ORIGINAL ARTICLE

A Comparative Assessment of Comprehensive Trail Making Test and Wisconsin Card Sorting Test Among Alcohol Dependence Patients

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ABSTRACT

Introduction: Alcohol, when used frequently, accelerates the ageing process, causes brain damage, and results in a reduced volume of grey and white matter, leading to frontal lobe abnormalities. The neurotoxicity resulting from alcohol overuse affects the higher functions of the brain. This study aimed to evaluate the effect of alcohol dependence on the executive functioning of the brain. **Methods:** This study was carried out as a case-control study among 60 patients with alcohol dependence and 60 controls. Assessment of executive function was carried out using the Comprehensive trail-making test (CTMT) and the Wisconsin card sorting test (WCST). Comparison between the alcohol dependence group and normal healthy controls were calculated using the Mann-Whitney U test as data followed a non-parametric distribution. **Results:** The mean age of the participants among the cases and controls was 38.3±5.5 years and 37.8±5.4 years, respectively. The results showed a significant difference in both WCST and CTMT between cases and controls ($p<0.05$). **Conclusion:** This study concludes that there was an impaired performance in executive functions in alcohol- dependence patients in early abstinence compared to normal controls showing frontal lobe impairment in alcohol-dependence patients.
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Keywords: Alcohol-dependence, Wisconsin card sorting test (WCST), Comprehensive trail-making test (CTMT), Neuropsychiatric

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INTRODUCTION

Alcohol dependence, which is characterised by excessive and frequent alcohol use, is fraught with many complications, which are physical, psychological, social, professional and legal. In physical complications, every system is involved, but the neurological system is particularly affected. Diagnosis of alcohol dependence is made when there are more than three of these symptoms present together in the previous year as per the criteria of ICD 10 (1). Among alcohol-dependence subjects, several studies have been reported on deficits of cognitive function, vitamin deficiency, executive functions, learning, memory, visuo-motor co-ordination, and abstraction due to the toxic effect of alcohol or withdrawal (2).

Alcohol dependence also impairs higher functions and higher-order cognitive functioning, which involves the ability to initiate, plan and regulate purposeful behavior, termed executive functioning (3). Studies have proposed that executive functioning is significantly damaged in alcohol dependence, and the impairment is sustained even after withdrawal. A meta-analysis reported less than one month as short abstinence, a time necessary for relapse prevention (4). A study observed that 45% of alcohol-dependent individuals have lingering deficits three weeks after cessation of alcohol use, and 15% retain deficits after one year of abstinence (5).

Several studies have determined the cognitive impairments in alcohol-dependent individuals using Montreal Cognitive Assessment (6), Mini-Mental State Examination (7). However, clinical neuropsychologists evaluate memory using the California Verbal Learning test and Doors and People test (8), Comprehensive trail making test (CTMT), Wisconsin Card Sorting Test (WCST), the Stroop Color Word test, and the Letter Fluency Test to evaluate executive functions (9,10).

The CTMT is a simple one to measure the range of cognitive processes, which includes; five visual search and sequencing tasks influenced by attention,

concentration, resistance to distraction, set-shifting, visual search, and sequencing demands (9,11). In addition, it is considered a significant association of overall measures of intelligence, particularly sensitive indicators of neurological impairment (12). The Trails 1–3, 4 and 5 are similar to Trial Making Test (TMT) Trails A and TMT Part B, respectively (13), and the trail scores by examinees are based on the completion time in seconds (9).

The WCST is a neurophysiological test that helps in evaluating higher-level cognitive processing and executive functions (14,15). The WCST consists of two sets of 64 response cards and represents four stimulus cards that vary in shape, colour, and number of elements. Upon completion, the higher-order cognitive operations are executive functions, and failure represents executive dysfunction (16). The WCST were applied in several neuropsychological studies to determine the cognitive performance among depression, schizophrenia (10), and epilepsy (17) were compared with the control subjects. CTMT and WCST have been developed and has been used world-wide as a measure of abstract reasoning and as a clinical neuropsychological instrument among various populations compared to the other neurological test batteries such as the tower of London test, Stroop test, Ammons quick tests (18).

Due to the paucity of studies in this area, there is a need to assess the executive functions in alcohol-dependent patients who might have executive function impairments and hence may face difficulties in carrying out relapse prevention using coping skills training during the early days of abstinence. Moreover, frontal lobe deficits interfere with relapse prevention efforts while rehabilitating alcohol-dependent patients after the detoxification phase is over. To our knowledge, there is a lack of study on cognitive operations, particularly on executive function among alcohol-dependence subjects in India.This study aimed to compare the executive functions between alcohol-dependence patients in early abstinence and normal healthy controls.

MATERIALS AND METHODS

Study setting

This study was carried out as a case-control study in the Department of Psychiatry among the outpatients visiting our tertiary care hospital (SRM Medical College and Hospital, Chennai) for a year between March 2015 and 2016.

Study participants

The study participants consisted of two groups –patients with alcohol dependence, who are in early abstinence (< 31 days) after detoxification treatment, including thiamine supplementationdiagnosed as per ICD-10, who are on de-addiction treatment, coming from the catchment areas of our tertiary care hospital. Controls - Normal healthy control group was attenders of patients who came to our hospital as per selection criteria, with age, education, and Intelligence Quotient (IQ) matched to cases.

Sample size and sampling

Based on the available literature, an effect size/Cohen's d for cognitive domains like executive function in early abstinence (0-31 days) was 0.534. Taking the anticipated effect size as 0.534 (moderate), desired statistical power as 0.8 (by convention) and the p-value at 0.05, the minimum sample size per group for a two-tailed t-test was calculated as 57 and was rounded off to 60 in each group. A total of 120 participants were selected by consecutive sampling.

Selection criteria

In this study, the alcohol dependence was diagnosed based on ICD 10 criteria and was on de-addiction treatment, which includes detoxification thiamine supplementation, in early abstinence (< 31 days) (16). In addition, the patients must be aged between 18-45 years, completed up to the eighth standard of formal education, according to Indian standards, and have IQ scores as per Raven's progressive matrices, ≥50th percentile. Subjects who have any history of psychiatric illness in the family or any other substance use other than alcohol in participants screened using MINI neuropsychiatric interview, history of long-term neurological or systemic illness and head injury with loss of consciousness were excluded for both case and controls from this study. Subjects matched for age, gender, IQ, and not having a history or current use of alcohol were considered control subjects. However, those with any history of, or the current status of, neuropsychiatric illnesses using MINI neuropsychiatric interview (Supplementary material) and IQ scores less than the 50th percentile in Raven's progressive matrix were excluded as controls from the study.

Ethical approval and informed consent

Ethical approval was obtained from the SRM Medical College Hospital and Research Centre, Institutional Ethics Committee (720/IEC, 2015), prior to the commencement of the study. Each participant was explained in detail about the study, and written informed consent was obtained from the participants prior to the data collection.

Data collection tools

Regarding alcohol consumption history, a structured interview schedule was used. All the study participants were screened for the presence of psychiatric disorders based on the MINI neuropsychiatric interview (18). Standard Raven's progressive matrices were used to assess the IQ levels. Any participant with a median IQ score ≥50 was included in the study. The cases and controls were matched by age, education and IQ.

Comprehensive Trail-Making Test

The CTMT-scaled scores are provided in the form of normalized T-scores given to all the subjects, with accompanying percentile ranks. Each Trail is assigned a qualitative description of the performance, which is based on the accompanying T-score, the grade has been described elsewhere (16). The T-scores of all the Trails are then summed up. Each T-score sum has a corresponding CTMT Composite Index score, which gives the overall performance in all 5 Trails. The number of trails to find the average or mean T-score divides the T-score sum. To determine the association between an individual trail score and the mean score of all 5 Trails, the examiner subtracts the mean of all five trail scores from each trail's T-score. The examiner then compares the difference between the values given in the Record booklet of the CTMT.

Wisconsin Card Sorting Test

WCST was used with four stimulus cards to evaluate the higher-level cognitive processing and execution. Overall, 128 response cards (two identical of 64 response cards) and the test were performed when the participant was expected to accurately sort every response card with one of the four stimulus cards through the feedback given to them based on a rule. Once the participant had made a specified number of consecutive correct matches to the initial sorting principle (usually done to the colour at first), the sorting principle changed abruptly to form or number without informing the subject, requiring them to employ feedback from the examiner to revise their strategy. The test continues through multiple such shifts in sorting principle among the three possible sorting categories of colour, form, and number (19). There were six WCST indices were used for analysis (14). The calculation of the results for WCST and CTMT data and other psychological tests was done with the help of the manuals (20) and cross-checked with the help of a trained clinical psychologist.

Statistical Analysis

Statistical Package for Social Sciences (SPSS ver. 16) was used for all the statistical analyses. Descriptive statistics were applied for the demographic details of the alcohol-dependence group and normal healthy controls. For categorical variables, the Chi-square test and for continuous variables t-test were used. Mann-Whitney U test was used to compare between the alcohol dependence and normal healthy control subjects.

RESULTS

Table 1 shows the socio-demographic characteristics of the study subjects. The mean age of both subjects are less than 40 years old and is not significantly differed (P=0.606) and the subjects are age-matched controls. Similar observation were noticed on the IQ among both case and control subjects (p>0.05). Among the two groups, there is a significant difference (p<0.05) was observed in religion, occupation and income. Overall results show in the alcohol-dependence group, about 52.8% were single and 47.6% were married, and 2 participants were divorced (50%) compared to 52.4%, 47.2% and 50% respectively, in control groups. A majority of the participants were Hindus (80.8%) as religion followed by Christians and others. The majority of the cases (43.3%) and controls (46.6%) had studied up to the higher secondary level of education. Most of them were semiskilled workers (35%), and 10% were unemployed in the alcohol dependence group compared to 38.3% of skilled workers in the control group (p<0.01). It was observed that the average monthly income was higher in the control group compared to the cases. Regarding the family, 58.3% belonged to the nuclear family in control subjects compared to 51.3% in alcohol dependence subjects. In both groups, the

Table I: Demographic characteristics between alcohol dependence and control subjects

Characteristics	Groups		P value
	Alcohol n (%)	Control n (%)	
Age#	38.30 ± 5.5	37.78 ± 5.4	0.606
IQ#	60.42 ± 12.4	60.83 ± 12.5	0.855
Marital Status			
Single	28 (52.8)	25 (47.2)	
Married	30 (47.6)	33 (52.4)	0.855
Divorced	2 (50)	2 (50)	
Religion			
Hindu	43 (71.7)	54 (90)	
Christian	14 (23.3)	3 (5)	0.015*
Others	3 (5)	3 (5)	
Education			
High School	1 (1.6)	1 (1.6)	
Higher Secondary	26 (43.3)	28 (46.7)	0.985
Diploma	10 (16.7)	9 (15)	
Graduate	23 (38.3)	22 (36.7)	
Occupation			
Unemployed	6 (10)	0	
Unskilled worker	3 (5)	1 (1.6)	
Semi-skilled worker	21 (35)	11 (18.3)	
Skilled worker	7 (11.7)	23 (38.3)	0.001**
Clerical	5 (8.3)	8 (13.3)	
Business	17 (28.3)	13 (21.7)	
Profession	1 (1.6)	4 (6.7)	
Family			
Nuclear	31 (51.7)	35 (58.3)	0.463
Joint	29 (48.3)	25 (41.7)	
Locality			
Urban	39 (65)	39 (65)	1.00
Rural	21 (35)	21 (35)	
Income			
No income	4 (6.7)	0	
Below 5000	2 (3.3)	0	
5000-10000	13 (21.7)	2 (3.3)	
10000-15000	16 (26.7)	13 (21.7)	
15000-20000	4 (6.7)	23 (38.3)	0.001**
20000-25000	4 (6.7)	5 (8.3)	
25000-30000	8 (13.3)	5 (8.3)	
30000-40000	8 (13.3)	8 (13.3)	
40000-45000	0 ()	2 (3.3)	
45000-50000	1 (1.6)	2 (3.3)	

IQ: intelligent quotient, #Mean ± SD, * p value<0.05, ** p-value <0.01

subjects belonged to urban (65%) localities compared to rural areas (35%).

Results were obtained when the WCST was used for comparing executive functions between alcohol dependence and controls using the Mann-Whitney U test with reference to the WCST manual. The results showed a significant difference in the perseverative errors between cases and controls (Table II). The observed difference was statistically significant ($p<0.05$). The total number of errors, number of categories, and number of trails administered, and number of correct responses were also statistically different ($p<0.05$). Statistically, a significant difference was observed between perseverative responses and non-perseverative errors and conceptual level responses between the groups. Perseverative error is mean rank of 46.1 in alcohol-dependence group and mean rank of 74.29 in control group indicating more perseverative error in alcohol-dependence group, as per reference from WCST manual higher the score better the performance. In the total number of errors the mean rank is 46.40 in alcohol-dependence group and control group (74.6) showing more errors in alcohol group as higher the score lesser the error according to WCST manual. The mean rank for the number of categories completed is 41.67 in the alcohol group which is lesser compared to the control group (79.33). The number of trials administered is higher (81.64) in the alcohol-dependence compared to the control group (31.6) which shows that alcohol group needed more number of trials to be administered than control group. The total number correct shows a mean rank of 50.72 in alcohol-dependence group and 70.28 in control group which shows that control group was more correct than alcohol-dependence group. The perseverative response (51.8) and the non- perseverative error (44.98) are lesser in alcohol-dependence group compared to control group 69.82 and 76.03 respectively as the performance is not higher in the alcohol-dependence group.

However, the conceptual level response in alcohol-dependence was mean rank of 69.8 as fails to attain the lower score compared to the control group score, 51.52. The better performance was observed in the control group (79.33) compared to the alcohol-dependence group (41.6) in the number of categories completed function. The trials to complete first category shows mean rank of 65.43 in alcohol-dependence group and 55.57 in control group which indicates that alcohol-dependence group took slightly more trials to finish first category, however there was no significant difference was observed ($p>005$). The failure to maintain set in alcohol-dependence group was a mean rank of 68.61 and 52.39 in control group which shows that alcohol-

Table II: Comparison of executive functions in alcohol dependents and normal controls using WCST applying Mann Whitney U test

Functions	Group	N	Mean Rank	Sum of Ranks	Z value	P value
Perseveration Error	Alcohol	60	46.71	2802.50	4.350	<0.001**
	Control	60	74.29	4457.50		
Total number of Errors	Alcohol	60	46.40	2784.00	4.448	<0.001**
	Control	60	74.60	4476.00		
Number of Categories Completed	Alcohol	60	41.67	2500.00	6.689	<0.001**
	Control	60	79.33	4760.00		
Number of trials administered	Alcohol	60	81.64	4898.50	7.008	<0.001**
	Control	60	39.36	2361.50		
Total number correct	Alcohol	60	50.72	3043.00	3.083	0.002**
	Control	60	70.28	4217.00		
Perseverative response	Alcohol	60	51.18	3071.00	2.940	0.003**
	Control	60	69.82	4189.00		
Non-perseverative error	Alcohol	60	44.98	2698.50	4.895	<0.001**
	Control	60	76.03	4561.50		
Conceptual level response	Alcohol	60	69.48	4169.00	2.860	0.004**
	Control	60	51.52	3091.00		
Number of categories completed	Alcohol	60	41.67	2500.00	6.689	<0.001**
	Control	60	79.33	4760.00		
Trials to compete first category	Alcohol	60	65.43	3926.00	1.561	0.119
	Control	60	55.57	3334.00		
Failure to maintain set	Alcohol	60	68.61	4116.50	2.721	0.007**
	Control	60	52.39	3143.50		
Learning to learn	Alcohol	60	60.36	3621.00	0.045	0.964
	Control	60	60.64	3638.50		

Note: ** Denotes significant at 1% level * Denotes significant at 5%

dependence had more difficulty to maintain set. There was no significant difference between both groups under the learning to learn function (p>0.05). Hence the results show on comparing the executive functions, alcohol dependence group performed low compared to control group subjects.

A comparison of CTMT for executive functions between alcohol dependents and controls using the Mann-Whitney U test was conducted (Table III). Results show that the mean rank of alcohol dependents and normal controls in CTMT Trail 1 was found to be 42.56 and 78.44, respectively, with a significant Z value of 5.657 (p<0.001**). The mean rank is significantly higher in normal controls than in alcohol dependents in Trail 2 is 42.95 and social drinkers is 78.05 with the significant Z value of 5.535 (p<0.001**). In addition, the mean rank of alcohol dependents in Trail 3 is 44.87and normal controls is 76.13 with the significant Z value of 4.935 (p<.0.001**). Furthermore, the mean rank of alcohol dependents in Trail 4 is 44 and social drinkers is 77 with the significant Z value of 5.205 (p<0.001**). The mean rank of alcohol dependents in Trail 5 is 47.13 and normal controls is 73.87 with the significant Z value of 5.295 (p<.001). The performance in trails were superior in normal controls when compared to alcohol dependence group with reference to CTMT manual. Thus, the alcohol dependence group had lower raw t scores as they took a long time to complete the trail when compared to the control group. Results conclude that the alcohol group performed poorly compared to the control group.

Table III: Comparison of executive functions in alcohol dependents and normal controls using Comprehensive Trail Making Test applying Mann-Whitney U test

Trials	Group	N	Mean Mark	Sum of Ranks	Z value	P value
Trail 1	Alcohol	60	42.56	2553.50	5.657	<0.001**
	Control	60	78.44	4706.50		
Trail 2	Alcohol	60	42.95	2577.00	5.535	<0.001**
	Control	60	78.05	4683.00		
Trail 3	Alcohol	60	44.87	2692.00	4.935	<0.001**
	Control	60	76.13	4568.00		
Trail 4	Alcohol	60	44.00	2640.00	5.205	<0.001**
	Control	60	77.00	4620.00		
Trail 5	Alcohol	60	47.13	2828.00	4.217	<0.001**
	Control	60	73.87	4432.00		

Note: ** Denotes significant at 1% level * Denotes significant at 5%.

DISCUSSION

This study was conducted to compare the executive functioning between alcohol-dependence patients and normal individuals who were matched. Results showed that the groups also matched in the locality and marital status. Hence, the confounding factors, which may affect executive functioning while comparing both these groups, were minimized. The benefit of matching also allowed for the use of raw scores of tests in the CTMT and WCST.

The present study found that the alcohol-dependence group performed poorly on executive functions when compared with normal controls. Alcohol dependent group showed impairment in the WCST test for executive functions when compared to the control groups. Areas of impairment in the alcohol dependence group were seen in perseverative response, perseverative error, the total number of errors and categories completed, failure to maintain set, non-perseverative error, number of trials administered, conceptual level response, trials to complete the first category and total number correct. The results showed that the mean rank of the perseverative error in alcohol-dependence group was 46.1 and 74.29 in the control group, indicating more perseverative error in alcohol dependence group, as per the reference from the WCST manual (higher the raw score, the better the performance) with a significant P value of <0.001** which shows a significant defect in perseverative error in alcohol dependence group.

The perseverative error is considered to be the most sensitive WCST measure of frontal lobe dysfunction. The increased perseverative errors found in the present study are the result of prefrontal cortex dysfunction caused by alcohol use. A study showed more perseverative errors in alcohol-dependence patients in his study when compared to social drinkers (21). Another study also showed similar results in their study that alcoholics made more errors than a group of normal controls (22,23). Results indicated that the mean rank of perseverative response in alcohol-dependence group is 51.8 and in the control group 69.82, which, interpreted according to the WCST manual as (higher the score, better response), has a significant p-value of 0.003**. These results were similar to the results of Guillot et al. 2010 (24), which found that perseverative response was significantly higher among alcohol dependents. However, that study failed to find differences in total errors and categories completed.

In this study, Pearson's correlation method was used to find the correlation between executive functions and drinking parameters. There was no correlation found between any drinking parameters and drinking variables except with binge patterns of drinking. A significant positive correlation was found between the total number of errors in WCST and drinking patterns (0.270*) in the present study. Further attempts were made to identify which pattern had more association with the total number of errors.

However, the results of the study by Saraswat et al. 2006 (25) also found no relationship between the duration of dependence and the amount of alcohol intake with executive functions. However, in addition to this, the study also found that the longer the period of abstinence

lesser the impairment. Similar results were seen in another study reported by Burhanglou et al. 2014 (26). These findings in the present study could have been because of certain genetic predispositions, quality variables like no relapses and individual predisposition with reference to alcohol intoxication and subsequent after effects. Higher-order processes that shape the downstream complications and consequences have to be considered in future. However, an in-depth analysis of other extraneous variables associated with several patterns of drinking needs to be done in large samples. Although researchers have discussed that the alcohol-dependence could be reversibility in the long term, few suggest that the deficits can lead to relapse resulting in long-term cognitive dysfunctions or alcohol-related dementia (26). Hence, there is a need for identification and treatment apart from detoxification addressing cognitive remediation, which could help with management. The findings of this study could pave the way for the intervention development and future implementation.

One of the limitation of this study is that the present analyses did not specifically examine a few other factors associated with executive cognitive function deficits, such as a family history of alcoholism, number of relapses etc. More scales to grade alcohol dependence and severity and correlation with executive cognitive function needs to be studied further as it is one of limitation of the study. The findings of the study extend to a community sample of men alone. The study is limited in not being inclusive of the female population and assessment of patients who have been abstinent for a longer duration. This study was conducted between 2015 -2016, hence, it will be updated with the larger number of samples in the near future.

CONCLUSION

This study concludes that there was a poor and impaired performance in executive functions in alcohol-dependence patients in early abstinence compared to normal controls identified by the use of WCST and CTMT executive function tests.

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