-informed, the mechanisms of change of the intervention implicate modifications in neurocognitive processes [58]. It is important to note that despite overall positive evidence, there are specificities in the effects of these interventions. While being one of the most heavily replicated and scalable interventions, cognitive bias modification currently has a greater level of support for the treatment of alcohol use disorders among people in residential treatment settings, and relative to other substances [59], and contingency management works better in people with SUD who have a history of previous treatment attempts and psychiatric comorbidities [60]. In the case of cognitive remediation, there is promising evidence on its ability to improve executive functions from small pilot studies [61], but still limited evidence from well-powered trials, especially about its effects on substance use-related outcomes such as craving, use reduction or abstinence [19]. There may also be unknown or unidentified indirect relationships between interventions and targets due to, for example, engagement of parallel or subordinate processes, but those were outside the scope of the study.

With regard to non-endorsed interventions, the experts were probably sensitive to the controversies associated with computerized cognitive training [62], which has shown limitations in terms of generalizability of benefits beyond trained tasks [63]. Mindfulness in the absence of explicit emotion regulation training was not supported by the experts despite its appeal among consumers, its efficacy for reducing substance misuse [64, 65] and being an active component of evidence-based interventions for SUD [54]. It is possible that the high degree of heterogeneity in mindfulness interventions, a dearth of studies examining their neurocognitive mechanisms in the context of addiction [66] and the mixed quality of available trials [65] deterred experts from endorsing. The heterogeneity of mindfulness interventions can be quantified and more clearly understood via careful reporting and examination of intervention mechanisms and key parameters of delivery [64]. Such components could then be mapped onto the cognitive-affective processes implicated in SUD; for example, using the targets identified by this consensus. Active engagement with cues (as per cognitive bias modification) and cognitive strategies (cognitive remediation) seems to be preferred over the more passive cue-exposure therapies. For other discarded interventions, such as interoceptive training and neuroscience-informed psychoeducation, the lack of research in a still emerging area may have prevented greater support from the experts.

The experts endorsed most of the initially surveyed techniques (10 of 11). This suite of techniques can be applied to design specific interventions and intervention regimens and to monitor consumers' engagement with active ingredients and its relationship with therapeutic outcomes. In this regard, our selection forms a toolbox that can contribute importantly to the standardization and systematic evaluation of cognitive training and remediation approaches in the context of SUD. Some of the techniques (e.g. repeated practice) seem better aligned with cognitive training approaches which seek to restore or reset specific cognitive skills whereas others, such as strategy learning or meta-awareness, are usually applied in the context of cognitive remediation [51]. However, an advantage of most of the techniques identified (e.g. guided practice, progressive difficulty and challenge, feedback, bias modification and goal-setting) is that they have potential to be transversally applied within several intervention approaches or combinations of approaches. Examples of suitable avenues include the combination of bias modification and feedback techniques in, for example, gamified versions of cognitive bias modification [67], bias modification and strategy learning techniques (e.g. cue-related episodic future thinking) [68] or feedback and strategy learning in combinations of contingency management and goal management [69].

Regarding delivery, the experts supported the role of cognitive training and remediation as an adjunct (rather than a stand-alone) treatment, which could be integrated in both abstinence-orientated and harm reduction programmes. The latter is particularly relevant, given increased appraisal of the value of substance use reduction as a therapeutic goal [70]. This amenability to different treatment philosophies, together with endorsement of the existing addiction treatment work-force and with specialized therapists as providers, speaks to the ecological validity and scalability of cognitive training and remediation in the context of standard addiction treatment. Experts also emphasized the need for individual-based delivery. Interestingly, this seemed to be at the cost of discarding group interventions, which include some well-validated approaches that are well accepted by providers and consumers. Through qualitative feedback coming from the experts, we understood that this prioritization of individual-based delivery is due to the perceived need for individualization of the cognitive training and remediation plan, as well as personalization of progress across the intervention. In terms of external support and preferred interfaces experts embraced multiple sources of support (treatment staff, specialists, family, artificial intelligence) and multiple/blended interfaces, which can be deemed appropriate depending on particular populations, settings and study designs. The accelerating effect of the current COVID-19 pandemic on remote intervention options probably played a role in leaning experts towards endorsement of telehealth, digital and fully automated approaches. That said, additional large-scale remote **intervention trials** for telehealth cognitive training and remediation approaches are still needed to ascertain the efficacy of this delivery format. Altogether, the consensus reflects eagerness to embrace the potential of digital health interventions, although caution is needed around the risk for these formats for over-promising and under-delivering [71].

Overall, we leveraged a well-established consensus-reaching method and engaged a diverse group of experts to obtain a comprehensive set of recommendations for the development and implementation of cognitive training and remediation interventions in the context of SUD. We used a two-tiered iterative approach involving both a steering committee and a larger pool of experts, which yielded extremely high retention rates, hence supporting the validity of our findings. The reliability of the experts' ratings across the two survey rounds was moderate to substantial, which is satisfactory in the context of consensus-formation, whereby participants are provided with overall panel agreement rates after the first round and asked to reflect upon their own responses in the context of this interim agreement during the second round. The scope of the consensus is unprecedented and our work may pave the way for a new generation of interventions in the SUD treatment arena. One limitation to address in future work is that of involvement of a broader forum of stakeholders, particularly those with lived experiences and first-line addiction clinicians. The current consensus may provide a roadmap for future participatory research involving researchers, clinicians and members of the community with lived experiences of substance use disorders, as well as their carers [72, 73]. The selected items could guide and facilitate co-production efforts that integrate the experts-based knowledge with consumers and families' goals, needs and preferences and thus contribute to development of more meaningful, tailored and feasible cognitive training and remediation interventions [74, 75]. Although cognitive training and remediation paradigms can sometimes be lengthy and repetitive, co-design approaches, together with gamification and adaptive difficulty settings for software-based tools, relating training/remediation approaches to therapeutic goals and employing trained therapists and a peer-support work-force who are skilled in building rapport and engagement may overcome feasibility challenges [76].

There are also other limitations to note, such as the modest response rates to our initial invitations (64%) which is, to some degree, expected given our unbiased approach (i.e. based on an independent systematic review) to identify a subsample of the experts. There was also substantial uncertainty (i.e. 'unsure' responses) regarding specific survey items, particularly those inquiring about the timing, frequency and duration of interventions, which highlights the need for more empirical research in this area. There was greater representation of invitees from certain geographical locations (e.g. Europe and North America over South America, Africa or Asia) and work settings (i.e. University-based versus clinic/hospital-based researchers). Although we achieved representation of the diversity of the research community in the field (regarding, for example, different career stages, locations and settings) within the Steering Committee (SC) and via the SC nominations, some aspects of our systematic review strategy, such as the non-inclusion of studies published in languages other than English or grey literature, or our selection of authors with at least two first/senior author publications in the field, may have disadvantaged representatives from developing countries and early career stages. The uneven representation of certain geographical locations such as Asia, Africa and the Middle East, as well as more broadly from

developing countries, remains a limitation that should be addressed in future studies when further developing and applying this consensus. Nonetheless, we engaged a similar number of male and female participants (45% female) and at least one representative from five continents and 13 countries, career stages and expertise (i.e. both cognitive training and rehabilitation experts included) and settings (both basic and clinical researchers and health practitioners were part of our sample) which, overall, support the diversity of our sample.

PRE-REGISTRATION

The study protocol was pre-registered on the Open Science Framework platform (<https://osf.io/xwipes/>) on 25 August 2021, prior to commencement of data collection.

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DECLARATION OF INTERESTS

A.V.-G. has received funding from Servier for consultancy work and Elsevier for editorial work and was part of the Scientific Advisory Board of Brainwell (Monclarity), which commercializes computerized cognitive training games, but has not received any honorarium or research funding from this company. E.G. has received payment for training clinicians in mindfulness and has been a consultant and licensor to BehaVR, LLC. V.M. and H.P. are Co-founders, Directors and shareholders of Cognitive Training Solutions Pty Ltd, which recently began commercializing the 'SWIPE' app, which delivers a form of cognitive bias modification. J.C.S. reports receiving research funding from Canopy Growth Corporation, DynamiCare Health, Ashley Addiction Treatment and the Cure Addiction Now Foundation. The remaining authors declare no conflicts of interest.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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