Imaging shows effects of alcohol use on brain

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Excessive alcohol use is one of the 10 leading causes of disease and injury in developed countries, accounting for 9.2% of the disease burden. It causes nearly one in 10 cases of ill health and premature death in Europe and is responsible for over 3% of worldwide deaths (1.8 million) every year and 4% of disability-adjusted life years lost (58.3 million). The health service in England and Wales pays up to British Sterling 1.7 billion (Euro 2.43 billion) per annum to treat alcohol-related conditions.

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Chronic alcoholic patients may suffer from Wernicke's encephalopathy (WE), a neurologic disorder that can start abruptly or emerge over a longer time period. It is characterized by nystagmus, ocular motor palsies, unsteadiness of stance and gait, and a confused, apathetic state. Symptoms may occur in isolation, but they more often occur in various combinations. Only a minority of patients present with the classic Wernicke's triad of nystagmus, ataxia, and confusion. Mammillary body atrophy is an irreversible marker of chronic WE that is best assessed on sagittal or coronal MRI. One group of researchers, however, has found no significant difference in the MRI prevalence of mammillary body atrophy between asymptomatic alcoholic patients and those with WE. Atrophy of the diencephalic or mesencephalic structures, characterized by dilatation of the third ventricle or aqueduct, may also point to a contribution of thiamine deficiency in the patient with chronic amnesia.

The characteristic MR findings in acute WE are high signal intensity on T2-weighted images in areas...
surrounding the third ventricle, aqueduct, and paramedian thalamic nuclei. Enhancement of mammillary bodies and the periventricular region of the third ventricle and periaqueductal area on postcontrast T1-weighted images can be observed. These findings can be resolved after thiamine supplementation. In the chronic phase of WE, T2 hyperintensity is no longer visible, but mammillary bodies and cerebellar vermis become atrophic and third ventricular enlargement is evident. High signal intensity on T2-weighted images can be resolved within 48 hours, and atrophic changes may appear as early as one week. These findings suggest a poor prognosis, even with thiamine supplementation.

WE remains a clinical diagnosis, without specific laboratory or ancillary markers. The selective vulnerability of the midline gray matter areas and their symmetric involvement allow neuroimaging to play an important ancillary role, however.

Osmotic myelinolysis is a toxic demyelinating disease seen in alcoholic, malnourished, or chronically debilitated adults. A large proportion of cases is associated with chronic alcoholism or rapid correction of hyponatremia, although the condition has also been observed in patients with normal sodium levels. The term "osmotic demyelinization syndrome" refers to pontine and extrapontine myelinolysis. A number of therapeutic options exist that can improve the prognosis of osmotic myelinolysis patients substantially.

Prompt MR scanning is increasingly facilitating antemortem osmotic myelinolysis diagnosis (Figure 1). Radiologic findings lag behind clinical observations, however, and the two do not always correlate. Unenhanced CT images are normal or demonstrate nonspecific hypodense lesions. Pontine and extrapontine lesions are hypointense on T1-weighted MRI and hyperintense on T2-weighted images. Transverse pontine fibers are most severely affected, while pyramidal tracts are usually spared. Contrast administration produces varying results, with the majority of lesions remaining unenhanced.

The globus pallidus and putamen show high intensity on T1-weighted MRI of patients with hepatic cirrhosis. This high signal is thought to be due in part to paramagnetic substances, especially manganese. Measurements of mean Mn concentration in postmortem examinations of hepatic cirrhosis have confirmed that its deposition may cause the high signal and nerve cell death in the globus pallidus. Signal within the globus pallidus enhances in accordance with prolongation of prothrombin time on T1-weighted MRI. This finding is also seen in patients with raised portal pressure and large varices.

Marchiafava-Bignami syndrome is a progressive neurologic disease most frequently seen in middle-aged or elderly, predominantly male, alcoholic patients (Figure 2). Acute presentation includes confusion, ataxic gait, dysarthria, and seizures, with progression to death in many cases. Other presentations include a variety of motor, sensory, and visual dysfunctions. These include apraxias and interhemispheric disconnection, which is manifested by constructional ability deficits and agraphia.

Fluid-attenuated inversion recovery (FLAIR) MR scans of patients in the acute phase show abnormal hyperintensity in the central layer of the corpus callosum. Spin-echo sequences show these same areas as having normal signal levels. Follow-up spin-echo images in the late phase demonstrate fluidlike intensity in the central layer of the corpus callosum. FLAIR MRI of patients with chronic Marchiafava-Bignami syndrome shows corpus callosal lesions as hypointense cores surrounded by hyperintense rims. This finding indicates central necrosis and peripheral demyelination. Marchiafava-Bignami syndrome is believed to cause discontinuous affection of the corpus callosum, and bilateral cutting of the cortex outflow. In addition to central necrosis and peripheral demyelination of periventricular lesions, MRI may indicate demyelination of the corpus callosum.

**ADDICTION AND WITHDRAWAL**

Functional imaging techniques such as PET and SPECT are emerging as a valuable adjunct to structural brain damage studies. Local changes in blood flow and energy metabolism, measured on either modality, help identify brain regions involved in specific sensory, motor, and cognitive functions. Such studies have revealed reduced blood flow and metabolic rates in certain brain regions of heavy drinkers, compared with those of teetotalers, even in the absence of measurable brain shrinkage. Biochemical changes and functional defects revealed by MRS and PET may reflect a decrease in the number or size of neurons or a reduction in the density of communication sites between adjacent neurons.

Functional imaging reveals that alcoholic subjects have diminished metabolic activity in several frontal brain regions such as the cingulate and orbitofrontal gyri, both early (two to three weeks after detoxification) and late in withdrawal (after up to eight weeks of abstinence). These findings suggest that long-term alcohol use produces significant damage to the neurotransmitter pathways in these.
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Imaging has also implicated impaired serotonin function in the severe depression that often accompanies withdrawal. Functional imaging has been used to help evaluate the effects of therapeutic drugs on withdrawal-induced craving. Imaging techniques permit researchers to study the link between brain and behavior, particularly mechanisms of alcohol addiction, with minimal risk to patients. Dynamic brain imaging enables investigations of subjects performing intellectual tasks and experiencing various emotions before, during, and after alcohol consumption.

Molecular techniques to study alcohol addiction and withdrawal include labeled ligands and MRS to monitor neurotransmitter pathway change. One of the most promising areas is the dopaminergic pathway in the brain. When dopamine cells fire, they release dopamine, and this message is transmitted by postsynaptic dopamine receptors. The dopamine D2 receptor is important in the reinforcing effects of drugs and alcohol that can lead to abuse. Radiolabeled ligands used to measure dopamine D2 receptors in addicted individuals have shown that D2 receptor availability is significantly decreased across a wide variety of types of drug addictions, and these decreases are observed both during early drug withdrawal and after protracted drug detoxification. Interestingly, dopamine D2 reductions have been documented in early-onset alcoholic individuals with family histories of alcoholism.

The probability of dopamine interacting with a receptor is a function of how much dopamine is liberated in the synapse and the number of receptors available. In alcohol addicts, the dopamine cells may fire, but the chance of an interaction is reduced because the number of receptors is significantly lower in such an individual. The addicted person thus learns that natural reinforcers are no longer exciting or motivating, as the changes in dopamine level are not large enough to signal the individual as salient stimuli.

PET and SPECT have contributed neuroimaging studies of the GABA-benzodiazepine receptor system showing that alcoholism is associated with reduced receptor levels in the brain, particularly in the frontal cortex. These reductions may occur in the absence of detectable gray matter atrophy, even in subjects who were abstinent for some time and were cognitively and neurologically normal.

Development of more receptor subtype selective tracers is required to enable us to better understand these metabolic changes. The opioid system is involved in mediating pleasurable effects of alcohol, and it may be related to craving and using selective labeled ligands. Some studies have found an increase in opioid receptor levels in both alcoholic subjects and opioid addicts immediately after detoxification, indicating that increases in opioid receptors may be fundamental to addiction. MRS measurement of alcoholic subjects has been reported to show regression of brain atrophy and metabolic recovery occurring at an early stage after abstinence from chronic alcohol use. MRS findings return to normal metabolic levels within weeks after detoxification. The recovery of normal N-acetylaspartate/creatine ratios is associated with improved performance on neuropsychological tests. These reversible choline signal changes support the hypothesis of altered cerebral metabolism of lipids in membranes or myelin in these patients.

Such studies could lead to better treatments and preventive measures because they provide information not available on conventional imaging in early stages of addiction. The integration of conventional and molecular imaging techniques with biomedical, psychosocial, and behavioral aspects of alcoholism promises improved prevention and treatment in the future.

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References

Disclosures:

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