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Effectiveness of an Integrated Intervention Program for Alcoholism (IIPA) for enhancing self-regulation: Preliminary evidence

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ABSTRACT

Objective: Alcoholism could be a core problem of self-regulatory failure. Several neurocognitive theories have hypothesized hypo-functioning or dysfunction of reflective (executive) system and heightened functioning of reactive (impulsive) system in self-regulatory failure implicated in drug addiction. Similarly, stress and affect dysregulation may breakdown self-regulation. The present study aimed to develop an Integrated Intervention Program for Alcoholism (IIPA) to enhance self-regulation and to test its effectiveness in the treatment of alcoholism.

Method: Individuals with early onset alcoholism (n = 50) were recruited after getting written informed consent. The study used randomized case control design. The participants were matched on age (+/−1 year) and education (+/−1 year). The TAU group received usual treatment for alcoholism which included pharmacotherapy, 6 sessions/week yoga and 3 sessions/week group therapy on relapse prevention. The intervention group received IIPA for 18 days along with usual treatment (except yoga sessions). The IIPA included several cognitive remediation tasks and mind-body exercise (Qigong and Tai Chi Chuan). Both groups were assessed on executive function tests and affect regulation scale at pre and post-intervention. The subjects were also followed up for 6 months to compare the abstinence between groups.

Results: Both groups were comparable at baseline. At post-intervention, the IIPA group showed a significant improvement compared to the TAU group on executive functioning and affect regulation. Follow-up results showed lower relapses in six months in the IIPA group.

Conclusion: Preliminary evidence showed that IIPA is effective in facilitating self-regulation. Further study may examine its utility and feasibility in other clinical conditions.

1. Introduction

Drug addiction such as alcoholism could be a core problem of self-regulatory failure (Heatherton and Wagner, 2011; Goldstein and Volkow, 2011; Baler and Volkow, 2006; George and Koob, 2010). Several neurocognitive theories have hypothesized the involvement of two brain's systems in drug addiction including alcoholism that is dysfunction or hypo-functioning of the reflective (executive) system and heightened functioning of the reactive (impulsive) system (Bechara, 2005; Verdejo-García and Bechara, 2009; Heatherton and Wagner, 2011). Dysfunctions of executive system generally associated with prefrontal cortex (Miller and Cohen, 2001; Miyake and Friedman, 2012) may produce abnormality in processing of reward, pain, stress, emotion and decision making that play a crucial role in addiction (George and Koob, 2010). Similarly, heightened impulses generally associated with limbic cortex may override or hijack weak executive control necessary for self-regulation and willpower to resist alcohol abuse (Bechara, 2005; Heatherton and Wagner, 2011).

It is well documented that alcoholism affects the functioning of prefrontal cortex by producing structural and functional impairments (Dirksen et al., 2006; Moselhy et al., 2001; Oscar-Berman and Marinkovic, 2003). Alcoholism produces a wide range of executive dysfunctions (Ratti et al., 2002; Koelega, 1995; Al-Zahrani and Elsayed, 2009; Ihara et al., 2000; Stavro et al., 2013; Loeber et al., 2009). Studies have reported that recovery of executive functions in alcoholism require control and long-term abstinence from 6 months to 2–3 years. In addition, some of the functions do not show improvement or show protracted minimal recovery in the abstinence period (Stavro et al.,

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2013; Mlinarics et al., 2009).

Several other factors such as stress, emotion dysregulation, and cue-induced craving also contribute substantially to alcohol use disorders. Stress can promote and enhance alcohol abuse, with the perhaps the primary purpose of getting relief from stress and anxiety (Koob, 2013; Pohorecky, 1991). Studies have demonstrated that heightened states of emotion and coping with stress is linked with the initiation and maintenance of alcoholism and relapse after treatment (Norman et al., 2007; Abbey et al., 1993; Dawson et al., 2005; Koob and Kreek, 2007; Sinha et al., 2006; Koob and Le Moal, 1997; Koob, 2013).

Application of neurocognitive theories of drug addiction could be useful in designing interventions to enhance treatment efficacy for persons with alcoholism. Several studies have demonstrated the effectiveness of cognitive remediation as a therapeutic intervention in various clinical conditions including Attention Deficit and Hyperactivity Disorders (ADHD) (Klingberg et al., 2005; Beck et al., 2010), schizophrenia (Adcock et al., 2009; Hegde et al., 2012; Wykes et al., 2011), substance use disorders (Bickel et al., 2011; Wiers et al., 2011), traumatic brain injury and stroke (Rohling et al., 2009; Cicerone et al., 2011; Chung et al., 2013).

The principle of cognitive rehabilitation/remediation is based on neural plasticity also known as brain plasticity (Keshavan et al., 2014; Vinogradov et al., 2012). Neuroplasticity is the ability of the nervous system to reorganize itself in response to intrinsic and extrinsic stimuli resulting in changes in functional neuronal networks due to the modifications of existing synapses or the formation of new synaptic interconnections (Berlucchi and Buchtel, 2009).

There are very few studies that have attempted to enhance executive functions in patients with alcoholism (Svanberg and Evans, 2013; Horton et al., 2015). Working memory and inhibitory control retraining are known to be effective in improving cognitive functions in patients with alcoholism (Houben and Wiers, 2009; Houben et al., 2011, 2012). However, these studies have been criticized due to methodological issues such as using college population, without face to face meeting via Internet, using tasks used for training for pre and post-assessment and use of non standardized cognitive training programs to treat neurocognitive deficits.

T'ai (or Tai) Chi (also pronounced as *Tai Chi Chuan* or *T*aiji) and Qigong (also pronounced as Chi Kung) are mind-body practices that originated from China (Birdee et al., 2009; Wang et al., 2013b) that have shown their effectiveness in several clinical conditions. For example, in ADHD (Hernandez-Reif et al., 2001), anxiety and depression (Wang et al., 2013a, 2014) and substance use disorders (Chen et al., 2010). Tai Chi and Qigong, both are a meditative form of exercise that requires coordinated gentle movements with mental focus, breathing, and relaxation for physical, mental, and spiritual cultivation (Lee and Lei, 1999).

Studies have hypothesized and described the mechanisms of change in exercise-based interventions. Tai Chi reduces the sympathetic nervous system activity and enhances relaxation (Motivala et al., 2006; Irwin et al., 2008), reduces stress, salivary cortisol levels and improves vitality (Jin, 1992). Tai Chi produces physiological effect by autoregulatory signaling pathways represented by limbic reward and motivation circuitry (Esch et al., 2007). Similarly, Qigong exercise helps in reducing plasma concentration of adrenocorticotropic hormone (ACTH), cortisol, and aldosterone hormone indicating that it impacts on Hypothalamic–Pituitary–Adrenal axis (Lee et al., 2004). Exercise contributes in neural/brain plasticity in regions implicated in drug addiction through chromatin remodelling (Gomez-Pinilla et al., 2011; Kumar et al., 2005; Wan et al., 2011).

The present study is an attempt to enhance executive functioning and affect regulation in persons with alcoholism to facilitate an optimal balance in activation/function of executive/reflective/prefrontal system and impulsive/reactive/limbic system. To meet this objective, an Integrated Intervention Program for Alcoholism (IIPA) was developed that had two components: a) cognitive remediation b) Qigong and Tai Chi Chuan exercises.

2. Material and methods

2.1. Research design

Randomized matched case control design with pre, post and follow up assessment was used in the present study.

2.2. Sample and procedure

The sample consisted of 50 male participants with a diagnosis of alcohol dependence as per International Classification of Diseases-10 (ICD-10) diagnostic criteria. Other inclusion criteria were: early onset alcohol dependence (alcohol dependence before 25 years of age), one or more first degree family members with alcohol dependence, age between 18 to 45 years. Participants were excluded from the study in presence of other substance dependence (except tobacco) such as cannabis; any major psychiatric disorders such as schizophrenia and mood disorders; self-reported major co-morbid medical or neurological disorders; severe memory impairments [score on Hindi Mental State Examination (HMSE) less than 24]; Family history of psychiatric disorders (other than alcohol dependence) in first degree family members; clinical impression of mental retardation and those who have received formal cognitive remediation or any form of meditation practices or structured psychological therapy in past one year.

Participants were allotted by randomly matched method into two groups: the intervention (IIPA) group (n = 25) and the treatment as usual (TAU) group (n = 25). They were matched on age (+/− 1 year) and education (+/−1 year). The procedure of allotment followed as: For example, if Mr. A, 25 years old, educated up to 8th standard who consented for voluntary participation in the study was allotted randomly into either IIPA or TAU group based on a standard randomization method. Suppose, he was allotted to the IIPA group then the next participant who matched the criteria of age (+/−1 year) and education (+/−1 year) with Mr. A was allotted to the TAU group and vice versa. The same procedure was followed to recruit other participants in the study. Participants were recruited from the inpatient setting of Centre for Addiction Medicine, NIMHANS, Bengaluru, India. The flowchart for the procedure is given in figure 1.

The present study was approved by the Institute's ethics committee (Ref. No.: NIMH/DO/SUB-COMMITTEE/2013). The study conformed to the provisions of the declaration of Helsinki. The trial was registered with Clinical Trial Registry-India (CTRI). The CTRI registration number is CTRI/2017/08/009346.

Baseline assessment was done in both groups after 3–4 days of detoxification. Thereafter, the TAU group received usual treatment for alcoholism as an inpatient for 18 days which included pharmacotherapy, yoga sessions in the group (6 sessions in a week) and relapse prevention sessions in the group (3 sessions in a week). The intervention group received IIPA (cognitive remediation and Qigong and Tai Chi Chuan exercises) in addition to usual treatment for alcoholism (except yoga sessions) as an inpatient for 18 days. It was decided that the intervention (IIPA) group need not attend yoga sessions in view of receiving another forms of mind-body practices (i.e., Qigong and Tai Chi Chuan). Yoga, Qigong, and Tai Chi are mind-body exercises that may differ in their origin and style of practice but they have common components such as graceful movements with the breathing exercise, awareness of self and integrating physical, mental and spiritual components to improve health and well-being (Wang et al., 2017). Post-intervention assessment was done after 18 days of usual treatment or IIPA with usual treatment. Participants were followed up for 6 months to compare the abstinence between the groups.

2.3. Tools

Socio-demographic data sheet: The socio-demographic data sheet was prepared to record demographic details and clinical information related to alcoholism such as onset of alcohol use, age of alcohol dependence, duration of alcohol use and dependence etc. **Mini-international Neuropsychiatry Interview (MINI)** (Sheehan et al., 1998): The M.I.N.I. version 6.0 was administered as a screening tool for Axis I disorders. **Family Interview for Genetic Studies (FIGS)** (Maxwell, 1992): The FIGS was used to gather diagnostic information about relatives in the pedigree being studied. **Short Alcohol Dependence Data Questionnaire (SADD)** (Raistrick et al., 1983): The SADD is a 15-items self-reported questionnaire. It is used to assess current alcohol dependence severity. **Hindi Mental State Examination (HMSE)** (Ganguli et al., 1995): The HMSE was used to assess and screen the patients with severe memory impairment. **Semi Structured Assessment for Genetics of Alcoholism-version II (SSAGA-II)** (Bucholz et al., 1994): Only sections on Attention Deficits and Hyperactivity Disorder (ADHD), Antisocial Personality Disorder (ASPD) and Conduct Disorder (CD) was administered for recording score of externalizing spectrum disorders.

2.3.1. Outcome measures for baseline and post assessment

Affect Regulation Checklist (ARC) (Moretti, 2003): The ARC has 12 items and it measures both, maladaptive (e.g., lack of control, suppression) and adaptive (reflection) regulatory aspects of affect. The ARC assesses regulatory characteristics independent to specific emotions and avoids confounding effects of emotional states. **Matrix Reasoning** (Wechsler, 1997a): The Matrix test from the Wechsler Adult Intelligence Scale-III (WAIS-III) was administered. It is primarily a test of intelligence and assesses non-verbal reasoning. **Controlled Oral Word Association (COWA) Test** (Spreen and Strauss, 1998): This test evaluates the spontaneous production of words beginning with a given letter within a limited amount of time. **Color Trails Test 1 and 2** (D'Elia et al., 1996): The Color trails test has two parts. Part 1 assesses speed for attention, simple sequencing, focused attention, perceptual tracking and visual search. While part 2 assesses mental flexibility and focused attention in addition to the above mentioned functions. **Five-Point Test** (Regard et al., 1982): This is a test to assess figural fluency. In this task, subjects are required to produce as many unique designs as possible by connecting the dots with straight lines. **Digit span** (Wechsler, 1997b): The forward condition assesses auditory short-term memory and attention, while backward condition measures working memory. **Spatial Span** (Wechsler, 1997b): This test assesses the ability to hold a visuospatial sequence of locations in working memory and then reproduce the sequence in same order (forward condition) and in reverse order (backward condition). **Stroop color-word interference test** (Golden, 1976): The Stroop test assesses inhibitory control and known to be sensitive to the functioning of the superior medial frontal lobe, including the anterior cingulate cortex (Stuss and Levine, 2002). **Game of Dice Task** (Brand et al., 2005): This task assesses decision making under risk conditions. In this task, subjects were asked to maximize a fictitious starting capital within 30 trials by guessing which a number of a single die will be thrown by the computer.

2.4. Integrated Intervention Program for Alcoholism (IIPA)

The IIPA was developed for the present study. It is applied as an inpatient based intervention program for 18 consecutive days. The number of sessions was decided in the view of feasibility and practicality. The IIPA included cognitive remediation (developed for the present study) and Qigong and Tai Chi Chuan exercises. The cognitive remediation was delivered in individual sessions while Tai Chi & Qigong were delivered in group sessions (in a group of 3–4 participants). Also, Psycho-education about IIPA and its possible benefits in alcoholism were discussed in 2–3 sessions, 15–20 minutes only. The brief description about the IIPA is given in Appendix A in Supplementary material.

2.5. Data analysis

All the clinical, behavioral and neuropsychological variables were tested for the normality using Shapiro-Wilk test and found to be normally distributed. Baseline comparisons were made between the two groups on all primary and secondary measures as well as on clinical and socio-demographic variables. Independent sample *t*-test was used for baseline comparison of continuous behavioral and neuropsychological outcome measures and chi-square test for comparison of categorical variables. Between group repeated measures analysis of variance (RMANOVA- 2 groups × 2 time points) was applied to examine the changes from pre to post intervention. Effect size in both groups was described by means of partial eta squared (η^2). Partial eta squared (η^2) of 0.01 to 0.05 indicates small effect size, 0.06 to 0.13 indicates medium effect size and 0.14 and above indicates a large effect size. Kaplan-Meier test was applied to see the significant difference between the two groups for better survival (abstinence) in 6 months follow up. All the statistical analyses were carried out using IBM-SPSS (v22) software.

3. Results

3.1. Socio-demographic characteristics

Subjects in both groups were in their early thirties with an average 11 years of formal education. There was no significant difference on age [IIPA group = 34.28 ± 5.33 (Mean ± SD), TAU group = 34.08 ± 5.73 (Mean ± SD); p = 0.899] and education [11.08 ± 2.48 (Mean ± SD), TAU group = 11.12 ± 2.45 (Mean ± SD); p = 0.955] as revealed by independent sample *t*-test. The groups were also comparable on socioeconomic status ($\chi^2 = 0.76$; p = 0.68) with the majority of participants from the middle (IIPA = 56%, TAU = 44%) and lower (IIPA = 36%, TAU = 44%) socioeconomic status in both the groups.

3.2. Comparison between the two groups on clinical variables

The variables such as the onset of alcohol use, the age of dependence, years of alcohol use, years of alcohol dependence, the quantity of alcohol use, the severity of alcohol dependence and externalizing traits were also documented and analyzed at baseline since they influence the nature and course of alcoholism as well as the severity of alcohol-related problems.

The descriptive and inferential statistics related to these variables are presented in Table 1. It shows that both groups were comparable in terms of age of onset of alcohol use, the age of dependence, total years of alcohol use, total years of alcohol dependence, and quantity of alcohol intake since one month and severity of alcohol use as assessed by Short Alcohol Dependence Data Questionnaire (SADDQ).

3.3. Medication received by the patients in both groups during study

All the patients received pharmacological treatment as an inpatient. Each patient was detoxified with diazepam. After the detoxification, 48% in the intervention group and 56% in the TAU group received Baclofen and Optineuron. Also, 32% in the intervention group and 28% in the TAU group received vitamin supplements. The pharmacological treatments for both groups were comparatively similar.

3.4. Comparison between two groups on outcome measures

A comprehensive neuropsychological assessment was used to assess the various domains of executive functioning such as mental flexibility, working memory, inhibitory control, and decision making. Results showed that both the groups were comparable on various measures of

Table 1
Group comparison on clinical variables at baseline.

Variables	IIPA group (n = 25) Mean ± SD	TAU group (n = 25) Mean ± SD	t value	p value
Age of onset (year)	18.64 ± 2.53	19.24 ± 3.09	−0.75	0.456
Age of dependence (year)	23.64 ± 2.61	23.96 ± 2.52	−0.44	0.662
Total years of alcohol use	15.28 ± 6.01	14.88 ± 5.81	0.24	0.812
Total years of alcohol dependence	10.60 ± 5.77	9.96 ± 5.10	0.42	0.680
Current alcohol consumption (in quarter or 180 ml) since one month	3.42 ± 1.017	3.40 ± 1.04	0.07	0.946
Externalizing traits	13.40 ± 3.80	11.12 ± 4.80	1.86	0.069
SADDQ	23.24 ± 8.66	23.32 ± 10.29	−0.03	0.976

SADDQ = Short alcohol dependence data questionnaire.

Table 2
Group comparison on neuropsychological measures and affect regulation at baseline.

Variables	IIPA group (n = 25) Mean ± SD	TAU group (n = 25) Mean ± SD	t value	p value
Reasoning				
Matrix	11.08 ± 3.56	11.44 ± 2.84	−0.40	0.694
Focused attention and speed of processing				
Color trail 1	86.12 ± 28.16	92.84 ± 32.54	−0.78	0.439
Mental/Cognitive flexibility and speed of processing				
Color trail 2	185.24 ± 55.42	208.76 ± 68.00	−1.34	0.186
Attention span and working memory				
Digit span F.	6.08 ± 1.15	6.84 ± 1.93	−1.69	0.099
Digit span B.	4.40 ± 1.47	5.40 ± 1.87	−2.10	0.041*
Spatial span F.	7.16 ± 1.49	7.60 ± 1.35	−1.09	0.280
Spatial span B.	5.72 ± 1.40	6.28 ± 1.49	−1.37	0.177
Verbal and figural fluency				
COWA	8.68 ± 3.04	9.55 ± 3.74	−0.90	0.373
Five point test	21.48 ± 7.77	24.04 ± 6.27	−1.28	0.206
Inhibitory control				
Stroop I.	156.21 ± 59.47	159.72 ± 56.33	−0.21	0.831
Decision making				
GDT Single	13.88 ± 8.46	13.68 ± 8.33	0.08	0.933
GDT Double	6.52 ± 5.54	7.00 ± 3.44	−0.37	0.714
GDT Triple	4.40 ± 4.25	4.56 ± 4.29	−0.13	0.895
GDT Quad	5.20 ± 5.61	4.76 ± 3.85	0.32	0.748
GDT Risky C.	20.40 ± 8.85	20.68 ± 6.95	−0.12	0.901
GDT Safe C.	9.60 ± 8.85	9.32 ± 6.95	0.12	0.901
GDT Net score	−10.80 ± 17.70	−11.36 ± 13.90	0.12	0.901
GDT FB	−8980.00 ± 6381.88	−8176.00 ± 5159.16	−0.49	0.626
Affect regulation				
Affect Dyscontrol	4.84 ± 2.41	4.40 ± 2.16	0.68	0.500
Affect Suppression	4.56 ± 1.78	4.68 ± 2.12	−0.22	0.829
Adaptive Reflection	4.08 ± 1.35	4.16 ± 1.77	−0.18	0.858

F = Forward condition, B = Backward condition, COWA = Controlled Oral Word Association Test, Stroop I = Stroop Interference Test, GDT = Game of Dice Task, C = Choices, Net score = Safe choices-Risky choices, FB = Final balance.
* Significant at 0.05.

executive functions and affect regulation at baseline (Table 2). However, there was a significant difference between two groups on verbal working memory at baseline. The mean score indicates that in comparison to the TAU group, the intervention (IIPA) group had poor performance on verbal working memory at baseline.

Pre to post-intervention results showed that the intervention group (IIPA) has significantly better performance on various domains of executive functions and affect regulation compared to the TAU group (Table 3). The effect size partial η^2 indicates that the magnitude of change was much high in the intervention (IIPA) group compared to the TAU group.

3.5. Comparison of abstinence for six months

Follow-up information regarding relapse and abstinence was obtained for the period of 6 months after post assessment in both the groups. Table 4(A) shows that there was the lower relapse and longer period of abstinence in the intervention (IIPA) group compared to the TAU group. It is seen that 11 (69% out of 16 known status) subjects in the TAU group had relapsed at 3 months as compared to the IIPA group which has only 4 (20%, out of 20 known status) relapses. At the end of 6 months follow up, 13 (87%, out of 15 known status) subjects relapsed in the TAU group which is higher than the IIPA group (n = 8/15, 53% among known status). A Kaplan-Meier test was applied to see the significant difference between the two groups for better survival (abstinence) in 6 months follow up. Results showed (Table 4(B)) that there was a significant difference between two groups ($p < 0.01$), and the estimated mean indicates a better abstinence in the IIPA group.

4. Discussion

The present study aimed to enhance self-regulation by facilitating optimal functioning between the executive/top-down prefrontal control and impulsive/limbic bottom-up regulation systems in individuals with alcoholism for their better treatment recovery. Results indicate that the IIPA along with the usual treatment had significantly better performance and large effect size on tests assessing various executive functions as compared to the usual/conventional treatment. Executive

Table 3
Comparison of groups for change in various domains of executive functioning and affect regulation from pre to post intervention (n = 25 in each group).

Variables	Time	IIPA group Mean ± SD	TAU group Mean ± SD	Time (T)	Group (G)	T × G	Within group pre to post	
							IIPA group	TAU group
Matrix reasoning test	Pre	11.08 ± 3.56	11.44 ± 2.84	F = 144.08	F = 3.92	F = 60.99	p= **0.001*****	p= **0.005****
	Post	16.56 ± 4.05	12.60 ± 2.83	p= **0.001*****	p = 0.054	p= **0.001*****	η^2= **0.80 L**	η^2= **0.16**
Color Trail-1	Pre	86.12 ± 28.16	92.84 ± 32.54	F = 12.89	F = 2.35	F = 0.91	p= **0.002*****	p = 0.069
(Time in sec.)	Post	67.84 ± 23.36	82.24 ± 27.96	p= **0.001*****	p = 0.132	p = 0.345	η^2= **0.18 L**	η^2= 0.07
Digit span test	Pre	6.08 ± 1.15	6.84 ± 1.93	F = 188.01	F = 1.20	F = 75.25	p= **0.001*****	p= **0.001*****
(Forward)	Post	9.28 ± 1.54	7.56 ± 1.78	p= **0.001*****	p = 0.278	p= **0.001*****	η^2= **0.84 L**	η^2= **0.21**
Spatial span test (Forward)	Pre	7.16 ± 1.49	7.60 ± 1.35	F = 94.12	F = 4.88	F = 33.88	p= **0.001*****	p= **0.009****
	Post	10.36 ± 1.29	8.40 ± 1.53	p= **0.001*****	p = 0.032	p= **0.001*****	η^2= **0.72 L**	η^2= **0.14**
COWA test	Pre	8.68 ± 3.04	9.55 ± 3.74	F = 148.08	F = 2.80	F = 44.45	p= **0.001*****	p= **0.001*****
	Post	15.57 ± 3.69	11.56 ± 3.74	p= **0.001*****	p = 0.101	p= **0.001*****	η^2= **0.79 L**	η^2= **0.24**
Five point test	Pre	21.48 ± 7.77	24.04 ± 6.27	F = 51.09	F = 0.30	F = 19.48	p= **0.001*****	p = 0.059
	Post	31.12 ± 9.26	26.32 ± 7.59	p= **0.001*****	p = 0.586	p= **0.001*****	η^2= **0.58 L**	η^2= 0.07
Color Trail- 2	Pre	185.24 ± 55.42	208.76 ± 68.00	F = 78.85	F = 6.91	F = 4.65	p= **0.001*****	p= **0.001*****
(Time in sec.)	Post	118.68 ± 31.07	168.20 ± 52.9	p= **0.001*****	p = 0.011	p= **0.036***	η^2= **0.56 L**	η^2= **0.32**
Digit span test	Pre	4.40 ± 1.47	5.40 ± 1.87	F = 107.12	F = 1.45	F = 64.04	p= **0.001*****	p = 0.103
(Backward)	Post	7.84 ± 1.21	5.84 ± 1.80	p= **0.001*****	p = 0.234	p= **0.001*****	η^2= **0.78 L**	η^2= 0.05
Spatial span test (Backward)	Pre	5.72 ± 1.40	6.28 ± 1.49	F = 103.92	F = 3.12	F = 30.45	p= **0.001*****	p= **0.002****
	Post	9.08 ± 1.15	7.28 ± 1.72	p= **0.001*****	p = 0.084	p= **0.001*****	η^2= **0.72 L**	η^2= **0.19**
Stroop interference test-Time (sec)	Pre	156.21 ± 59.47	159.72 ± 56.33	F = 79.67	F = 1.61	F = 9.43	p= **0.001*****	p= **0.001*****
	Post	101.32 ± 29.03	132.93 ± 55.34	p= **0.001*****	p = 0.210	p= **0.004****	η^2= **0.60 L**	η^2= **0.26**
GDT	Pre	13.88 ± 8.46	13.68 ± 8.33	F = 16.14	F = 3.68	F = 12.49	p= **0.001*****	p = 0.734
Single choices	Post	5.76 ± 5.64	13.16 ± 7.83	p= **0.001*****	p = 0.061	p= **0.001*****	η^2= **0.37 L**	η^2 = 0.01
GDT	Pre	6.52 ± 5.54	7.00 ± 3.44	F = 1.12	F = 0.30	F = 0.08	p = 0.347	p = 0.587
Double choices	Post	7.84 ± 6.55	7.76 ± 5.36	p = 0.295	p = 0.862	p = 0.777	η^2= 0.02	η^2 = 0.01
GDT	Pre	4.40 ± 4.25	4.56 ± 4.29	F = 4.15	F = 2.47	F = 5.30	p= **0.004****	p = 0.852
Triple choices	Post	7.68 ± 5.13	4.36 ± 4.04	p= **0.047***	p = 0.123	p= **0.026***	η^2= **0.16 L**	η^2 = 0.01
GDT	Pre	5.20 ± 5.61	4.76 ± 3.85	F = 3.82	F = 2.32	F = 4.00	p= **0.007****	p = 0.975
Quad choices	Post	8.72 ± 8.46	4.72 ± 5.29	p = 0.056	p = 0.134	p= **0.051***	η^2= **0.14 L**	η^2 = 0.01
GDT Risky choices (Single + Double)	Pre	20.40 ± 8.85	20.68 ± 6.95	F = 9.26	F = 3.36	F = 10.67	p= **0.001*****	p = 0.876
	Post	13.60 ± 9.39	20.92 ± 7.66	p= **0.004****	p = 0.073	p= **0.002****	η^2= **0.29 L**	η^2 = 0.01
GDT Safe choices (Triple + Quad)	Pre	9.60 ± 8.85	9.32 ± 6.95	F = 9.26	F = 3.36	F = 10.67	p= **0.001*****	p = 0.876
	Post	16.40 ± 9.39	9.08 ± 7.66	p= **0.004****	p = 0.073	p= **0.002****	η^2= **0.29 L**	η^2 = 0.01
GDT Net score	Pre	−10.80 ± 7.69	−11.36 ± 13.90	F = 9.26	F = 3.36	F = 10.67	p= **0.001*****	p = 0.876
(safe choices – risky choices)	Post	2.80 ± 18.77	-11.84 ± 15.32	p= **0.004****	p = 0.073	p= **0.002****	η^2= **0.29 L**	η^2 = 0.01
GDT	Pre	−8980.00 ± 6381.88	−8176.00 ± 5159.16	F = 16.28	F = 1.96	F = 12.30	p= **0.001**	p = 0.711
Final balance	Post	−3368.00 ± 3299 .97	−7784.00 ± 5733.29	p= **0.001**	p = 0.168	p= **0.001**	η^2= **0.37 L**	η^2 = 0.01
Affect Dyscontrol	Pre	4.84 ± 2.41	4.40 ± 2.16	F = 43.73	F = 1.88	F = 16.65	p= **0.001*****	p = 0.080
	Post	1.80 ± 1.63	3.68 ± 2.17	p= **0.001*****	p = 0.18	p= **0.001*****	η^2= **0.54 L**	η^2= 0.06
Affect Suppression	Pre	4.56 ± 1.78	4.68 ± 2.12	F = 5.27	F = 5.34	F = 9.37	p= **0.001*****	p = 0.591
	Post	2.88 ± 1.94	4.92 ± 2.10	p= **0.026***	p = 0.025	p= **0.004****	η^2= **0.23 L**	η^2= 0.01
Adaptive reflection	Pre	4.08 ± 1.35	4.16 ± 1.77	F = 23.56	F = 1.14	F = 4.33	p= **0.001*****	p = 0.056
	Post	5.68 ± 1.35	4.80 ± 1.71	p= **0.001*****	p = 0.291	p= **0.043***	η^2= **0.33 L**	η^2= 0.07

* $p < 0.05$.
** $p < 0.01$.
*** $p < 0.001$] [L = large effect size].

functions play crucial role in self-regulation and mediate reward processing, emotional regulation, inhibition of impulses, and decision making (Cicerone et al., 2000; Mischel et al., 2011; Kerr and Zelazo, 2004; George and Koob, 2010). Continuous long-term substance abuse such as alcoholism attenuates the PFC ability to monitor and inhibit the addictive behaviors (Volkow et al., 2003; Goldstein and Volkow, 2002; Kalivas and Volkow, 2005; Everitt and Robbins, 2005). This may result in loss of self-control and indulgence in addictive behaviors despite harmful consequences to the individual.

Persistent use of alcohol may lead to more habitual and automatic drinking behavior recruiting the appetitive drive regions and decreased self-regulation/control results from the decreased frontal executive control (Everitt and Robbins, 2005). Therefore, we assume that improving executive functions through the integrated intervention program (i.e., IIPA) might potentially enhance the regulatory executive function/self control. The enhanced executive control could regulate the neural networks that elicit impulsive and disinhibited behavior through top-down regulation. It is well established that mind-body exercises (such as Tai Chi and Qigong) not only promote health benefits but also improve cognitive functions and self regulation (Chiesa et al., 2011). Hence, integrating the training for executive functions and mind-body exercises forms a unique method of treatment to treat the dysregulated executive hypoactive executive function and hyperactive limbic system in alcoholism.

Alcoholism-related behavior can be highly habitual and automatic (Tiffany and Conklin, 2000; Tiffany, 1990) and individuals may often be unaware of the factors that influence their decision to drink (Wiers et al., 2007, 2011). Long-term alcohol abuse causes the brain to become sensitized to alcohol and associated stimuli (Robinson and Berridge, 2000, 1993). Hence, alcohol-related stimuli can induce a conditioned motivational state in the sensitized brain. This may lead to the search for alcohol and ingest it without experiencing the pleasure. Several studies have indicated that a change in drinking behavior is possible by changing alcohol-related cognitive processes such as changing the expectancy or experimenting with attending alcohol cues (Field et al., 2005; Wiers et al., 2011). To reduce the implicit automatic biases or cue reactivity to the alcohol-related cues, the present study has a cognitive remediation task (i.e., Affect & Self-regulation and Memory Enhancement Task) in which participants were required to encode and recall non-alcoholic words in the presence of alcohol related stimuli. Therefore, requiring them suppress or inhibit strong habitual, prepotent response to alcohol cue which could potentially increase hyperactivation

Table 4
(A) Follow-up information about relapse and abstinence for 6 months. (B) Comparison for survival time in 6 months follow up.

(A) Time Period	Group	Relapse N (%)	Abstinence	Unknown/Not available status
1 Month	IIPA (n = 25)	1 (4%)	21 (84%)	3 (12%)
	TAU (n = 25)	4 (16%)	14 (56%)	7 (28%)
2 Months	IIPA (n = 25)	3 (12%)	19 (76%)	3 (12%)
	TAU (n = 25)	9 (36%)	7 (28%)	9 (36%)
3 Months	IIPA (n = 25)	4 (16%)	16 (64%)	5 (20%)
	TAU (n = 25)	11 (44%)	5 (20%)	9 (36%)
4 Months	IIPA (n = 25)	6 (24%)	10 (40%)	9 (36%)
	TAU (n = 25)	12 (48%)	3 (12%)	10 (40%)
5 Months	IIPA (n = 25)	7 (28%)	8 (32%)	10 (40%)
	TAU (n = 25)	12 (48%)	3 (12%)	10 (40%)
6 Months	IIPA (n = 25)	8 (32%)	7 (28%)	10 (40%)
	TAU (n = 25)	13 (52%)	2 (8%)	10 (40%)

(B) Group	Estimate Mean	SE	X^2Log-rank (Mantel-Cox)	df	p
IIPA	5.01	0.36	6.62	1	**0.010****
TAU	3.55	0.47			

** $p < 0.01$.

in the limbic or impulsive system. For successful performance on this task, a patient must direct his attention away from alcohol-related stimuli. Therefore, it can be assumed that the practice of this task could have reduced the implicit attentional biases related to drinking behavior. Similarly, the enhanced executive functions (such as working memory, inhibitory control, and mental flexibility) in the IIPA group would have contributed in better regulation of thought and behavior (Friedman et al., 2008; Miyake and Friedman, 2012). This is further corroborated from the pre to post intervention performance on simulated gambling task (GDT). The GDT assesses decision making with known probability of win and loss and selections of risky choices (i.e., highly rewarding but low win probability) that produce negative outcome (loss) reflect poor executive functioning and impulse control risk (Bechara et al., 2005; Everitt and Robbins, 2005; Redish et al., 2008; Cservenka and Nagel, 2012). Results showed that participants in the IIPA group had more advantageous selections at post-intervention while there was no significant difference in the TAU group.

Several research findings suggest that individual at high risk for substance abuse may have difficulty in regulating autonomic arousal effectively (Tarter et al., 1999). Studies have shown that a high relapse rate occur in a heightened state of emotion (Norman et al., 2007; Lloyd and Turner, 2008; Dawson et al., 2005). Cessation of a drug may elicit withdrawal symptoms which is associated with subjective symptoms of negative affect such as dysphoria, depression, irritability and dysregulation of brain reward circuitry (Koob and Le Moal, 1997; Weiss and Koob, 2001). Acute withdrawal elicits dysregulation of drug reinforcement system and stress neurotransmitter system that could lead to vulnerability to relapse. Results showed that the IIPA group had a significant reduction in maladaptive affect regulation strategies such as affect dyscontrol and affect suppression. It can be argued that improvement in affect regulation could be attributed to the improvement in executive functions mediated by the PFC and its circuitry. The PFC is recruited for temporal organization of behavior and purposeful goal-directed activity through two networks which includes both executive network and limbic network (Abernathy et al., 2010; Moghaddam and Homayoun, 2008). The orbitofrontal cortex, a primary region of the limbic network inhibits the irrelevant behavior and relays processed information to the executive control network of the dorsolateral prefrontal cortex (Abernathy et al., 2010). Thus, the entire fronto-temporal-amygdala circuits is involved in emotional regulation (Eslinger et al., 1996; Stuss and Benson, 1986).

It may be presumed that improved executive functions could have enhanced the functioning of frontal areas and its cortical and subcortical networks and thereby facilitating better affect regulation. Similarly, on the other hand, mind-body exercises (Qigong and Tai Chi Chuan) are known to regulate affect. Exercise activates the same reward pathways which are involved in drug addiction. It increases dopamine concentration and dopamine receptor binding (MacRae et al., 1987; Greenwood et al., 2011) and decreases glutamate in the striatum which may protect against overstimulation of glutamatergic receptor in case of chronic drug abuse (Guezennec et al., 1998). Exercise may also influence the brain plasticity through chromatin remodelling at regions implicated in drug addiction (Gomez-Pinilla et al., 2011; Kumar et al., 2005; Wan et al., 2011).

Lastly, relapse prevention is a challenging work in the field of addiction treatment including treatment of alcoholism (Kirshenbaum et al., 2009; Menon and Kandasamy, 2018). The impaired self control may make it more difficult for addicted individuals to resist the temptation of drink (Campanella, 2016). The integrated intervention program for alcoholism (IIPA) was designed to improve the neurocognitive deficits which are important for executive control, reduce implicit attentional biases and motivation for drinking (cue-related craving), improve affect regulation, diminish stress and enhance well-being. Based on the results, we argue that IIPA could facilitate better functioning resulting in lower relapse rate and a longer period of abstinence in the intervention (IIPA) group as compared the control (TAU) group. Survival analysis showed that there was a significant difference between the two groups for better survival (abstinence) in 6 months follow up. This indicated durability of gains produced by the IIPA.

There are several limitations in this study. First, the present study had small sample size. A large sample size could have facilitated more generalizability. Second, this study used randomized case control design; a randomized control design with blind rating could have helped in arriving at more robust conclusions. Third, a documentation of the status of anti-craving medication such as Baclofen during the follow-up could have provided more understanding about effectiveness of the IIPA with regard to the abstinence. Fourth, high attrition and lack of follow-up assessment of executive functions are other limitations of this study. Several factors can cause a high attrition rate in long term follow-up. One very important factor is low socioeconomic status which can influence treatment adherence (Littlejohn, 2006; Fiscella et al., 2000; Bernheim et al., 2008). Financial cost in travelling and/or multiple follow-up visits may contribute for high attrition in patient belonging to the lower socio-economic status. In the present study, 36% patients in the IIPA group and 44% in the TAU group were from the lower socio-economic status and this could be one of the reasons for high attrition

rate at 6 months follow-up. This study provides preliminary evidence of the effectiveness of Integrated Intervention Program for Alcoholism (IIPA). In addition, a few participants (n = 5) were unwilling to continue with IIPA program after few initial sessions. This could be due to lengthy session of the cognitive remediation program of the IIPA. Future studies may consider reducing the length of the session by reducing the number of task used in the program and also tailor the program to suit the cognitive profile of the individual patients. Despite these limitations, the preliminary evidence form this study suggests that the Integrated Intervention Program for Alcoholism (IIPA) is an effective treatment method to improve neurocognitive functions as well as affect regulation in patients with alcoholism.

5. Conclusion

To the best of our knowledge, the present study is the first one which has integrated cognitive remediation and mind-body exercises (Qigong and Tai Chi) to address self-regulatory mechanism in persons with alcoholism. The integration approach is used for ameliorating not only the neurocognitive deficits but also targeting the affect dysregulation, stress and cue-induced craving. The IIPA could potentially be used in other similar clinical conditions such as externalizing behaviors, other substance use disorders and behavioral addictions including pathological gambling and gaming addiction.

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Conflict of interest statement

All other authors declare that they have no conflicts of interest.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.ajp.2019.05.006.

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