

# Alcohol Related Brain Damage

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**Abstract:** Chronic excessive alcohol intoxications evoke cumulative damage to tissues and organs. We examined prefrontal cortex (Brodmann's area (BA) 9) from 20 human alcoholics and 20 age, gender, and postmortem delay matched control subjects. H & E staining and light microscopy of prefrontal cortex tissue revealed a reduction in the levels of cytoskeleton surrounding the nuclei of cortical and subcortical neurons, and a disruption of subcortical neuron patterning in alcoholic subjects. BA 9 tissue homogenization and one dimensional polyacrylamide gel electrophoresis (PAGE) proteomics of cytosolic proteins identified dramatic reductions in the protein levels of spectrin  $\beta$  II, and  $\alpha$ - and  $\beta$ -tubulins in alcoholics, and these were validated and quantitated by Western blotting. We detected a significant increase in  $\alpha$ -tubulin acetylation in alcoholics, a non-significant increase in isoaspartate protein damage, but a significant increase in protein isoaspartyl methyltransferase protein levels, the enzyme that triggers isoaspartate damage repair in vivo. There was also a significant reduction in proteasome activity in alcoholics. One dimensional PAGE of membrane-enriched fractions detected a reduction in  $\beta$ -spectrin protein levels, and a significant increase in trans-membranous  $\alpha 3$  (catalytic) subunit of the Na<sup>+</sup>, K<sup>+</sup>-ATPase in alcoholic subjects. However, control subjects retained stable oligomeric forms of  $\alpha$ -subunit that were diminished in alcoholics. In alcoholics, significant loss of cytosolic  $\alpha$ - and  $\beta$ -tubulins were also seen in caudate nucleus, hippocampus and cerebellum, but to different levels, indicative of brain regional susceptibility to alcohol-related damage. Collectively, these protein changes provide a molecular basis for some of the neuronal and behavioural abnormalities attributed to alcoholics.

**Keywords:** Alcohol, behavioral Abnormalities, intoxication

## 1. Introduction

The brain, like most body organs, is vulnerable to injury from alcohol consumption. The risk of brain damage and related neurobehavioral deficits varies from person to person. This article reviews the many factors that influence this risk, the techniques used to study the effects of alcoholism on the brain and behavior, and the implications of this research for treatment. (1 Alcohol dependence, also known as alcoholism, is characterized by a craving for alcohol, possible physical dependence on alcohol, an inability to control one's drinking on any given occasion, and an increasing tolerance to alcohol's effects [American Psychiatric Association (APA) 1994].)

About half of the nearly 20 million alcoholics in the United

States seem to be free of cognitive impairments. In the remaining half, however, neuropsychological difficulties can range from mild to severe. For example, up to 2 million alcoholics develop permanent and debilitating conditions that require lifetime custodial care (Rourke and Löberg 1996). Examples of such conditions include alcohol-induced persisting amnesic disorder (also called Wernicke-Korsakoff syndrome) and dementia, which seriously affects many mental functions in addition to memory (e.g., language, reasoning, and problem-solving abilities) (Rourke and Löberg 1996). Most alcoholics with neuropsychological impairments show at least some improvement in brain structure and functioning within a year of abstinence, but some people take much longer (Bates et al. 2002; Gansler et al. 2000; Sullivan et al. 2000). Unfortunately, little is known about the rate and extent to which people recover specific structural and functional processes after they stop drinking. However, research has helped define the various factors that influence a person's risk for experiencing alcoholism-related brain deficits, as the following sections describe.

## 2. Aetiology

When alcohol enters the body, it travels from the stomach and intestines through the bloodstream to various organs. In the liver, spikes in blood alcohol content caused by heavy drinking overload its ability to process alcohol. So, excess alcohol journeys from the liver to other parts of the body, like the heart and central nervous system. Subsequently, alcohol moves through the blood-brain barrier, affecting the brain's neurons directly. There are over 100 billion interconnected neurons in the brain and central nervous system. As a toxic substance, drinking alcohol can damage, or even kill, neurons.

Alcohol is often described as a "downer" because it slows down signals sent between neurons. Additionally, certain automatic brain processes controlled by the cerebellum and cerebral cortex are impaired or slowed (i.e. breathing, balance, processing new information). It also slows GABA neurotransmitters, resulting in slurred speech, lethargic movements, and reduced reaction time. Conversely, alcohol causes the rapid release of glutamate neurotransmitters (responsible for dopamine regulation in the reward center of the brain). This creates the "warm, fuzzy" feelings many associate

with drinking.

These short-term effects of alcohol, though potentially dangerous on their own, mask the long-term damage alcohol can cause. Damage to the hippocampus region (responsible for memory creation) is severely affected by drinking and “blackouts,” leading to short-term memory loss and brain cell death. Repeated blackouts, a clear sign of excessive drinking, can result in permanent damage that inhibits the brain from retaining new memories. For example, an individual may be able to recall past events with perfect clarity but not remember having the conversation a few hours later.

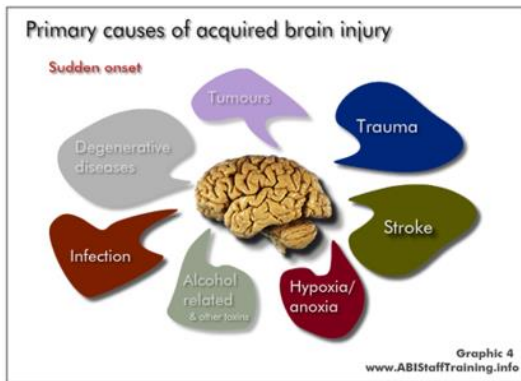


Fig. 1. Primary causes of acquired brain injury

### 3. Signs and symptoms

*Cognitive and memory problems:*

**Memory loss:** A person is unable to remember directions to familiar places or has trouble remembering appointments or recalling what they have just done or should be doing.

**Difficulty with familiar tasks:** A person may struggle with an everyday task like using their phone or confused about the layout of their home or how to prepare a meal.

**Difficulty in processing new information:** Not being able to recall times, dates appointments they have recently been given, or to remember people they have just met.

**Depression and irritability:** This can also include apathy, a lack of interest in people or events and a lack of spontaneity or motivation.

**Poor judgement and loss of inhibition:** A person may be too trusting of strangers or respond inappropriately for example by removing their clothes in public.

**Difficulty concentrating:** It can be hard for people with ARBD to focus on one thing for more than a few minutes, which can makes everyday tasks difficult.

**Poor choices and decisions-making:** A person may not see any reasons to think about changing their drinking and may not seek or accept help. They may have difficulty in weighing up options or making sensible decisions. They may also be vulnerable to manipulation, coercion and abuse by others.

**Physical problems:** Damage to liver, stomach and pancreas: all of which can affects brain function.

**Pins and needles and numbness or burning sensation in arms**

**and legs;** this can increase the risk of falls and accidents.

**Slow, wide, stumbling gait(ataxia):** this can make it difficult for someone to walk, and they may find balancing difficult.

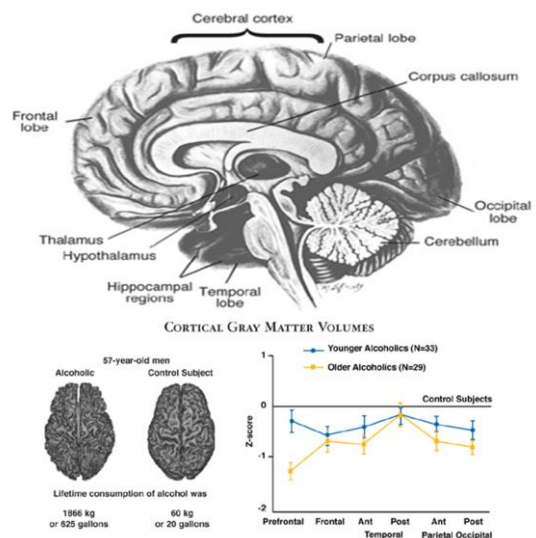
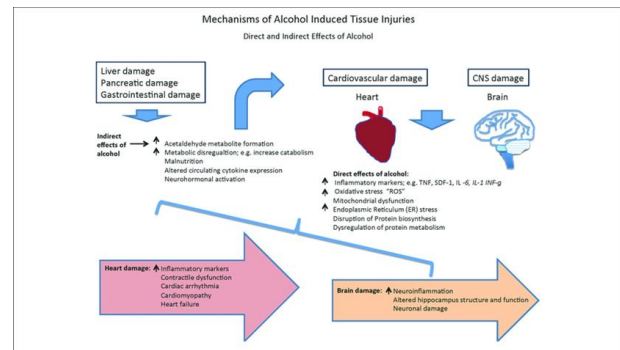
**Poor temperature control, muscle weakness and disturbed sleep patterns:** these are all caused by shrinkage of the brain and by tissue damage.

#### A. Wernicke-Korsakoff's Syndrome

The most severe form of ARBD is known as Wernicke-Korsakoff's Syndrome (WKS), and was named after the two doctors who first recognized it. It is caused by a lack of vitamin B1 (thiamine) in the body, which in turn is a result of long-term heavy drinking.

In the past, Wernicke-Korsakoff's Syndrome (WKS) was used as an umbrella term to describe all types of ARBD and alcohol-related dementias. However, the term Alcohol-Related Brain Damage (or Alcohol-Related Brain Impairment) is a much more useful term, as WKS is actually a very specific form of ARBD. WKS is made up of two separate elements: Wernicke's Encephalopathy and Korsakoff's Psychosis.

#### B. Pathophysiology



#### C. Diagnosis

Generally, an individual will develop alcohol-related brain damage after 10 to 20 years of heavy drinking (though some

have developed brain damage in less time). Women may develop alcohol-related brain damage in a shorter time span due to body size. People between the ages of 45 and 60 are the most commonly diagnosed group because it takes time for symptoms to appear. Oftentimes, when patients finally receive a diagnosis, much of the damage is permanent. Yet, the brain is a powerful organ and capable of regeneration to an extent. Through early intervention and treatment, some brain impairment can be halted, or even reversed.

#### D. Treatment

Depending on the severity of brain damage, patients may receive either preventative, restorative, or end-of-life supportive medical care. There are no cures for alcohol-related brain damage. For those with WKS, thiamine and vitamin supplements can improve brain function. Early diagnosis of alcohol-related dementia, hepatic encephalopathy, and FAS can halt alcohol-related brain damage and lifestyle changes may even reverse deterioration. However, for all forms of alcohol-related brain damage, quitting drinking is the best first step.

Brain damage caused by alcohol represents a gradual decline in brain function and health. For people suffering from an alcohol dependency, there is time to get help and to begin to rehabilitate yourself. All treatment for AUDs and alcohol-related diseases starts with a complete detox to free the body of harmful substances. Most medical professionals recommend some form of inpatient detox at a rehab facility. This increases comfortability for the individual as well as their chances of a successful recovery. Through proper detox, abstinence, and a healthy diet, brain scans show some effects of heavy drinking can be undone. Alcohol treatment medications like Acamprosate and Naltrexone may be prescribed to block the effects of a relapse or reduce alcohol cravings.

#### 4. Conclusion

Alcoholics are not all alike; they experience different subsets of symptoms, and the disease has different origins for different people. Therefore, to understand the effects of alcoholism, it is important to consider the influence of a wide range of variables. Researchers have not yet found conclusive evidence for the idea that any one variable can consistently and completely account for the brain deficits found in alcoholics. The most plausible conclusion is that neurobehavioral deficits in some alcoholics result from the combination of prolonged ingestion of alcohol, which impairs the way the brain normally works, and individual vulnerability to some forms of brain damage. Characterizing what makes alcoholics “vulnerable” remains the subject of active research.

In the search for answers, it is necessary to use as many kinds of tools as possible, keeping in mind that specific deficits may be observed only with certain methods, specific paradigms, and particular types of people with distinct risk factors. Neuroscience provides sensitive techniques for assessing changes in mental abilities and observing brain structure and

function over time. When techniques are combined, it will be possible to identify the pattern, timing, and distribution of the brain regions and behaviors most affected by alcohol use and abuse. Electromagnetic methods (ERP and MEG) specify the timing of alcohol-induced abnormalities, but the underlying neural substrate (i.e., the anatomical distribution of the participating brain areas) cannot be unequivocally evaluated based on these methods alone. Conversely, the hemodynamic methods (fMRI, PET, and SPECT) have good spatial resolution but offer little information about the sequence of events. Drawing on the respective advantages of these complementary methods, an integrated multimodal approach can reveal where in the brain the critical changes are occurring, as well as the timing and sequence in which they happen (Dale and Halgren 2001). Such confluence of information can provide evidence linking structural damage, functional alterations, and the specific behavioral and neuropsychological effects of alcoholism. These measures also can determine the degree to which abstinence and treatment result in the reversal of atrophy and dysfunction.

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