EXECUTIVE DYSFUNCTION IN ALCOHOL DEPENDENT INDIVIDUALS: A CASE CONTROL STUDY

Neethi Valsan[1], Shijin Ammanam Veetil[2], Saibunisa Beevi[3]

[1]Assistant Professor, Department of Psychiatry, Jubilee Mission Medical College & Research Centre.
[2]Assistant Professor, Department of Psychiatry, Government Medical College.
[3]Professor & HOD, Department of Psychiatry, Jubilee Mission Medical College & Research Centre.

ABSTRACT

BACKGROUND

The use of alcohol is increasingly prevalent in our country. Being a neurotoxin, it tends to affect elective mental capacities. Frontal lobe is found to be most affected by chronic alcohol use.

AIM

To study the executive functions in alcohol dependent individuals and to determine any relationship with alcohol intake variables.

MATERIALS AND METHODS

30 recently detoxified alcohol dependent individuals attending the De-addiction Clinic of Medical College, Kottayam, was compared to 30 controls on four tests of executive functions, namely, Controlled Word Association Test, Trail Making Test, Stroop Test, and Wisconsin Card Sorting Test.

Statistical analysis of the data has been done using the Statistical Package for Social Sciences (SPSS Windows version 10).

RESULTS

Executive function was significantly impaired in the alcohol dependent individuals when compared to normal controls in all the four tests. On analysing the effect of drinking variables on executive functioning, the performance of patients is seen to improve with abstinence in Stroop. Those with a positive family history of ADS in the first degree relatives produced fewer words in verbal fluency.

CONCLUSION

As the executive impairment remains more or less stable irrespective to the chronicity or amount of alcohol use, it could be assumed that the executive dysfunction observed is a trait marker rather than a state dependent variable.

KEYWORDS

Executive Dysfunction, Frontal Lobe Dysfunction, Prefrontal Cortex, Neuropsychological Tests, Alcohol Dependence Syndrome.

HOW TO CITE THIS ARTICLE: Valsan N, Veeti SA, Beevi S. Executive dysfunction in alcohol dependent individuals: A case control study. J. Evid. Based Med. Healthc. 2016; 3(47), 2351-2356. DOI: 10.18410/jebmh/2016/519

INTRODUCTION: The use of alcohol is increasingly prevalent in our country and remains associated with innumerable social, economic and health problems. Being a neurotoxic substance, it is common for the occurrence of brain problems among patients, not only in the first days of withdrawal, but also months after the last use of the substance (Pfefferbaum et al, 1995).[1]The deleterious effects of alcoholism on cognitive functioning were reported in the literature as early as the 1880s by Wernicke (Wernicke, 1881)[2] and Korsakoff (Korsakoff, 1887),[3] followed by Hamilton in 1906 (Hamilton, 1906)[4] and Fisher in 1910 (Fisher, 1910).[5]

Financial or Other, Competing Interest: None.
Submission 17-05-2016, Peer Review 02-06-2016,
Acceptance 09-06-2016, Published 11-06-2016.
Corresponding Author:
Dr. Neethi Valsan,
Appt. 4B, Tower 1, Alukkas Bhavanam,
Olarikkara, Thrissur-680012, Kerala.
E-mail: neethivalsan@yahoo.co.in
DOI: 10.18410/jebmh/2016/519

By the 1960s, the studies by Fitzhugh and co-workers introduced the clinical neuropsychological model in the study of cognitive function in alcoholism, and marked the beginning of systematic research in this area (Fitzhugh et al., 1960; Fitzhugh et al., 1965).[6] Alcohol tends to affect elective mental capacities rather than having a diffuse impact on mental functions. Many recent studies based on neuropsychological and neuroradiological data support 'frontal lobe hypothesis' showing frontal lobe to be more susceptible to alcohol-related brain damage than other cerebral regions.

Frontal lobe deficits adversely affect an individual's ability to learn new information and integrate new skills with prior learning experiences. These impairments tend to interfere with relapse prevention strategies directed at the rehabilitation of alcohol dependent patients after the detoxification phase is over (Bates et al, 2002).[7] These cognitive deficits may be amenable to retraining. Therefore, early detection and intervention may have an impact on the overall prognosis.

Though chronic alcohol ingestion can trigger deficits in anterior frontal lobe structure and functions, whether it can be recovered once the consumption ends remains an unanswered question. And, to what extent the alcohol consumption variables affect the frontal lobe functions, also remains a 'Grey Area'. The limited effort in this direction has produced inconclusive results. Moreover, there are very few studies undertaken with these perspectives in our country. This study, therefore, attempts to examine the executive functions and their association with alcohol consumption variables like duration and severity of dependence and period of abstinence.

AIMS AND OBJECTIVES:

- To study the executive functions in alcohol dependent individuals.
- To study the relationship between executive dysfunction and alcohol intake variables.

MATERIALS AND METHODS: Male subjects in the age group of 18-50 with a diagnosis of "Alcohol Dependence Syndrome", as per ICD-10 DCR and confirmed by two consultants, were recruited from among the patients attending the DE addiction Clinic and Psychiatry Outpatient Department, Medical College, Kottayam over a period of 1 year.

STUDY GROUP:

Inclusion Criteria:

- Abstinent from alcohol for at least 10 days.
- Right handed.
- At least 5 years of formal education.

Exclusion Criteria:

- Evidence of mental sub normality.
- History or cross-sectional evidence of other psychiatric illnesses.
- Presence of clinically apparent medical/neurological illness (Wernicke-Korsakoff syndrome, epilepsy, head injury, CVA, diabetes mellitus, thyroid dysfunction).
- H/O any other substance abuse except tobacco.
- Presence of Colour blindness.
- Subjects with self-reported visual/ auditory impairment.

Among the patients attending the clinic only 30 patients satisfied the criterion and were included in the study group.

CONTROL GROUP: Matched for age and education, was selected from caregivers of patients from ophthalmology ward who had no history of harmful use of alcohol or dependence and fulfilling the exclusion criteria for the cases.

INSTRUMENTS:

1. **Specially designed intake Proforma:**
    1. **Socio-Demographic Details:** To record the subject's age, gender, education, occupation, marital status, religion, type of family, income.
    2. **Clinical Profile:** Information regarding the following variables was recorded:
        a. Age of onset of drinking.
        b. Total duration of alcohol use.
        c. Duration of dependence.
        d. Average amount of alcohol intake (in units).
        e. Presence of withdrawal seizures, delirium or alcohol induced psychotic episodes.
        f. Period of Abstinence in the last 1 year.
        g. Positive family history.
2. **ICD-10 Criteria for Alcohol Dependence Syndrome.**
3. **SADQ Questionnaire.**
4. **Neuropsychological Tests.**

To assess executive functions, trail making test, Stroop colour word test, controlled oral word association test and Wisconsin card sorting tests were employed.

Procedure: After noting down the socio-demographic details, the alcohol dependent subjects and the control subjects were administered the neuropsychological tests by the researcher, in the same order, and carried out under similar conditions for all the subjects. Duration of assessment was approximately 45 minutes to 1 hour, and varied with patients' performance in the tests. The performance of cases and controls on these tests were compared. An intragroup analysis was done among the cases to study the effect of drinking variables on executive functioning. All the procedures followed in this study were approved by the ethical committee of our institution.

STATISTICAL ANALYSIS: Statistical analysis of the data has been done using the Statistical Package for Social Sciences (SPSS Windows version 10). For interval/ ratio level data, mean was computed and t test is used to study the difference between mean values. For nominal level measurements, the differences are compared in terms of percentages. When there were wide variations in data, as reflected in standard deviation, equivalent non-parametric test (Mann Whitney U) was applied. For continuous data, when more than two means were involved ANOVA (F test) was used. For qualitative data, to study the differences in observations, Chi square test was used. For all these tests, the statistical significance was fixed at 5% level (0.05).

OBSERVATIONS AND DISCUSSIONS: 30 recently detoxified alcohol dependent individuals attending the De-addiction clinic of medical college, Kottayam, was compared to 30 controls on four tests of executive functions, namely, Controlled Word Association Test, Trail Making Test, Stroop Test, and Wisconsin Card Sorting Test.

Demographic Profile of Cases: The mean age of cases is 39.9 yrs. that show a patient group of younger age as against the earlier studies (Brandt et al, 1983; Parsons et al, 1971).[8]Increased age could be a confounding factor as normal ageing can lead to cognitive deficits or there may be an unidentified dementing process going on.

The mean number of years of education is 9.03 and that of controls is 9.33 years. Since the premorbid IQ could not be assessed, a minimum number of years of formal education was sought to be included in the study. Age of onset of drinking was 16.23 years, which is the adolescent stage where exploring different pleasure giving activities is one of the important priorities. This could have led the patients to start consuming alcohol at this age. The mean years of regular use of alcohol were 17.76. The mean duration of dependence among the cases was 3.97 yrs. This short-term of dependence is probably due to younger age of the sample and could be confounded by the patients' recall bias.

The average amount of alcohol use was 23.21±12.63 units. The mean of maximum period of abstinence was 51.3 days. Positive family history of ADS in first degree relatives was obtained in 21 patients. The mean SADQ score was found to be 31.40 which suggests severe alcohol dependence (severity >30).

TESTS OF EXECUTIVE FUNCTIONS:

Cases vs. controls:

Verbal Fluency: Mean score for verbal fluency for cases is 21.17, whereas that for the controls is 32.43, showing a significant difference between the two groups. This is in agreement with studies done earlier (Dao-Castellano et al, 1998; Brokate et al, 2003).[9][10] There are studies which disagree with our finding like Ratti MT et al, 2002,[11] Karl Mann et al 1999[12] and Ihara& Berrios, 2000.[13] In these studies, the mean yrs. of education of the patients are higher than that in the current study. Oscar-Berman, Kirkley, Gansler & Couture (2004)[14] has showed that education may play a role, because low education led to a reduced performance in alcoholics, but not in controls.

	Category	Mean (No. of. Words)	Std. Deviation	Mann-Whitney U	Sig
SA	Case	7.00	3.322	217.500	.001
	Control	10.47	3.866		
NA	Case	6.23	2.431	249.500	.003
	control	9.07	4.025		
PA	Case	7.93	3.258	142.000	.000
	Control	12.90	4.708		
Total	**Case**	**21.17**	**7.465**	**172.500**	**.000**
	Control	**32.43**	**11.796**		

Table 1: Controlled Word Association Test

Trail Making Tests: Time taken for TMT part B showed a mean of 203.93 sec. for cases whereas the controls took significantly lesser time for completion i.e. 70.5 sec. (p=0.00). The time difference between part B and A also showed significant difference between the two groups, a mean of 123.06 sec. for cases and 34.44 sec. for controls (p=0.00). This finding is similar to other studies (Dao-Castellano et al, 1998; Ratti MT et al, 2002: Karl Mann et al 1999; Ihara & Berrios, 2000; Noel X et al, 2001; S.J.C. Davies, 2005; Goldstein RZ et al, 2004)[9][11][12][13][15][16][17]

Tests	Category	Mean	Std. Deviation	Mann-Whitney U	sig
TMT A	Case	77.50	34.810	127.000	.000
	control	38.63	11.458		
TMT B	Case	203.93	106.895	68.000	.000
	Control	70.50	26.898		
TMT B-A	Case	123.07	84.217	92.500	.000
	Control	32.13	22.413		

Table 2: Trail Making Tests

*Significance at less than or equal to 0.05.

There is significant difference between the case and controls in respect to the time taken to complete Trails A and B and B-A.

Stroop Test: Time taken for Stroop W was 118.7 sec. in cases as against 94.7 sec. for controls (p=0.017). Cases took more time for Stroop C (439.67 sec.) than controls (217.9 sec.). The difference is statistically significant (p=0.00). The time difference between the two tests Stroop C-W was also significantly increased for cases (p=0.00). This is in agreement with earlier studies (Dao-Castellano et al, 1998; Ihara & Berrios, 2000; Noel X et al, 2001; M. T. Ratti et al, 2002; Goldstein RZ et al, 2004).[17]

	Category	Mean	Std. Deviation	Mann-Whitney U	p
STROOP W	Case	118.70	47.030	246.000	.003
	Control	94.70	25.748		
STROOP C	Case	439.67	217.322	75.000	.000
	Control	217.90	44.621		
STROOP CW	Case	324.53	210.108	127.000	.000
	Control	123.20	45.176		

Table 3: Stroop Test

*Significance at less than or equal to 0.05.

Statistically significant differences were found for all the subtests of Stroop between cases and controls.

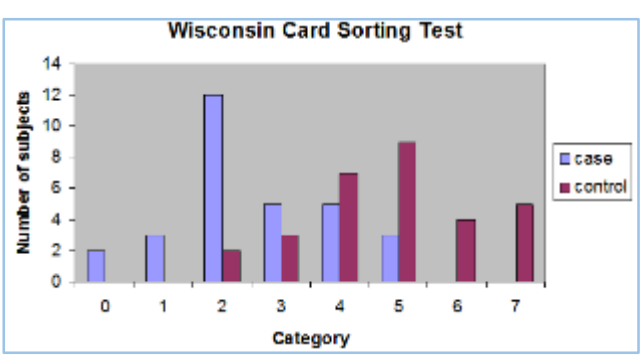

Fig. 1

Among controls, majority (30%) made 5 categories, whereas majority of the cases (40%) made only 2 categories.

Wisconsin Card Sorting Test: Majority of the cases (40%) completed only 2 categories whereas majority of the controls (30%) could complete 5 categories (p=0.00). Cases made more perseverative errors than controls and the difference was statistically significant (p =0.00) which has been replicated in earlier studies (Tarter, 1973; Ihara & Berrios, 2000; M. T. Ratti et al, 2002).[18][13] Thus, executive function was significantly impaired in the alcohol dependent individuals when compared to normal controls in all the four tests. Poor performance in alcohol dependent individuals on tests of executive functions have been demonstrated by researchers using other tests as well as neurophysiological measures such as positron emission tomograms (Adams et al, 1993),[19] which gives further emphasis to our findings.

Effect of drinking variables on executive functions:
Age of First Drink: Patients were divided into three groups: those who had onset less than 15 yrs., 15-20 yrs. and more than 20 years. No significant difference was observed in their performance in any of the four.

Years of Dependence: Comparison was made between the performances of cases with duration of dependence of less than 4 years and more than or equal to 4 years of dependence.

None of the tests showed significant difference between the groups. The mean years of dependence obtained in the current study was 3.9 yrs. with only two patients having more than 8 yrs. of dependence. This poor representation of those with greater years of dependence in the sample could explain the absence of significant relationship observed in the study.

The Sample Group Was Divided into Three: Those with abstinence <3 months, 3-6 months and >6 months. Of the four tests, Stroop W and C were found to be less impaired with increasing periods of abstinence (Table 4). But, there were lesser number of subjects with period of abstinence of more than 3 months in the current study. So, a conclusive opinion is difficult and study needs replication with a better representative sample.

SADQ Score: Based on the SADQ score, the patients were divided into 'Mild' (<16), 'Moderate' (16–30) and 'Severe' dependence (>30). Majority (53.3%) of the patients came under severe dependence. There were no differences observed in the four tests among the different groups.

Tests	Age of First Drink	Years of Dependence	Amount of Use	Periods of Abstinence	SADQ Score
Verbal Fluency	.060	.690	.584	.497	.859
Trail Making Tests TMT A	.102	.586	.606	.420	.323
TMT B	.276	.884	.753	.485	.230
TMT B-A	.438	.852	.710	.485	.234
Stroop Tests STROOP C	.129	.205	.974	**.012***	.344
STROOP C-W	.146	.227	.934	**.049***	.392
Wisconsin Card Sorting Tests					
WCST ERRORS	.592	.509	.739	.465	.464
WCST CAT	.411	.824	.723	.470	.181

Table 4

Of the four tests, Stroop W and C were found to be less impaired with increasing periods of abstinence (Table 4). But, there were lesser number of subjects with period of abstinence of more than 3 months in the current study. So, a conclusive opinion is difficult and study needs replication with a better representative sample.

Tests	Withdrawal Seizures	Withdrawal Delirium	Induced psychosis	Other sub. Used	FA/H
Verbal Fluency	0.918	0.811	.359	0.7	**.003***
TMT A	.441	.520	.365	.573	.845
TMT B	.346	.958	.889	.146	.366
TMT B-A	.157	.935	.867	.135	.275
STROOP W	.201	.226	.334	.922	.205
STROOP C	.994	.904	.540	.541	.208
STROOP W-C	.828	.985	.368	.504	.386
WCST ERRORS	.597	.359	.244	.156	.305
WCST CAT	.918	.848	.208	.259	.466

Table 5

*Significance at less than or equal to 0.05.

Subjects were subdivided into two groups: those with a positive history and those with negative history. Statistical correlation could be found among the tests for verbal fluency (p=0.03) in those with positive family history. Though there was a trend towards a positive correlation between impairment in TMT B and Stroop Tests and a positive family history, it did not reach statistical significance. This difference in performance between the two groups could not be attributed to genetic factors alone as various other variables like duration of dependence and the average amount of alcohol consumed had not been controlled for and thus may have confounded the result.

The other variables like past history of delirium tremens, withdrawal seizures and psychotic episodes were found to have any significant effect on the tests for executive dysfunction. However, the diagnoses of these conditions were based on historical data which could be erroneous due to recall bias. To overcome this, ideally patient with the above diagnosis should be identified cross-sectionally and cognitive functions should be tested in the asymptomatic stage during the next follow-up.

Thus, to summarise, the alcohol dependent individuals performed worse than the controls. They produced lesser number of words in verbal fluency, took more time for completion of Trail Making tests, took more time to read in Stroop C and Stroop W and completed less number of categories and made more perseverative errors in Wisconsin Card Sorting Tests. Thus, chronic use of alcohol produces impairment in strategic planning, organised searching, sequencing skills and set shifting, response inhibition and cognitive flexibility.

On analysing the effect of drinking variables on executive functioning, the performance of patients is seen to improve with abstinence in Stroop. Those with a positive family history of ADS in the first degree relatives produced fewer words in verbal fluency when compared to those with a negative family history. But, otherwise, as the executive impairment remains more or less stable irrespective to the chronicity or amount of alcohol use, it could be assumed that the executive dysfunction observed is a trait marker rather than a state dependent variable. Moreover, this assumption is further supported by studies done in non-alcoholic population with a positive family history which showed that positive family history have independent, additive deleterious effects on cognitive-perceptual functioning (Drejer et al., 1985; Tarter et al., 1989; Corral et al., 2002).[20][21][22]

The improvement in the cognitive dysfunction with abstinence suggests that alcohol does exert a neurotoxic effect on prefrontal lobes albeit its effect is only transient. Further researches, employing prospective methods, needs to be undertaken for confirmation of this hypothesis.

CONCLUSION: Thus, to conclude, the presence of executive dysfunction may be a trait marker of alcohol dependence syndrome and its relation with the drinking variables needs to be further followed up in prospective studies.

LIMITATIONS:

- The study cannot be generalised to a larger population as it was conducted in a small sample.
- The study design was cross-sectional. A longitudinal assessment of the deficits would have been more appropriate.
- Extensive assessment of frontal lobe functions with a wide array of tests was not done.
- Lack of consideration for the nutritional status of the patients.

REFERENCES

1. Pfefferbaum A, Sullivan EV, Mathalon DH, et al. Longitudinal changes in magnetic resonance imaging brain volumes in abstinent and relapsed alcoholics. Alcoh Clin Exp Research 1995;19(5):1177-1191.
2. Wernicke C. Lehrbuch der Gehirnkrankheiten fur Aerzte und Studirende. Theodor Fisher, Kassel U. Berlin 1881;2:229–242.
3. Korsakoff S. Disturbance of psychic activity in alcoholic paralysis. Vestn Klin Psichiat Neurol 1887;4(2):1–102.
4. Hamilton CL. Alcohol and the mind. Illinois Med J 1906;9:39–46.
5. Fisher JT. Mental defects following the use of alcohol. S Calif Practitioner 1910;25:569–572.
6. Fitzhugh L, Fitzhugh K, Reitan, R. Adaptive abilities and intellectual functioning of hospitalized alcoholics: further considerations. Quarterly Journal of Studies on Alcohol 1965;26(3):402-411.
7. Bates ME, Bowden SC, Barry, D. Neurocognitive impairment associated with alcohol use disorders: implications for treatment. Experimental & Clinical Psychopharmacology 2002;10(3):193-212.
8. Parsons OA, Tarter RE. Conceptual shifting in chronic alcoholics. Journal of Abnormal Psychology 1971;77(1):71-75.
9. Dao-Castellana MH, Samson FL, Syrota A. Frontal dysfunction in neurologically normal chronic alcoholic subjects: metabolic & neuro-psychological findings. Psychol Med 1998;28(5):1039-1048.
10. Brokate B, Hildebrand H, Eling P, et al. Frontal lobe dysfunctions in Korsakoff's syndrome and chronic alcoholism: continuity or discontinuity? Neuropsychology 2003;17(3):420–428.
11. Ratti MT, Soragna D, Sibilla L, et al. Cognitive impairment and cerebral atrophy in heavy drinkers. Prog neuropsychopharmacol Biol Psychiat 1999;23(2):243-258.
12. Mann K, Gunther A, Stetter F, et al. Rapid recovery from cognitive deficits in abstinent alcoholics: a controlled test-retest study. Alcohol & Alcoholism 1999;34(4):567-574.
13. Ihara H, Berrios GF. Group & case study of the dysexecutive syndrome in alcoholism without amnesia. J Neurol Neurosurg Psychiatry 2000;68(6):731-737.

14. Oscar-Berman M, Eckardt M, Warren K. Neuropsychological vulnerabilities in chronic alcoholism. Review of NIAAA's Neuroscience and Behavioral Research Portfolio. NIAAA Publications, Bethesda 2000;p.437–471.
15. Davies SJ, Pandit SA, Feeney A, et al. Is there cognitive impairment in clinically healthy abstinent alcohol dependence? Alcohol & alcoholism 2005;40(6):498–503.
16. Noel X, Linden VM, Schnidt N. Supervisory attentional system in non-amnesic alcoholic men. Archives of General Psychiatry 2001;58(12):1152-1180.
17. Goldstein RZ, Leskovjan AC, Hoff AL, et al. Severity of neuropsychological impairment in cocaine and alcohol addiction: association with metabolism in the prefrontal cortex. Neuropsychologia 2004;42(11):1447-1458.
18. Tarter RE. An analysis of cognitive deficits in chronic alcoholics. The Journal of Nervous and Mental disease 1973;157(2):138-147.
19. Adams KM, Gilman S, Koeppe RA, et al. Neuropsychological deficits are correlated with frontal hypometabolism in positron emission tomography studies of older alcoholic patients. Alcohol clin exp res 1993;17(2):205-210.
20. Drejer K, Theilgaard A, Teasdale TW, et al. A prospective study of young men at high risk for alcoholism: neuropsychological assessment. Alcohol Clin Exp Res 1985;9(6):498–502.
21. Tarter RE, Jacob T, Bremer DL. Specific cognitive impairment in sons of early onset alcoholics. Alcohol Clin Exp Res 1989;13(6):786-789.
22. Corral M, Holguín SR, Cadaveira F. Neuropsychological characteristics of young children from high-density alcoholism Families: a three-year follow-up. J Stud Alcohol 2003;64(2):195–195.