European Journal of Molecular & Clinical Medicine (EJMCM)
ISSN: 2515-8260 Volume 09, Issue 03, 2022

Original research article

Study of Executive Dysfunction in Persons with Alcohol Dependence Syndrome

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Abstract

Background: Alcohol dependence syndrome is a chronic disorder resulting indisturbances of various cognitive function areas. Neuro-anatomical and functional changes of the brain most often affect the prefrontal cortex of the brain and the hippocampus.

Methods: A study was conducted for a period of Two year, Department of psychiatry GMC, Bettiah. A total of 30 cases diagnosed with ADS admitted as psychiatry inpatients and 30 healthy controls wereincluded for the study after taking written informed consent. These patients were evaluated using Mini International Neuropsychiatric Interview (MINI-6), Clinical Institute Withdrawal Assessment of Alcohol Scale, Revised (CIWA-Ar), Severity of Alcohol Dependence Questionnaire (SADQ), Trail making Test-A and B (TMT-A andB), Digit Span Test(DST), Word list, Stroop test(STR), Tower of Hanoi (TOH). Clinical details were noted during the course of interview.

Results: Compared with controls, persons with alcohol dependence syndrome presented impaired learning abilities which included immediate and delayed, working memory, cognitive flexibility, and in response inhibition.

Conclusion: This study has shown the presence of significant executive dysfunction in patients with alcohol dependence syndrome.

Keywords: Executive function, Alcohol Dependence Syndrome, Neuropsychology.

Introduction

Substance abuse disorders are an important subject of interest for health professionals, especially mental health. It has implications on individual health, familial and social consequences, criminal and legal problems, and the effects on national productivity and economy. These disorders include substances like nicotine, alcohol, cannabis, opiate, etc. Addiction is a psychological and physiological dependence on a substance or behaviors over which a person has lost his control. The person has craving, salience, tolerance tothe effects of substance/behavior, withdrawal symptoms, loss of control, and uses the substance/behavior despite harm. Among the different substances, alcohol is commonly used and is one of the most prevalent. Its major constituent is ethanol which is a amphiphilic substance, i.e., it dissolves both in lipids and water. It is this lipophilic aspect of ethanol which enables it tocross blood brain barrier and have interactions with the brain. It is one of the extensively studied

topic from time immemorial and has significantly evolved over time. Clinical research in India has focused mainly on alcohol and substance related comorbidity.Neurobiological research is on preliminary levels and mainly focused on identifying high-risk individuals.(1)

Causes of Alcohol Dependence Syndrome, Addiction is a disease either inherited or developed from genetic, psychological or social factors. Earlier alcohol dependence was considered to be derived from social and psychological causes. The initiation of alcohol intake probably depends largely on social, religious and psychological factors. There are various psychological, psychodynamic, behavioural and sociocultural theories that explain the cause of addiction to alcohol. Various researchers in multiple domains of medicine have proven the role of the frontal lobes in addiction. The neocortex differentiates humans from animals and is also the one which is susceptible to the effects of alcohol as well as the reason for addiction in individuals with defects in the prefrontal cortex(PFC). The other areas affected are the cerebellum and limbic system. Frontal Lobes: They are the largest region of cortex in humans. They have five parallel, though interacting, subcircuits: motor, oculomotor, dorsolateral, orbitofrontal, and anterior cingulate.(2) The prefrontal cortex lies anterior to the premotor cortex. It is divided into dorsolateral PFC (DLPFC), the medial/cingulate PFC (ACC), and the orbital PFC/orbitofrontal (OFC). OFC is also interchangeably used with ventromedial PFC. The DLPFC and ACC are associated with executive function networks and the OFC with the inhibitory as well as limbic control of executive functions.(3) Imaging studies haveshown decrease in gray matter in prefrontal cortex in individuals with alcohol dependence associated with executive dysfunction.(4) Ethanol is a substance that affects the brain area involved in reinforcement. PFC receive input from the dopamine, norepinephrine, serotonin, and acetylcholine neurotransmitter systems. The glutamatergic projections from PFC control the dopaminergic projections from cortex to nucleus accumbens core.(5) Alcohol increases dopamine release in nucleus accumbens and blunts the glutamatergic transmission from PFC. Chronic alcohol use deranges the dopaminergic balance in the PFC. (6) Executive function is the ability to formulate, initiate, regulate, and schedule other cognitive activities.(7) It includes sustained and selective attention, mental flexibility, response inhibition, supervisory control of action, and resistance to interference.(8) Alcohol use for longer periods makes way for deficits in planning, risk assessment, decision making capacity.(9) It is unclear if these deficits are causal in the development of dependence, or are interactive with each other and highly unlikely they are epiphenomenal, i.e., unrelated to each other.(10) Alcohol dependence has physical, psychological and social consequences which can lead to poor quality of life. There have been extensive studies on the topic with the neurobiological studies gaining precedence in the recent past.

Objectives

The objective of the current study was to determine the executive function deficits in persons with Alcohol Dependence Syndrome (ADS).

Review of Literature

These are a group of mental processes aimed at higher mental functioning. These include working memory, attention, impulse control, mental flexibility.(11) Planning, judgement and decision making are other aspects of executive functions.The difficulties in complex mental tasks have been attributed to the frontal lobes by various studies.(3) The other structures involved in executive functions are anterior cingulate cortex, basal ganglia, possibly the dorsomedial thalamic nucleus and cerebellum, and the ventral mesencephalon. But conventionally, the concept of executive control has been attributed to the function of the frontal lobes.(12) Tower tests: These are tower of London, Hanoi and Toronto. They measure

planning and judgement, working memory and inhibition. Towers of Hanoi and London do measure similar tasks but differ slightly. They are used interchangeably by researchers and the difference needs to be kept in mind.(13, 14) Impairments of frontal lobe patients on TOH can be additionally due to short term memory deficits along with goal-sub goal conflict resolution difficulties and not planning alone.(15) Chanraud et al. studied the relationship between brain morphological alterations, executive performance, and drinking history of alcohol dependent individuals and compared it with healthy individuals. They used voxel based morphometry MRI and testslike Wisconsin Card Sorting Test (WCST), Stroop test, TMT-B, letter fluency test and letter sequencing tests. It showed alteration in gray and white matter volume, especially in frontal and cerebellar regions, was associated with impairment of executive function inthe patients.(4) Goudriaan et al. did a cross-sectional study of 49 pathological gamblers, 48 abstinent ADS persons, 46 Tourette's syndrome patients and 49 normal controls comparing using avariety of tests testing different domains of executive functions. The tests showed poor response inhibition, mental flexibility, planning and time estimation in gamblers as well as ADS subjects.(16) In a literature review by Bates et al, they have described the cognitive dysfunctions due toalcohol dependence as multifactorial and unequal in terms of executive domains affected.They have further extrapolated from the literature review about importance of cognitive evaluation in management and rehabilitation of ADS patients.(7) Scheurich has described response inhibition as well as impaired decision making as prominent deficits with minimal simple working memory problems in ADS individuals.(25) A recent literature review by Oscar-Berman et al. has mentioned of executive deficits to result of chronic alcohol use which may be associated with structural changes in thebrain. The frontocerebellar systems underlie the deficits in executive dysfunctions.(17), van Hemel-Ruiter et al. studied the role of executive control moderation over attentional bias for alcohol stimuli and showed it to be significant only in persons with poor control.(18) Montgomery et al. in their systematic review and metaanalytic study have concluded about similarities in executive impairments in heavy social drinkers and dependent individuals in terms of switching, inhibition and semantic memory deficits.(19).

Material and methods

It was a case control study design and patients and healthy controls were recruited over aperiod of Two year. 30 cases were taken who were inpatients in psychiatry ward diagnosed with alcohol dependence syndrome (ADS) in Government medical college and Hospital, Bettiah. 30 age and sex matched controls were chosen from the healthy population within hospital premises and 10 kms around the hospital premises.

Consecutive sampling was done to select the study subjects. All consenting patients and healthy controls were recruited as the study sample as per the inclusion and exclusion criteria.

Inclusion criteria

Adult patients (18-60 years) with Alcohol Dependence Syndrome (ADS) admitted in the psychiatry ward, Formally educated up to class 5.

Exclusion criteria

Patients in delirium, independent epilepsy, dementia or any other neurodegenerative brain disorder, H/o head injury. Co-morbid severe mental illness and intellectual disability, Patients with co-morbid substance use other than nicotine.

The consecutive patients diagnosed with alcohol dependence syndrome (ADS) admitted in Psychiatry ward at GMC, Bettiah. were included in the study after taking informed consent after a period of abstinence. Similarly, controls were chosen from healthy population within

hospital premises and 10kms around the hospital premises. A total of30 cases and 30 controls were assessed for a period of two years from, All the patients were assessed using appropriate scales and data was collected.

It consists of words of familiar objects like vehicles, tools, animals and body parts. There are two word lists A and B, with 15 different words in each list. List A is presented at the rate of one per second during 5 successive trials. Patient is asked to recall after each trial. Word list is given after 5 trials followed by immediate recall of same. This is followed byimmediate recall of List A. After a delay of 20 minutes, words from List A are again recalled to form delayed recall score.

Results

Table 1: Demographics and Clinical Variables

Sl. No	Variable	Controls (n=30)	Cases (n=30)	p value
1	Age (Mean±SD)	33.93±10.63	41.93±8.63	0.002
2	Education N(%)			
	Above 10^{th} grade	27(90)	21(70)	0.053
	Below 10^{th} grade	3(10)	9(30)	
3	SADQ (Mean±SD)	22.33±12.67	-	
4	Age of Dependence(Mean±SD)	25.87±4.67	-	

A total of 30 ADS cases and 30 healthy controls were included in the study. The mean age of controls was 33.93 years with a standard deviation of 10.63 years. The mean ageof cases was 41.93 years with a standard deviation of 8.63. The difference was significant(p value of 0.002). 90 percent (27) of controls were educated above 10^{th} grade, whereas 70 percent (21) of test population were educated above 10^{th} grade. The p value was trending towards significance. In view of the above differences, linear regression was done to remove any confounding effects. The mean SADQ score of cases was 22.33 with a standard deviation of 12.67, indicating the study population had mild, moderate and severe dependence cases. The mean age of dependence of the cases was 25.87 years with a standard deviation of 4.67 years.

Description of executive function test results

Trail making test: The p value of TMT A of 0.002 is significant and means thatthe focused attention and visuo-motor speed of cases was poorer than controls. TMT B had a p value of 0.008 which indicates that the cases had poorer mentalflexibility compared to controls. Only 90% of cases completed TMT B and the rest were not able to complete it due to difficulties, Digit span test: Both the Digit span-forward and backward shows significance indicating patients had poorer attention and working memory. Tower of Hanoi: This test did not show a significant difference between cases andcontrols, except the 3 disk time and errors which shows poorer performance in cases. 3 disk task was done by 22 cases and 27 controls, and the rest were not ableto do the task. 4 disk task was done by 18 cases and 15 controls respectively. The 5 disk task was done by 7 cases and 10 controls. The rest were not able to complete the tests due to difficulty, Stroop test: There was no significance in the interference scores of cases and controls, but the p value is trending towards significance, Auditory verbal learning test: The p value is significant for all the 5 trials of List A, immediate recall and delayed recall indicating the cases have impaired learningand memory.

Discussion

This study included 30 alcohol dependent persons and 30 healthy controls. As per this study, alcohol dependent persons had poorer performances in both TMT A and B compared to controls. Poorer response in TMT A indicates impaired attention and visuo- motor speed and in TMT B indicating impaired set shifting and flexibility.

These results are comparable to the results got by Saraswat et al. wherein the patients have fared poorlyboth in TMT A and B.(20) This study showed no difference in cognitive deficits in patients based on their severity of drinking unlike the study by Sanchez-Craig et al.which suggests that drinking pattern of patients correlates with the TMT results. These are on similar lines to Day et al. which suggested chronic alcohol use affects both TMT Aand B.(21) One study by Guillot et al. has shown no difference in TMT A in initialphases of acute alcohol use, but difference in TMT B in initial phases of alcohol use as well as at higher levels of alcohol in the body. The TMT results of this study are also comparable to the results of Ratti et al. which compared 22 male alcoholics with 22 matched controls for frontal dysfunction and found significance in Trail making tests.(22)The results are also comparable to the studies done by Houston et al. and Moriyama et al. who have found significant differences in Trail making tests. Stroop interference showed only a trend significance in the current study which can be comparable to the study by Ratti et al. which had similar findings on Stroop.(22) This indicates that response inhibition has been largely unaffected in the study population. A study by Bechara et al. also has not found significant difference in Stroop test.(23) But in a community sample study by Houston et al., there's a clearer poor result in Stroop test inheavy drinking individuals. Tower of Hanoi has not shown any significance in our study between the alcohol dependent individuals and controls. This study did not find any domain defects in planning and programming. However, Weissenborn R et al. in their study have shown executive function deficits in their study using Tower of London suggesting impaired executive functioning in social drinkers and impaired spatial working memory and pattern recognition in binge drinkers.(24) Our results do not corroborate the same with respect to the tower tests, which may be because of the small sample size and sampling method involved. In the above study, there was significant impairment in memory in domains of verbal learning, immediate and delayed recall. These are comparable to the findings of studies by Nowakowska K et al. and Houston et al. who have significant difference in WCSTand verbal fluency and in digit span tests respectively. In view of the above findings, the current study has showed the attentional deficits, difficulties in mental flexibility, with impaired learning and immediate and delayed recall. Most of the findings are in line with the previous studies done as mentioned in the review of literature except that our study has not found a significant difference in in set shifting and stroop test, though there was trend towards the same.

The findings of attentional deficits, difficulties in mental flexibility, along with impaired learning and immediate delayed recall have a negative bearing on the natural course of alcohol use. These impairments underlie the causes of multiple relapses in persons with alcohol dependence.

Conclusion

The study has shown that persons with alcohol dependence have executive deficits in verbal learning, immediate and delayed recall, focused attention and mental flexibility. In the light of above findings, it is important to evaluate alcohol dependence patients for cognitive deficits as they are not known in routine evaluation. Further studies are requiredto strengthen the above findings and research in neuropsychology for cognitive deficits should be emphasized.

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