

**NEUROPSYCHOLOGICAL ASSESSMENT OF ALCOHOL
DEPENDENT PATIENTS – A COMPARATIVE STUDY**

**DISSERTATION SUBMITTED FOR
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BONAFIDE CERTIFICATE

This is to certify that the dissertation entitled **“NEUROPSYCHOLOGICAL ASSESSMENT OF ALCOHOL DEPENDENT PATIENTS – A COMPARATIVE STUDY”** is a bonafide record work done by **Dr. Karthikeyan.R** under my direct supervision and guidance, submitted to the Tamil Nadu Dr.M.G.R Medical University regulation for **M.D Branch XVIII – Psychiatry**.

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DECLARATION

I, **Dr. KARTHIKEYAN. R** solemnly declare that the dissertation titled “**NEUROPSYCHOLOGICAL ASSESSMENT OF ALCOHOL DEPENDENT PATIENTS – A COMPARATIVE STUDY**” has been prepared by me. I also declare that this bonafide work or a part of this work was not submitted by me or any other for any award, degree, diploma to any other University board either in India or abroad.

This is submitted to The Tamilnadu Dr. M. G. R. Medical University, Chennai in partial fulfillment of the rules and regulation for the award of M.D degree **Branch – XVIII (Psychiatry)** to be held in April 2013.

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INTRODUCTION

Substance abuse becomes an enormous problem worldwide. The substance abuse and its direct and indirect complications have many medical, social and economic consequences. Alcohol is socially and legally accepted substance of abuse. Because of its wide availability, aggressive marketing and relatively cheap price attracts the common man for pleasure seeking. Gupta. *Set al*(2008)

It became a major public health issue especially in developing countries. Currently rapid changes have occurred in alcohol use in India. The change includes early age of initiation of alcohol intake, excessive consumption of spirits to the point of intoxication and blackout, binge drinking and taking alcohol when they are alone to combat boredom. In India 95% of alcohol consumed in the form of spirit(exp. Whisky, rum, brandy, vodka), they have high alcohol content (40-47%). But in western societies they take more amounts of beer and wine, which have low alcohol content. These factors add to the risks encountered by the western population.

Addressing alcohol related problems it not only limited to biomedical field; it involves socioeconomic and political dimensions also. Terence. *Get al* (1987). The main factor which affects the alcohol related problems is policy making. For example some State Governments in India banned alcohol in their states; they have relatively low level of alcohol related problems than the states in which alcohol is sold by the Government owned shops, when excluding problems due to illicit alcohol sales.

Alcohol affects every part of the body, from hair to nail. The first and foremost organ which is influenced and damaged is the brain, especially frontal lobe. From head to toe alcohol greys the hair, accelerates the aging process, and causes more wrinkles in face, it produces telanectaciae, gynaecomastia, ascites, malnutrition and its complications. In gastro intestinal tract it causes peptic ulcer, chronic liver diseases, and pancreatitis. It affects respiratory diseases like aspiration pneumonia. It affects cardiovascular system like dilated cardiomyopathy, atrial fibrillation and increase proneness to develop myocardial infarction. Alcohol is one of the leading causes for

cancers, especially oropharyngeal and gastrointestinal cancers. Simon *et al* (2005), Meiret *al*(2005).

Persons who take alcohol have impaired judgement and excessive impulsivity, they tend to drive vehicle under the influence of alcohol which many times proved to be fatal. They are prone to falls and subsequent orthopaedic complications. They tend to have head injuries ranges from subtle repeated unnoticed head injuries to severe intracranial injuries. One of the common causes of confused state in alcoholic is chronic subdural haematoma.

Alcohol increases the desire and takes away the performance; it is partially true in sexual function. Initially alcohol appears to increases the sexual desire, but chronic alcoholics have reduced libido, erectile dysfunction and they become impotent because of various physical complications, one of the cause is testicular atrophy associated with chronic liver disease.

The neuropsychiatric complications of alcohol include head injury and its sequelae, blackouts, cerebellar degeneration, central pontinemyelinolysis, marchiafavabignami disease, wernickes

encephalopathy and seizures. Psychiatric complications are intoxication, withdrawal effects, abuse and dependence, delirium tremens, psychosis, mood disorder, personality change, anxiety disorder, amnesia, dementia, sexual dysfunctions, hallucinosis and sleep disorders. Many of the impulsive suicidal attempts occurred in intoxicated state for trivial reasons, if they are not intoxicated, they will not attempt suicide for trivial reasons. (Simon *et al*, 2005, Meiret *al*, 2005)

Alcohol affects the attendance in occupational setup due to hangover, withdrawal effects and associated complications. It affects the occupational well-being of the person. Alcohol is the main harbinger of the quarrels in road sides and in domestic violence. Many of the crimes occurred under the influence of alcohol. Thus alcohol affects the mental Physical and social integrity of the individual. Rafael *et al* (2011), Christopher *et al*(1998), Karen *et al*(2012).

Alcohol abuse and dependence are chronic disorders. They have structural and functional disturbances in brain. In simple terms alcohol abuse or alcoholism is characterized by regular and excessive use of

alcohol causing physical, interpersonal, social and occupational problems. Repeated use in unwarranted situations like driving in intoxicated state. Alcohol dependence is characterized by repeated alcohol related difficulties for the past twelve month period in at least three functional areas. It causes many neuropsychiatric complications which have high morbidity and mortality.

Persons who abuse alcohol may have vulnerability to develop other substance abuse because of their genetic and environmental vulnerability. The most common comorbid substance of abuse by the alcohol dependent patients is tobacco, next is cannabis. 50-90% of treatments seeking people for alcohol related problems are tobacco smokers. Drobos. J (2002) postulated that combined use of alcohol and tobacco has classical conditioned cue reactivity, leads to craving for both substances. Prendergast *et al*(2002) postulated that the tobacco use counteract with alcohol effects on cognition and motor coordination.

There is a large vacuum in the research data regarding alcohol related health, social and economic impact in India. It impairs the progress

towards the right health care policy making in India. In many alcohol related epidemiological studies at some point of time there was 80% of the population using alcohol, in that 20% have problem due to alcohol. Western literature estimated that the life time prevalence of alcohol dependence is 12-15% for men, 5-8% for women. In India one fifth of hospital admissions, 18% of psychiatric admissions, 20% of brain injuries, 60% of road traffic accidents are related to alcohol intake. Role of alcohol in domestic violence is enormous, one third of husband engaged in domestic violence are in intoxicated state, according to WHO study (2004)

Acute and chronic use of alcohol is associated with neurocognitive deficits ranges from mild to moderate cognitive impairment to severe Korsakoff's syndrome. The aim of the present study is to assess the cognitive dysfunctions associated with alcohol dependence syndrome and to gain better knowledge about it and try to implement findings into day to day clinical practice.

REVIEW OF LITERATURE

Alcohol is socially accepted and permitted by law of land as a recreational substance. But it causes many adverse events in all parts of life. We all know the acute effect of alcohol that impairs the

cognitive functions. But the chronic effects of alcohol on the neuropsychological functions are also important. They are subtle dysfunctions, can be revealed only through systematic neuropsychological testing. The alcohol dependent patient himself is not aware of the fact that he is having the subtle neurocognitive impairment which is required for normal day to day functions. Whenever there is delay between cause and effect the person is not taking the risk factor as serious one. In the review of literature various issues were discussed regarding alcohol and its effect on cognitive functions.

India is having second largest population, which has become the third largest market for alcoholic beverages. The changing social norms, increased availability, urbanization, relaxation of overseas trade rules, high intensity marketing, and poor level of awareness have contributed to the increased use of alcohol in Indian population. Benegal. V(2005).

Alcohol dependence is a cluster of cognitive, behavioral and physiological phenomena that may develop after repeated alcohol use.

They have strong desire to use alcohol, impaired control over their behavior, inspite of knowing the harmful effect continues the pattern of increased intake, giving priority to alcohol intake than any other pleasurable activities in life, tolerance to the effect of alcohol, withdrawal symptoms when alcohol is not taken. Baboret *al*(2001).

First we discuss about the basic concepts of alcohol then the effect of alcohol on brain and its functions.

Pharmacology of alcohol:

Alcohol is chemically defined as having OH group. The most common alcohols of health care significance are ethyl alcohol, methyl alcohol and isopropyl alcohol. The term alcohol generally refers to ethyl alcohol, which is widely available for recreational and industrial use. The chemical formula of alcohol is $\text{CH}_3\text{CH}_2\text{OH}$. It is a clear odourless fluid which is easily mixes with water.

When ingested 80% of the alcohol is absorbed in small intestine, especially in duodenum, rest in the stomach. In empty stomach about 50% of the alcohol is absorbed in 15mins, peaks in 20 mins. The rate of absorption is affected by food, rate of ingestion,

drugs, volume and concentration of alcohol and the carbonation of drink. Alcohol distributed to every fluid compartment of the body. Alcohol is metabolized by alcohol dehydrogenase which converts it into acetaldehyde, subsequently by aldehyde dehydrogenase to acetic acid. The alcohol is excreted via kidneys. 10-15% of the alcohol excreted unchanged via lungs and kidneys.

Neuropharmacology of alcohol

Alcohol generally considered as a central nervous system depressant, in large doses it functions like general anaesthetic. In small doses it has euphoric effect; this effect is mediated by action on mesolimbic dopaminergic system and nucleus accumbens. GABAergic neurotransmitter system mediates anxiolytic and relaxation effects.

There is no conclusive idea about the specific alcohol related receptors like many of the substance of abuse. But it is postulated that the effect is mediated by alteration of the fluidity of the bilayer lipid neuronal membrane that may affect the neurotransmitter system and ion channels. Alcohol has effect on major neurotransmitter system

like opiod, glutamate, serotonin and GABA. It indirectly affects the dopamine level in ventral tegmental area and mediate reward pathway.

Epidemiology of alcohol related problems

Studies regarding substance abuse are a topic of interest for many public health issues, studies from 1968 to 2000 focuses on alcohol related problems. A meta-analysis by Reddy and Chandrasekhar (1998) revealed that overall substance use prevalence is 6.9/1000 for India with rural and urban rates of 7.3 and 5.8/1000 population. The rates in men and women were 11.9 and 1.7% respectively. A study in southern rural India showed that 14.2% of the sample had hazardous use of alcohol. This was assessed using AUDIT. Similar study in a tertiary hospital, Sampathet *al*(2007) revealed 17.6% of the inpatients have hazardous use of alcohol.

The national household survey of drug use is first of its kind in India which systematically collected data regarding nationwide prevalence of drug use, Ray(2004). Following tobacco alcohol become the next common substance of abuse.It accounted for 21.4% followed by

cannabis (3%) and opioids (0.7%). 17-26% of the studied population satisfied the ICD-10 criteria for alcohol dependence, which contributed to 4% of the general population prevalence, Pratimamurthy et al(2010). The drug abuse and monitoring system, Ray (2004) which evaluates the substance of abuse in inpatient population found that the major substance were alcohol (43.9%), opioids (26%) and cannabis (11.6%).

When considered the age the mean age of initiation of alcohol intake was 20.8 ± 5.9 year. World health organization states that two billion persons consume alcoholic beverages and 76.3 million people have diagnosable alcohol related disorders worldwide, Theotoka.I(2006).

Alcohol use is increased alarmingly in the less than 21 age group from 2% to 14% in the past 15yrs, according to studies in Kerala by Alcohol and Drug information Centre India, a local NGO. The age of first use of alcohol dropped to 13yrs. The study by NIMHANS has shown that the average age of initiation of alcohol intake reduced from 28yrs to 20 years from 1980 to recent times. The National Survey (study sponsored by the Ministry of Social Justice

and Empowerment and the United Nations Office on Drugs and Crime, 2004) revealed that among adult men, about 21% were current drinkers and about 17% were regular user of alcohol, and among those seeking treatment about 44% were alcohol users. The most recent data on alcohol use is available from the National Family Health Survey (NFHS-3, 2007) Data collected in 2005-06, published in September 2007. It showed that about 32% were current users of alcohol and between 4 and 13% were daily users. The proportion of users among rural and urban population is very similar (32% and 31% respectively).

There is a threefold increase risk of alcoholism in relatives of alcoholics. Some studies found that there are upto eight fold increases in drug related problem in alcoholic's siblings, Karen *et al* (2012). A lowered age of onset is associated with more severe alcohol dependence and consequent complications. A recent Indian study reported that the age of onset of alcohol use in a hospital based population was 18yrs and the age of onset of dependence was 27 yrs. They found that these subjects developed the first criteria of

dependence after six years of alcohol used and then requires only four year to develop the dependence syndrome as per ICD-10.

Jhonsonpradeep *et al*(2010)

The pitfall of Indian studies is, alcohol related data collected while collecting data for other major mental illnesses. Surya *et al* (1964) surveyed 510 households (2731) in southern India. His study reveals a prevalence of 3.6/1000. Gopinath (1968) reported prevalence of 2.36/1000. Likewise the prevalence in various Indian studies ranges from 1.38 to 4.8 per 1000 in India, Saxena S(1999).

Standard drink:

While discussing about alcohol the concept of standard drink comes. Many studies describe alcohol intake in units of standard drink. But the standard drink varies from country to country. (International Center for Alcohol Policies, 1998). When using the term standard drink it adds to the challenge that it doesn't translated semantically or literally into any Indian language. Studies discovered that more people

pour more amount of alcohol than standard sizes. White (2003); Madhabika *et al* (2008).

In India the size is varying from region to region and it differs from the international standards and the people also tend to use the quantity according to that. Some of the quantific measures of the Indian alcoholic beverages are given below. Madhabika *et al* (2008).

1. Beer (5%)- 650ml, 750ml, 330ml
2. Strong beer(8%)- 650ml, 750ml
3. Wine(12-15%)- 750ml
4. Glasses-90ml
5. Bottles-750ml
6. Foreign liquor-30ml
7. Indian liquor-40-60ml
8. Patiala or burra peg-80ml
9. Country liquor sachets-44ml, 200ml
10. Delhi bottles-1 lit, 750ml
11. Urrack, feni(40-70%) 'pint' or half bottle-375ml
12. Quarter- 180ml

13.Premixed drinks(4.6%)- 275ml

Likewise Indian measures vary from international standards.

One standard drink includes,

330ml of beer \times 5% \times 0.79 (conversion factor) = 13gm of ethanol

140ml of wine (one glass) \times 12% \times 0.79 =13.3gm of ethanol

40ml of spirit \times 40% \times 0.79 = 12.6gm of ethanol

This shows that there is variation in the alcohol content as per the standard drink. Santanuet *al* (2012).

Neurocognitive functions

The cognitive functions can be discussed under many headings, but the important functions affected in alcoholism are briefly discussed here.

Attention impairment

Attention is a complex of abilities including maintenance of alert state filtering of relevant information, set shifting, orienting to new stimuli. Attention physiologically reduced in sleep, dreams, hypnotic states, fatigue, and boredom. It may pathologically decrease in organic states, epilepsy, and in psychosis. Narrowing of attention also prominent in depression. A severe deficit in attention is a feature in hyperkinetic disorder. That may be also observed in hypomania and mania. In psychosis alternation of perception is associated with change of attention. Selected tests for attention includes Digit span, Digit vigilance test, Paced auditory serial addition test, Visual memory span. In substance abuse disorders, subtle alteration in attention is present.

Memory impairment

Memory has three stages or components; they are encoding, storage and retrieval. Memory can be typed according to the time duration of memory to immediate memory, recent memory, and long term memory. There are other types of classifications also. The disturbances of memory can be organic due to brain damage,

psychogenic as occurring in many psychiatric conditions. Research findings found that verbal and spatial memories are processed differently by left and right hemisphere. For learning new material, memories plays a major role for collecting new information, matching with the previous information and store the new information, retrieve as and when required. In chronic alcoholics there is deficit in many areas like working memory, short term memory and retrieval. This kind of deficit is also found in Alzheimer's dementia and schizophrenia. Test for memory include Wechsler memory scale, California verbal learning test, Rey Osterrieth complex figure test, Benton visual retention test, Rey auditory verbal learning test, brief visuo-spatial memory tests.

Executive function:

It is ability to maintain an appropriate mental set in order to fulfill a future goal. The component of executive function are planning, filtering competing information, maintain a goal and excluding other irrelevant things from the goal. Many times executive function discussed under the heading of intelligence quotient, but

actually they are partially overlapping separate entities, because, in lesions of frontal lobe executive function is affected much, but intelligence quotient is relatively stable, Glass *et al* (2009), Gary *et al*(2012). Tests for executive dysfunction includes Wisconsin card sorting test, Trail making tests, Stroop testing and Category test.

Working memory:

It is part of short term memory which is concerned facts related to a task currently in use, Candice (2006). Working memory typically affected in schizophrenia, mania, and dementia. In alcohol dependents it is comparable to deficits found in Alzheimer's dementia. The test for working memory includes working memory rating scale, Rivermead behavior memory test, speed and capacity of language processing test, reading decision test, non-word memory test and children test for non-word repetition.

Verbal fluency:

Verbal fluency broadly divided into semantic and phonological. Semantic fluency refers to the ability to produce as much words in a particular category like naming animals. In phonological fluency the

subject has to produce as many words as possible, beginning with particular letter with time limitation. This verbal fluency is typically affected in schizophrenics, in alcohol dependent individuals there is conflicting evidence regarding word fluency in various studies. Tests include Boston diagnostic aphasia examination, Boston naming test, Animal naming test, Token test, and Controlled oral word association test.

Cognitive functions and alcoholism:

Acute effects of alcohol:

The effects of alcohol are not uniform on all neurocognitive functions. The alcohol affects mainly the motor control and cognitive control of behavioral functioning. It affects fine motor control and ability to perform multiple task at a time. Alcoholics have impairment in reaction time, dual task performance and fine motor skills according to the blood alcohol level. The well-known factor is whenever a person is intoxicated he is having slurred speech. Because speech requires fine motor control, coordination and timing, they find difficult in reading a passage swiftly. Other system significantly

affected by alcohol is vestibular apparatus. There are two types of nystagmus associated with alcohol. One is positional alcohol nystagmus, it is subdivided into two categories I and II. PAN I is characterized by same side nystagmus when head is down, it occurs in peaking alcohol concentration; it starts from 40 mg/dl. PAN II occurs 5-10hrs after drinking during elimination phase. It is exactly opposite to PAN I. another type of nystagmus is horizontal gaze nystagmus, which is jerky movement of eye when looking at sides, with upright position of head; it starts to occur in 80 mg/dl concentration of alcohol.

To assess the person is acutely intoxicated to the point of not able to carry out his personal work, like driving, many test used. They are called as field sobriety tests. One leg stand test, walk and turn test, horizontal nystagmus test and alphabet test are some of the field sobriety tests which is used by US traffic Dept for to assess the acute effect of alcohol in addition to blood and urinalysis.

Chronic effects of alcohol on neurocognition:

The relationship between alcohol intake and cognitive dysfunction is a debatable topic when considering the long term effect. Some studies reveals alcohol significantly affects the cognitive functions, while others reports that there is no clear association between alcohol intake and cognitive deterioration unless there is brain damage as in korsakoff's syndrome. Iracemaleroiet *al*(2002). Other possible factors discussed are the cognitive deficit preceded the alcohol intake and it may contribute to faulty decision making of alcohol use and its continuation.

The chronic effects of alcohol on the cognitive functions may be due to direct toxic effect of alcohol, metabolic abnormalities, subtle head injuries and comorbid physical complications, Zinn. *Set al*(2004);Pratimamurthy*et al*(2010).

Alcoholics have predominantly frontal lobe dysfunction (58%) and short term memory loss (32%). Studies say that they have working memory impairment also. Dementia due to chronic alcoholism is rare (4%), eventhough it is on the rise nowadays.

Alcoholics have deficit in executive functions like abstract thinking, cognitive flexibility, inhibition of competing responses, visual scanning, set shifting, decreased problem solving, nonverbal abstract skills and depressed new learning skills. Nowakowska. *Ket al* (2008); Karen *et al*(2012), Glass *et al*(2009) and Madhabika*et al*(2008). They are prone to develop perseveratory mistakes in neuropsychological tests. Alcohol cues affect automatic cognitive processes in both dependent and non-dependent drinkers, Miles cox *et al*(2003). In addition they have deficit in verbal fluency, spatial imagination and flexibility of closure also, Scheurich. A *et al* (2004). Most alcoholics exhibit mild to moderate deficiency in intellectual functioning.

Alcohol significantly affects the quality and pattern of sleep. It is well known that sleep disturbances is associated with disturbance in learning new things, processing of new memory, decreased attention, concentration and problem solving skills, Brower *et al*(2001); Kern-Hage*et al* (2004);Winerman (2006);Nortan. *Fet al*(2011).

High frequencies, volume, long duration of alcohol intake, pattern of alcohol intake are influencing the cognitive impairment and blackout. Lee. *et al*(2009), White *et al*(2003). Park and Noblewerethe first to demonstrate that drinking pattern affects the cognitive functions.Kokavec. *Aet al*(1999).

Alcohol and cognitive functions have J or U shaped relationship. Mild to moderate alcohol intake affect the cognitive profile favourably, but excessive consumption has deleterious effect. Brittonn *Aet al*(2004), Gupta *Set al*(2008),Tilia*et al*(2004).

There is an increased frequency of cognitive impairment as age progresses, verbal fluency, working memory and frontal lobe functions are affected as equal in patients with Alzheimer's disease. Alcoholics are comparable to mild cognitive impairment patients, but the cognitive profile of alcohol dependent patients in distinct from that of Alzheimer's disease, Liappas. *Iet al*(2007), but there is no association between alcohol consumption and development of Alzheimer's disease, Iracemalero*iet al*(2002).

Structural and functional abnormalities in brain due to alcohol:

Research findings suggest that alcohol dependent patients have morphological abnormalities of brain, abnormal glucose and amino acid metabolisms, disturbances in monoaminergic and cholinergic transmitter system, vascular and microcellular abnormalities.

Brain of alcohol dependent patients is smaller than general population. It is due to loss of cortical neurons. This loss is prominent in frontal, prefrontal, hypothalamus and cerebellum. The aforementioned areas are centres for higher mental functions which are damaged in alcoholics. Cerebellum maintains gait, balance and assist in learning process. These functions are altered in alcohol dependent patients, Edith V. Sullivan *et al*(2002), Gupta. *Set al*(2008), Noel *et al*(2002). There is less number of neuronal losses in basal ganglia, nucleus basalis and raphe nuclei. They have atrophy of cerebrum, cerebellum, widened ventricles and sulci. These changes are independent of wernickes encephalopathy, Gupta. *Set al*(2008)

Morphological and functional imaging studies found that they have altered cerebral vasculature, parenchymal and subarachnoid haemorrhage, ischemic infarcts, decreased frontal glucose utilization

and hypo metabolism in frontal lobe, Rafael Coullaut-Valera *et al* (2011), Zinn. S *et al*(2004), Gupta. *Set al*(2008).

Alcohol is a neurotoxin, it cause damage of mitochondria, facilitate apoptosis of neurons and causes oxidative damage by excitotoxicity, Timothy *et al*(2007), Paulo *et al*(2004).

Alcoholics use different neural network to finish a task in hand than the general population. If he is abstinent for few weeks, he has the chance to form new neuronal connections, Edith. *Vet al*(2002). Eventhough adolescents have the capacity to form new connections quickly than the adults; they are very much vulnerable to the effect of alcohol. They have reduced P300 amplitude and abnormalities, Pratimamurthy *et al*(2010), repeated withdrawal in them associated with more neuronal loss and cognitive impairment. Interestingly right hemispheric functions are more affected left hemispheric functions. Zinn. *Set al*(2004).

Studies says that even social drinkers who take 21 or more standard drink (12gm of alcohol) per week have deficit in mental functions. The common problems in them are memory, learning, abstraction,

problem solving, and psychomotor processing difficulties. They take more time to complete the task in hand, implies they have impaired working memory, Paulo J *et al*(2004).

MODELS FOR EXPLAINING ALCOHOL-RELATED BRAIN DAMAGE:

There are various theories which explain cognitive deficit in alcoholics, some of them are,

1. Tuck and Jackson (1991) found that subtle neuropsychological abnormalities precedes neurological abnormalities and without any gross brain abnormalities by 10yrs. The cognitive deficit in alcoholics postulated due to underlying brain abnormalities and subclinical head injuries, Edith V. Sullivan *et al*(2002), Christopher C.H. cook *et al*, (1998), National institute on alcohol abuse and alcoholism No.53, (July 2001)
2. Others discuss in terms of premature aging hypothesis due to alcohol, Ryan & Butter (1984). This finding is supported by imaging, not by neuropsychological testings. There were conflicting results. Some studies present correlation, Fein *et*

al(1990); Hochla& Parson(1982), other studies found no consistent findings, Shelton, Parsons &Leber, (1984); Beckers, Butters, Hermann &Dangelo(1983). Eckardt, *et al* (1995) found in 18-35 years age group, they are free from cognitive deficit, inspite of significant alcohol use, Karen.D(2012).

3. Some discuss in terms of impulsivity which is heavily depend upon cognitive functions. They says that the high impulsive behavior associated with alcoholics which may be highly automatic, so they are prone to develop cognitive errors and faulty decision making which contributed to alcohol intake behavior. Others discuss that addictive substances on long term use impairs the control over impulsivity that in turn affect executive functions, Reinout W. wierset *al*(2009), Javadsalehifadardiet *al* (2009), Abigail K. rose *et al*, (2008).

4. Many studies says that whenever there is cognitive impairment in alcoholics it may be due to underlying structural brain abnormalities, severest of it is korsakoff's syndrome, it is characterized by severe persistent memory impairment and

deterioration in the sense of time, WHO (1994). It is one of the sequel of chronic and excessive intake of alcohol. The cause may be direct toxic effect of alcohol and thiamine deficiency. Degeneration of mammillary bodies, thalamic nuclei, cerebellum, periaqueductal grey, frontal lobe and subcortical areas observed.

The accompanying table lists the prevailing models, Oscar–Berman (2000). The factors discussed in one hypothesis is not mutually exclusive from the factors discussed in other hypothesis, they are interrelated.

Hypotheses Proposed To Explain the Consequences of Alcoholism for the Brain

<i>Hypotheses Emphasizing the Personal Characteristics Associated With Vulnerability</i>	
Characteristic	Hypothesis
Aging	Premature aging hypothesis: Alcoholism accelerates aging. Brains of alcoholics resemble brains of chronologically old nonalcoholics. This may occur at

	the onset of problem drinking (“accelerated aging”) or later in life when brains are more vulnerable (“increased vulnerability” or “cumulative effects”).
Gender	Alcoholism affects women more than men. Although women and men metabolize alcohol differently, it is not yet clear if women’s brains are more vulnerable than men’s brains to the effects of alcoholism.
Family history	Alcoholism runs in families; thus, children of alcoholics face increased risk of alcoholism and associated brain changes.
Vitamin deficiency	Thiamine deficiency can contribute to damage deep within the brain, leading to severe cognitive deficits.
<i>Hypotheses Emphasizing the Vulnerability of Brain Regions or Systems</i>	
Region/System	Hypothesis
Entire brain	Vulnerable to cerebral atrophy.
Limbic system, thalamus, and hypothalamus	Vulnerable to alcohol-induced persisting amnesic disorder (also known as Wernicke–Korsakoff

	syndrome).
Frontal lobe systems	More vulnerable to the effects of alcoholism than other brain regions/systems.
Right hemisphere	More vulnerable to the effects of alcoholism than the left hemisphere.*
Neurotransmitter systems (e.g., gamma-aminobutyric acid [GABA], glutamate, dopamine, acetylcholine, and serotonin systems)	Several neurotransmitter systems are vulnerable to effects of alcoholism.

Positive aspects of alcohol:

Alcohol has many positive effects also. It increases high density lipoprotein, decrease low density lipoprotein, regulates clotting mechanisms, Gupta.*Set al*(2008). Cross sectional studies done among U.S blacks, French men and women, Japanese Americans showed

there is significant better performance in neuropsychological test in moderate drinkers than nondrinkers, Meir J. Stampfer *et al*(2005).

Mechanisms for possible positive association of alcoholism and cognition are,

1. Persons with better educational status consume alcohol moderately so they may have better cognition, Nowakowska. *Ket al* (2008).
2. Moderate consumption indirectly implies that the person is having good physical, mental and socioeconomic position, Rita Z. Golstein *et al*(2004).
3. Alcohol reduce vascular incidence and improves vascularity, insulin sensitivity, fibrinogen level, fibrinolytic activity and platelet function. It reduce the cerebral occlusion and increase cerebral blood flow which may explain the good cognitive abilities, Britton. *Aet al*(2004), Meir J. Stampfer *et al* (2005).
4. Moderate alcohol consumption increases the acetylcholine in the brain which is associated with better cognitive functions, Lydia Krabbendam *et al*(2000).

Some studies quote that 1 to 14.9 gm of alcohol per day actually reduces the cognitive impairment in women. There is evidence that even 6yrs of heavy consumption of alcohol is not associated with cognitive decline, but alcohol increases the vulnerability of the brain to other diseases, Jill E. Green *et al*(2004). There is an inverse association for all types of alcoholic beverages, Meir J. stampfer *et al*(2005).

Comparison with other substance of abuse:

About 80-95% of alcohol dependence patients are regular smokers, Hurt *et al*(1994); Pomerleau *et al*(1997); Romberger and Grant(2004), among treatment seekers 50-90% are heavy smokers. Some suggest that nicotine which is one of the active substances in tobacco may counteract the adverse effects of alcohol on cognition and motor incoordination, prendergast *et al*(2002). But neuroimaging and neurocognitive measures clearly find difference between smokers and nonsmokers in alcohol dependent patients. Smokers have more neocortical grey matter loss, with increased temporal lobe white matter Timothy C. durazzo *et al*(2007).

Smoking itself can affect executive skills, learning, memory, processing speed and cognitive efficiency. Smoking adversely affects cognitive functions in addition to alcohol, Timothy C. Durazzo *et al*(2009)

Recent results suggest that smoking affect the information processing speed whereas alcoholism affect widespread functions in various Neurocognitive domains, J.M. Glass *et al*(2009).

Paraherakis, Charney & Gill(2001) reported that persons with alcohol and benzodiazepine addiction have higher level of cognitive impairment than patients dependent on other substances. (Substance use and cognitive impairment, Virginia office of substance abuse services, (march 2004). Compared to cocaine, alcohol has more detrimental effect on attention, executive functioning, Rita Z. Golstein *et al*(2004).

Treatment implications:

People lacks motivation when there is a delay between risk taking behavior and the consequences, so there is an immediate need for a tool to assess the cognitive impairment in alcohol dependent

patients Gupta. *Set al* (2008). Questionnaires used for alcohol misuse such as AUDIT, Conigrave *et al*(1995), Paddington alcohol test, Smith *et al*(1996), alcohol problem questionnaire, Drummond(1990) and SADQ, Stockwell *et al*(1983) were not designed to assess cognitive difficulties. Even though the patients often worry about the memory problem, they were not aware of the subtle abnormality. Clinically healthy above average IQ persons also have deficit in routine testing. Some studies recommend trail A and trail B making test for routine clinical use in clinically healthy alcohol dependent patients, Theotoka. I(2006).

Routine neuropsychological functions identify cognitive deficit in 45% of the alcohol dependent patient in 3 weeks, 15% after 1yr of abstinence, Zinn. *Set al* (2004), Nadia solowij, katy A. jones *et al*(2011). Short term memory loss and perceptuomotor coordination are the most difficult to overcome with time, Frank Norton *et al* (2011).

Alcoholics readily accept the problem of drinking but 50% of them relapse in 3 months, Javadsalehifadardiet *al*(2009) because

alcoholics with high degree of cognitive impairment have poor overall prognosis, Noel. *Xet al*(2002). Alcoholics with deficit in learning, memory, executive functions have difficulty in interpreting information provided to them, especially in the early part of abstinence, Nowakowska. *Ket al*(2008).

The three week detoxification programme affect the drive to take alcohol but the cognitive functions remain impaired after three weeks, so new neurocognitive strategies should be implemented after 3 weeks. That will reduce the rate of relapse, Liappas. *I et al* (2007), Marina cordovil de souse uva *et al*(2010), Paulo J cunha *et al*(2004).

Recovery is a lifelong process. Family members should assist the patient in controlling the impulsivity, reestablish the executive functions, personal and occupational activities needs revisit because they have reduce capacity to control over their activities. The main aim of treatment process is to educate the patient about the cognitive deficits and assist him to come out the deficits, Norton. *Fet al*(2011). But Morgenstern and Bates argue that there is no relationship between

recovery and cognitive deficit.(National institute on alcohol abuse and alcoholism No.53, July 2001)

Cognitive deficit have implication in day to day functioning of the individual. First step in the treatment schedule of any substance abuse disorder is identifying the damage in brain due to the substance of abuse, because it has implication in treatment outcome, Rafael coullaut-valera *et al* (2011).

Hence, with the above perspective, the present study titled “Neuropsychological assessment in alcohol dependence patients- A comparative study” was carried out with the following aim, objective and hypothesis.

NEED FOR THE STUDY

1. Alcohol related problem is on the rise, it is important to stress the neurotoxic effect of alcohol.
2. To quantify the neurotoxic effect of alcohol and translate it into clinical practice
3. To include the cognitive function assessment in the routine examination schedule of alcohol dependence patients.

METHODOLOGY

AIM

ToStudy Neurocognition among alcohol dependent patients and compare it with non-alcoholic controls.

OBJECTIVE OF THE STUDY

- i. To assess the Neuropsychological functions in alcohol dependence patients.
- ii. To assess the association between various alcohol related parameters like duration, quantity, frequency and SADQ score with cognitive functions.
- iii. Compare the findings with the non-alcoholic controls.

INCLUSION CRITERIA:

- Patients meeting ICD 10-RDC (research diagnostic criteria) criteria for alcohol dependence.

Patients and controls:

- In the age group between 21-50yrs.
- Education status 8thStd and above.
- Those who give informed consent for the study.

EXCLUSION CRITERIA:

- Patients with past and present history of obvious neuropsychiatric complications.

- Substance use other than alcohol and tobacco.

Patients and controls:

- Persons having comorbid psychiatric, neurologic and medical illnesses.
- Persons are on or used drugs known to cause cognitive dysfunction.
- Those who are not consented for the study.

HYPOTHESIS:

1. Alcohol dependence patients have significantly high Neurocognitive dysfunction than the controls.

2. Attention impairment, executive function and working memory are the most common Neurocognitive functions affected in alcohol dependence patients in comparison to controls.
3. Duration of alcohol intake affects verbal memory more than the nonverbal memory.
4. Quantity of alcohol intake doesn't affect the attention and executive functions in alcohol dependence patients.
5. Patients with severe alcohol dependence have more Neurocognitive deficits.

MATERIAL AND METHODS

The methodology adopted for the present study titled **“Neuropsychological assessment of alcohol dependent patients –a comparative study”** is dealt under the following heads:

- i. Selection of locale and samples
- ii. Semi structured proforma for demographic and clinical details
- iii. Mini international neuropsychiatric interview
- iv. Alcohol dependence questionnaires (AUDIT, SADQ)
- v. Conduct of neuropsychological Test
 - Rey osterrieth complex figure test
 - Trail making A and B tests
 - Rey Auditory verbal Learning test
 - Digit Span
 - Stroop test
 - Animal Naming Test
 - Cowat (controlled oral word association test)
- vi. Scoring, Interpretation and statistical analysis of data
- vii. Discussion, summary and conclusion

SELECTION OF THE LOCALE AND SAMPLES:

The study is conducted in Department of psychiatry, Government Rajaji hospital, Madurai during the period of March 2012 September 2012. The prior permission from institutional ethical committee was obtained. The patient population is chosen from inpatients who were admitted in de-addiction unit of Department of psychiatry. Controls were selected from the attenders of patients in medical and surgical ward who was not taken alcohol. The age, sex and education matched control group was selected. Since the patients admitted for alcohol dependence treatment were males, controls also chosen as males. Based on the inclusion and exclusion criteria 30 cases and 30 controls were selected.

The purpose of the study was explained to the participants in regional language. Oral as well as written consent was obtained before the conduct of the study. After the selection of participants they were examined by two senior psychiatric consultants of department of psychiatry. After their approval subjects were included in the study.

First the proforma for sociodemographic profile and clinical details was filled up. Then structured mental status examination was done to diagnose alcohol dependence syndrome and to rule out the other major psychiatric illnesses. MINI is used for this purpose. The study was monitored by senior psychiatric consultants in the department. The cases referred to alcohol dependent patients, controls referred to non - alcoholics. They used interchangeably in the result and discussion.

SCORING, INTERPRETATION AND STATISTICAL ANALYSIS

The above neuropsychological tests were administered, scoring done according to the standard procedure as per the manual. The scores thus obtained were tabulated, analyzed and interpreted. **SPSS 20** is used for statistical analysis. Measure of central tendency, chi square test for categorical variables, student 't' test for quantitative measures used. Correlational analysis used to correlate various test findings with other variables.

SEMI STRUCTURED PROFORMA FOR SOCIOECONOMIC AND GENERAL MEDICAL DETAILS

A pretested proforma was developed to elicit the socio- economic background including details on age, occupation, marital status, dwelling, socioeconomic status and religion. Based on the details collected, **Kuppusamy socio economic scale, S.E.Gupat and B.P.Sethi (1978), Kuppusamy(1961)** was used to assess the socio economic status. General medical details also collected, if any medical illness present they were excluded from the study.

SOCIO ECONOMIC SCALE (S.E.GUPAT AND B.P.SETHI (1978), KUPPUSAMY (1961))

Socioeconomic scale consists of scores based on three variables namely education, occupation, and income on the basis of ten point scale. It consists of ten categories are grouped with 5 social class namely very high, high, upper middle, lower middle and very low. The 10 point scale consists of 200 scores with equal class interval. The inter-rater reliability is found to be very high (R=0.9).

This scale incorporates guidelines to score children, dependent person, married, and unmarried subjects. His general principle applied that the initial scores deals remarkable lower 8 position. The next 60 scores related to average to slightly above position and the scores between 100-200 pertains to the higher position.

**MINI INTERNATIONAL NEUROPSYCHIATRIC
INTERVIEW:**

It is a short structured interview. It is developed by psychiatrists and clinicians in the USA and Europe, for DSM-IV and ICD-10 psychiatric disorders. It is designed to be used in epidemiological and multicenter clinical trials. It takes around 15 mins to complete. It has many variations like: the M.I.N.I.-Screen, the M.I.N.I.-Plus, and the M.I.N.I.-Kid, Sheehan DV *et al*(1998).

ALCOHOL DEPENDENCE QUESTIONNAIRES:

AUDIT:

Alcohol use disorder identification test is a screening instrument which is specifically designed for international use, Edith V. Sullivan *et al*(2002). It is a 10 point questionnaire with 0-4 scores per question. It has a maximum score of 40. A score of 8 or more associated with hazardous drinking, more than 13 in women, 15 in men associated with dependence pattern of alcohol use. It needs 2 mins to complete the questionnaire, SantanuGhosh *et al*(2012).

SEVERITY OF ALCOHOL DEPENDENCE QUESTIONNAIRE (SADQ)

Severity of alcohol dependence questionnaire assesses the alcohol dependence severity, developed in Maudsley hospital. It covers speed of withdrawal symptom onset, physical and affective withdrawals, craving and frequency of alcohol consumption. It is scored in a 4 point scale, from 0 to 3. A score more than 16 is associated with mild; 16-30 is associated with moderate; more than 30 with severe pattern of dependence.

NEUROPSYCHOLOGICAL TEST BATTERY:

Neuropsychological assessment was carried out to assess the extent of impairment in particular skill and to attempt to determine the area of the brain which is impaired. A core part of neuropsychological assessment is the administration of neuropsychological tests for the formal assessment of cognitive function. It is essential that neuropsychological assessment also include an evaluation of the person's mental status. The test battery is chosen carefully after discussing it with senior psychiatrist and clinical psychologist. The following tests were administered for all the subjects.

1. REY OSTERRIETH COMPLEX FIGURE TEST (ROCF)

A complex figure task was developed by Andre Rey (1941); most recently translated by Corwin & Bylsma (1993) to examine both perceptual processing and visual memory in brain-damaged individuals. Paul Alexander Osterrieth (1944); translated by Corwin and Bylsma, (1993) standardized Rey's procedure and provided a

numerical scoring system based on the presence or absence of structural elements in the individual's reproduction of the figure. The Rey-Osterrieth Complex Figure Test remains a central test in the practice of neuropsychology Lezak (1995). As Boone (2000) notes, the ROCF has become one of the most commonly used neuropsychological tests in both clinical and research paradigms, and it is referenced in over 200 publications. The test consists of a timed (but not time-limited) trial in which the individual copies a complex two-dimensional geometric figure, followed by an immediate recall trial. Individuals are not forewarned that they will be asked to recall the figure they have copied. The modern administration also includes a delayed recall task. The amount of time until delayed recall varies, from 20 minutes to 40 minutes, however, a 30-minute interval is generally used.

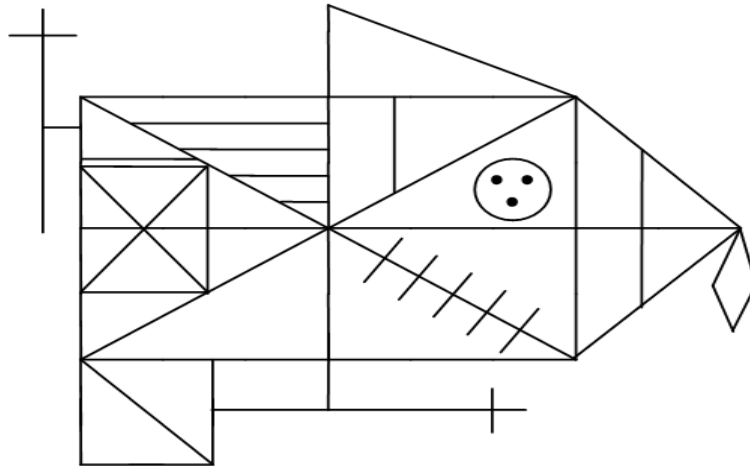


Figure 1. The Rey-Osterrieth Complex Figure.
Typically 20cm in length.

The Rey Osterrieth Complex Figure (ROCF) is a “pen and paper” neuropsychological test used to evaluate neurological dysfunction in visual perception and long term visual memory. A subject is asked to copy the complex figure and then reproduce it from memory. The reproduction has both immediate recall and delayed recall phase. It is widely used in research and clinical environments. The Osterrieth scoring system is the most popular system of many scoring systems available that produce a quantitative score for the accuracy of the drawing. The figure is split in to eighteen identifiable areas, each of which is considered separately and marked on the accuracy of its position and the distortion exhibited, using the scale.

The eighteen identifiable areas each scores 0, 1, and 2 according to the accuracy, placement and correctness of the drawing. If they miss one part it scores 0, less accurate reproduction 1, and correct reproduction scores 2. The total score is 36 according to the classical scoring system. Osterrieth defined adult average score on the copy phase is 32 and on the recall production to be 22.

2. THE TRAIL MAKING TEST (TMT)

The Trail Making Test (TMT) is one of the most popular neuropsychological tests and is included in most test batteries. The TMT provides information on visual search, speed of processing, scanning, mental flexibility, and executive functions, Tombaugh *et al*(2004).

Both parts of the Trail Making Test consist of 25 circles distributed over a sheet of paper. In Part A, the circles are numbered 1 – 25, and the patient should draw lines to connect the numbers in ascending order. In Part B, the circles include both numbers (1 – 13) and letters (A – L); as in Part A, the patient draws lines to connect the

circles in an ascending pattern, but with the added task of alternating between the numbers and letters (i.e., 1-A-2-B-3-C, etc.). The patient should be instructed to connect the circles as quickly as possible, without lifting the pen or pencil from the paper. Time the patient as he or she connects the "trail." If the patient makes an error, point it out immediately and allow the patient to correct it. Time taken to complete the trail and number of errors made is noted.

3. REY AUDITORY VERBAL LEARNING TEST (RAVLT)

Rey Auditory Verbal Learning Test (RAVLT) evaluates memory and learning. The test was administered according to its original standards: Fifteen translated nouns (list A) were read by the examiner, followed by subject's free recall (A1-A5), five times consecutively. Before every recall examiner read aloud the set of words to the patient with 1 sec gap between words. After the fifth recall, the examiner read a further list (list B) of 15 new words, followed by the subject's free recall (B). Immediately after and 20 minutes later, another recall of list A(A6 and A7) were assessed. A recognition test, with 15 words from List A intermingled with 14 new

words, was read to the subjects, who should identify which words belonged to the original list and which were new. The RAVLT has proven useful in evaluating verbal learning and memory, including proactive inhibition, retroactive inhibition, retention, encoding versus retrieval, and subjective organization. In the recognition trail, the hits are scored separately. Omissions and commissions errors also noted.

4. DIGIT SPAN TEST

Digit span is a measure of attention. Both forward and backward digit span recall have been widely used to assess short-term memory and working memory. The subjects were asked to repeat the string of numbers presented by the examiner who read it aloud one per second. The length of the string varies from 3 to 9 digits. The string is presented to subject after finishing the previous string correctly; whenever the subject makes two consequent mistakes in the same length of string the test can be stopped. Same procedure is followed for digit backward with one alteration that the subject has to exactly reverse the sequence of the number string which is read by the examiner.

5. STROOP COLOUR TEST

The Stroop task is included in many neuropsychological batteries as a measure of selective attention. This brief five minute test is applicable for those between the ages of 15 and 90. It assesses cognitive processing and provides valuable diagnostic information on brain dysfunction, cognition, and psychopathology. This test measures the ease with which a perceptual set can be shifted according to changing demands and by suppresses a habitual response in favor of an unusual one. The pre frontal areas are essential for response inhibition.

Three cards with 100 names present are used. In the first card 100 colour names printed in black and white. In second card coloured ~~xxxx~~ symbols printed in red, green and blue mixed. In third card name of the colour printed in other colour, for example red name is printed in blue colour. The subject is asked to read the card column wise with the time limit of 45 sec. In first card subject has to read the name of the colour, second card colours should be identified, third card he has to tell the colour of the word, not to read the letter. This

cause interference needs cognitive flexibility, response inhibition and selective attention to complete the task. Scoring done as per manual.

6. ANIMAL NAMING TEST (ANT)

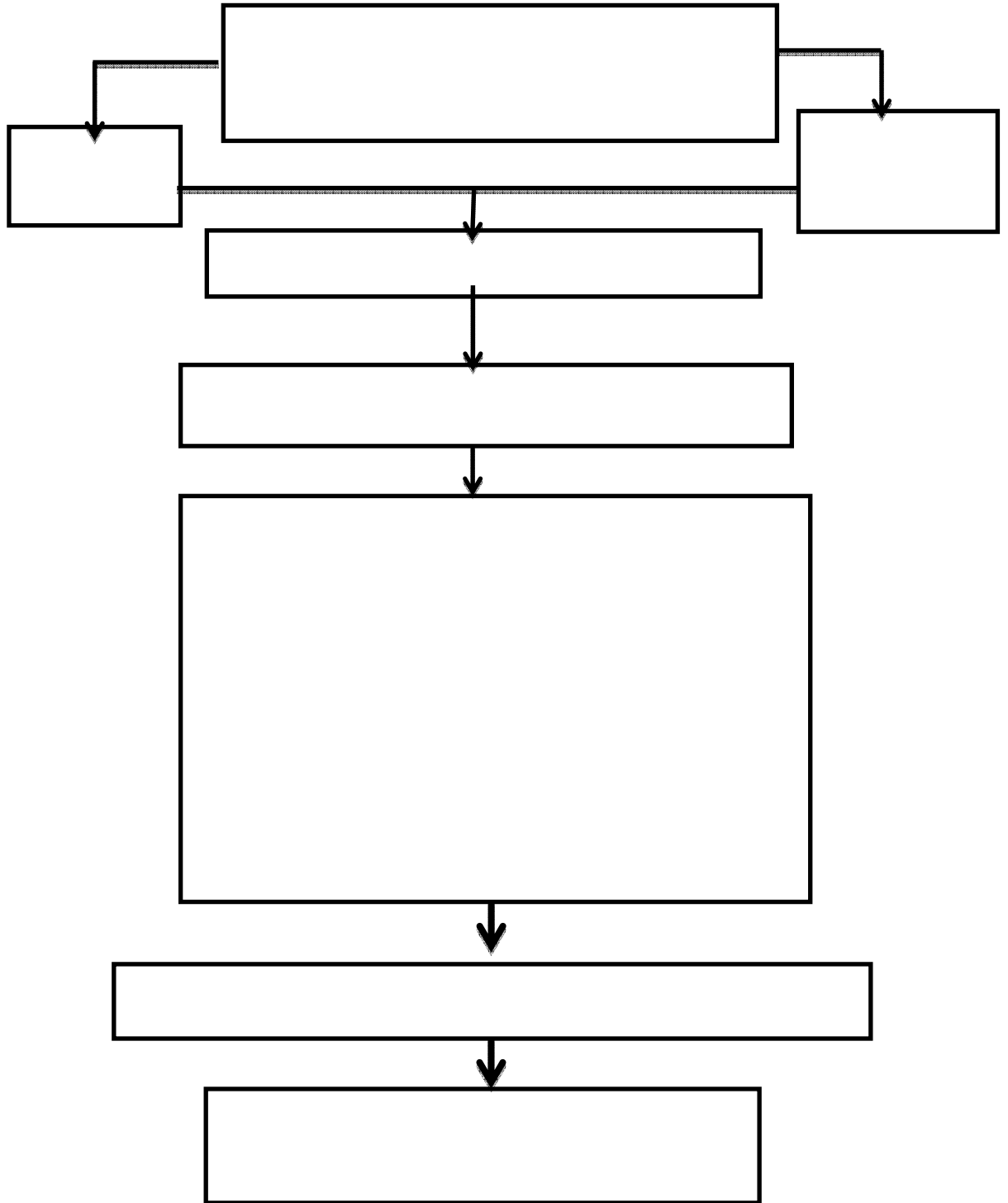
Animal Naming Test is a measure of categorical verbal fluency which is one form of verbal fluency. In this, it is the content of the words rather than the phonetic similarity of the words that is regulated. The subject generates words which belong to a particular category. Subject is asked to generate the names of animals as many as possible in one minute time. The subject is asked to exclude the names of fishes, birds and snakes. The total number of new words generated forms the scores.

7.CONTROLLED ORAL WORD ASSOCIATION TEST (COWAT)

The Controlled Oral Word Association Test (COWAT) is a measure of a person's ability to make verbal associations to specified letters (i.e., C, F, and L). This measure is a useful component of a neuropsychological battery as it is able to detect changes in word

association fluency often found with various disorders. The test assess phonetic fluency, the person has to produce nouns starting with specific letter for one minute. That should not include names. Likewise three letters given, 1min for each letter. The test was administered with three tamil letters. (க,ம,ப)

EXPERIMENTAL DESIGN



RESULTS

TABLE 1

**COMPARISON BETWEEN SOCIODEMOGRAPHIC PROFILE
OF ALCOHOL DEPENDENT AND NON ALCOHOLICS**

NO	VARIABLES	CASES (N=30)	PER CENT	CONTROLS (N=30)	PER CENT	P VALUE
1	Age(in years) 21-30 31-40 41-50	8 18 4	27 60 13	10 17 3	33 57 10	0.534
2	Education Middle High Higher Sec >high sec	7 16 4 3	23 54 13 10	12 13 1 4	41 43 3 13	0.312
4	Marital status Married Unmarried	25 5	83 17	20 10	67 33	0.136
5	Domicile Urban Rural	17 13	57 43	20 10	67 33	0.426
6	Religion Hindu Muslim Christian	26 4 0	87 13 0	27 2 1	90 7 3	0.431
7	SES Lower middle Middle Upper middle	1 26 3	3 87 10	6 23 1	20 77 3	0.093

*p < 0.005 , ** p < 0.001 (SES –Socio – Economic Status)

Table 1 shows, about 27 and 33 per cent of the subjects were in the age group of 21-30 years while 60 and 57 per cent of the subjects were in the age group of 31-40 years and only 13 and 10 per cent of the subjects were in the age group of 41-50 years in alcohol and non-alcohol group respectively.

About 23 and 41 per cent of the subjects had completed middle school of education, 54 and 43 per cent of the subjects had completed high school, 13 and 3 per cent of the subjects educated upto higher secondary grade, 10 and 13 percent were graduated in cases and controls respectively.

Almost 83 and 63 per cent of the subjects were married and remaining 17 and 33 per cent were unmarried in case and control group respectively.

About 57 and 67 per cent of the subjects were living in urban area, while remaining 43 and 33 per cent of the subjects were from rural area in case and control group respectively.

Almost 87 and 90 per cent of the subjects were Hindus; while 13 and 7 were Muslims in alcohol and non-alcohol group respectively. Only 3 per cent of the subjects were Christians in control group.

Majority of 87 and 77 per cent of the subjects belonged to middle income; while 3 and 20 percent were from lower middle income class and 10 and 3 percent were from upper middle income class in case and control group respectively.

There is no statistical difference in socio-demographic profile between cases and controls.

TABLE – 2

**COMPARISON BETWEEN TOBACCO USE IN ALCOHOL
DEPENDENT AND NONALCOHOLICS**

Variable		Case(N=30)		Control (N=30)	
		Number	Per cent	Number	Per cent
Tobacco abuse	Present	29	97	6	20
	Absent	1	3	24	80

*p < 0.005, ** p < 0.001

P value 0.000001**

This table aims at comparing the use of tobacco in both case and control groups. Majority 97 per cent of the subject in alcohol dependent group had the habit of tobacco use while only 20 per cent of the subjects uses tobacco in non- alcohol dependent group. 3 per cent of the subjects did not use tobacco in alcohol dependent group and 80 percent in non-alcohol group respectively.the difference is statistically significant at 1 percent level.

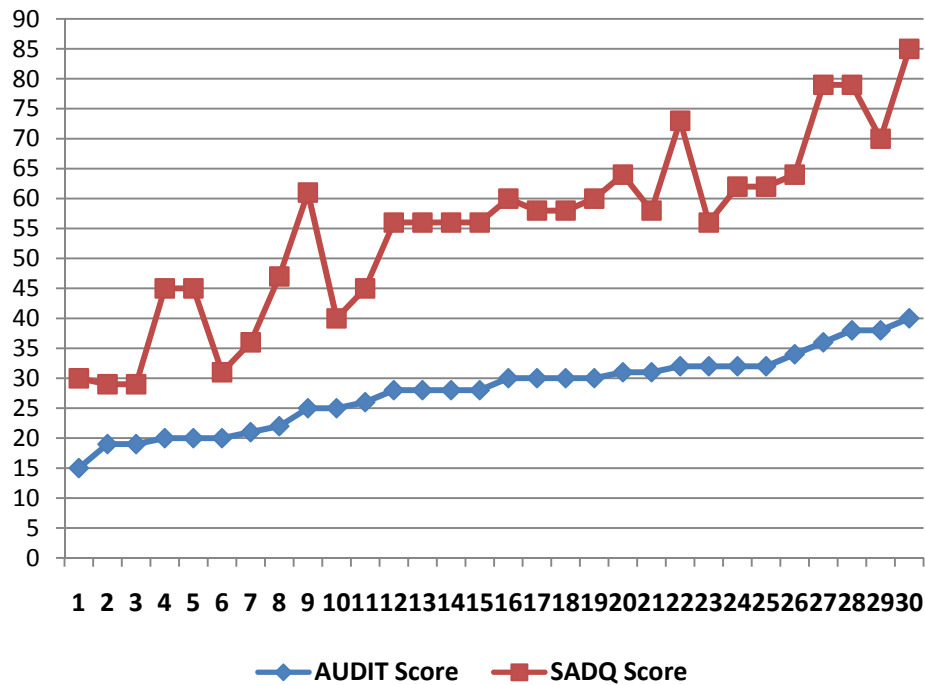
TABLE – 3

SEVERITY OF ALCOHOL DEPENDENCE

VARIABLE		CASE (N=30)	
		NUMBER	PER CENT
(SADQ Score	Mild	7	23
	Moderate	15	50
	Severe	7	23
	Very severe	1	4

Figure – I

AUDIT AND SADQ SCORE



For assessing the alcohol dependence two questionnaires applied, one is AUDIT, which screened people for alcohol dependent or not. All cases scored more than 15 in AUDIT score, implies they were dependent on alcohol. Then to assess the severity of alcohol dependence SADQ was applied. About 22 percent fell into mild dependence, 50 in moderate dependence, 23 percent in severe

dependence and 4 percent in very severe dependence according to the SADQ score.

TABLE 4

DURATION OF DAILY ALCOHOL INTAKE

VARIABLE		CASE(N=30)	
		NUMBER	PER CENT
Duration of alcohol intake (in years)	< 5	1	3
	6-10	11	37
	>10	18	60

Table 4 shows the total duration of alcohol intake in the alcohol dependent patients. 3 percent takes alcohol less than 5 years, 37 percent takes alcohol between 6 and 10yrs, 60 percent of the case taking alcohol for more than 10 yrs.

TABLE 5

QUANTITY OF INTAKE OF ALCOHOL

Quantity/day	Number	Per cent
6 standard drinks	5	16
7-12 standard drinks	11	37
>12 standard drinks	14	47
Total	30	100

Table 5 shows the quantity of intake of alcohol was studied among the selected subjects in order to assess the intensity of alcoholism. Data revealed that 47 per cent of the subjects drank more than 12 standard drinks per day while almost 37 per cent of the subject's drink ranges from 6-12 standard drinks per day and only 16 per cent drank 6 standard drinks per day.

TABLE – 6
MEAN SCORE OF REY OSTERRIETH COMPLEX FIGURE TEST

S.NO	VARIABLES	CASE (N=30)	CONTROL (N=30)	t VALUE
1	Rey copy	35.06±1.57	34.83±1.60	0.538
2	Rey Immediate recall	26.50±5.54	29.63±4.06	-2.379*
3	Rey delayed recall	26.60±6.45	29.30±4.40	-1.930

*p < 0.005, ** p < 0.001

The table depicts that the mean score of Rey Osterrieth complex figure test. Alcohol dependent group scored 35.06± 1.57, 26.50±5.54, 26.60±6.45 in Rey copy, immediate recall and delayed recall phase respectively; while the non – alcohol group scored 34.83±1.60, 29.63±4.06 and 29.30±4.40 in Rey copy, immediate recall and Delayed recall phase respectively. There is a significant difference between two groups in immediate recall phase of the test.

TABLE – 7

MEAN TIME TAKEN TO COMPLETE TRAIL MAKING TEST

VARIABLES		CASE (N=30) In seconds	CONTROL (N=30) In seconds	t VALUE
Trail Making Test	Trail A	61.00±26.38	52.73±19.57	1.481
	Trail B	107.80±39.60	63.20±15.79	5.917**

*p < 0.005, ** p < 0.001

FIGURE - 2

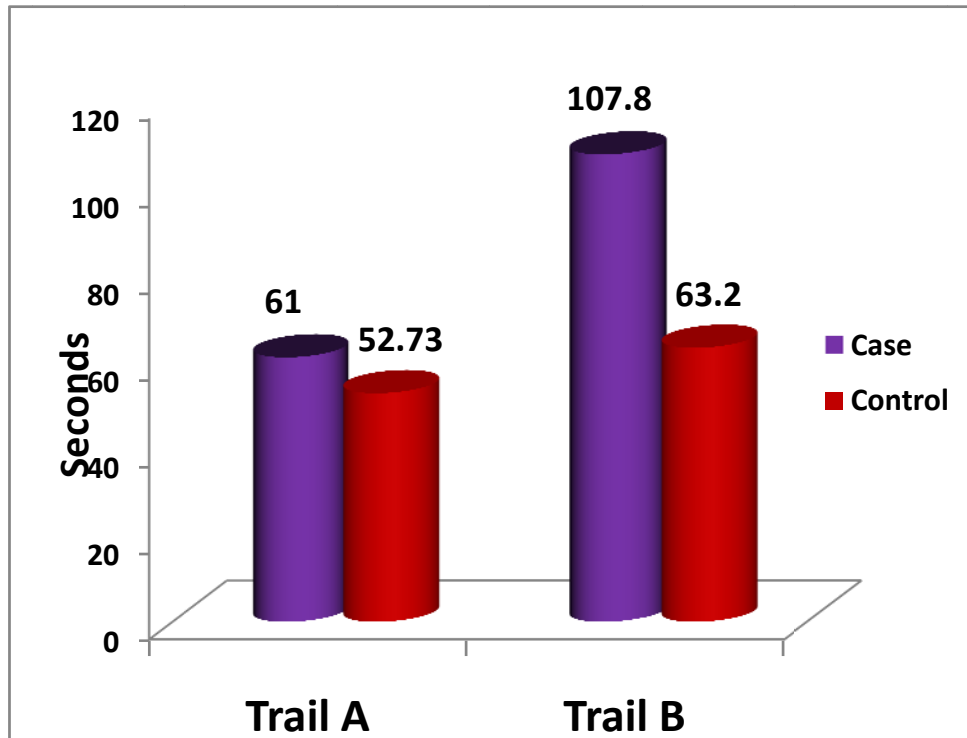


Table 7 and figure -2 shows the result of trail making A and B tests. In trail A cases and controls scores, 61.00 ± 26.38 and 52.73 ± 19.57 respectively. In trail B cases and controls scores, 107.80 ± 39.60 and 63.20 ± 15.79 respectively. There is a significance difference in the trail B test between cases and controls at 1 percent level.

TABLE – 8

**MEAN SCORE OF REY AUDITORY VERBAL LEARNING
TEST**

S.N O	VARIABLE	CASE (N=30)	CONTROL (N=30)	t VALUE
1	RAVLT 1	6.83±2.29	8.17±2.39	-2.323*
2	RAVLT 2	8.17±1.98	10.06±1.89	-4.080**
3	RAVLT 3	9.67±2.35	11.33±2.12	-3.453**

4	RAVLT 4	10.93±2.18	12.53±1.99	-2.943**
5	RAVLT 5	10.90±2.19	13.13±1.65	-4.553**
6	List B	5.53±2.28	6.73±1.85	-2.272*
7	IR A	9.90±2.38	11.70±2.29	-2.964**
8	DR A	8.73±3.07	11.77±2.14	-4.241**
9	Recognition	26.60±2.06	28.20±1.27	-3.565**
10	Omission	1.20±1.67	0.47±1.04	-1.959
11	Commission	1.20±1.13	0.33±0.61	3.563**

*p < 0.005, ** p < 0.001

IR A- immediate recall list A; DR A- delayed recall list

FIGURE -3

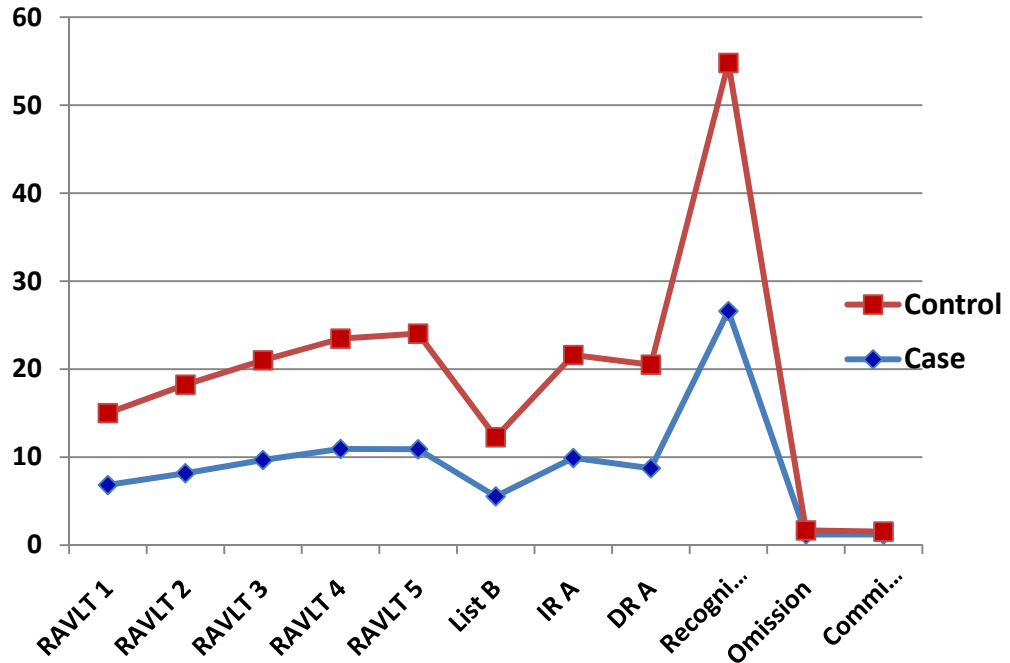


Table 8 and figure - 3 shows, Rey auditory verbal learning test mean score for recall 1 was 6.83 and 8.17; recall 2 was 8.17 and 10.06, recall 3 was 9.67 and 11.3; recall 4 was 10.93 and 12.53 and recall 5 was 10.90 and 13.13 in alcohol and non- alcohol group respectively. The mean recall score of list B was found to be 5.53 and 6.73; immediate recall was 9.90 and 11.70 and delayed recall was 8.73 and 11.7 in alcohol and non- alcohol group respectively. The mean score of recognition was found to be 26.60 and 28.20; while omission was 1.20 and 0.61; commission was 1.20 and 0.33 in alcohol

and non – alcohol group respectively. There was a statistically significant difference between cases and controls in recall 2, 3, 4, 5, immediate recall A, delayed recall A, recognition and commission error at 1 percent level, in recall 1 and list B at 5 percent level. There is no significant difference in omission error.

TABLE - 9

MEAN SCORE OF DIGIT SPAN TEST

VARIABLE		CASE (N=30)	CONTROL (N = 30)	t VALUE
Digit span test	Digit forward	6.87±1.50	7.37±1.79	-1.077
	Digit backward	4.30±1.32	5.70±1.84	-3.475**

*p < 0.005, ** p < 0.001

Table 9 depicts the results of digit forward and digit backward tests. In digit forward tests cases and controls scored 6.87±1.50 and 7.37±1.79 respectively. In digit backward test they scored 4.30±1.32 and 5.70±1.84 respectively. There was a statistically significant difference observed at 1% level in digit backward test between cases and controls.

TABLE – 10

MEAN SCORE OF STROOP TEST RESULTS

Variable	Case (N=30)	Control(N=30)	t value
Stroop 1	83.33±19.30	92.90±10.08	-2.399*
Stroop 2	48.50±11.71	51.80±9.63	-1.338
Stroop 3	29.43±9.65	37.23±13.05	-2.442*

*p < 0.005, ** p < 0.001

FIGURE -4

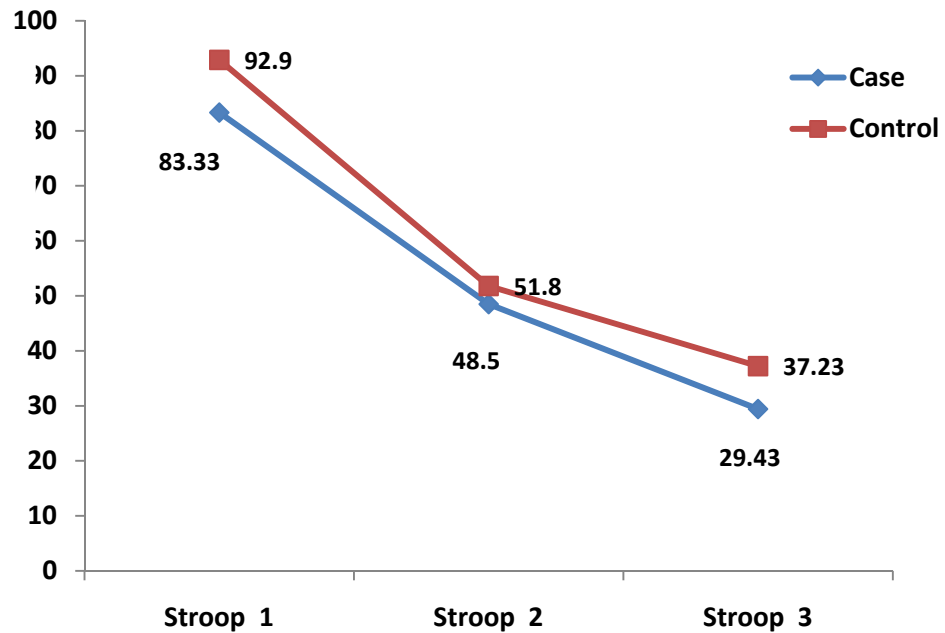


Table 10 and figure - 4 depicts the result of Stroop test. In Stroop 1, cases and controls scored 83.33 ± 19.30 and 92.90 ± 10.08 respectively. In Stroop 2 they scored 48.50 ± 11.71 and 51.80 ± 9.63 respectively. In Stroop 3 they scored 29.43 ± 9.65 and 37.23 ± 13.05 respectively. There was a statistically significant difference in Stroop test 1 and 3 between these two groups observed at 5% level.

TABLE - 11

MEAN SCORE OF ANIMAL NAMING AND COWAT TEST

VARIABLE	CASE (N=30)	CONTROL(N=30)	t VALUE
ANT	11.47±2.83	12.46±3.46	-1.422
COWAT	19.20±4.82	22.33±5.91	-2.195*

*p < 0.005, ** p < 0.001

FIGURE - 5

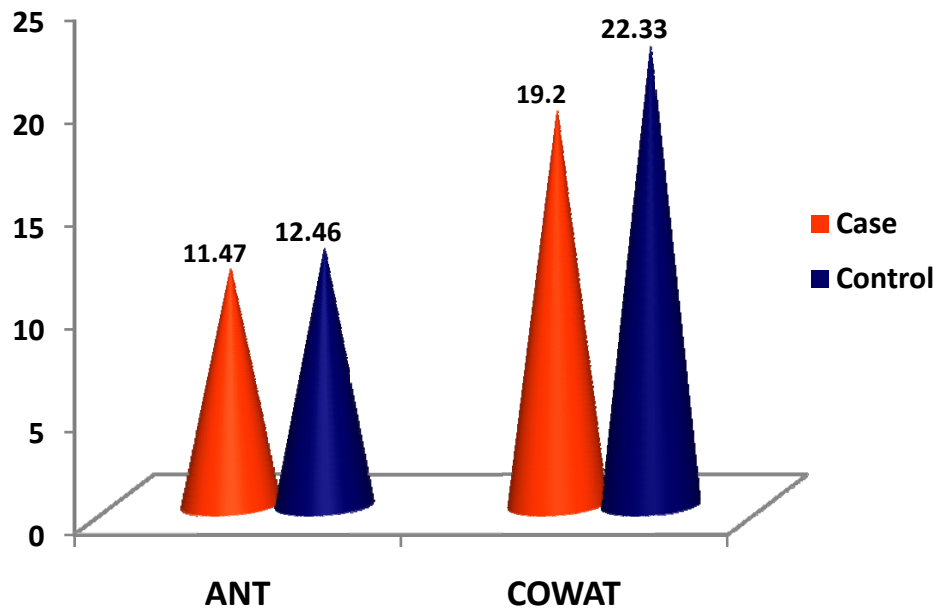


Table 11 and figure – 5 depicts the results of animal naming and controlled oral word association test. Alcohol dependent and non-alcoholics scored 11.47 ± 2.83 and 12.46 ± 3.46 respectively in animal naming test. They scored 19.20 ± 4.82 and 22.33 ± 5.91 in COWAT. There was a statistically significant difference observed in COWAT test between case and controls at 5% level.

TABLE 12**CORRELATION BETWEEN DRINKING INDICES AND TEST RESULTS**

VARIABLES	DURATION	QUANTITY	SADQ SCORE
REY COPY	0.008 (0.965)	0.125 (0.512)	-0.244 (0.193)
REY IR	0.183 (0.334)	0.266 (0.156)	0.241 (0.200)
REY DR	0.146 (0.440)	0.207 (0.272)	0.332 (0.073)
Trail A	0.083 (0.664)	0.056 (0.769)	0.042 (0.824)
Trail B	-0.180 (0.341)	-0.187 (0.321)	-0.077 (0.686)
RAVLT 1	-0.153 (0.420)	0.015 (0.938)	0.096 (0.616)
RAVLT 2	-0.112 (0.555)	-0.104 (0.585)	-0.292 (0.118)
RAVLT 3	-0.023 (0.903)	-0.170 (0.370)	-0.319 (0.086)
RAVLT 4	0.013 (0.947)	-0.074 (0.699)	-0.003 (0.988)
RAVLT 5	-0.061 (0.750)	-0.208 (0.270)	-0.340 (0.066)
LIST B	0.220 (0.243)	-0.181 (0.339)	-0.165 (0.382)
IR A	0.192 (0.308)	0.136 (0.472)	0.077 (0.684)
DR A	0.218 (0.248)	0.114 (0.548)	0.204 (0.278)
RECOGNITION	0.222 (0.238)	-0.025 (0.894)	-0.122 (0.522)
OMMISION	-0.107 (0.572)	0.052 (0.784)	0.263 (0.160)
COMMISION	-0.237 (0.207)	0.098 (0.607)	-0.031 (0.869)
DIGIT FORWARD	0.125 (0.570)	0.301 (0.106)	-0.145 (0.445)
DIGIT BACKWARD	0.124 (0.515)	0.017 (0.927)	-0.078 (0.680)
STROOP 1	-0.138 (0.466)	-0.042 (0.826)	0.160 (0.397)
STROOP 2	-0.017 (0.929)	-0.252 (0.179)	0.185 (0.328)
STROOP 3	-0.142 (0.454)	-0.113 (0.552)	-0.163 (0.391)
ANT	0.131 (0.490)	0.028 (0.885)	-0.009 (0.962)
COWAT	0.054 (0.777)	-0.122 (0.519)	-0.079 (0.679)

Data are r value (p value)

Table 12 depicts the correlation between the various alcohol related indices like duration of daily alcohol intake, quantity of alcohol intake (converted into standard units) and severity of alcohol dependence (assessed by severity of alcohol dependence questionnaire) and neuropsychological test results. There is no statistically significant difference observed between the alcohol indices and test scores.

DISCUSSION

The present study aimed at assessing the neurocognitive functions in alcohol dependent patients. Then the results were compared with the results of the controls. The same neurocognitive test battery is applied to both the groups. The study is designed, keeping in mind the possible adverse cognitive effects of alcohol. The subjects selected carefully after ruling out any major neuropsychiatric illnesses, because major psychiatric illnesses like schizophrenia, bipolar mood disorder and depression are having their own cognitive dysfunction profiles. The role of withdrawal effect of alcohol, benzodiazepines used for detoxification process, physical illnesses, fatigue, motivational factors in doing the neuropsychological tests are addressed, all possible efforts are made to reduce the confounding factors.

The neuropsychological test battery applied to the patients in single sitting, after atleast one week of abstinence from alcohol. Patients in acute withdrawal state have tremor which may interfere in tasks like drawing Rey osterrieth complex figure test and trial making tests. Then they have anxiety, sleep disturbance which have

their negative consequences in learning, memorizing and executive functions.

The tests administered are intended to test attention, executive function, short term memory, working memory, nonverbal, verbal memory and verbal fluency.

In this study majority of the patients belongs to 31-40 age group. Patients have started their first alcohol intake in their late teens. Then they slowly developed the daily intake pattern of alcohol use. They fulfilled the criteria for alcohol dependence atleast for the past 2 to maximum of more than 10 yrs. Johnson Pradeep *et al*, 2010, in his study discussed that average age of onset of alcohol intake is 18yrs, they take another 6yrs to have the first criteria for dependence, in another 4 yrs they become full blown alcohol dependence patients. The findings in the present study are in concordance with the findings of the above mentioned study.

The subjects selected with the education status at and above the 8th Std to reduce the bias of educational qualification interferes with performance of the test, it possibly reduce the IQ factor

confounding the test results. Since there is no statistically significant difference between the cases and controls regarding education and socioeconomic status the possibility of intelligence confounding the result is ruled out.

In the patients 83% of the persons were married. In controls 63% of them were married. In considering the marital status of the patients, it is one of the important factors which bring the patient to the hospital. Patients admit that because of influence of wife and children they came for deaddiction treatment. This factor can be further used to bring the patient to health care personnel. Marriage certainly influence the duration of alcohol intake and quantity of intake. It prolongs the period to develop the dependent pattern of alcohol intake.

The urban rural difference is not significant in the present study, (57% from urban, 43% from rural of cases). The finding is in concordance with the Family Health Survey (NFHS-3, 2007) Data collected in 2005-06, published in September 2007, showed that

proportion of users among rural and urban population is very similar (32% and 31% respectively).

Considering the religion Hindu's predominates (87%) and majority from middle socioeconomic class. These factors can be taken as mere representation of the cross section of the population because there is no statistically significant difference between cases and controls. But one factor should be thought of is the religious prohibition of alcohol in Muslims reduce the incidence of drinking in their population. Middle income people join together and take alcohol for pleasure in the beginning of their alcohol usage, but at last they lose most of their revenue in buying alcohol. This has major public health impact not only on the life of the patient but also on the life of the family members also.

Alcohol and tobacco are like conjoined twins, they are abused together in most of the situations. People who are willing to quit alcohol are not willing to quit tobacco. They considered tobacco as an innocuous substance. There are two forms of tobacco use which predominate in Tamil Nadu are smoking and chewing. In the present

study, 97% of the patient population smoke tobacco to the level of dependence. This finding is consistent with several literatures, Hurt *et al*(1994); Pomerleau *et al*(1997); Romberger & Grant(2004), Timothy C. Durazzo & Stefan Gazdzinski(2007). In the controls only 20% are smokers, their pattern of smoking is also not severe. Whenever assessing effect of alcohol on the brain and other systems, tobacco use is a major hurdle, because various substances in tobacco affects the whole system, so it complicate the picture and we cannot assess the sole effect of alcohol.

For alcohol dependence AUDIT questionnaire and SADQ questionnaire were applied. AUDIT is used for screening, 70% of the patients scored more than 26 out of the maximum score of 40. SADQ categorize the dependence severity. In that 50% scored for moderate, 27% scored for severe and very severe categories. Cumulatively 77% of the patients have significant dependence to alcohol. The questionnaires assess the alcohol dependence with various parameters like duration, quantity, physical and psychological craving and withdrawal, but they typically lack the quality to assess the cognitive

functions, Theotoka.I, (2006), Gupta.*Set al*, (2008), Conigrave*et al*(1995), Stockwel*et al.*, (1983).

Sixty per cent of the cases took alcohol for more than 10yrs that too almost daily, 47% of them consume more than 360ml (more than 12 standard drinks) per day, cumulatively 84% consume more than 180ml (6 standard drinks) daily. This shows that they are heavy consumer of alcohol. There are no International standards in local shops. The standard in Tamil Nadu is 90ml and 180ml (3-6 standard drink). Patients consume roughly 50gm to 160gm of alcohol per day. There is no significant association between the duration, quantity and severity of dependence was found in the present study. Hamin lee, SungwonRoh*et al*(2009), white.A.*Met al*(2003) found that duration of alcohol intake, pattern and quantity of intake significantly affects the cognitive functions. The present study doesn't correlate with the above study. When considering the overall results patients have significantly performed worse than controls. Other alcohol related factors may influence the outcome. Alcohol itself is a neurotoxin which independently influences the result.

When considering the results of test batteries controls clearly outperformed the cases in all tests. But the significance level varies. In Rey Osterrieth complex figure test significant difference is observed between cases and controls in the immediate recall phase. This shows patients have problem in retrieval of the information which they have processed in the immediate past. Since there is no significant difference in copy and delayed recall, visual memory and motor skills is not significantly affected. Patients with executive dysfunction have retrieval problems which is the function of frontal cortex rather than temporal cortex. This findings is in concordance with the results of Zinn.S and Roy stein *et al* (2004) findings.

The trial making tests shows difference in performance between cases and controls, which is significant with trial B test at 1 percent level. It clearly implies that the alcohol dependence patients have reduced information processing speed, visual scanning, cognitive flexibility and executive functions comparing to controls. These findings are comparable with findings of Noel *et al* (2001), Zinn.Set *al* (2004). The discrepancy between patients and controls in the test

signifies the impairment in various neurocognitive functions in alcohol dependent patients. Patients have deficit in timed task and visual scanning, which poses demand on working memory. It implies alcohol significantly affect the executive function and working memory.

The Rey auditory verbal learning test findings shows that cases have significant delay in the recall of words in all phases of test. They have significant difference at 1% level in most of the phases. Nadia solowiji, katy A. Jones *et al*(2011) found that delayed recall in verbal learning tests is associated with duration, frequency and quantity of alcohol consumption. But the findings of the present study don't correlate with the above mentioned study.

But patients recalled less no of words than controls and they have difficulty in free recall when proactive and retroactive inhibition is present. This implies that they have executive and working memory impairment than the controls. These functions belong to frontal and prefrontal cortex. The patient group has decreased verbal memory; this finding is supported by Daig.I, Mahlberg.R(2012).

In digit span test, case scored less than the controls; It is significant at 1% level in digit backward test. It shows significant impairment of attention, working memory and immediate memory. This findingsis comparable with the results of Frank Norton and LavaniaHalay (2011).

In Stroop test, alcoholics performed worse than the controls, it is significant at 5% level in Stroop 1 and 3. This shows that alcoholics have poor selective attention, speed of information processing, reduction in cognitive flexibility and executive function comparing to non-alcoholics. This findings are comparable with Sharma *et al* (2001) and Marina Cordovil de souse uvaet *al* (2010) findings.

In verbal fluency alcohol dependents recalled less number of words than the controls. There is significant difference in phonetic fluency assessed by COWAT at 5% level. In the verbal fluency test the individual has to actively search code and recall the words from semantic network. This is a function of frontal lobe. The active search and semantic organization and process were impaired in patient group.

Sometimes this dysfunction can be compared with the dysfunction in Alzheimer disease, Ioannisiappas, Iouliatheotoka *et al*(2007).

In correlational analysis there was no significant association between the duration, quantity and severity of alcohol dependence and the various neuropsychological test findings. The findings in the present is not correlating with the findings of, Hamin lee *et al*(2009), White *et al*, (2003) studies.

There are many studies which supports that moderate alcohol consumption favors the better cognitive functions, Jill E. Green *et al*, (2004), Meir J. Stampfer *et al* (2005), Lydia krabbendam *et al* (2000). There is no study which says that heavy alcohol consumption doesn't affect the cognitive function. Some studies gives explanation that the cognitive functions are not direct consequence of alcohol intake, but due to associated factors like premorbid intelligence, personality and brain abnormalities. The patients participated in the study more enthusiastically than the controls, inspite of that they performed lower than the controls. The findings of the present study clearly depicts alcohol dependence patients have significant impairment in working

memory and executive function which can be explained by the neurotoxic effect of alcohol which adversely affects the frontal lobe.

To summarize the findings of the present study, alcohol dependent patients have significant deficit in attention, working memory, executive function, impaired verbal memory and verbal fluency. Patients have difficulty in information processing, visual scanning, retrieval of facts, verbal and nonverbal recall and cognitive flexibility. The functions mentioned above are mediated by prefrontal and frontal cortex. The findings also supported by previous studies in this area.

The study is attempted to assess the neurocognition in alcoholics and to demonstrate the deficit in them. Since alcohol marketing is become aggressive in the recent past, it needs biomedical evidence to prove its ill effect to assist in policy making. This study is aimed at right population and at right time, when voice started to arise in the public health side to ban alcohol in the state.

In acute phase of the recovery alcohol patients having reduce information processing, but they appeared to be well

motivated. It is one of the reasons why most of them relapsed in 3-6 month period.

Patients spontaneously reports that they have difficulty in recalling names, they have slowness in their work, difficulty in memorizing cell numbers, not able to drive swiftly and make careless mistakes. Those findings objectively confirmed by the systematic testing of executive function, working memory and various other functions in the present study.

Alcohol had become the great hazard in the modern community especially in this part of country. There is lack of systematic data about the alcohol related neuropsychiatric complications. The research work on alcohol and its various health complications is a never ending process, it needs constant updates. Having data related to the population whom we serve enriches our clinical decision making; hence an attempt was made in the study to test the Neurocognition in Indian population.

LIMITATIONS OF THE STUDY

1. It was a cross sectional study, no follow up study was made.

2. The test administered in hospital based severe alcohol dependence patients, so it may not be extrapolated to general community.
3. The sample size is small.
4. The systemic and mental illnesses are ruled out with basic investigations in addition to clinical findings. Imaging is not attempted to rule out structural defects.
5. The main limiting factor is tobacco use, which is heavy in alcohol dependence patients, it affects the cognitive functions as alcohol, but this factor cannot be eliminated in the present study.

CONCLUSION

To summarize, the present study done with the aim of assessing neurocognitive functions in alcohol dependent patients. Based on the findings in our study the following conclusions were made.

1. Alcohol dependent patients have significant deficit in neurocognitive functions than non alcoholics.
2. Alcohol dependent patients have significant dysfunction in executive function, working memory and attention than non alcoholics.
3. Duration of alcohol intake is not significantly correlated with the verbal and nonverbal memory.
4. Quantity of alcohol intake doesn't affect the attention and executive function.
5. Severity of alcohol dependence measured with SADQ doesn't correlated with the Neurocognitive dysfunction.

The findings confirm the hypothesis that alcohol dependence patients have impairment in executive functions, working memory, short term memory, set shifting, selective attention, cognitive flexibility, visual memory and information processing speed. The findings also

corroborated with the previous literature evidence. But there is no significant correlation observed between duration, quantity and severity of alcohol dependence and various neuropsychological test findings. It disproves other hypothesis. But they cumulatively affect neurocognition. The functions affected by alcohol are predominantly mediated by prefrontal and frontal cortex.

The findings can be used in various treatment programmes, while discussing about the management strategies. Since patient have limited capacity to process the information given to them in the acute phase of the treatment, information can be given to family members and ask the family members to keenly instruct and reinstruct the patient about the ill effect of alcohol. The routine examination can include basic neuropsychological testing to identify possible subtle cognitive deficits, early in all alcohol dependent patients. Trail making test can be easily incorporated in the day to day practice while assessing the alcohol dependence patients. This study adds to the armamentarium of studies related to alcohol. But it is the first step of a long journey of bringing the patient out of the ill effect of alcohol.

In future the early identification of it cognitive dysfunction in alcohol misuse disorder can be attempted, because it is more common than alcohol dependence in the community. It can be included in public health information materials like printing a crab picture in the tobacco related products.

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