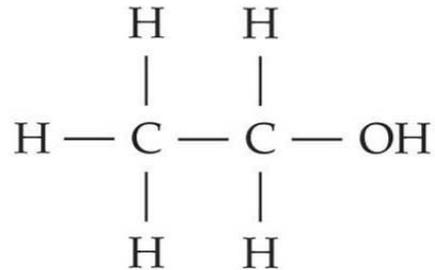


Addiction and the Brain (PSGY1005)

Alcohol



Ethyl alcohol (ethanol)



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The University of
Nottingham

UNITED KINGDOM • CHINA • MALAYSIA

Outline

- Relevance of alcohol to individual and society: alcohol-associated harms
- Psychopharmacology of alcohol
 - Primary neuropharmacological targets of alcohol
 - Acute psychological effects of alcohol
 - Psychological effects of chronic (excessive) alcohol consumption



Pieter Bruegel, Fight between carnival and lent (1559)

HOW THE WORLD
TREATS WIDOWS

SAVING
OUR OCEANS

WILDCATS: OUT
OF THE SHADOWS

NATIONAL GEOGRAPHIC

THE BIRTH OF

BOOZE

Our 9,000-Year
Love Affair
With Alcohol

FEBRUARY 2017

THE SCIENCE OF WHOPI GOLDBERG

MODERN LIFE IN THE ANCIENT AMAZON

FURTHER: THE UNIVERSE HAS EYES

<http://www.nationalgeographic.com/magazine/2017/02/alcohol-discovery-addiction-booze-human-culture/>



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in London and
Manchester
guardian.co.uk

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Alcohol 'more harmful than heroin or crack'

Lancet study reopens debate on drug
classification and curbs on drinking

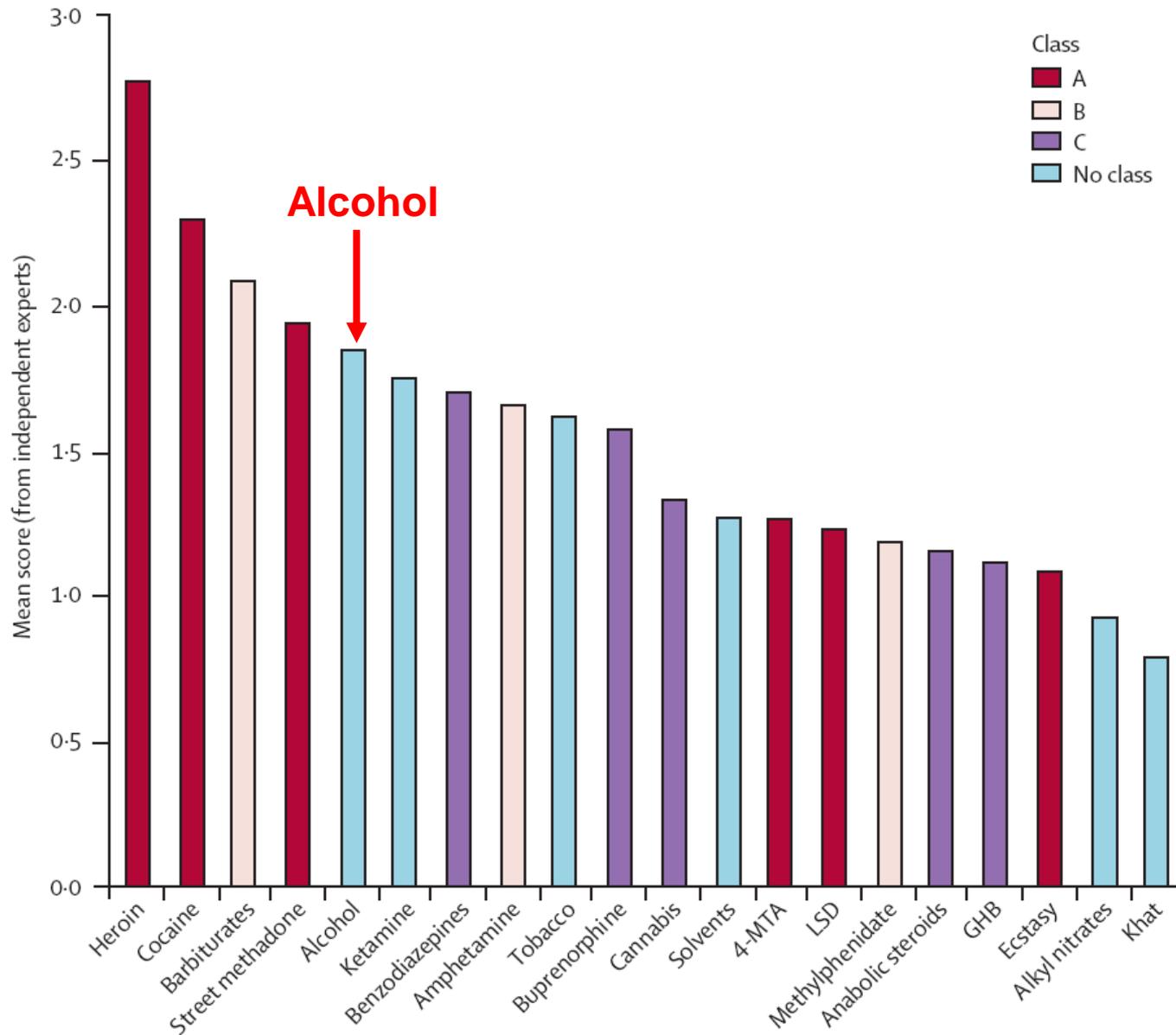
Harms associated with drugs

| Parameter | | | |
|---------------|-------|--------------------------|------------------|
| Physical harm | One | Acute | To users |
| | Two | Chronic | |
| | Three | Intravenous harm | |
| Dependence | Four | Intensity of pleasure | |
| | Five | Psychological dependence | |
| | Six | Physical dependence | |
| Social harms | Seven | Intoxication | To others |
| | Eight | Other social harms | |
| | Nine | Health-care costs | |

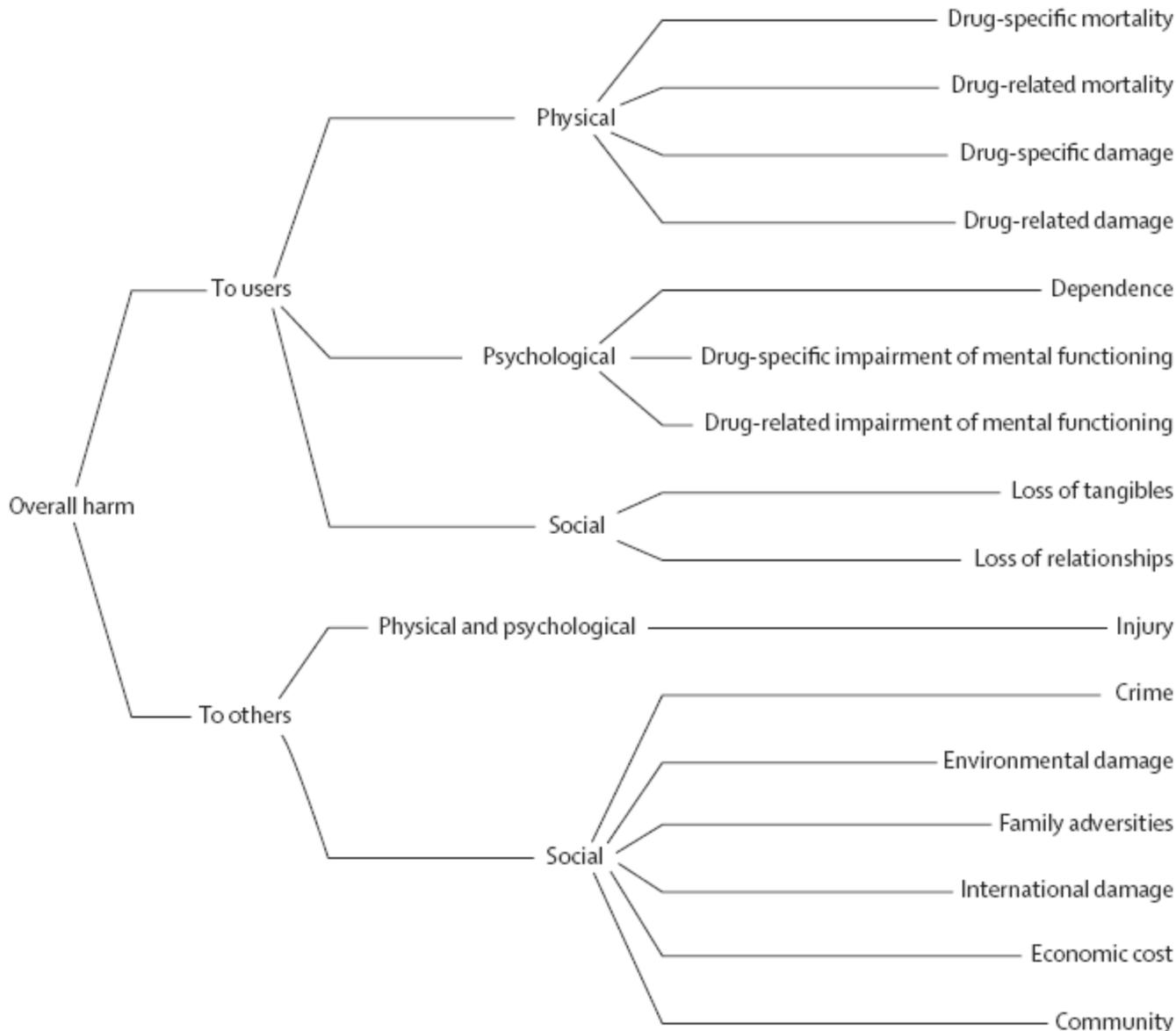
Development of drug harm scale:

- Experts assign score (0-3) for each parameter
- Parameters are averaged to yield overall harm score

Harmfulness of different drugs

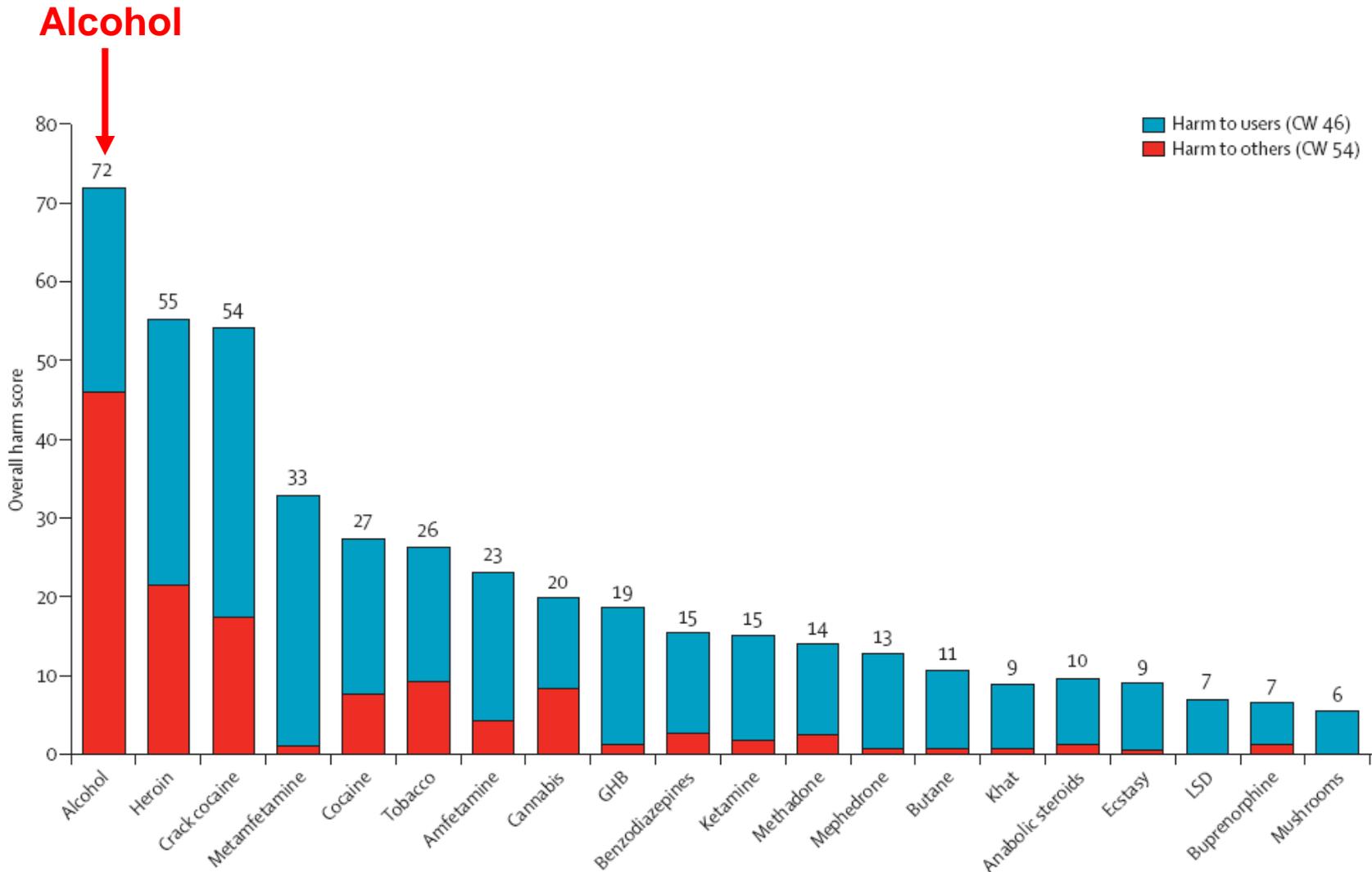


Harms associated with drugs: Improved criteria and weighting



- 16 criteria (9 in 2007 study)
- Scores from 0-100 (0-3 in 2007 study)
- Differential weighting of criteria to indicate their different importance

Harmfulness of different drugs



The suggestion that alcohol is more harmful than crack is based on:

a) an expert assessment of drug harms to users.

b) an expert assessment of drug harms to others (i.e., society).

c) both a) and b).

d) none of the above.

“On the basis of these data it is clear that the present UK drug classification system is not simply based on consideration of harm.”

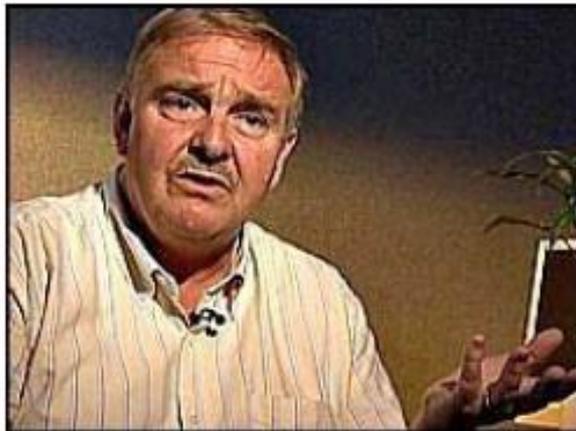
“They also [support] that aggressively targeting alcohol harms is a valid and necessary public health strategy.”

Page last updated at 18:23 GMT, Friday, 30 October 2009

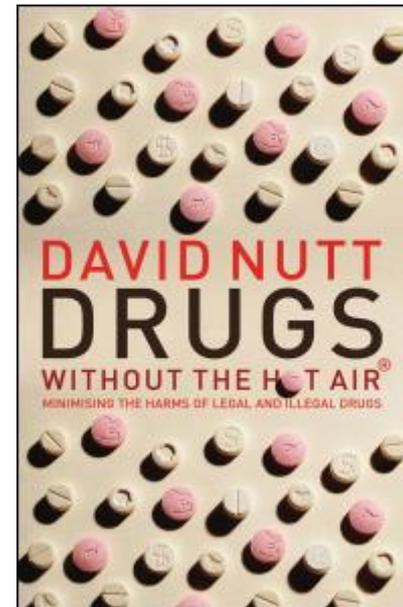
Profile: Professor David Nutt

By Dominic Casciani
BBC News, Home Affairs

Professor David Nutt has been sacked as the government's top drugs adviser after a rollercoaster of a relationship with two home secretaries over the last 12 months.



David Nutt: Scientist who clashed with policy



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Psychological effects of alcohol



“If recreational drugs were tools, alcohol would be a sledgehammer. Few cognitive functions or behaviors escape the impact of alcohol . . .”

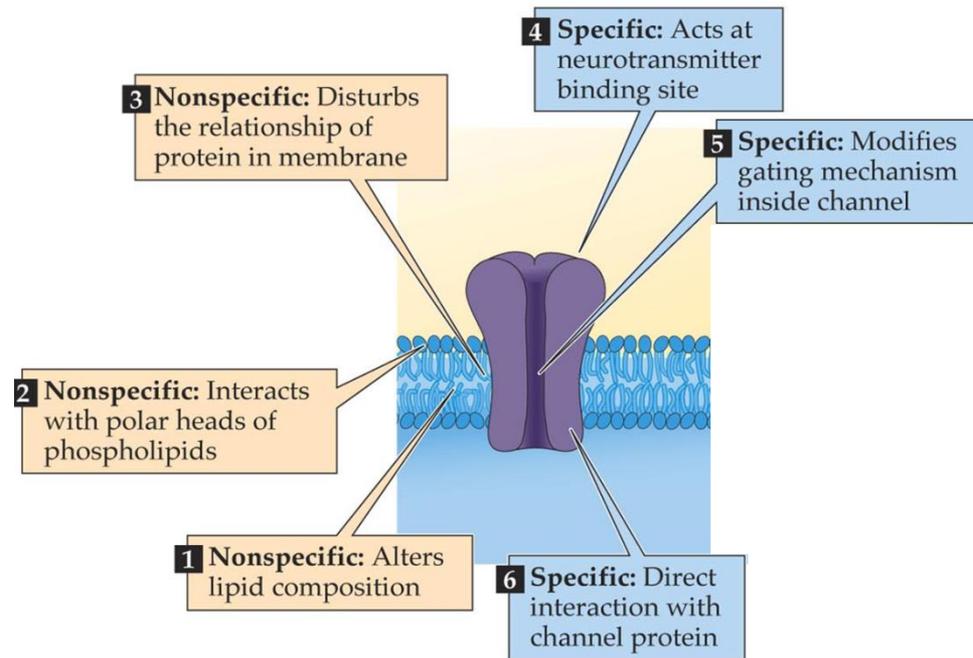
White (2003) Alcoh. Res. Health 27:186

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)



Primary neuropharmacological targets of alcohol



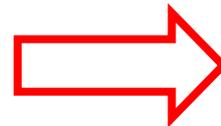
PSYCHOPHARMACOLOGY, Figure 9.13 © 2005 Sinauer Associates, Inc.

Complex neuropharmacology

- Nonspecific effects – interactions with lipid bilayer; mainly at higher concentrations
- Specific effects – interaction with ligand-gated ion channels (i.e., neurotransmitter receptors) and voltage-gated ion channels; at concentrations within range achieved by common alcohol consumption

First hit

- Neurotransmitter receptors (NMDA, GABA-A, Glycine, 5-HT₃, nACh)
- Voltage-gated ion channels (L-type Ca²⁺ channels, GIRKs)



Cascade of synaptic events involving many neurotransmitters

Psychological effects of alcohol depend on complex interactions between many variables

VARIABLES AFFECTING THE EFFECTS OF ETHANOL IN HUMANS

Environmental variables (social cues)

Cognitive Set (expectancy) (see boxes 9.2 and 9.3 in text book)

Mood, arousal, personality factors

Age and sex of subjects

Exposure to other drugs (coffee, nicotine, etc.) and nutritional state of the subjects

Variables related to ethanol ingestion:

Dose

Rate of ingestion

Time of testing post ingestion; time of day

Type of beverage ingested (role of congeners)

TABLE 9.2 Blood Alcohol Concentration and Effects on Behavior

| BAC | Effects on behavior |
|-----------------------|---|
| .02–.03 | Minimal effects; slight relaxation; mild mood elevation |
| .05–.06 | Decreased alertness; relaxed inhibitions; mildly impaired judgment |
| .08 [*] –.10 | Loss of motor coordination; slower reaction times; less caution |
| .14–.16 | Major impairment of mental and physical control; slurred speech; exaggerated emotions; blurred vision; serious loss of judgment; large increases in reaction time |
| .20–.25 | Staggering; inability to walk or dress without help; tears or rage with little provocation; mental confusion; double vision |
| .30 | Conscious but in a stupor; unaware of surroundings |
| .45 | Coma; lethal for 50% of the population |

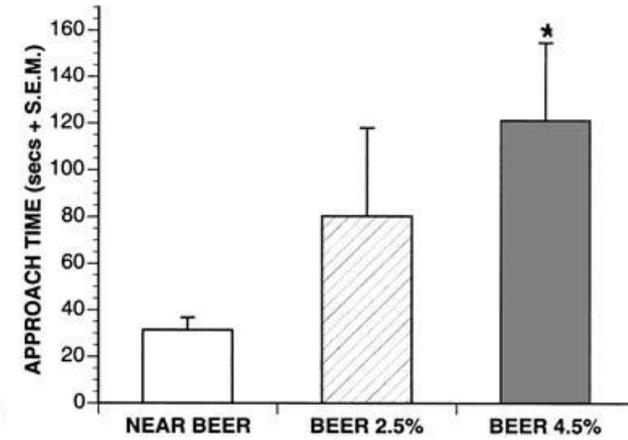
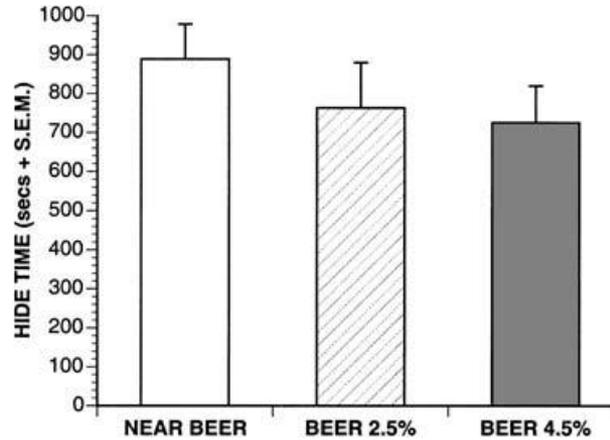
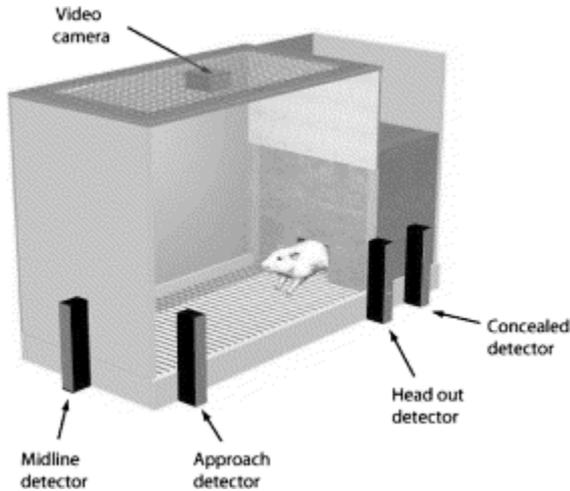
***Legal driving limit in UK, except for Scotland, where the limit is 0.05**

Alcohol-induced reduction in tension and anxiety

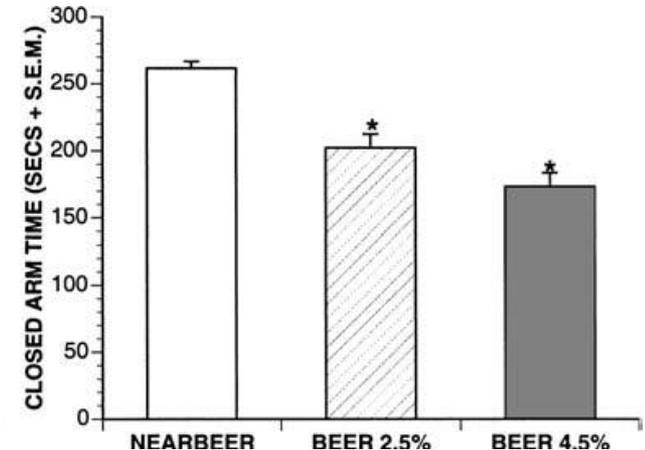
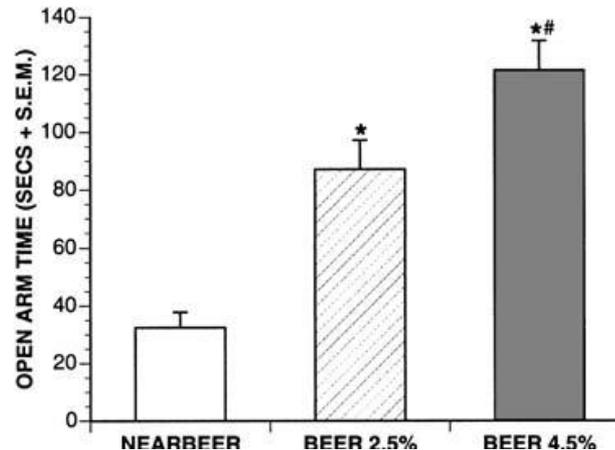
- View that alcohol reduces tension and anxiety – and that this effect is a major contributor to alcohol consumption and abuse – is widely held, even though studies on human subjects have reported variable effects on measures of anxiety (e.g., self report, autonomic arousal) (Wilson, 1988, BehavResTher 26:369; Kushner et al., 2000, ClinPsycholRev 20:149).
- Similar to classical anxiolytics, such as benzodiazepines, alcohol acts as indirect agonist at GABA-A receptors, i.e. enhances the response of the major inhibitory neurotransmitter GABA (Harris & Mihic, 2004, PNAS 101:2).
- Comorbidity of anxiety disorders and alcohol abuse (Kushner et al., 2000, ClinPsycholRev 20:149).
- Alcohol relatively consistently reduces measures of anxiety in rodents (e.g., Blanchard et al., 1993, ProgNeuropsychopharmacol&BiolPsychiat 17:171 and next slide).

Beer drinking in rats reduces anxiety

Cat odour avoidance test

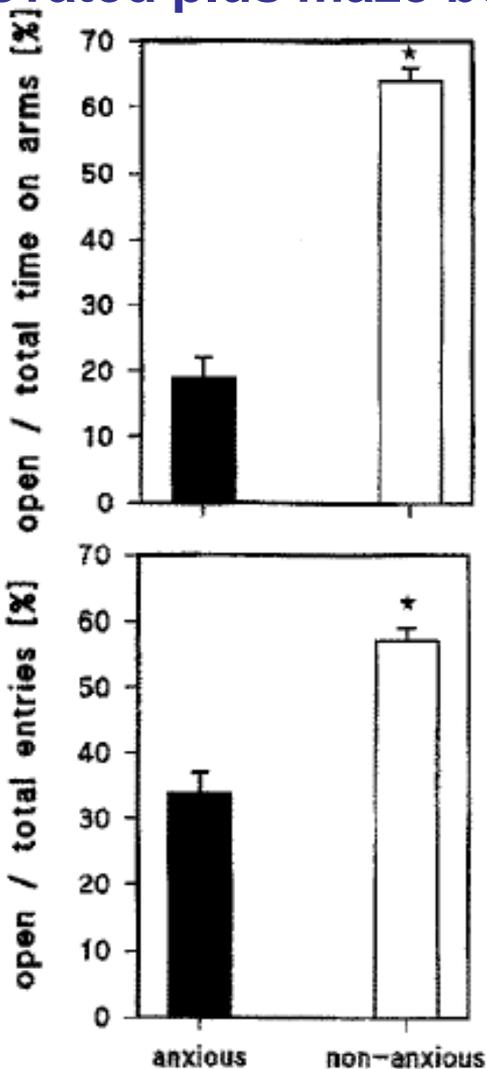


Elevated plus maze test

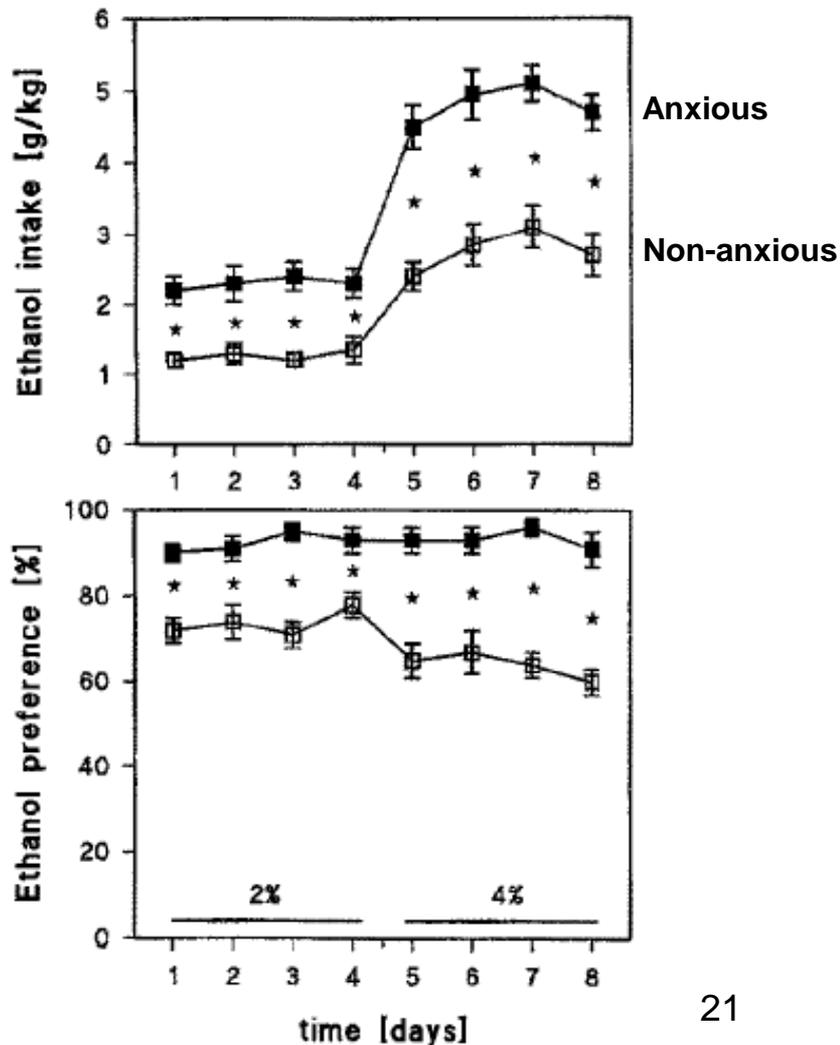


Anxiety predicts ethanol self-administration in rats

Anxious and non-anxious rats
(elevated plus maze behaviour)



Higher alcohol self-administration in anxious rats



Which of the following supports the hypothesis that alcohol decreases anxiety?

- a) Alcohol causes rats to spend less time on the open arms on the elevated plus maze.**
- b) Alcohol acts as indirect agonist at GABA-A receptors, i.e. enhances the response of the major inhibitory neurotransmitter GABA.**
- c) Alcohol causes rats to spend more time on the open arms on the elevated plus maze test.**
- d) b) and c).**

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)



Next lecture!

Selected reading – Alcohol 1

Textbook chapter:

Chpt. on Alcohol – for general overview

Excellent other book:

Nutt, David. *Drugs - without the hot air : Minimising the harms of legal and illegal drugs*, UIT Cambridge Ltd., 2012.

<https://ebookcentral.proquest.com/lib/nottingham/detail.action?docID=5285796>

For today's topics, see especially chpts 2,3 and 6.

Selected overviews of topics discussed today:

DJ Nutt, LA King, LD Phillips (on behalf of the Independent Scientific Committee on Drugs) (2010) Drug harms in the UK: a multicriteria decision analysis. *Lancet* 376:1558-1565.

V Vengeliene, A Bilabo, A Molander, R Spanagel (2008) Neuropharmacology of alcoholism. *Br. J. Pharmacol* 154:299-315.

Kushner MG, K Abrams, C Borchardt (2000) The relationship between anxiety disorders and alcohol use disorders: a review of major perspectives and findings. *Clinical Psychology Review* 20:149-171.

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

Some questions for revision

- Is alcohol harmful? Which criteria do we need to consider?
- What are the neuropharmacological targets of alcohol?
- What evidence is there to suggest that alcohol reduces anxiety?

The exam MCQs related to alcohol will all be based on the material dealt with in my two lectures on alcohol.

The MCQs put up during the lecture give you a good idea of the level of detail I would expect a student to know or understand, respectively, in order to do well in the exam.

If you understand the material, so that you can answer the lecture MCQs and the revision questions well, you should have no difficulties with the exam MCQs.