Combining approach bias modification with working memory training during inpatient alcohol withdrawal: an open-label pilot trial of feasibility and acceptability

Victoria Manning[1,2]*, Katherine Mroz[1,2], Joshua B. B. Garfield[1,2], Petra K. Staiger[3,4], Kate Hall[3,4], Dan I. Lubman[1,2] and Antonio Verdejo-Garcia[5]

Abstract

Background: According to contemporary neurocognitive models, addiction is maintained by the biasing of information-processing and decision-making systems towards relatively automatic, impulsive, reward-seeking responses to drug-related stimuli, and away from more controlled, deliberative, "reflective" states of processing that could result in decisions to delay or avoid drug use. Cognitive training programs aimed at either countering "impulsive" processing or enhancing "reflective" processing alone have shown promise. However, there has been no attempt to simultaneously target both aspects of processing with a combined training program. We aimed to test the feasibility and acceptability of a novel 'dual-training' program targeting both processes during residential alcohol withdrawal, and to measure abstinence rates following discharge.

Methods: Thirty-seven patients undergoing alcohol withdrawal at a residential unit participated in this open-label pilot feasibility study. We tested a 4-session program of dual cognitive training targeting both impulsive (approach bias) and reflective (working memory) aspects of processing. Descriptive statistics were used to examine feasibility (training uptake and completion rates) and acceptability (withdrawal from the study; participants' ratings of the tasks). Alcohol abstinence rates were examined 2-weeks post-discharge.

Results: Seven participants withdrew after commencing training. Twenty-six (70%) completed the 4-session training protocol, and four completed 3 sessions before discharging. Among participants who provided ratings, nearly all (93%) rated the training as interesting. Most (87%) indicated that they felt it had improved their attention. However, most did not feel it had decreased their craving for alcohol. At 2-weeks post-discharge, 16 (53%) participants reported abstaining from alcohol. For comparison, an earlier pilot trial in the same setting found a 68% abstinence rate with approach bias training alone, and 47% abstinence in a non-training control group.

Conclusions: Dual training during residential alcohol detoxification appears to be both acceptable and feasible, suggesting that future research is warranted to test its effectiveness at reducing likelihood of relapse.

Keywords: Alcohol use disorder, Working memory, Approach bias, Cognitive bias, Cognitive training, Detoxification, Withdrawal

* Correspondence: Victoria.Manning@monash.edu
[1]Monash Addiction Research Centre and Eastern Health Clinical School, Monash University, 110 Church Street, Richmond, Victoria 3121, Australia
[2]Turning Point, Eastern Health, 110 Church Street, Richmond, Victoria 3121, Australia
Full list of author information is available at the end of the article

Background

Contemporary neurocognitive models suggest that in alcohol use disorder (AUD), information-processing and decision-making are biased towards relatively automatic, implicit processes which drive initial approach tendencies [1, 2]. According to these models, normative information processing involves a series of iterations which progressively allow more associations and contextual information to be activated, enabling evaluation and response selection to move from more automatic to more reflective styles. In AUD, however, rapidly-activated, automatic impulses become sensitised to alcohol-related stimuli, resulting in strong activation of alcohol-approach tendencies, (i.e. approach bias [3, 4]), before more reflective processing styles are engaged. The ability to engage reflective processing may be further undermined by the neurocognitive deficits that are common among people with AUD [5, 6]. Increased approach bias has been found to have cross-sectional associations with increased hazardous drinking [7, 8], and to prospectively predict increased drinking after treatment in problem drinkers seeking to reduce their drinking [9], although one study found the opposite effect (lower approach bias predicting relapse) [10]. Importantly, however, approach bias can be reduced in alcohol dependent individuals through computerised approach bias modification (ABM) training, which has been shown to lead to reduced relapse rates [11–14]. Indeed, a recent systematic review suggests that ABM is effective in reducing a range of addictive behaviours [15], including alcohol use when applied as an adjunctive approach for individuals with AUDs [16].

Impairment in working memory, which refers to the ability to maintain and manipulate goal-relevant information, and which is thus implicated in reflective control [17], is one of the neurocognitive deficits most commonly observed among people with AUD [5, 6]. Such WM deficits make it harder to implement strategies to circumvent habitual behaviours, such as impulsive alcohol-approach tendencies, and can therefore hamper treatment outcomes [18]. Research has shown poorer WM among individuals with higher alcohol approach bias [19]. Cognitive training designed to improve WM capacity has shown promising results, including improved performance on WM tasks [20], reductions in delay discounting (the tendency to prioritise immediate small rewards over larger, delayed rewards) [21], and reductions in heavy drinking, particularly among individuals with high approach bias [22]. Therefore, strategies that both dampen approach bias and strengthen WM could improve treatment outcomes, yet to date this has not been explored, despite the fact that both ABM and WM training are low-cost, non-invasive, easy-to-administer interventions.

Treatment for AUD often commences with inpatient detoxification. Research has shown that the initial weeks of abstinence are a period of neuroplasticity and neural reorganisation [23–25], making this a potentially opportune time to modify neurocognitive processes. However, if detoxification is not followed by post-withdrawal treatment, around 85% of patients relapse [26]. Early relapse prevents subsequent engagement in post-withdrawal treatment. This highlights the importance of examining adjunctive interventions during residential withdrawal to prevent rapid relapse and increase the chance of ongoing post-withdrawal treatment engagement.

Our pilot study of a 4-session course of ABM during detoxification significantly reduced rates of early relapse relative to a control condition [12]. We expected that adding WM training to ABM ("dual-training") would increase abstinence rates even further. Nevertheless, before executing costly randomised controlled trials, it is important to establish whether dual-training is acceptable and feasible (e.g., tolerated and completed) during detoxification treatment. The aim of the current pilot study was to examine the feasibility and acceptability of a novel computerised 'dual-training' program combining ABM and WM training during inpatient withdrawal, and examine rates of abstinence at 2-week follow-up relative to those observed in our earlier study with ABM-alone or sham-training.

Methods

Design and setting

We conducted an open-label single-group feasibility study in a residential alcohol and other drug withdrawal unit in the Melbourne metropolitan area. We aimed to measure outcomes related to feasibility (rate of uptake, rates of training completion) and acceptability (rate of withdrawal of consent to participate, participants' ratings of the training tasks). We also conducted a 2-week follow-up to assess alcohol use following discharge from withdrawal treatment.

Participants

Inpatients undergoing alcohol withdrawal were assessed for eligibility in consultation with nursing staff. Those deemed eligible ($N = 42$) were approached on the fourth day of detoxification. Forty-one provided consent, of whom 37 commenced training (as shown in Fig. 1). Inclusion criteria were: alcohol as the primary drug of concern; aged 18–60 years; able to understand English; and weekly or more alcohol use in the past month. Exclusion criteria were: a diagnosed intellectual disorder; neurological illness; traumatic brain injury with loss of consciousness exceeding 30 minutes; or current psychotic episode (as assessed by clinical staff).

Fig. 1 Recruitment and participant flow diagram
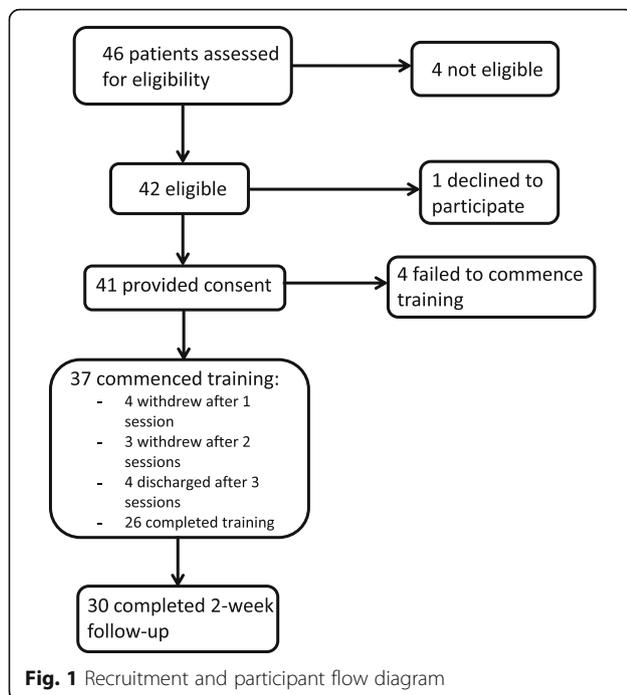
Materials
Alcohol use
Participants' alcohol use was measured using the Time-line Follow-back (TLFB) interview method [27]. At the baseline interview, participants were asked to recall their alcohol consumption in the 30 days prior to admission. At the 2-week follow-up, the TLFB was conducted via telephone interview, covering the 14 days following discharge from detoxification.

Acceptability
Acceptability of the dual-training program was informed by a three-item measure administered after completing training. Items were 'I found the task improved my attention', 'I found the task decreased my craving for alcohol' and 'I found the task interesting', with response options of 'Strongly Agree', 'Agree', 'Unsure', 'Disagree', and 'Strongly Disagree'.

Alcohol craving
The Alcohol Craving Questionnaire – Short Form – Revised (ACQ-SF-R) [28] was administered before participants commenced the first session of training and after their final session of training. Scores on the ACQ-SF-R can range from 1 to 7, with higher scores indicating stronger cravings.

Severity of alcohol dependence
The Severity of Alcohol Dependence Questionnaire community sample version (SADQ-C) [29] was used to measure symptoms of physical dependence on alcohol. Scores on the SADQ-C can range from 0 to 60, with higher scores indicating greater severity of dependence. A score of 16–30 is believed to indicate moderate dependence and a score over 30 indicates severe dependence.

Interventions
Approach Bias Modification Training (ABM)
We used a training version of the Alcohol Approach -Avoidance Task [14] implemented with E-Prime 2.0 software. Participants were instructed to pull a joystick in response to pictures in a horizontal (landscape) orientation, and push a joystick in response to pictures in a vertical (portrait) orientation. Pulling the joystick caused the image to expand on the screen, making the image seem to move "towards" the participant. Pushing the joystick caused the image to shrink, making it appear to recede into the distance. Images of 40 alcoholic and 40 non-alcoholic beverages commonly available in Australia were used, with each image appearing 3 times per session (i.e. 240 trials per session). Landscape-oriented pictures always contained images of alcoholic beverages. Portrait-oriented images always contained pictures of non-alcoholic beverages. Each session lasted approximately 15 min.

Working memory training
Participants completed five WM tasks each day, administered through the training application 'Brainwell', a program created by Monclarity LLC [30]. Prior to commencing the first training session, participants completed a cognitive 'fitness test' involving three 60-s tests of memory, attention, and problem solving, to calibrate initial difficulty to their level of functioning. The training tasks were gamified and adaptive, increasing and decreasing in difficulty in real-time depending on performance. Similar to facets of WM targeted by other training studies, [21, 22, 31] the tasks aimed to strengthen monitoring and updating abilities, spatial span, memory capacity, and visuo-spatial WM. The 10-trial spatial span task and the 5-trial monitoring and updating task each took approximately 5 min. The remaining 3 tasks (one memory capacity task and two visuo-spatial WM) each required participants to complete as many trials as possible in a 3-min period.

Procedure
A researcher conducted sessions in a private room inside the detoxification unit. Baseline assessment and the first training session occurred on day four of detoxification. Participants completed a demographic information form, followed by the TLFB. Participants then commenced. Daily training sessions continued on the following 3

Manning *et al. Substance Abuse Treatment, Prevention, and Policy* (2019) 14:24

Page 4 of 6

days, with the fourth and final session occurring on day 7 of detoxification. Each session involved WM training followed by ABM. The fourth session of training was followed by the acceptability questionnaire. Acceptability was also indexed by the number of participants who withdrew consent to participate after commencing training. Feasibility of the intervention was indexed by the rate of uptake and the rate of completion of the 4-session protocol. Two weeks following discharge, alcohol use was assessed in a telephone interview.

Statistical analyses

Descriptive statistics were generated using IBM SPSS version 25.

Results

Participants' baseline characteristics are shown in Table 1.

Feasibility

Of 42 patients invited to participate, only 1 patient declined participation and 37 of the 41 (90%) who agreed to participate commenced training. Of these 37 participants, 26 (70%) completed all 4 sessions of training. Four participants completed only 1 session, three completed 2 sessions, and four completed 3 sessions. These rates of uptake and completion suggest good feasibility of delivering dual training during detoxification.

Acceptability

Seven (18%) of the 37 participants who commenced training withdrew consent prior to completing training. Task ratings from the 30 participants who did not withdraw, shown in Table 2, indicated that a large majority found the tasks interesting (93% either 'strongly agreed' or 'agreed') and felt they improved their attention (87% either 'strongly agreed' or 'agreed'). This suggests that training was acceptable to a large majority of participants. However, the majority (53%) were 'unsure' if the training reduced their alcohol craving. Nevertheless, ACQ-SF-R scores revealed that there was a small but significant reduction in alcohol craving between the first (mean = 3.7) and final sessions (mean = 3.0) of training (t (29) = 3.788, p < .001).

Alcohol abstinence

Of the 30 participants who completed the 2-week follow-up, 16 (53%; 95% CI: 36–70%) reported abstaining from alcohol in the 14-days following discharge. Nonetheless, this was only slightly (6%) higher than we observed with sham-training in our previous pilot of ABM alone [12].

Discussion

The study findings suggest that engaging patients in computerised WM and ABM training during residential alcohol withdrawal treatment is feasible. Most participants found dual training to be acceptable, rating it as interesting and helpful in terms of perceived improved attention. The two-week abstinence rate was similar to what we previously observed following no ('sham') training in our earlier study [12] and lower than we observed with ABM alone (absent WM training). However, it is important to note that this was a feasibility study which was not powered to examine effectiveness, and the estimated abstinence rate may lack precision due

Table 1 Participants Characteristics

	M/n	SD/%
Age (M years /SD)	42.7	8.9
Gender (n/% female)	17	46
Born in Australia (n/%)	32	89
Any post-secondary education (n/%)	22	59
Receiving unemployment or disability support benefits (n/%)	17	46
Relationship status (n/% single)	21	57
Any psychiatric comorbidity[b] (n/%)	32	87
Family history of AUD (n/%)	24	65
Total drinking days in past month (M/SD)	27.2	5.4
Standard drinks[a] in the past month (M/SD)	497.0	263.3
SADQ-C score (M/SD)	28.6	12.5
Anti-craving medications at admission (n/%)[c]	15	44

AUD alcohol use disorder, *SADQ-C* Severity of Alcohol Dependence Questionnaire (community version), *SD* standard deviation
[a]In Australia, a 'standard drink' is defined as 10 g (i.e. 12.7 ml) of pure alcohol
[b]Psychiatric diagnoses included depression (n = 24), anxiety disorders (n = 24), bipolar disorder (n = 7), post-traumatic stress disorder (n = 3), and other disorders (n = 3)
[c]Data on whether anti-craving medications were administered at admission was missing for 3 participants

Manning *et al. Substance Abuse Treatment, Prevention, and Policy* (2019) 14:24

Page 5 of 6

Table 2 Percentage of participants endorsing each rating of the training tasks (N = 30)

	Strongly agree	Agree	Unsure	Disagree	Strongly Disagree
I found the task interesting	50	43	3	0	3
I found the task improved my attention	23	63	13	0	0
I found the task decreased my craving for alcohol	7	20	53	20	0

to the small sample size (note the 95% confidence interval extends from 36 to 70%).

We expected that adding WM training to ABM (dual training) could enhance abstinence rates, given that previous studies supported the effectiveness of WM training for substance use disorders [22, 32]. However, these previous studies adopted multi-session training protocols (e.g., 25 sessions delivered over one month). Thus, our 4 sessions were likely insufficient to have a positive impact on relapse rates, and future studies should consider testing this approach in settings where longer training is possible (e.g. post-withdrawal rehabilitation), or use post-discharge "booster" training sessions. Our findings regarding feasibility and acceptability suggest that a large proportion of patients would engage with such neuro-cognitive interventions, making them a worthwhile investment for future research. Limitations of this study include the lack of acceptability questionnaire assessments among the 7 participants who withdrew (meaning acceptability may be over-estimated). Moreover, the acceptability questionnaire was just a 3-item instrument that provides very limited feedback, and did not distinguish between the ABM and WM training. Self-reported alcohol outcomes were also not objectively-verified.

Conclusions

Our findings indicate that dual-training is acceptable and feasible during alcohol withdrawal. We cannot draw conclusions regarding the effectiveness of this intervention from a small single-group, open-label study. However, considering the likelihood that WM training requires more than 4 sessions to be effective, we would suggest that larger trials designed to test the efficacy of this dual-training approach either be in treatment settings where longer courses of WM training are possible (e.g., post-withdrawal rehabilitation programs), or incorporate post-discharge "booster" sessions into their protocol.

Abbreviations
ABM: Approach bias modification; AUD: Alcohol use disorder; TLFB: Timeline follow-back; WM: Working memory

Availability of data and materials
Data collected from individual participants will not be made publicly available, due to conditions of ethical approval regarding confidentiality. Data may only be made available to researchers for additional analyses subject to further ethical approval. Those interested in further analyses of data produced may contact the corresponding author.

Authors' contributions
VM, PKS, KH, DIL, and AV conceived of the study, developed the protocol, and secured funding. VM also supervised the research team that conducted recruitment and data collection, and was involved in writing and editing the final version of this manuscript. KM recruited participants, collected and analysed data, wrote the first draft of this manuscript, and assisted with further editing of later drafts. JBBG was also involved in data collection and analysis and contributed to writing and editing this manuscript. All authors were involved in reviewing and editing the manuscript, and approve this final version.

Ethics approval and consent to participate
Ethical approval was acquired from the Eastern Health Human Research Ethics Committee (EHHREC; Reference E34–2015). Participants were provided with written and verbal explanation of the study prior to being asked to sign a consent form, as approved by the EHHREC.

Consent for publication
Not applicable

Competing interests
AV is a member of the scientific advisory board of Monclarity but receives no funds from them. DIL has provided consultancy advice to Lundbeck and Indivior, and has received travel support and speaker honoraria from Astra Zeneca, Janssen, Lundbeck, Shire and Servier. However, these organisations have no role in the present study, and do not conceivably stand to gain or lose from the publication of this manuscript. No other authors have any competing interests to declare.

Publisher's Note
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Author details
[1]Monash Addiction Research Centre and Eastern Health Clinical School, Monash University, 110 Church Street, Richmond, Victoria 3121, Australia. [2]Turning Point, Eastern Health, 110 Church Street, Richmond, Victoria 3121, Australia. [3]School of Psychology, Deakin University, Locked bag, Geelong 2200, Australia. [4]Centre for Drug use, Addictive, and Anti-social Behaviour Research (CEDAAR), Deakin University, Locked bag, Geelong 2200, Australia. [5]School of Psychological Sciences & Monash Institute of Cognitive and Clinical Neurosciences, 18 Innovation Walk, Clayton Campus, Wellington Road, Monash University, Melbourne, Victoria 3800, Australia.

References
1. Cunningham WA, Zelazo PD. Attitudes and evaluations: a social cognitive neuroscience perspective. Trends Cogn Sci. 2007;11(3):97–104.
2. Gladwin TE, Figner B, Crone EA, Wiers RW. Addiction, adolescence, and the integration of control and motivation. Dev Cogn Neurosci. 2011;1(4):364–76.

3.   Ernst LH, Plichta MM, Dresler T, Zesewitz AK, Tupak SV, Haeussinger FB, et al. Prefrontal correlates of approach preferences for alcohol stimuli in alcohol dependence. Addict Biol. 2014;19(3):497–508.

4.   Wiers CE, Stelzel C, Park SQ, Gawron CK, Ludwig VU, Gutwinski S, et al. Neural correlates of alcohol-approach bias in alcohol addiction: the spirit is willing but the flesh is weak for spirits. Neuropsychopharmacology. 2014; 39(3):688–97.

5.   Le Berre AP, Fama R, Sullivan EV. Executive functions, memory, and social cognitive deficits and recovery in chronic alcoholism: a critical review to inform future research. Alcohol Clin Exp Res. 2017;41(8):1432–43.

6.   Manning V, Teo HC, Guo S, Wong KE, Li TK. Neurocognitive functioning and treatment outcome following detoxification among Asian alcohol-dependent inpatients. Subst Use Misuse. 2016;51(2):193–205.

7.   Christiansen P, Cole JC, Goudie AJ, Field M. Components of behavioural impulsivity and automatic cue approach predict unique variance in hazardous drinking. Psychopharmacology. 2012;219(2):501–10.

8.   Kersbergen I, Woud ML, Field M. The validity of different measures of automatic alcohol action tendencies. Psychol Addict Behav. 2015;29(1): 225–30.

9.   Martin Braunstein L, Kuerbis A, Ochsner K, Morgenstern J. Implicit alcohol approach and avoidance tendencies predict future drinking in problem drinkers. Alcohol Clin Exp Res. 2016;40(9):1945–52.

10.   Spruyt A, De Houwer J, Tibboel H, Verschuere B, Crombez G, Verbanck P, et al. On the predictive validity of automatically activated approach/ avoidance tendencies in abstaining alcohol-dependent patients. Drug Alcohol Depend. 2013;127(1–3):81–6.

11.   Eberl C, Wiers RW, Pawelczack S, Rinck M, Becker ES, Lindenmeyer J. Approach bias modification in alcohol dependence: do clinical effects replicate and for whom does it work best? Dev Cogn Neurosci. 2013;4:38–51.

12.   Manning V, Staiger PK, Hall K, Garfield JBB, Flaks G, Leung D, et al. Cognitive Bias modification training during inpatient alcohol detoxification reduces early relapse: a randomized controlled trial. Alcohol Clin Exp Res. 2016;40(9):2011–9.

13.   Rinck M, Wiers RW, Becker ES, Lindenmeyer J. Relapse prevention in abstinent alcoholics by cognitive bias modification: clinical effects of combining approach bias modification and attention bias modification. J Consult Clin Psychol. 2018;86(12):1005–16.

14.   Wiers RW, Eberl C, Rinck M, Becker ES, Lindenmeyer J. Retraining automatic action tendencies changes alcoholic patients' approach bias for alcohol and improves treatment outcome. Psychol Sci. 2011;22(4):490–7.

15.   Kakoschke N, Kemps E, Tiggemann M. Approach bias modification training and consumption: a review of the literature. Addict Behav. 2017;64:21–8.

16.   Wiers RW, Boffo M, Field M. What's in a trial? On the importance of distinguishing between experimental lab studies and randomized controlled trials: the case of cognitive Bias modification and alcohol use disorders. J Stud Alcohol Drugs. 2018;79(3):333–43.

17.   Wiers RW, Gladwin TE, Hofmann W, Salemink E, Ridderinkhof KR. Cognitive Bias modification and cognitive control training in addiction and related psychopathology: mechanisms, clinical perspectives, and ways forward. Clin Psychol Sci. 2013;1(2):192–212.

18.   Noel X, Sferrazza R, Van Der Linden M, Paternot J, Verhas M, Hanak C, et al. Contribution of frontal cerebral blood flow measured by (99m)Tc-Bicisate spect and executive function deficits to predicting treatment outcome in alcohol-dependent patients. Alcohol Alcohol (Oxford, Oxfordshire). 2002;37(4):347–54.

19.   Sharbanee JM, Stritzke WG, Wiers RW, Young P, Rinck M, MacLeod C. The interaction of approach-alcohol action tendencies, working memory capacity, and current task goals predicts the inability to regulate drinking behavior. Psychol Addict Behav. 2013;27(3):649–61.

20.   Khemiri L, Brynte C, Stunkel A, Klingberg T, Jayaram-Lindstrom N. Working memory training in alcohol use disorder: a randomized controlled trial. Alcohol Clin Exp Res. 2018.

21.   Bickel WK, Yi R, Landes RD, Hill PF, Baxter C. Remember the future: working memory training decreases delay discounting among stimulant addicts. Biol Psychiatry. 2011;69(3):260–5.

22.   Houben K, Wiers RW, Jansen A. Getting a grip on drinking behavior: training working memory to reduce alcohol abuse. Psychol Sci. 2011;22(7):968–75.

23.   Bartsch AJ, Homola G, Biller A, Smith SM, Weijers HG, Wiesbeck GA, et al. Manifestations of early brain recovery associated with abstinence from alcoholism. Brain. 2007;130(Pt 1:36–47).

24.   van Eijk J, Demirakca T, Frischknecht U, Hermann D, Mann K, Ende G. Rapid partial regeneration of brain volume during the first 14 days of abstinence from alcohol. Alcohol Clin Exp Res. 2013;37(1):67–74.

25.   Willoughby AR, de Zambotti M, Baker FC, Colrain IM. Partial K-complex recovery following short-term abstinence in individuals with alcohol use disorder. Alcohol Clin Exp Res. 2015;39(8):1417–24.

26.   Batra A, Muller CA, Mann K, Heinz A. Alcohol dependence and harmful use of alcohol. Dtsch Arztebl Int. 2016;113(17):301–10.

27.   Sobell LC, Sobell MB. Timeline Followback user's guide: a calendar method for assessing alcohol and drug use. Toronto: addiction Research Foundation; 1996.

28.   Singleton EG, Tiffany S, Henningfield JE. Alcohol craving questionnaires (ACQ-NOW and ACQ-SF-R) background, scoring, and administration. Baltimore: Division of Intramural Research, NIDA, NIH; 2014.

29.   Stockwell T, Sitharthan T, McGrath D, Lang E. The measurement of alcohol dependence and impaired control in community samples. Addiction. 1994; 89(2):167–74.

30.   Monclarity LLC. Brainwell 2013 [Available from: www.brainwell.com].

31.   Wanmaker S, Leijdesdorff SMJ, Geraerts E, van de Wetering BJ, Renkema PJ, Franken IH. The efficacy of a working memory training in substance use patients: a randomized double-blind placebo-controlled clinical trial. J Clin Exp Neuropsychol. 2018;40(5):473–86.

32.   Rupp CI, Kemmler G, Kurz M, Hinterhuber H, Fleischhacker WW. Cognitive remediation therapy during treatment for alcohol dependence. J Stud Alcohol Drugs. 2012;73(4):625–34.