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ALCOHOL AND BRAIN SHRINKAGE

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Article QUICK LINKS :

[Imaging and Alcoholism: A Window on the Brain](#) /
[Alcohol's Effects on Brain Structure and Function](#) /
[Relating Structure and Function to Behaviour](#) /
[Mechanisms of Addiction / Treatment of Alcoholism](#) /
[Appendix : Imaging Techniques](#)
[References](#)

IMAGING AND ALCOHOLISM : A WINDOW ON THE BRAIN

The processes that initiate and maintain alcoholism are regulated by interactions among nerve cells (i.e., neurons) in the brain. These mechanisms interact with emotional, cognitive, and social factors to determine an individual's response to alcohol consumption. Imaging techniques¹ allow scientists to study the link between brain and behaviour with minimal risk to the patient.

Using imaging, scientists can watch the brain in action as a person performs intellectual tasks, reacts to the environment, or experiences emotions. Data obtained before, during, and after a person has consumed alcohol can be compared and analysed. Imaging offers the promise of integrating biomedical, psychosocial, and behavioural aspects of alcoholism, leading to improved prevention and treatment. This Alcohol Alert illustrates some current and potential applications of imaging to alcoholism research.

ALCOHOL'S EFFECTS ON BRAIN STRUCTURE AND FUNCTION

Results of autopsy studies show that patients with a history of chronic alcohol consumption have smaller, lighter, more shrunken brains than non-alcoholic adults of the same age and gender¹. This finding has been repeatedly confirmed in living alcoholics using structural imaging techniques, such as computed tomography (CT) and magnetic resonance imaging (MRI). Structural imaging reveals a consistent association between heavy drinking and physical brain damage, even in the absence of medical conditions previously considered to be clinical indicators of severe alcoholism (e.g., chronic liver disease or alcohol-induced dementia).

Imaging reveals shrinkage to be more extensive in the folded outer layer (i.e., cortex) of the frontal lobe ², which is believed to be the seat of higher intellectual functions. In men, vulnerability to frontal lobe shrinkage increases with age (2-4). Current studies will determine if the same effect occurs in women. Repeated imaging of a group of alcoholics who continued drinking over a 5-year period showed progressive brain shrinkage that significantly exceeded normal age-related shrinkage ⁵. The rate of frontal cortex shrinkage in this study correlated approximately with the amount of alcohol consumed ⁵.

Shrinkage also occurs in deeper brain regions, including brain structures associated with memory ⁶⁻⁸, as well as in the cerebellum, which helps regulate coordination and balance ⁹. Limited research suggests that women may be more susceptible than men to alcohol-related brain shrinkage ¹⁰⁻¹¹.

The detection of structural brain damage is complemented by results of functional imaging techniques, such as positron emission tomography (PET) and single photon emission computed tomography (SPECT). By measuring local changes in blood flow and energy metabolism, PET and SPECT can help identify brain regions involved in specific sensory, motor, or cognitive functions. Such studies consistently reveal decreased blood flow and metabolic rates in certain brain regions of heavy drinkers compared with those of non-alcoholic's ^{12, 13}, even in the absence of measurable shrinkage ¹⁴. Structural and functional defects revealed by magnetic resonance spectroscopy (MRS) and PET may reflect a decrease in the number ¹⁵ or size ^{16, 17} of neurons or a reduction in the density of communication sites between adjacent neurons ^{16, 17}.

RELATING STRUCTURE AND FUNCTION TO BEHAVIOUR

A key goal of imaging in alcoholism research is to detect changes in specific brain regions that can be correlated with alcohol-related behaviours. Imaging of the cerebellum has linked both shrinkage ^{9, 18} and decreased blood flow ¹⁹ to impaired balance and gait. Such impairment may cause falls among older alcoholics, leading to head injury that may exacerbate brain dysfunction. Studies of cognitive performance, however, have found no consistent relationship between shrinkage of the frontal cortex and impairment of short-term memory and problem-solving ^{1, 20}, functions typically disrupted by frontal lobe damage. Conversely, some studies have found an approximate correlation between shrinkage of memory-related brain structures (e.g. mammillary bodies) and the degree of memory impairment ⁷. Functional imaging studies show that frontal lobe blood flow ²¹ and metabolism ¹² may decrease in alcoholics before significant shrinkage or major cognitive problems become detectable ^{13, 21}.

Cognitive functions and motor coordination may improve at least partially within 3 to 4 weeks of abstinence ²⁰ accompanied by at least partial reversal of brain shrinkage ^{22, 23} and some recovery of metabolic functions in the frontal lobes ²⁴ and cerebellum ^{17, 25}. Frontal lobe blood flow continues to increase with abstinence, returning to approximately normal levels within 4 years ²⁶. Relapse to drinking leads to resumption of shrinkage ²³, continued declines in metabolism and cognitive function ²⁴, and evidence of neuronal cell damage ²⁵.

MECHANISMS OF ADDICTION

Studies using animals or cultured slices of brain tissue have identified chemical messengers (i.e., neurotransmitters) and neuronal pathways that may help mediate alcohol's effects. Functional imaging studies are confirming and extending these results. For example, a neuronal pathway involving the neurotransmitter dopamine has been implicated in the development of alcoholism. Non-alcoholic social drinkers administered a mildly intoxicating dose of alcohol¹⁹ and alcoholic subjects experiencing craving for alcohol²⁷ exhibit decreased blood flow in parts of the brain where dopamine is present. Imaging studies also provide evidence for disrupted response of the neurotransmitter serotonin, which appears to interact with dopamine in the development of alcoholism²⁸.

Functional imaging reveals that alcoholics have diminished metabolic activity in several frontal brain regions early and late in withdrawal^{29, 30}. In non-alcoholics, benzodiazepine sedatives, some of which are commonly used to treat alcohol withdrawal, produce a temporary alcohol-like impairment of coordination and cognition accompanied by an overall decrease in the brain's metabolic rate. In alcoholics, some frontal brain regions exhibit a smaller metabolic change following benzodiazepine administration than is seen in non-alcoholics. These results may indicate a diminished capacity for dampening excessive neuronal activity, possibly weakening a person's ability to inhibit behaviour³⁰. Among non-alcoholic social drinkers, the effects of benzodiazepines on specific brain regions as assessed by PET³¹ and functional MRI³² differ between persons with and without a family history of alcoholism. Therefore, an abnormal reaction to benzodiazepines may represent a pre-existing risk factor for alcoholism rather than a consequence of long-term alcohol consumption.

A promising application of functional imaging is in the study of cognitive and emotional processes involved in addiction, craving, and relapse. For example, preliminary studies have correlated craving for cocaine with increased metabolism in a neuronal network that integrates emotional and cognitive aspects of memory³³. Similar mechanisms implicated in craving for alcohol may help account for individual differences in vulnerability to alcoholism³⁴.

TREATMENT OF ALCOHOLISM

DIAGNOSIS: Routine clinical applications of imaging include detecting conditions that commonly co-occur with alcoholism, such as residual brain damage from head trauma³⁵, various psychiatric disorders³⁶, and alcohol-induced organic brain disorders characterized by dementia or amnesia³⁷.

WITHDRAWAL: Up to 15 percent of alcoholics experience seizures during withdrawal, and the likelihood of having such seizures, as well as their severity, increases with the number of past withdrawal episodes. In a structural imaging study of alcoholics who had undergone seizures, Sullivan and colleagues³⁸ found shrinkage on both sides of the brain behind the frontal lobes. It is not known whether seizures cause the shrinkage or result, in part, from pre-existing damage to the area.

Investigators have used PET and SPECT to locate and quantify sites on neuronal surfaces where neurotransmitters implicated in the development of alcoholism interact with the neuron. Results of such research has implicated impaired serotonin function in the severe depression that often accompanies withdrawal ³⁹. Functional imaging is also being used to help evaluate the effects of naloxone on withdrawal-induced craving ⁴⁰. This medication is chemically related to the anti-craving medication naltrexone (ReVia™).

PSYCHOSOCIAL Therapies: Higgins ⁴¹ describes the concept of neurobehavioral treatment, which emphasizes learning-based approaches to relapse prevention while paying special attention to the neurobiologic changes that accompany abstinence. For example, a common treatment strategy involves the development of skills for recognizing and coping with environmental influences or emotional states that may induce craving and trigger drinking. This approach requires the ability to monitor and evaluate one's behaviour and learn from failed efforts ⁴¹. Researchers are using functional imaging to investigate the basis for impairment of these cognitive functions ⁴².

APPENDIX : IMAGING TECHNIQUES

Structural imaging depicts a three-dimensional "slice" of the brain, showing more detail than a conventional X ray. CT is a refinement of x-ray technology, whereas MRI interprets signals emitted by the brain in the presence of a strong magnetic field ⁴³. These techniques are commonly used to help diagnose certain medical conditions (e.g. tumours) as well as in research.

Functional imaging techniques in common use include PET, SPECT, and modifications of magnetic resonance technology ^{14, 43}. PET and SPECT provide computer-generated, colour-coded, three-dimensional images of the distribution within the brain of radioactive substances injected into the bloodstream. These images can be used to detect changes in blood flow in specific brain regions or to determine the locations of various neurotransmitters or receptors. Functional MRI can locate and assess levels of brain activation associated with motor, sensory, or cognitive processes that may be impaired by alcohol over time at intervals as short as a few seconds ⁴⁴. MRS can detect specific molecules, including alcohol itself ⁴⁵, and can detect metabolic changes underlying deterioration of neuronal structural integrity ⁴³.

Imaging and Alcoholism: A Window on the Brain-A Commentary by NIAAA
Director Enoch Gordis, M.D.

Imaging technology has helped alcohol researchers to study how alcohol damages internal organs, such as the brain and the liver. More recent advances in imaging techniques are allowing investigators to also study alcohol dependence itself. Scientists are beginning to measure alcohol's effects on mood, emotional states, craving, and cognition while simultaneously assessing metabolic, physiologic, and neurochemical function in the brain. These innovations in imaging technology will help not only the alcohol field, but also all fields of medicine where biology and behaviour are so closely linked.

For more information or to make an appointment please contact us on (02) 9637 9998 during business hours.

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