Alcohol-Related Brain Disorders

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Chronic and excessive alcohol use leads to a spectrum of Alcohol-Related Brain Disorders (ARBD), which invariably include some form of neurocognitive impairment.

There are multiple pathways to the development of ARBD related to:

(a) The direct neurotoxicity of alcohol on neurons and neuro-transmitter systems (including increased glutamate and excitotoxicity)
(b) The effects of sub-acute or chronic thiamine and nutritional deficiencies
(c) Effects of traumatic brain injuries (often as the result of intoxication), cerebro-vascular disease, and any underlying genetic predisposition.

In any individual, these effects frequently operate together to varying degrees.

In addition, these different aspects of neurotoxicity may result in different patterns of neurological disease (as evidenced by neuro-imaging studies), which in turn may present with different patterns of neuro-cognitive impairment, sometimes with partial reversibility. This is depicted in Table 1 below.

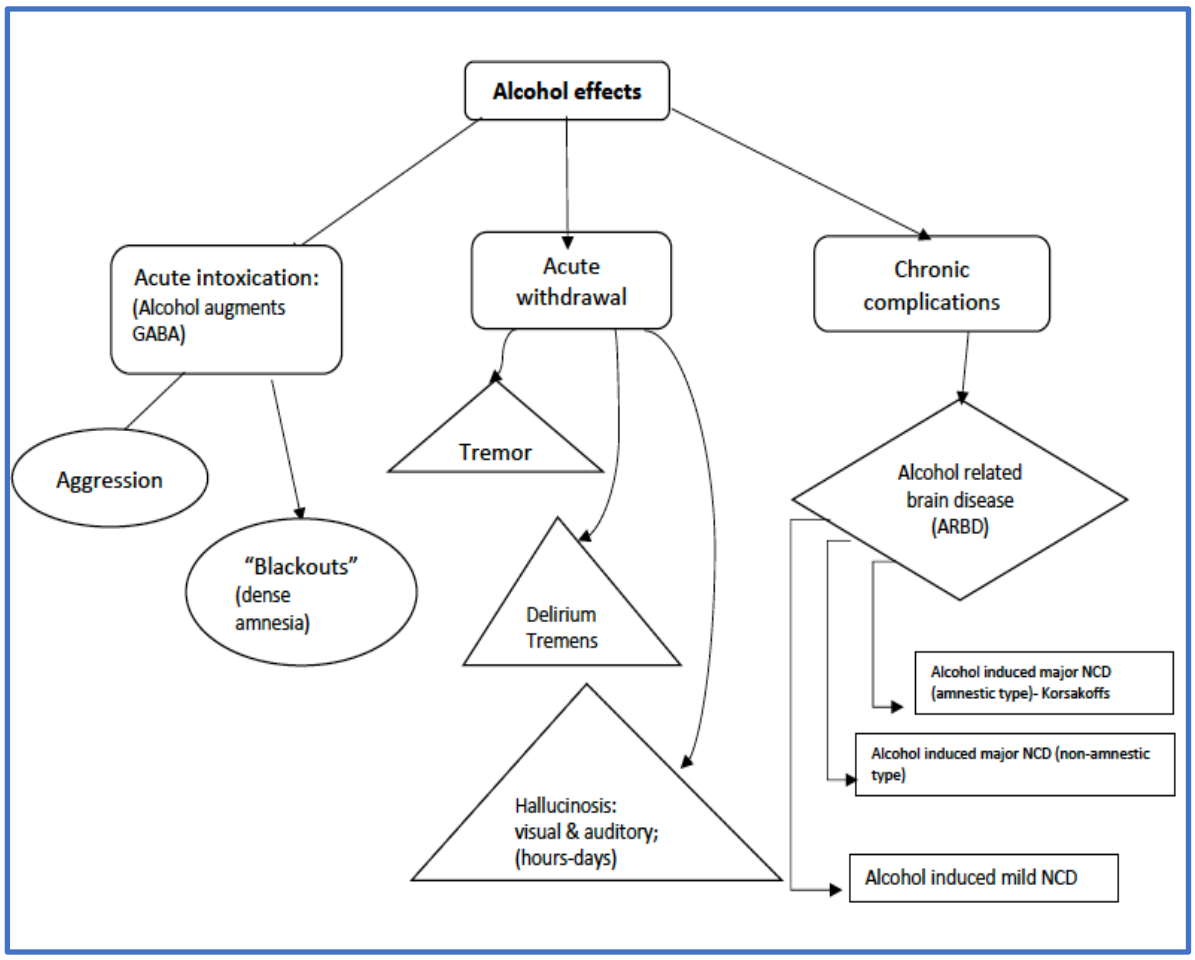
Table 1. ARBD Neuro-toxicities and Biotypes

Mechanism	Neuro-transmitter	Thiamine deficiency	Chronic neuronal loss
Description	GABA effects through proximity of alcohol receptor (often acute picture); Glutamate effects (often chronic picture)	Alcohol interferes with thiamine storage and metabolism, and also impairs nutritional intake	Effects of long term Glu excitotoxicity, recurrent TBI and CVD (usually small vessel)
Clinical	CNS depression (slowing, staggering, amnesia and blackouts), and disinhibition possibly through Glu effects	Wernicke's Encephalopathy (WE)- confusion, opthalmoplegia and ataxia; some progress to Korsakoff's Syndrome (KS)- See below.	Persisting amnestic neurocognitive disorder, often with dysexecutive features.
Neuro-imaging	Global atrophy, frontal atrophy, fronto-cerebellar dysfunction	Mammillary bodies and thalamic radiations, peri-aqueductal areas affected. KS might display frontal lobe changes.	Global atrophy. Frontal atrophy. Callosal thinning. Small vessel disease.
Treatment	Benzodiazepines for acute withdrawal	Thiamine and other nutritional replacement	Manage vascular risk factors. Ensure abstinence
Prognosis	Recovery is typical after 2-12 weeks	Partial recovery in 25-50%. 25% have persistent symptoms	If no improvement after 3 months, typical picture is persistent symptoms or gradual decline

Clinical Syndromes seen in ARBD

An outline of these is shown in Figure 1 below.

Direct effects of alcohol can be divided into acute intoxication, acute withdrawal and long-term complications that can persist even with sustained abstinence. The focus of the rest of this chapter will be on the chronic complications of alcohol use, as this is where the bulk of the neuropsychiatric consequences are seen in clinical practice.



Other psychiatric features of chronic alcohol use:

Psychiatric symptoms are common in chronic alcohol use. There is a bidirectional relationship between these two states. The most common co-morbid conditions include – anxiety disorders, depression, suicidality, other substance use disorders and sleep disorders.

Table 2. ARBD - Complications of chronic use

Clinical Syndrome:	**Wernicke's encephalopathy**	**Korsakoff's syndrome**	**Alcohol related NCD (major & mild)**
Description	Thiamine deficiency resulting in acute neurological deficits	Chronic thiamine deficiency resulting in anterograde & retrograde memory loss with or without confabulations.	Can be a subacute presentation with gradual cognitive decline. DSM criteria are met for NCD
Clinical	Altered mental state or memory changes. Ophthalmoplegia Cerebellar dysfunction	Disproportionate impairment in memory (episodic) & learning with relative sparing of the other domains. Apathy prominent	Prominent dysexecutive features and variable memory impairment.
Neuro-imaging	On MRI signal hyperintensity in the mamillary bodies, dorsomedial thalami, periaqueductal area,3rd ventricle can be classically seen. (2)	Enlargement of ventricles. Disproportionate Subcortical white matter loss (3).	Age- inappropriate cerebral atrophy.
Treatment	IV thiamine replacement	Anecdotal evidence for use of cholinesterase inhibitors and memantine (3)	Placement in specialized residential settings. Behavioral interventions (3)
Prognosis	Ocular symptoms improve rapidly with iv thiamine. Residual deficits in memory and learning are common. (3)	Poor, recovery is rare and they require some form of ongoing supervision.	Overall, poor for major NCD with ongoing cognitive deterioration expected over the coming years.

Other (rare) neurological syndromes in chronic alcohol use:

1.Alcoholic cerebellar degeneration

The anterior and superior cerebellar vermis is disproportionally affected in some chronic alcohol users. Presents clinically with gait instability and unsteadiness in the lower limbs. May progress to poor co-ordination and tremor in the arms, dysarthria, and intermittent visual changes. They are unable to tandem walk on neuro exam. Overall, only partial recovery even with total abstinence is ever achieved. Nutritional supplementation and physical therapy is advised (3).

2. Marchiafava-Bignami disease

A rare demyelinating disorder and necrosis of the corpus callosum and surrounding white matter. Seen in undernourished chronic alcohol users. Has a variable course characterized by neurocognitive impairment, spasticity, dysarthria, and immobility. Management includes alcohol cessation and adequate nutritional supplementation (3).

Conclusion

Excessive, chronic alcohol use is associated with a myriad of neuropsychiatric complications, most notably cognitive impairment as a feature of alcohol related brain disease. These ARBD are a feature of thiamine deficiency, direct neurotoxic effects of alcohol, or both.

Timeous assessment and management of these conditions is important to prevent further impairment and possibly reverse some of the ARBD effects with complete abstinence and thiamine administration.

References:

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3) Uptodate.com