C81ADD Psychology of Addiction

Alcohol

\[
\begin{array}{c}
H \\
\vdots \\
C \\
\vdots \\
H
\end{array}
\begin{array}{c}
H \\
\vdots \\
C \\
\vdots \\
H
\end{array}
\begin{array}{c}
\text{Ethyl alcohol (ethanol)}
\end{array}
\]

Tobias Bast

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Selected aspects of the psychopharmacology of alcohol (ethanol)

• Primary neuropharmacological targets of alcohol

• Acute psychological effects of alcohol
  - Decreased tension/anxiety (anxiolysis)
  - Impaired memory (amnesia, ‘black out’)
  - Directly ‘rewarding’ effects of alcohol?

• Psychological effects of chronic (excessive) alcohol consumption
  - Neuropharmacological adaptations, withdrawal symptoms and alcohol dependence
  - Severe and chronic cognitive deficits due to brain shrinkage (Wernicke-Korsakoff Syndrome)
Alcohol-induced memory loss (‘amnesia’)

• Alcohol interferes with memory, especially with the encoding of new information into long-term declarative memory. Alcohol-induced anterograde amnesia may range from little memory lapses (‘cocktail party memory deficits’) to ‘fragmentary’ or ‘en bloc black outs’, i.e. partial or complete absence of memory, for experiences under alcohol influence, if large amounts of alcohol have been drunken rapidly (‘binging’).

• Aaron White and colleagues (2002, JAmErCollHealth 51:117) asked 772 undergraduates the following question:

"Have you ever awoken after a night of drinking not able to remember things that you did or places that you went?"

51% of those who had ever consumed alcohol answered YES.

Possible mechanisms of alcohol-induced amnesia I:
State-dependence

• Information encoded/learnt in a drugged state, may be remembered better if tested in a comparable drugged state, than in a non-drugged state (Overton, 1964, JCompPhysiolPsychol 57:3). Such state-dependence of memory may partly account for alcohol-induced amnesia.

• Experiments testing for state-dependence typically include 4 groups in a 2X2 design:

<table>
<thead>
<tr>
<th>Group</th>
<th>Encoding drug state</th>
<th>Retrieval drug state</th>
</tr>
</thead>
<tbody>
<tr>
<td>AA</td>
<td>alcohol</td>
<td>alcohol</td>
</tr>
<tr>
<td>SS</td>
<td>sober</td>
<td>sober</td>
</tr>
<tr>
<td>AS</td>
<td>alcohol</td>
<td>sober</td>
</tr>
<tr>
<td>SA</td>
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• Alcohol has been shown to render some aspects of declarative memory state dependent. There is also evidence for asymmetric state dependence, i.e. retrieval was especially reduced in the AS group, but less so in the SA group.

State-dependent effect of alcohol on word-association memory

Word-association test

- **Learning phase (Day 1):** Subjects were asked to respond to 10 words with the first word that comes to mind.

- **Recall phase (Day 2):** Subjects were cued with the words and asked to recall their response from Day 1.

<table>
<thead>
<tr>
<th>Group</th>
<th>Word association Errors</th>
</tr>
</thead>
<tbody>
<tr>
<td>AA</td>
<td>2.50 ± 1.57</td>
</tr>
<tr>
<td>SS</td>
<td>1.25 ± 1.14</td>
</tr>
<tr>
<td>AS</td>
<td>4.58 ± 2.13</td>
</tr>
<tr>
<td>SA</td>
<td>2.25 ± 1.43</td>
</tr>
</tbody>
</table>

Which finding supports state-dependent recall?

a) Recall is worse in group AA than in SS.

b) Recall is better in group AA than in AS.

c) Both a) and b).

d) None of the above.

Difference between AA and AS groups is best explained by state-dependence.

Goodwin et al. (1969) Science 163:1358
Possible mechanisms of alcohol-induced amnesia I: State-dependence

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• Alcohol has been shown to render some aspects of declarative memory state dependent. There is also evidence for asymmetric state dependence, i.e. retrieval was especially reduced in the AS group, but less so in the SA group.

• However, state-dependency appears to account mainly for little memory lapses or fragmentary blackouts – en block blackouts seem to be due to other mechanisms (Goodwin, 1969, BrJPsychiatry 115:1033-1038).

Possible mechanisms of alcohol-induced amnesia II:
Selective interference with hippocampal memory mechanisms

- Alcohol mainly interferes with encoding of new declarative information, similar to damage to the hippocampus (such as in patient H.M.). Thus, interference with hippocampal synaptic mechanisms of memory may contribute to alcohol-induced amnesia.


- For example, alcohol disrupts the induction of hippocampal long-term potentiation (LTP) – an activity-dependent long-lasting increase in synaptic strength and a candidate physiological mechanism of memory (Bliss & Collingridge, 1993, Nature 361:31).

Long-term potentiation (LTP): the basics

Glutamate vesicles release glutamate, which binds to AMPA receptors, allowing an increase in sodium current. This leads to an increase in AMPA receptor numbers and efficiency, resulting in LTP (increased AMPA receptor numbers and efficiency).


Neuroscience - Science of the Brain: An Introduction for Young Students; p. 28 (http://www.bna.org.uk/publications/brain_sci.html)
Possible mechanisms of alcohol-induced amnesia II: Selective interference with hippocampal memory mechanisms

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Many of alcohol's effects are unpleasant – why do so many people consume alcohol?
Meso-corticolimbic dopamine system and reward

Rewards activate meso-corticolimbic dopamine transmission

For critical review see:
Intracerebral microdialysis to measure neurotransmitters

Westerink (1995) Behav Brain Res 70:103
Drugs of abuse, including alcohol, increase accumbal dopamine levels

Chronic excessive alcohol use can lead to alcohol dependence

### Neuropharmacological adaptations to repeated and chronic alcohol use contribute to dependence:

- **Tolerance** in response to repeated use leads to reduced acute alcohol effects
- **Long-term compensatory changes** in neural mechanisms in response to chronic excessive alcohol use lead to chronic psychological changes when sober

- Compensatory changes are opposed to acute effects of alcohol

**TABLE 9.4** Diagnostic Criteria of Substance Abuse and Substance Dependence

<table>
<thead>
<tr>
<th>Substance abuse</th>
<th>Substance dependence</th>
</tr>
</thead>
<tbody>
<tr>
<td>occurs when the drug</td>
<td>occurs when the drug fulfills the criteria for abuse and also includes:</td>
</tr>
<tr>
<td>impairs the ability of the individual to function at school, at work, or in the home.</td>
<td>development of tolerance;</td>
</tr>
<tr>
<td>causes legal problems like arrests for violence or driving under the influence.</td>
<td>physiological or cognitive signs of withdrawal at abstinence;</td>
</tr>
<tr>
<td>is used in a dangerous manner.</td>
<td>frequent desire and effort to reduce drug use;</td>
</tr>
<tr>
<td>is used despite legal, social, or medical problems.</td>
<td>preoccupation with securing, consuming, and recovering from drug use so that most daily activity is directed by the drug.</td>
</tr>
</tbody>
</table>

*Source: American Psychiatric Association, 1994.*

Withdrawal hyperexcitability

Altered balance between excitatory and inhibitory neurotransmission in response to chronic alcohol:

- Decreased GABA-A receptor function (compensating for acute GABA enhancing effects of acute alcohol)
- Increased glutamate receptor stimulation and function (compensating for decreased glutamate release and decreased NMDA receptor function in response to acute alcohol)

Possible effects:

- Many withdrawal symptoms: seizures, tremor, withdrawal anxiety, alcohol craving
- Excitotoxic brain damage (resulting in long-term cognitive deficits)

Amy Winehouse 'died from seizure as body shocked from lack of alcohol'

Amy Winehouse’s family believe she died from a seizure as her body couldn’t cope with her sudden decision to stay off alcohol for three weeks, it has been reported.

Related Tags:
Amy Winehouse

Amy Winehouse's family believed she died after ignoring doctor's orders to wean off alcohol gradually

Metro, 28 July, 2011

http://www.metro.co.uk/showbiz/870656-amy-winehouse-died-from-seizure-as-body-shocked-from-lack-of-alcohol
Reduced dopamine transmission during withdrawal

Possible effect:
Reduced sensitivity to (natural) rewards and reduced motivation

Chronic excessive alcohol consumption may cause alcohol tolerance and withdrawal symptoms:

a) by inducing compensatory neurophysiological changes that are opposite to the effects of acute alcohol.

b) by inducing neurotoxicity.

c) both a) and b).

d) none of the above.
Severe cognitive impairments and brain shrinkage associated with chronic excessive alcohol consumption

Wernicke-Korsakoff Syndrome:
• Caused by thiamine deficiency, most commonly in association with alcoholism
• Wernicke Syndrome: acute stage, characterised by ophthalmoplegia (paralysis of eye muscles), confusion, ataxia
• Korsakoff Amnesia: remains after treatment of acute Wernicke Syndrome if thiamine deficiency lasted too long; global impairment in forming new declarative memory; severe brain ‘shrinkage’, especially striking degeneration of the mammilary bodies

Cognitive deficits and brain shrinkage in ‘uncomplicated’ alcoholics
Even alcoholics without WKS, may present with deficits in sensori-motor and executive functions, learning and memory and show marked fronto-cerebellar brain damage.

Brain shrinkage associated with chronic excessive alcohol use

Control

Wernicke-Korsakoff Syndrome

Intact mammilary bodies

Degenerated mammilary bodies

Brain shrinkage associated with chronic excessive alcohol use

Selected reading – Alcohol II

Textbook chapter:
Chpt. 9, Alcohol – for general overview

Selected overviews of topics discussed today:


All articles, as well as all references given in lecture, are available online via Nottingham University access.
Questions for revision

• How may alcohol interfere with our memory?

• By which common mechanism may drugs of abuse, including alcohol, act as ‘reward’?

• Which neuropharmacological adaptations may lead to alcohol dependence?

• Can you drink your brain away? Which neurodegenerative changes are associated with alcoholism?

The MCQs related to alcohol will all be based on the material dealt with in my two lectures on the psychological effects of alcohol. If you understand the material, so that you can answer the revision questions well, you should have no difficulties with the MCQs.