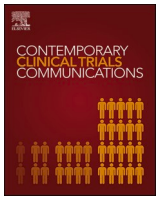
Contemporary Clinical Trials Communications 29 (2022) 100969

Contents lists available at ScienceDirect

Contemporary Clinical Trials Communications

journal homepage: www.elsevier.com/locate/conctc



Protocol for a cluster randomised crossover pilot trial of Goal Management Training^{+} (GMT^{+}) for methamphetamine use disorder

Alexandra C. Anderson [a,b,*], Alex H. Robinson [a,b], Dan I. Lubman [b,c], Antonio Verdejo-Garcia [a,b,*]

[a] School of Psychological Sciences and Turner Institute for Brain and Mental Health, Monash University, Melbourne, Victoria, Australia
[b] Monash Addiction Research Centre, Monash University, Victoria, Australia
[c] Turning Point, Eastern Health Clinical School, Monash University, Victoria, Australia

ARTICLE INFO

Keywords:
Cognitive remediation
Goal management training
Methamphetamine
Addiction
Pilot trial
Executive functions

ABSTRACT

Background: Methamphetamine use disorder (MUD) is associated with executive dysfunctions, which are linked with poorer treatment outcomes. However, current treatments for MUD do not directly address cognition. We recently modified Goal Management Training (now Goal Management Training^{+}; GMT^{+}), a group-based intervention originally designed to improve executive functions after brain injury, to enhance suitability for MUD. Here, we describe the rationale and design of a trial which aims to determine the acceptability and feasibility of GMT^{+} during residential rehabilitation for MUD, and its impact on executive functions and clinical outcomes.
Methods: We used a cluster randomised crossover design: participants are randomised at the cluster level to receive either GMT^{+} or psychoeducation-control (Brain Health Workshop; BHW). GMT^{+} is delivered in four 90-min weekly sessions and includes a between-session journal with 10-min daily activities. The program targets attention, impulse control, goal-setting, and decision-making. BHW is a health-oriented intervention that delivers information about the brain and promotes healthy exercise, diet, and sleep. It is matched to GMT^{+} on program format, length, and time with therapists. We will recruit forty-eight participants with MUD from residential treatment services. Our primary outcomes are acceptability, feasibility, and self-reported executive functioning. Secondary outcomes include craving, quality of life and cognitive performance. Outcome assessments are performed at baseline, post-interventions, 4-week follow-up, and 12-week follow-up.
Conclusions: This study will provide GMT^{+} feasibility and acceptability data and will indicate initial efficacy on executive functions and clinical outcomes in residential treatment for MUD. Information from this pilot trial will inform a powered RCT.

Providing effective treatment for methamphetamine use disorder (MUD) is becoming a critical need. Methamphetamine is a highly addictive stimulant, and the second most common illicit drug used worldwide, with approximately 27 million people using amphetamines in 2019 [1]. Methamphetamine is an important contributor to the global burden of disease and is associated with a range of harmful consequences, including physical and mental health conditions, disadvantaged social circumstances, risk of suicide, and increasing rates of unintentional death [2–6]. Underlying the core features of MUD (including loss of control over substance use and continued use despite harmful consequences) are deficits in executive functions, namely, the higher-order cognitive skills that enable goal-oriented behavior [7–9]. Executive dysfunctions have been shown to persist during early abstinence from methamphetamine, a period when people may be engaging in treatment services [10].

Executive functions encompass different skills such as working memory (or on-line updating of information), inhibition (controlled suppression of prepotent responses; impulse control), flexibility and decision-making [11,12]. Deficits in these executive functions have predicted treatment drop-out, poorer perceived quality of life, and drug relapse in people with stimulant use disorders [13–16]. However, current gold-standard treatments for MUD do not improve cognitive dysfunctions and have shown limited overall efficacy [3,17,18]. There is therefore a significant need to include interventions that train executive functions as an adjunct to standard addiction treatments. Residential rehabilitation facilities, a gold-standard treatment option, are

* Corresponding authors. Turner Institute for Brain and Mental Health, Monash University, 18 Innovation Walk, Clayton, VIC, 3800, Australia.
E-mail addresses: alexandra.anderson@monash.edu (A.C. Anderson), antonio.verdejo@monash.edu (A. Verdejo-Garcia).

https://doi.org/10.1016/j.conctc.2022.100969
Received 4 May 2022; Accepted 7 August 2022
Available online 11 August 2022

well-suited to incorporating novel adjunct interventions. This is because these treatment facilities can provide a motivated and available population, and patients can benefit from improved cognitive-executive skills to achieve their own therapeutic goals [19,20].

Goal Management Training (GMT) is a cognitive remediation program originally designed to improve executive dysfunction after brain injury [21] and has shown early promise at improving executive functions in substance use disorders [22–26]. GMT trains executive functions via strategy learning and application of meta-cognitive skills to personal goals. However, its original materials were catered to people with greater cognitive deficits and different demographics and lifestyles than people with MUD. To adapt GMT to the needs of people with MUD and treatment providers, we conducted a re-development process using input from these end-users within a co-design approach [27]. The modified program, GMT$^+$, includes four weekly modules focussing on different executive functions that are typically impaired in MUD, including attention, inhibition, goal setting (working memory), and decision-making [14,28–30].

This paper describes the protocol of a pilot trial of GMT$^+$ for MUD treatment. The primary objective is to determine whether GMT$^+$ is acceptable and feasible in the context of residential treatment for MUD, and whether it has a positive effect on executive functions, compared to psychoeducation-control. Secondary outcomes include reductions in substance use and craving, treatment retention rates, quality of life, personal goal attainment, and cognitive performance in tests of inhibition and decision-making.

1. Material and methods

This protocol is in accordance with the guidelines for Good Clinical Practice, SPIRIT, and CONSORT 2013. The interventions are described in accordance with the TIDieR checklist. This study is prospectively registered with anzctr.org.au (ACTRN12621000172808).

1.1. Trial design

This is a four-week, between-groups, single-blind (assessors) cluster-randomised crossover trial comparing GMT$^+$ versus Control in terms of acceptability and effects on executive functions. The primary outcomes are (i) acceptability, indicated by the proportion of people who withdraw consent prior to engaging in GMT$^+$ and participants ratings of the program in a purpose-designed scale, (ii) feasibility, indicated by the proportion of participants who complete four sessions of GMT$^+$, and (iii) benefit for executive functions, indicated by a validated self-report of executive functioning measured immediately after the end of interventions. We will also conduct follow-ups at four weeks and twelve weeks following the intervention to assess longevity of effects and secondary outcomes.

We selected a psychoeducation-based active comparator (Brain Health Workshop; BHW) to determine the superiority of GMT$^+$. Psychoeducation delivers informational content about the impact of substance use on the brain and body and how lifestyle choices can help to improve their health. This intervention is superficially similar to GMT$^+$ (health-focussed and enjoyable) and permits a similar format and exposure to therapists without actively training executive functioning.

1.2. Study setting

Recruitment and data collection will take place across either two or three residential addiction treatment sites in metropolitan and regional Victoria, Australia. The participating organisations are therapeutic community models of treatment, which focus on achieving positive lifestyle changes, group living, and increasing opportunities for responsibility and growth [31]. Therapeutic communities are abstinence-based approaches and individuals may detox prior or at the beginning of their treatment stay. There are between 18 and 100 people with drug and alcohol addictions residing at participating treatment sites.

1.3. Eligibility criteria

Participants must be aged between 18 and 50; meet the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) [32] criteria for MUD, measured with the Mini-International Neuropsychiatric Interview (MINI) [33]; seeking and/or engaged in addiction treatment; have sufficient English language proficiency to understand the intervention content; and be intending to stay at the treatment setting for long enough to complete the intervention (see Fig. 1). Clients will be ineligible if they meet the DSM-5 criteria for psychosis or schizophrenia; have severe cognitive impairment, indicated by a score lower than 16 on the Montreal Cognitive Assessment (MoCA) [34]; or if they are currently taking benzodiazepines.

1.4. Interventions

1.4.1. GMT$^+$

General Description. GMT$^+$ is a modified cognitive remediation program for MUD. It is delivered in a group setting and includes meta-cognitive strategies to train executive functions that are disrupted in MUD [attention, inhibition, goal setting (working memory), and decision-making] and opportunities to practice building control over these functions with in-session and between-session activities.

Approach/Active ingredients. GMT$^+$ exerts its training effect through strategy learning in session. Clients engage in experiential learning about cognitive slips (i.e., accidental errors) through in-session activities, e.g., sorting pictured postcards into incorrect piles due to inattention to specific details. Facilitators then teach specific strategies related to that executive function and clients repeat the activity with improved performance. This is further supported by character examples and discussions of real-world slips, (including substance-related slips and general functioning, e.g., within relationships or employment) and ongoing practice and reflection in the between-session journal activities. Participants make a GMT$^+$ bracelet in session 1 that is worn around their wrist as a reminder to practice GMT$^+$ skills in everyday situations, (e.g., regularly pausing to prevent impulsive responding).

Contents. GMT$^+$ includes four modules that are delivered weekly using presentation slides. Each module is dedicated to training a unique executive function. Module 1 (Be Aware) trains attention; participants are taught to notice when they start to 'zone out' or are in 'autopilot' mode and use mindfulness strategies to redirect attention back to the present moment. Module 2 (Pause) trains impulse control; participants are taught to pause regularly to maintain or regain focus on a current task and to reduce automatic emotionally driven responses. Module 3 (Envision Goals) trains goal setting and working memory; participants are taught how to check their current goals or task instructions to shield them from distractions. Module 4 (Decide) trains decision-making; participants are taught to consider future-focussed decisions and consider longer-term goals when making short-term decisions.

Participants receive a printed journal with daily activities to reflect on GMT$^+$ skills and progress towards achieving life goals. Some activities require GMT$^+$ skills during completion (four per week), and other activities are designed to help participants to reflect on the consequences of applying GMT$^+$ skills throughout the day (three per week). Materials are further described in our paper outlining the collaborative redesign [27] and may be requested for research purposes by contacting the corresponding authors.

Delivery. GMT$^+$ is a face-to-face, therapist-guided intervention, that will be delivered by doctoral students in clinical psychology, with a minimum of six years training in psychology. Groups will include between 4 and 6 participants, are delivered weekly, and run for 90 min. Peers interact throughout the group, engaging in open discussions about personal experiences with methamphetamine, cognitive slips, and their

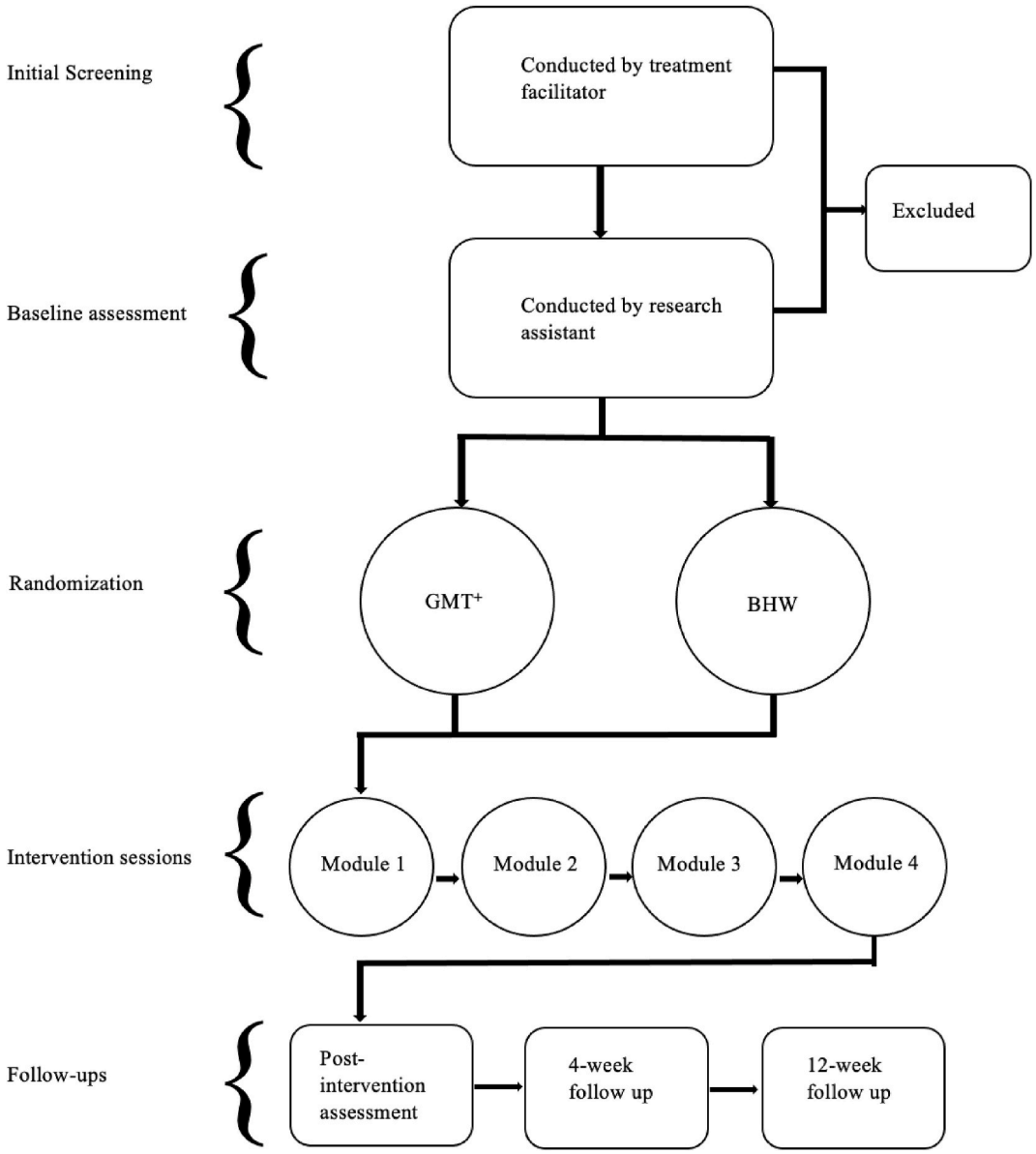


Fig. 1. Participant flow through the trial phases.

consequences. They also complete in-session activities together and share their experiences with the activities and how they might use GMT^{+} strategies to help overcome similar everyday slips.

The journal activities for each module are introduced at the end of each session. Facilitators discuss the instructions and assess participants' comprehension. The journal takes approximately 10 min per day to complete and is designed to be completed individually. However, peer discussion about the program and skills practice over the week is encouraged. Journal activities are discussed at the beginning of the next session with peers and facilitators, and further instruction or guidance is provided if required. See Supplementary Material A for attendance monitoring.

1.4.2. BHW

General Description. BHW is a manualized active control intervention that maintains a health-promotion focus. The program delivers psychoeducation material about cognitive dysfunction in MUD and healthy lifestyle choices. BHW was modelled off the control intervention employed by Levine and colleagues [21], although includes substantial changes to increase methamphetamine-related content and to enhance similarity to GMT^{+}. BHW is matched to GMT^{+} with respect to format, group discussions, time spent with facilitators, and between-session homework duration.

Approach/active ingredients. Although BHW includes information about the brain and different cognitive functions, it does not explicitly train executive function. Psychoeducation content is presented, and the group engages in discussions and hands-on activities related to the module content. Examples of BHW activities include making alphabet letters out of blocks, juggling balls, and sorting meal recipe cards from most to least healthy. Participants are not provided with cognitive strategies and the activities are not designed to evoke slips. The BHW journal includes the opportunity for participants to reflect on the benefits of healthy lifestyle changes.

Contents. As with GMT^{+}, there are four weekly modules, delivered using presentation slides. Module 1 provides basic information about brain anatomy and cognition, the impact of long-term methamphetamine use, and an introduction to neuroplasticity. Modules 2–4 provide content that is focused on healthy living. Module 2 focuses on healthy exercise, Module 3 focuses on healthy diet, and Module 4 focuses on healthy sleep. Each session includes psychoeducation content related to

the weekly topic, group-based discussions about cognition and lifestyles during methamphetamine use, suggested lifestyle changes to promote neuroplasticity (e.g., choosing a Mediterranean diet), and interactive activities.

Participants receive a printed journal to reflect on the health-related content in between sessions. Some activities are designed to reinforce psychoeducational content (e.g., identifying foods consistent with a Mediterranean diet), while other activities are designed to reflect on healthy lifestyle changes over the week (e.g., maintaining a meal diary, an exercise planner, or a sleep diary). The materials may be requested by contacting the authors.

Delivery. As with GMT^{+}, BHW is a face-to-face, therapist-guided intervention that will be delivered by clinical psychology doctoral students. It includes weekly 90-min sessions with 4–6 participants. Peers interact throughout the group, engaging in open discussions about personal experiences with methamphetamine, unhealthy lifestyle choices, and physical and cognitive health consequences. Similar to GMT^{+}, they complete in-session activities together and share their experiences with lifestyle recommendations and practices.

The journal activities are also introduced at the end of each session and facilitators provide instructions and assess comprehension. Journal completion takes approximately 10 min daily and should be completed individually, although peer discussion during the week is also encouraged. Journal activities are discussed at the beginning of the next BHW session with peers and facilitators to assess for comprehension and engagement.

Table 1
Description of secondary outcomes, characterization variables, process variables and moderators, and assessment timings.

Outcome	Measure	Description	Assessment point
Secondary Outcomes			
Inhibition	Cognitive Impulsivity Suite (CIS) [39]	The CIS includes three separate gamified tasks that capture different aspects of cognitive inhibition, including attentional control, information gathering, and feedback monitoring/shifting.	Baseline Post-intervention
Delay Discounting	Kirby 27-item Delay Discounting Task (DDT) [40]	This self-reported questionnaire presents hypothetical monetary amounts. Participants select between receiving an immediate smaller amount or a delayed larger amount. The DDT provides an indication of how sensitive individuals are to delay.	Baseline Post-intervention
Decision making	Iowa Gambling Task (IGT) [41]	A computer-based intervention that requires participants to make selections from four decks of cards with a goal of making as much game-based currency as possible. An overall net score is provided (i.e., general decision-making ability), while computational modelling can provide values of mechanisms driving each participant's behavior.	Baseline Post-intervention
	Two Staged Task (2ST) [42]	A computer-based intervention that requires participants to make two sets of choices to earn in-game rewards. These choices occur in a task structure where different environmental states link to one another. The 2ST measures two types of decision-making: model-free (retrospective and repetitive) and model-based (prospective and goal-orientated).	Baseline Post-intervention
Severity of methamphetamine dependence	Severity of Dependence Scale [43]	Five-item self-report questionnaire indicating the degree of dependence on methamphetamine.	Baseline 4-Week FU 12-Week FU
Methamphetamine use over the past month	Timeline Follow Back interview (TLFB) [44]	The TLFB captures information about the amount and frequency of methamphetamine use over the past month, providing quantitative estimates of drug use.	Baseline 4-Week FU 12-Week FU
	Hair toxicology	We will assess recent methamphetamine use and abstinence from methamphetamine using an objective biomarker of hair toxicology.	Baseline 4-Week FU 12-Week FU
Methamphetamine craving	Penn Alcohol Craving Scale (PACS) [45]	The PACS is a five-item questionnaire capturing frequency, intensity, and duration of thoughts about using methamphetamine. We used a modified version of this scale to reflect craving about methamphetamine.	Baseline 4-Week FU 12-Week FU
Treatment retention	N/A	Audit of the study database to determine the proportion of participants who are still enrolled at the treatment facility 4 weeks after the interventions.	4-Week FU
Quality of life	World Health Organization Quality of Life (WHOQOL_Bref) [46]	A 26-item measure of an individual's subjective assessment of their position in life in the context of four domains of wellbeing: psychological, social, physical, and environmental.	Baseline 4-Week FU 12-Week FU
Goal achievement	Goal Attainment Scaling (GAS) [47]	The GAS is an individualised outcome measure involving standardised goal selection and goal scaling	Post-intervention 4-Week FU
Characterization Variables			
Psychiatric disorders	Mini International Neuropsychiatric Interview [33]	Structured diagnostic interview for major DSM-5 diagnoses	Baseline
Cognitive impairment	Montreal Cognitive Assessment (MoCA version 8.3) [34]	A brief screening tool designed to capture mild cognitive impairment	Baseline
Intelligence	National Adult Reading Test [48]	A single word oral reading test with 50 irregular words that participants are not able to decipher through guess work and must therefore rely on former knowledge.	Baseline
Process Variables			
Group therapy alliance	Group Session Rating Scale [49]	Four-item visual analogue scale, capturing group therapy alliance on relationship, goals and topics, approach, and the overall fit.	At the end of each intervention session
Moderators			
Working memory	Letter-Number Sequencing Task; Wechsler Adult Intelligence Scale (4th ed; WAIS-IV) [50]	A combination of letters and numbers are presented to participants, and they are tasked to recall them in sequential order, first starting with numbers, then with letters.	Baseline Post-intervention
Trait impulsivity	UPPS-P Impulsive Behavior Scale- short version [51]	A 20-item measure of five trait aspects of impulsivity. This includes negative urgency, positive urgency, sensation seeking, (lack of) premeditation, and (lack of) perseverance.	Baseline Post-intervention

Note. Baseline assessments occur within approximately one week of the first intervention session; post-intervention assessments take place within approximately one week following intervention completion; 4-week FU and 12-week FU assessments take place 4 and 12 weeks after intervention completion.

2. Measures

2.1. Primary outcome measures

Acceptability of GMT$^+$. Acceptability of GMT$^+$, compared to BHW, will be assessed by the proportion of people who withdraw consent prior to engaging in GMT$^+$, and participants' ratings of the program on a 4-item acceptability scale [35], administered at post-intervention. Participants respond to items assessing whether they found that the program (1) improved their attention, (2) helped them to focus on their goals, (3) reduced their craving for methamphetamine, and (4) was interesting. Response options included "strongly agree", "agree", "unsure", "disagree", or "strongly disagree".

Feasibility of GMT$^+$. Feasibility of GMT$^+$ will be indicated by the proportion of participants who complete GMT$^+$, assessed by performing an audit of the study database at post-intervention. Feasibility will be demonstrated if at least 80% of the sample complete the intervention.

Executive functions. Change in executive functioning from baseline to post-intervention will be assessed with the Behavior Rating Inventory of Executive Function – Adult Version [36] (BRIEF-A). The BRIEF-A is a self-report measure capturing an adult's own perception of their executive functioning in their everyday environment. It includes 75 items and nine subscales. Participants indicate how often each item has been a problem over the past month, with response items including "never", "sometimes", and "often". The primary outcome is the Global Executive Composite, which provides an overall summary score. Higher scores indicate greater difficulty with executive functioning. The BRIEF-A has demonstrated excellent test-retest reliability (r = 0.93 to 0.94) and criterion validity in substance use populations [37,38].

2.2. Additional outcome measures

Secondary outcomes, characterization variables, process variables, and moderators are outlined in Table 1, along with the assessment timepoints. See Supplementary Material B for detailed descriptions of each measure.

2.3. Participant timeline

Only one treatment group is run at a time to avoid leakage of information between groups by participants residing at the facility. Each round of treatment delivery (or period) will last seven to eight weeks, including initial treatment and baseline assessments (week 1), delivery of interventions (weeks 2–5), post-intervention assessments (week 6) and washout period (weeks 7-8). See Table 2 for the planned testing and intervention schedule at each site. The estimated maximum recruitment time is 14 months, including treatment administration across two or three sites, and the maximum expected study duration is 18 months, accounting for follow-up assessments.

2.4. Treatment allocation

Randomisation occurs at the cluster level. Two pre-determined sequences, generated by an independent statistician, will be randomly applied to a treatment setting. Each sequence contains four treatment periods. Sequence 1 will deliver BHW (period 1), GMT$^+$ (period 2), GMT$^+$ (period 3), and BHW (period 4). Sequence 2 will deliver GMT$^+$ (period 1), BHW (period 2), BHW (period 3), and GMT$^+$ (period 4). In this design, each treatment will be delivered an equal number of times across settings and will follow itself and the alternate treatment at least once. Once the first group of participants have completed baseline assessments at the first treatment site, the setting will randomly be assigned sequence 1 or sequence 2 by a researcher who is not involved in performing assessments or delivering the treatments, and the first cluster will receive the treatment allocated to period 1 of that sequence. The second treatment setting will follow the alternative sequence. If a

Table 2
Anticipated testing and intervention schedule at each treatment site.

Week	Period 1 baseline testing	Period 1 intervention	Period 1 post-assessment and wash-out	Period 2 baseline testing	Period 2 intervention	Period 2 post-assessment and wash-out	Period 3 Baseline testing	Period 3 Intervention	Period 3 post-assessment and wash-out	Period 4 baseline testing	Period 4 intervention	Period 4 post-assessment and wash-out
	Week 1	Weeks 2–5	Weeks 6–8	Week 9	Weeks 10–13	Weeks 14–16	Week 17	Weeks 18–21	Weeks 22–24	Week 25	Weeks 26–29	Weeks 30–32
Site 1 Sequence 2	Test phase 1	GMT$^+$	Test phase 2	Test phase 1	BHW	Test phase 2	Test phase 1	BHW	Test phase 2	Test phase 1	GMT$^+$	Test phase 2
Site 2 Sequence 1	Test phase 1	BHW	Test phase 2	Test phase 1	GMT$^+$	Test phase 2	Test phase 1	GMT$^+$	Test phase 2	Test phase 1	BHW	Test phase 2
Site 3 Sequence 2	Test phase 1	GMT$^+$	Test phase 2	Test phase 1	BHW	Test phase 2	Test phase 1	BHW	Test phase 2	Test phase 1	GMT$^+$	Test phase 2

Note. Follow up assessments will be conducted off-site. Test phase 1 = baseline assessment; Test phase 2 = post-intervention assessment; GMT$^+$ = Goal Management Training$^+$; BHW = Brain Health Workshop. Site 3 will be introduced if we are not able to recruit sufficient participants who meet eligibility to be able to commence a treatment group (e.g., four eligible participants). The above intervention administration order is an example, based on Sequence 2 being randomly allocated to Site 1.

third treatment setting is required to increase participant numbers, the treatment setting will match the sequence applied at the first setting.

2.5. Procedure

The researchers facilitating the interventions (AA and AR) will inform participants about the study at each treatment setting. Once approximately six participants express interest in the trial, we will start the research protocol. Participants will provide written informed consent. Research officers, blind to intervention allocation, will then administer the baseline assessment battery (including the BRIEF-A and measures indicated in Table 1) with each participant. Once a minimum of four participants have completed the baseline assessments and meet eligibility, the treatment will commence. The interventions will be delivered over a four-week period. The research officer will then contact the treatment centre to arrange on-site post-intervention assessments, and to obtain information on treatment retention. The research officer will also contact participants to arrange follow-up assessments, which are conducted at a university or a local library. Participants may withdraw consent from the trial at any stage.

3. Analysis plan

3.1. Sample size

As we are allowing between four to six participants in each group, the target sample size was set between 32 and 48 participants (between 16 and 24 in each condition). The sample size in our pilot trial is pragmatically determined to factor in two sites (although a third site may be added to support participant numbers), four sequential groups, and a maximum of six participants in each group. The primary outcome is the BRIEF-A GEC difference between baseline and post-intervention. In a recent study, Marceau and colleagues [24] applied cognitive remediation for substance use disorder in a residential treatment context. The baseline mean GEC was 59.44 (SD = 11.19) and the covariate-adjusted, post-intervention mean was 53.07 (SD = 6.94). With consideration of pilot sample size, and assuming a similar post-intervention effect and between four and six participants in each of the eight groups, our trial has 80% power to detect treatment differences in the scenarios outlined in Table 3.

3.2. Statistical methods

Statistical analyses will be performed using the most appropriate procedures in MATLAB R2022a, R 4.1.3 and Genstat. We will follow the intention-to-treat principle in primary and secondary analyses, and include all randomised participants, irrespective of program completion or whether they were lost to follow-up. We will also complete per protocol analyses to determine any differences.

3.3. Primary outcomes

Acceptability (dimensional ratings data) and feasibility (proportion data) will be analysed using descriptive statistics, and Chi square or t-test analyses comparing the GMT$^+$ and BHW groups. We will assess change in executive functioning with linear mixed modelling. Random effects will be the treatment sites, participants within groups, and repeated assessments within participants. Fixed effects will be time (pre versus post), treatment (BHW versus GMT$^+$), their interaction, and periods (four levels, if they are aligned across sites). We will assess diagnostic plots of residuals to indicate potential departures from assumptions; in the event of violations, we may conduct analyses on transformed data. We will calculate Hedges' g effect sizes for the BRIEF-A outcome to quantify pre-post changes in GMT$^+$, compared to the control (BHW).

3.4. Research ethics approval

Monash University Human Research Ethics Committee approved this research and trial (Reference Number 12364).

4. Discussion

This will be the first study to determine whether GMT$^+$ is feasible and acceptable within MUD treatment, and whether it has a positive impact on executive functioning and clinical outcomes. Executive dysfunction is a core feature of MUD, which has been linked with earlier treatment drop out and higher rates of relapse [14,16]. By strengthening executive functions as part of standard treatment, we expect to empower people with MUD to self-regulate and better align their behavior with their long-term goals.

We anticipate that GMT$^+$ will be well tolerated by people with MUD, indicating acceptability of the intervention. GMT$^+$ has been customized to the specific needs of patients and treatment providers. We focused on enhancing the engagement of the intervention materials and in-session activities, and integrated real-world examples of personal goals that are highly salient to people with MUD. The content is also relevant to their experience in therapeutic communities (e.g., building interpersonal relationships, keeping personal responsibilities and goals at the treatment centre front of mind). Such customized approaches, where the intervention has been matched to consumers' identity and goals, have been found to enhance the feasibility of intervention implementation [52]. We also tailored the program to an appropriate difficulty level and to the relevant executive dysfunctions exhibited by people with MUD. This is important to ensure that clients are adequately challenged, yet able to demonstrate cognitive improvement [53]. This is expected to increase the likelihood of treatment completion, providing feasibility of the intervention.

We expect that participants with MUD who are enrolled in GMT$^+$ will show a greater overall improvement in executive functions than those enrolled in BHW. Although BHW is an active control intervention that is superficially similar to GMT$^+$, it does not include active 'training' ingredients to enhance awareness of cognitive errors or provide strategies to build executive control. Psychoeducation around healthy brain functioning, and the benefits of sleep, diet, and exercise also feature in existing treatment programs which have limited efficacy [3]. We have

Table 3
BRIEF-A effect size estimates for groups of four or six participants.

Number of subjects per group	Pre-expo mean (all groups)	Post-expo mean BHW (A)	Post-expo mean GMT$^+$ (B)	*SD* Sites	*SD* Groups	*SD* Participants	*SD* Obs	*SD* Total	*ICC* Groups	*ICC* Participants	Effect Size
6	59.5	57.5	53.43	2.23	2.45	11.00	3.47	12.00	0.453	0.047	−0.339
4	59.5	57.5	52.44	2.23	2.45	11.00	3.47	12.00	0.453	0.047	−0.422
4	59.5	57.5	53.43	2.23	2.45	9.25	2.80	10.22	0.453	0.066	−0.398

SD Total = the square root of the sum of the squared SDs for sites, groups within sties, subjects within groups and observations within subjects. ICC groups = Variance of Sites/(Variance of Sites + Variance of Groups). ICC subjects = Variance of Groups/(Variance of Groups + Variance of Subjects). Effect Size = Difference in post-exposure means/(SD Total). Power calculations for each scenario are based on 5000 simulations, a REML analysis of each simulated trial and calculation of the t-test for the treatment by time interaction contrast.

already seen preliminary evidence of the benefit of GMT on areas of executive functioning in earlier trials in substance use disorders [22,25], and the program has been further tailored to target the cognitive difficulties associated with MUD (i.e., attention problems, poor inhibition or difficulty controlling impulses, difficulty shielding goals from distractions, and preferencing short-term over long-term decisions) [9,29,54].

5. Strengths and limitations

There are several strengths to our trial protocol. We have tailored the intervention to the specific needs of MUD and have an initial indication of acceptability, based on qualitative feedback from people with MUD and treatment providers during the intervention redevelopment stage [27]. We are employing an active control intervention, comparable to GMT^{+} in time spent with facilitators, group-based format, and in the number and style of in-session group activities and between session journal activities. This will permit us to determine whether the specific ingredients of GMT^{+} are relatively more effective than the comparator treatment [55]. Further, the trial is being conducted across multiple treatment centres which will enhance representativeness of different treatment contexts across sites.

Our eligibility criteria are intentionally inclusive to mirror real-world presentations. We allow for depressive and anxiety disorders and have only ruled out disorders linked to severe neurocognitive impairment, including schizophrenia, psychosis, and intellectual disability, as individuals may not benefit from executive function training given deficits in more basic skills [56–58]. There is also strength in the selected outcomes in this study. Our primary outcome of change in executive functioning uses a measure that reflects behavior in everyday environments, which is ideal to detect relevant and real-world changes resulting from the intervention. Further, we have selected a range of purposeful cognitive measure to be able to assess underlying mechanisms that may contribute to improved impulse control, decision making and treatment outcomes.

There are also some limitations and practical considerations likely to arise during this trial. This trial is operating during the COVID-19 pandemic in Australia and will likely be faced with ongoing public health and safety measures, including brief or extended lockdown periods. This may result in necessary changes to how the trial is delivered, including the implementation of online assessments and intervention sessions, or unexpected delays if treatment centres elect to suspend research activities. COVID-19 safety protocols will be implemented to mitigate risk. Any changes to the research protocol and clinical procedures will be carefully documented throughout the trial.

Participants are recruited on the basis that they provide an intention to attend four intervention sessions. In some cases, sessions may be missed due to illness or requirements of the treatment centre (for example, attending an essential appointment, or being temporarily removed from group activities due to inappropriate conduct). In such situations, we will provide participants with a brief recap of missed content at the subsequent session they attend and will encourage further discussion with co-clients in their treatment group to catch up. It is not possible to provide individual catch up sessions due to the group nature of the program and logistical constraints of finding a suitable time for the treatment centre, facilitators, and the participant.

Treatment drop-out is another challenge that is expected [59,60]. However, a secondary aim of this study is to address whether the anticipated improvement in executive functioning in the GMT^{+} group is associated with improved outcomes, including longer treatment retention. As people with MUD are frequently lost to follow-up assessments in clinical trials (up to 50%) [61], we anticipate this as a limitation to achieving 4- and 12-week follow-up outcomes. We have attempted to reduce contact barriers by collecting primary and secondary contact details. Attendance barriers are minimized by offering to meet participants at a library close to their residential location and by communicating positive regard and acceptance of the participant's engagement in follow-up assessments if treatment goals were not achieved or sustained (e.g., returning to methamphetamine use).

6. Conclusions

This trial will determine whether GMT^{+} is acceptable and feasible as an add-on intervention during residential treatment for MUD and provide preliminary evidence for the effectiveness of GMT^{+} at improving executive functions and clinical outcomes. Although GMT has demonstrated initial promise at improving executive functions in stimulant use disorder, this is the first trial to test the benefits of the revised intervention (GMT^{+}) and in people with MUD. If GMT^{+} is found to be beneficial, it may present as an ideal adjunct intervention to administer in addiction treatment settings, as it could be administered by the existing treatment workforce after appropriate training. If the results of this pilot trial are favourable, the data will be used to inform a fully powered randomised controlled trial.

Author contributions

AA and AVG take responsibility for the integrity of all aspects of the manuscript. Study concept and design: AVG and DL (lead), AA and AR (supporting). Reviewing the study concept and protocols: All authors. Drafting of the manuscript: AA. Critical revision of the manuscript for important intellectual content: All authors.

Funding

This study was funded by The National Centre for Clinical Research on Emerging Drugs Research Seed Funding Grant (NCR3SF10). AA and AR are funded by the Australian Government Research Training Program. DL is supported by an NHMRC Investigator grant (1196892). AVG is supported by a Medical Research Future Fund, Next Generation of Clinical Researchers CDF2 Fellowship (MRF1141214).

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

AVG has received funding from Servier for consultancy work and Elsevier for editorial work. No pharmaceutical grants were received in the development of this study. DL has provided consultancy advice to Lundbeck and Indivior, and has received travel support and speaker honoraria from Camurus, Indivior, Janssen, Lundbeck, Shire, and Servier. These organisations do not stand to benefit from this project. DL has been an investigator on an untied education grant from Sequirus, as well as an investigator-led grant from Camurus, both unrelated to the current work.

Acknowledgments

The authors would like to thank Associate Professor John Reynolds for assistance provided with the simulation-based sample size calculation.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.conctc.2022.100969.

References

[1] United Nations Office on Drugs and Crime, World Drug Report 2021, 2021. New York, United Nations.
[2] S. Darke, S. Kaye, R. McKetin, J. Duflou, Major physical and psychological harms of methamphetamine use, Drug Alcohol Rev. 27 (3) (2008 May) 253–262.

[3] M. Farrell, N.K. Martin, E. Stockings, A. Bórquez, J.A. Cepeda, L. Degenhardt, et al., Responding to global stimulant use: challenges and opportunities, Lancet 394 (2019) 1652–1667.

[4] R.J. Tait, S. Whetton, M. Shanahan, K. Cartwright, A. Ferrante, D. Gray, et al., Quantifying the societal cost of methamphetamine use to Australia, Int. J. Drug Pol. 62 (2018 Dec 1) 30–36.

[5] S. Darke, S. Kaye, J. Duflou, Methamphetamine-related death is an under-addressed public health problem, Addiction 112 (12) (2017) 2204–2205.

[6] B. Han, W.M. Compton, C.M. Jones, E.B. Einstein, N.D. Volkow, Methamphetamine use, methamphetamine use disorder, and associated overdose deaths among US adults, JAMA Psychiatr. 78 (12) (2021 Sep 22) 1329–1342. https://jamanetwork.com/journals/jamapsychiatry/fullarticle/2784468.

[7] N.P. Friedman, A. Miyake, L.J. Altamirano, R.P. Corley, S.E. Young, S.A. Rhea, et al., Stability and change in executive function abilities from late adolescence to early adulthood: a longitudinal twin study, Dev. Psychol. 52 (2) (2016 Feb 1) 326–340.

[8] R.Z. Goldstein, N.D. Volkow, Dysfunction of the prefrontal cortex in addiction: neuroimaging findings and clinical implications, Nat. Rev. Neurosci. 12 (2011) 652–669.

[9] S. Sabrini, G.Y. Wang, J.C. Lin, J.K. Ian, L.E. Curley, Methamphetamine use and cognitive function: a systematic review of neuroimaging research, Drug Alcohol Depend. 194 (2019) 75–87.

[10] S.L. Simon, A.C. Dean, X. Cordova, J.R. Monterosso, E.D. London, Methamphetamine dependence and neuropsychological functioning: evaluating change during early abstinence, J. Stud. Alcohol Drugs 71 (3) (2010) 335–344.

[11] A. Miyake, N.P. Friedman, M.J. Emerson, A.H. Witzki, A. Howerter, T.D. Wager, The unity and diversity of executive functions and their contributions to complex "frontal lobe" tasks: a latent variable analysis, Cognit. Psychol. 41 (1) (2000 Aug 1) 49–100.

[12] A. Verdejo-García, M. Pérez-García, Profile of executive deficits in cocaine and heroin polysubstance users: common and differential effects on separate executive components, Psychopharmacology (Berl) 190 (4) (2007 Mar 29) 517–530.

[13] E.M. Barreno, S. Domínguez-Salas, C. Díaz-Batanero, Ó.M. Lozano, J.A.L. Marín, A. Verdejo-García, Specific aspects of cognitive impulsivity are longitudinally associated with lower treatment retention and greater relapse in therapeutic community treatment, J. Subst. Abuse Treat. 96 (2019 Jan 1) 33–38.

[14] S. Domínguez-Salas, C. Díaz-Batanero, O.M. Lozano-Rojas, A. Verdejo-García, Impact of general cognition and executive function deficits on addiction treatment outcomes: systematic review and discussion of neurocognitive pathways, Neurosci. Biobehav. Rev. 71 (2016) 772–801.

[15] A.J. Rubenis, R.E. Fitzpatrick, D.I. Lubman, A. Verdejo-Garcia, Impulsivity predicts poorer improvement in quality of life during early treatment for people with methamphetamine dependence, Addiction 113 (4) (2018 Apr) 668–676.

[16] L. Stevens, A. Verdejo-García, A.E. Goudriaan, H. Roeyers, G. Dom, W. Vanderplasschen, Impulsivity as a vulnerability factor for poor addiction treatment outcomes: a review of neurocognitive findings among individuals with substance use disorders, J. Subst. Abuse Treat. 47 (1) (2014) 58–72.

[17] M.P. Paulus, J.L. Sewart, Neurobiology, clinical presentation, and treatment of methamphetamine use disorder: a review, JAMA Psychiatr. 77 (9) (2020) 959–966.

[18] M.-L. Brecht, D. Herbeck, Time to relapse following treatment for methamphetamine use: a long-term perspective on patterns and predictors, Drug Alcohol Depend. 139 (2014) 18–25.

[19] C. Eberl, R.W. Wiers, S. Pawelczack, M. Rinck, E.S. Becker, J. Lindenmeyer, Approach bias modification in alcohol dependence: do clinical effects replicate and for whom does it work best? Dev Cogn Neurosci 4 (2013 Apr 1) 38–51.

[20] R.W. Wiers, Cognitive training in addiction: does it have clinical potential? Biol. Psychiatry. Cogn. Neurosci. Neuroimaging 3 (2) (2018) 101–102.

[21] B. Levine, T.A. Schweizer, C. O'Connor, G. Turner, S. Gillingham, D.T. Stuss, et al., Rehabilitation of executive functioning in patients with frontal lobe brain damage with Goal Management Training, Front. Hum. Neurosci. 5 (2011). Available from: http://journal.frontiersin.org/article/10.3389/fnhum.2011.00009/abstract.

[22] J.P. Alfonso, A. Caracuel, L.C. Delgado-Pastor, A. Verdejo-García, Combined goal management training and mindfulness meditation improve executive functions and decision-making performance in abstinent polysubstance abusers, Drug Alcohol Depend. 117 (1) (2011) 78–81.

[23] K.B. Casaletto, D.J. Moore, S.P. Woods, A. Umlauf, J.C. Scott, R.K. Heaton, Abbreviated Goal Management Training shows preliminary evidence as a neurorehabilitation tool for HIV-associated neurocognitive disorders among substance users, Clin. Neuropsychol. 30 (1) (2016 Jan 2) 107–130.

[24] E.M. Marceau, J. Berry, J. Lunn, P.J. Kelly, N. Solowij, Cognitive remediation improves executive functions, self-regulation and quality of life in residents of a substance use disorder therapeutic community, Drug Alcohol Depend. 178 (2017 Sep) 150–158.

[25] C. Valls-Serrano, A. Caracuel, A. Verdejo-Garcia, Goal Management Training and Mindfulness Meditation improve executive functions and transfer to ecological tasks of daily life in polysubstance users enrolled in therapeutic community treatment, Drug Alcohol Depend. 165 (2016) 9–14.

[26] A.C. Anderson, G.J. Youssef, A.H. Robinson, D.I. Lubman, A. Verdejo-Garcia, Cognitive boosting interventions for impulsivity in addiction: a systematic review and meta-analysis of cognitive training, remediation and pharmacological enhancement, Addiction 116 (12) (2021 Dec 1) 3304–3319.

[27] A.C. Anderson, A.H. Robinson, E. Potter, B. Kerley, D. Flynn, D.I. Lubman, A. Verdejo-Garcia, Development of Goal Management Training+ for methamphetamine use disorder through collaborative design, Front. Psychiatr. 13 (2022), 876018, https://doi.org/10.3389/fpsyt.2022.876018.

[28] N.R. Moallem, K.E. Courtney, L.A. Ray, The relationship between impulsivity and methamphetamine use severity in a community sample, Drug Alcohol Depend. 187 (2018) 1–7.

[29] S. Potvin, J. Pelletier, S. Grot, C. Hébert, A. Barr, T. Lecomte, Cognitive deficits in individuals with methamphetamine use disorder: a meta-analysis, Addict. Behav. 80 (2018 May 1) 154–160.

[30] H. Mizoguchi, K. Yamada, Methamphetamine use causes cognitive impairment and altered decision-making, Neurochem. Int. 124 (2019 Mar 1) 106–113.

[31] What are therapeutic communities?, National Institute on Drug Abuse (NIDA) [Internet]. [cited 2022 Mar 28]. Available from: https://nida.nih.gov/publications/research-reports/therapeutic-communities/what-are-therapeutic-communities.

[32] American Psychiatric Association (APA), Diagnostic and Statistical Manual of Mental Disorders: DSM-5, DSM-V, fifth ed., 2013. org.db29.linccweb.org/10.1176/appi.

[33] D.V. Sheehan, Y. Lecrubier, K.H. Sheehan, P. Amorim, J. Janavs, E. Weiller, T. Hergueta, R. Baker, G.C. Dunbar, The Mini-International Neuropsychiatric Interview (M.I.N.I): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10, J. Clin. Psychiatr. 59 (Suppl. 20) (1998) 22–33.

[34] Z.S. Nasreddine, N.A. Phillips, V. Bédirian, S. Charbonneau, V. Whitehead, I. Collin, et al., The montreal cognitive assessment, MoCA: a brief screening tool for mild cognitive impairment, J. Am. Geriatr. Soc. 53 (4) (2005 Apr 1) 695–699.

[35] V. Manning, J.B.B. Garfield, K. Mroz, S.C. Campbell, H. Piercy, P.K. Staiger, et al., Feasibility and acceptability of approach bias modification during methamphetamine withdrawal and related methamphetamine use outcomes, J. Subst. Abuse Treat. 106 (2019 Nov 1) 12–18.

[36] R.M. Roth, G.A. Gioia, P.K. Isquith, BRIEF-A: Behavior Rating Inventory of Executive Function-Aadult Version, Psychological Assessment Resources, 2005.

[37] R.M. Roth, C.E. Lance, P.K. Isquith, A.S. Fischer, P.R. Giancola, Confirmatory factor analysis of the Behavior Rating Inventory of Executive Function-Adult Version in healthy adults and application to attention-deficit/hyperactivity disorder, Arch. Clin. Neuropsychol. 28 (5) (2013 Aug 1) 425–434.

[38] E. Hagen, A.H. Erga, K.P. Hagen, S.M. Nesvåg, J.R. McKay, A.J. Lundervold, et al., Assessment of executive function in patients with substance use disorder: a comparison of inventory- and performance-based assessment, J. Subst. Abuse Treat. 66 (2016 Jul 1) 1–8.

[39] A. Verdejo-Garcia, J. Tiego, N. Kakoschke, N. Moskovsky, K. Voigt, A. Anderson, et al., A unified online test battery for cognitive impulsivity reveals relationships with real-world impulsive behaviours, Nat. Human Behav. 5 (11) (2021 May 27) 1562–1577.

[40] K.N. Kirby, N.N. Maraković, Delay-discounting probabilistic rewards: rates decrease as amounts increase, Psychon. Bull. Rev. 3 (1) (1996) 100–104.

[41] A. Bechara, S. Dolan, N. Denburg, A. Hindes, S.W. Anderson, P.E. Nathan, Decision-making deficits, linked to a dysfunctional ventromedial prefrontal cortex, revealed in alcohol and stimulant abusers, Neuropsychologia 39 (4) (2001) 376–389, https://doi.org/10.1016/S0028-3932(00)00136-6.

[42] N.D. Daw, S.J. Gershman, B. Seymour, P. Dayan, R.J. Dolan, Model-based influences on humans' choices and striatal prediction errors, Neuron 69 (6) (2011) 1204–1215, https://doi.org/10.1016/j.neuron.2011.02.027.

[43] M. Gossop, S. Darke, P. Griffiths, J. Hando, B. Powis, W. Hall, et al., The Severity of Dependence Scale (SDS): psychometric properties of the SDS in English and Australian samples of heroin, cocaine and amphetamine users, Addiction 90 (5) (1995 May 1) 607–614.

[44] L.C. Sobell, M.B. Sobell, Timeline Follow back User's Guide: A Calendar Method for Assessing Alcohol and Drug Use, Addiction Research Foundation, Toronto, 1996.

[45] B.A. Flannery, J.R. Volpicelli, H.M. Pettinati, Psychometric properties of the penn alcohol craving scale. Vol. 23, Alcohol Clin. Exp. Res. 23 (1999) 1289–1295.

[46] B. Murphy, H. Herman, G. Hawthorne, T. Pinzone, H. Evert, Australian WHO QOL Instruments: User's Manual and Interpretation Guide, Australian WHO QOL Field Study Centre, Melbourne, Australia, 2000.

[47] L. Turner-Stokes, Goal attainment scaling (GAS) in rehabilitation: a practical guide, Clin. Rehabil. 23 (4) (2009 Jan 29) 362–370.

[48] P. Bright, E. Hale, V.J. Gooch, T. Myhill, I. van der Linde, The national adult reading test: restandardisation against the wechsler adult intelligence, Scale—Fourth edition 28 (6) (2016 Sep 1) 1019–1027.

[49] K. Quirk, S. Miller, B. Duncan, J. Owen, Group Session Rating Scale: preliminary psychometrics in substance abuse group interventions, Counsell. Psychother. Res. J. 13 (3) (2013) 194–200.

[50] D. Wechsler, Wechsler Adult Intelligence Scale, fourth ed., Pearson, Sydney, Australia, 2008.

[51] M.A. Cyders, A.K. Littlefield, S. Coffey, K.A. Karyadi, Examination of a short English version of the UPPS-P impulsive behavior scale, Addict. Behav. 39 (9) (2014 Sep 1) 1372–1376.

[52] L. Yardley, L. Morrison, K. Bradbury, I. Muller, The person-based approach to intervention development: application to digital health-related behavior change interventions, J. Med. Internet Res. 17 (1) (2015 Jan 1) e30.

[53] A. Medalia, T. Herlands, A. Saperstein, N. Revheim, Treatment planning, in: A. Medalia, T. Herlands, A. Saperstein, A. Revheim (Eds.), Cognitive Remediation for Psychological Disorders: Therapists Guide, Oxford University Press, 2017, https://doi.org/10.1093/med-psych/9780190608453.003.0006.

[54] R.E. Fitzpatrick, A.J. Rubenis, D.I. Lubman, A. Verdejo-Garcia, Cognitive deficits in methamphetamine addiction: independent contributions of dependence and intelligence, Drug Alcohol Depend. 209 (2020 Apr 1), 107891.

[55] P. Karlsson, A. Bergmark, Compared with what? An analysis of control-group types in Cochrane and Campbell reviews of psychosocial treatment efficacy with substance use disorders, Addiction 110 (3) (2015 Mar 1) 420–428.

[56] E.A. Demetriou, C.Y. Song, S.H. Park, K.L. Pepper, S.L. Naismith, D.F. Hermens, et al., Autism, Early Psychosis, and Social Anxiety Disorder: a transdiagnostic examination of executive function cognitive circuitry and contribution to disability, Transl. Psychiatry 8 (1) (2018 Sep 24) 1–10.
[57] M.L. Thai, A.K. Andreassen, V. Bliksted, A meta-analysis of executive dysfunction in patients with schizophrenia: different degree of impairment in the ecological subdomains of the Behavioural Assessment of the Dysexecutive Syndrome, Psychiatr. Res. 272 (2019 Feb 1) 230–236.
[58] M. Spaniol, H. Danielsson, A meta-analysis of the executive function components inhibition, shifting, and attention in intellectual disabilities, J. Intellect. Disabil. Res. 66 (1–2) (2022 Jan 1) 9–31.
[59] J. Grigg, V. Manning, S. Arunogiri, et al., Methamphetamine Treatment Guidelines: Practice Guidelines for Health Professionals, second ed., Turning Point, Richmond, Victoria, 2018.
[60] S.N. Lappan, A.W. Brown, P.S. Hendricks, Dropout rates of in-person psychosocial substance use disorder treatments: a systematic review and meta-analysis, Addiction 115 (2) (2020 Feb 1) 201–217.
[61] R. Cook, B. Quinn, K. Heinzerling, S. Shoptaw, Dropout in clinical trials of pharmacological treatment for methamphetamine dependence: the role of initial abstinence, Addiction 112 (6) (2017 Jun 1) 1077–1085.