UCL School of Pharmacy

Inhalants

Solvent and volatile substance abuse 2025

What is VSA?

- **Solvent and volatile substance abuse (VSA)** is an increasing problem concern in many nations and communities, particularly where poverty, prejudice and lack of opportunity are common.

- **Several factors also contribute to VSA** - peer pressure, broken or dysfunctional families, low academic performance at school, alcohol or drug abuse, physical or sexual abuse.

What is VSA?

- **VSA, often referred to as "solvent/inhalant abuse" or "sniffing",** is the deliberate inhalation of organic volatile chemicals found in many everyday products, such as:-

- solvent-based adhesives **("glue sniffing"),**
- butane gas **(cigarette lighter refills), aerosols,** and numerous other products **(*e.g.* N_20)**, for the purposes of achieving euphoria or intoxication

What is VSA?

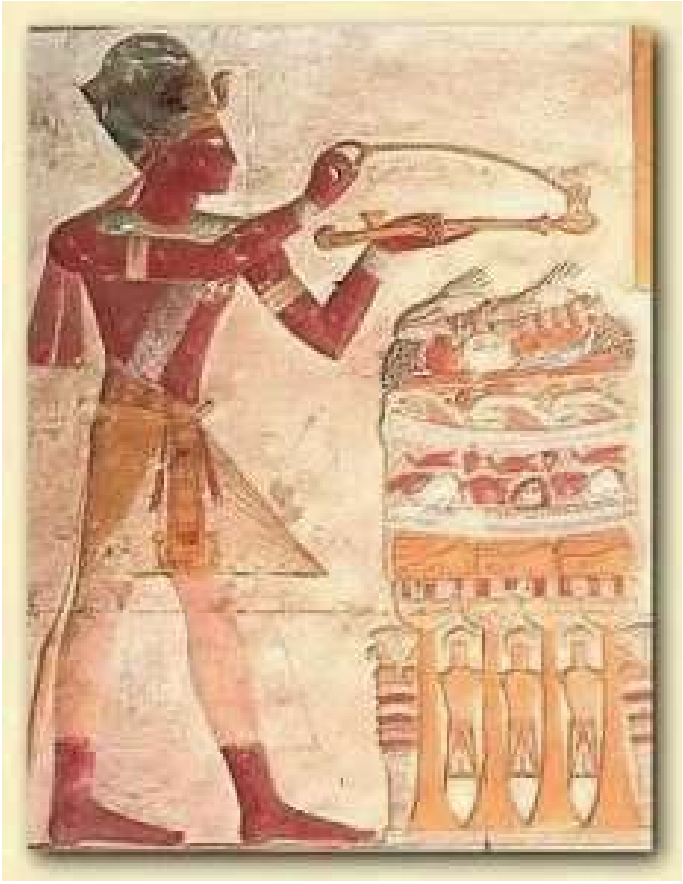
- The phenomenon is not new. There are references to the inhalation of vapours to induce a trance-like state in **Greek** and **Egyptian** history.

Temple of Apollo - Delphi

Pythia was "the oracle of Delphi," a priestess at the temple of Apollo who provided divine but obscure messages for her human subjects to interpret.
The natural fumes rising from cracks in the earthen floor contained gases (ethylene, methane) whose inhalation may have inspired the oracle's speech.

What is VSA?

- The phenomenon is not new. There are references to the inhalation of vapours to induce a trance-like state in **Greek** and **Egyptian** history.

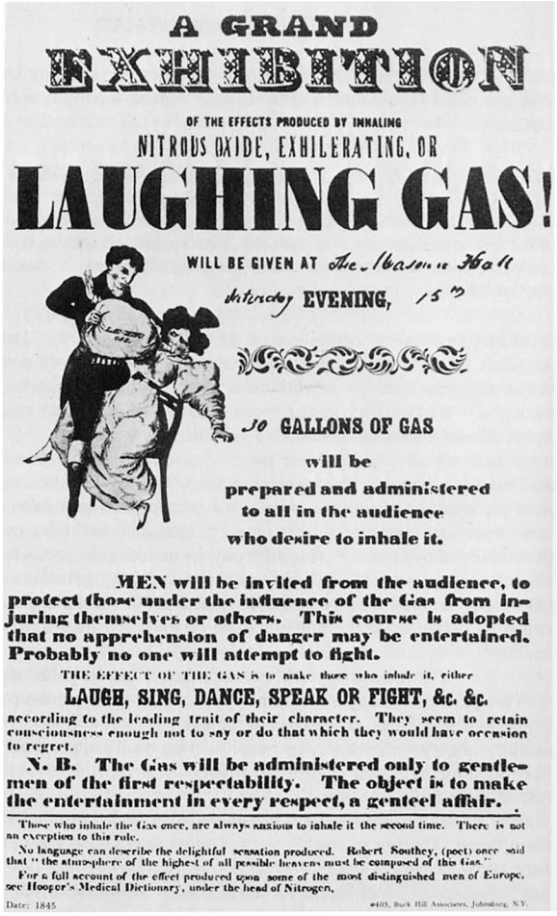


Burning of Frankincense

The Egyptians also burnt various herbs, spices, flowers, barks, woods and resins as part of religious ceremonies in temples – in particular: **Frankincense** was burned at sunrise, **Myrrh** at noon and **Kyphi** (a very popular incense containing a mixture of aromatic ingredients) at sunset. It is still made and sold today!

What is VSA?

- **Joseph Priestley discovered N_2O in 1772.** During the 19th century, the inhalation of anaesthetics such as **N_2O** (laughing gas) and **ether** became a recreational activity.



A GRAND

EXHIBITION

OF THE EFFECTS PRODUCED BY INHALING

NITROUS OXIDE, EXHILERATING, OR

LAUGHING GAS!

WILL BE GIVEN AT The Masonic Hall

this day EVENING, 15th

30 GALLONS OF GAS

will be

prepared and administered

to all in the audience

who desire to inhale it.

MEN will be invited from the audience, to protect those under the influence of the Gas from injuring themselves or others. This course is adopted that no apprehension of danger may be entertained. Probably no one will attempt to fight.

THE EFFECT OF THE GAS is to make those who inhale it, either

LAUGH, SING, DANCE, SPEAK OR FIGHT, &c. &c.

according to the leading trait of their character. They seem to retain consciousness enough not to say or do that which they would have occasion to regret.

N. B. The Gas will be administered only to gentlemen of the first respectability. The object is to make the entertainment in every respect, a genteel affair.

Those who inhale the Gas once, are always anxious to inhale it the second time. There is not an exception to this rule.

No language can describe the delightful sensation produced. Robert Southey, (poet) once said that "the atmosphere of the highest of all possible heavens must be composed of this Gas."

For a full account of the effect produced upon some of the most distinguished men of Europe, see Hooper's Medical Dictionary, under the head of Nitrogen.

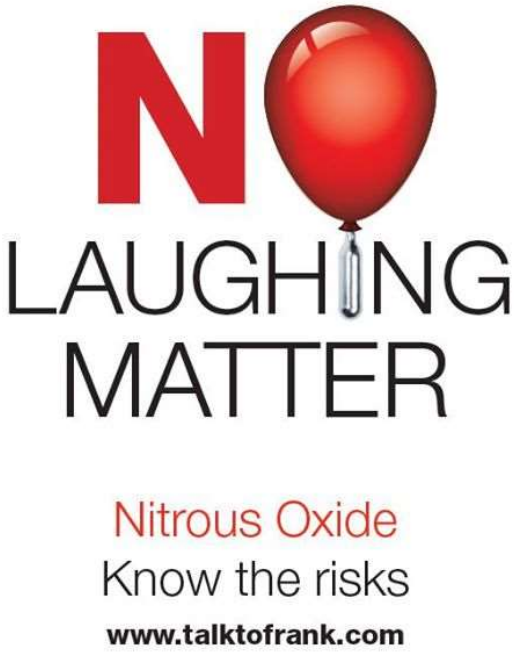
Date: 1845

What is VSA?

- More recently, **N_2O** has increased in popularity as a recreational inhalational drug of abuse- and was classed as a "legal high" -obtained from small disposable metal cartridges used as a propellant inside of whipped cream dispensers ("whippets") or balloons sold filled with the gas. It is now considered as the second most commonly used recreational drug in England and Wales after cannabis. It is possible to become addicted to N_20.

What is VSA?

- 56 deaths were associated with the misuse of N_2O between 2001 and 2020. A teenager died after inhaling the gas (also called 'hippy crack') at a house party in SE London in July 2015. Chronic abusers can develop Vitamin B_{12} deficiency leading to toxic myeloneuropathy. **The UK government has recently banned the sale and possession of N_2O for recreational use (March 2023).**



Types of product being abused?

There are over 1,000 products which are commonly available and subject to abuse.

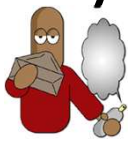
Any organic compound which is gaseous or which will easily vaporise at room temperature, has a psychoactive effect and *does not produce highly irritating effects* can be misused.

Types of product being abused?

- **Volatile gases,** solvents, solvent based glues lighter fuels (butane gas), thinners, spray paint, dry cleaning fluids, correcting fluids (Tipp-Ex, etc.), magic markers, nail polish remover, toluene, surgical spirit, petrol; moth balls; shoe dyes;
- **Aerosols** deodorants, hair sprays, furniture polish, pressurised products;
- **Anaesthetic gases** nitrous oxide, ether, halothane;
- **Nitrites** amyl nitrite ('poppers') and butyl nitrite.

Methods of use: -various

- **'Sniffing' -** Directly sniffing products from their containers



- **'Bagging' -** Pouring substances into plastic bags and inhaling from the bag, or even putting bag over the head

- **Spraying aerosol sprays directly into the open mouth** this can be **highly dangerous,** as death can occur due to vaso-vagal inhibition of the heart, causing a profound **bradycardia** or even **asystole**

- **'Huffing'** a handkerchief, rag, sleeve or collar of the abuser's clothing is soaked with the volatile solvent, and the moistened cloth is placed over the nose and mouth.

Teenager died inhaling deodorant

BBC NEWS

A teenager died after inhaling gas from a fabric spray which her mother initially thought she used to mask cigarette smell, an inquest has heard.

Helen Coffey, 14, died a week after she was found collapsed in her family home in Cardiff in April 2005.

Teenager died inhaling deodorant

BBC NEWS

A teenage girl in Derby (UK) died suddenly after spraying aerosol deodorant on a blanket in her bedroom and breathing in the fumes –her devastated parents have called for clearer labels on the products warning of the dangers.

Giorgia Green, 14, suffered cardiac arrest and died after breathing in the fumes in May 2022 in what her parents say was a preventable accident.

Dangers of VSA

- **Anyone who experiments with volatile substances is placing him or herself at serious risk of Sudden Sniffing Death due to:**

- **Choking on vomit.**
- **Heart failure** as a result of the direct toxic effects of the substance - certain solvents, are arrhythmogenic- sensitizing the heart to the effects of noradrenaline
- **Suffocation** through the use of plastic bags over the head during administration.
- **Accidents** while intoxicated

Dangers of VSA

- **~40 % of solvent-related deaths occur after a single sniffing episode.** Unlike other drugs there is no known safe dose or safe method of use. **Between 2001 and 2020, 714 people in England and Wales died as a result of using volatile substances.**
- **Most VSA-associated deaths involve butane gas found in cigarette lighters and propane gas found in some deodorant sprays**. Inhalation of glues has accounted for far fewer of the deaths.

Dangers of VSA

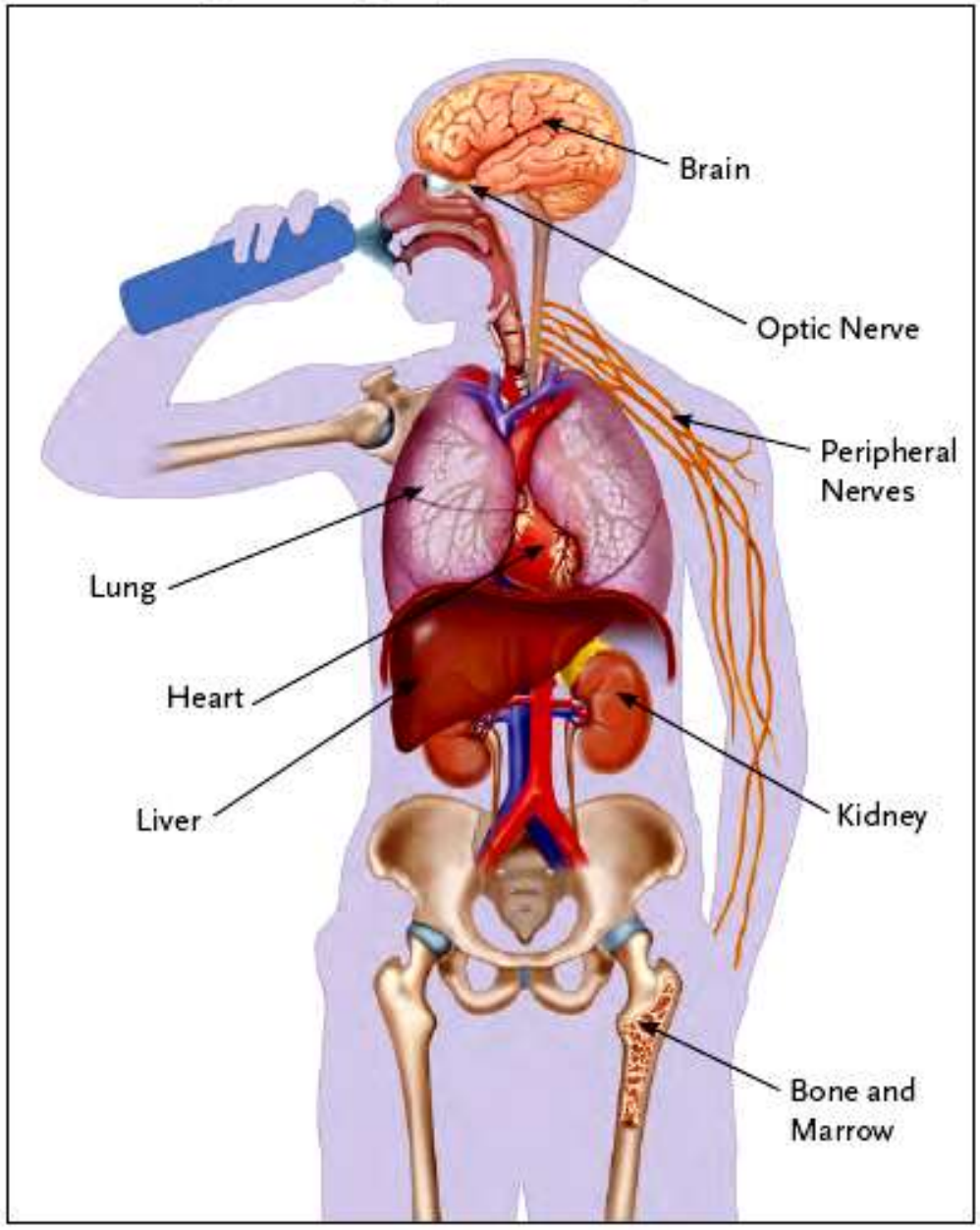
Other serious health problems in chronic sniffers

- **Respiratory difficulties;** liver malfunction; kidney damage; metabolic and electrolyte disturbances; blood abnormalities

- **Peripheral and CNS damage,** particularly cerebral, cerebellar and brain stem atrophy - damage to optic nerve; peripheral neuropathy

Dangers of VSA

FIGURE 2. Organs Damaged by Inhalant Exposure



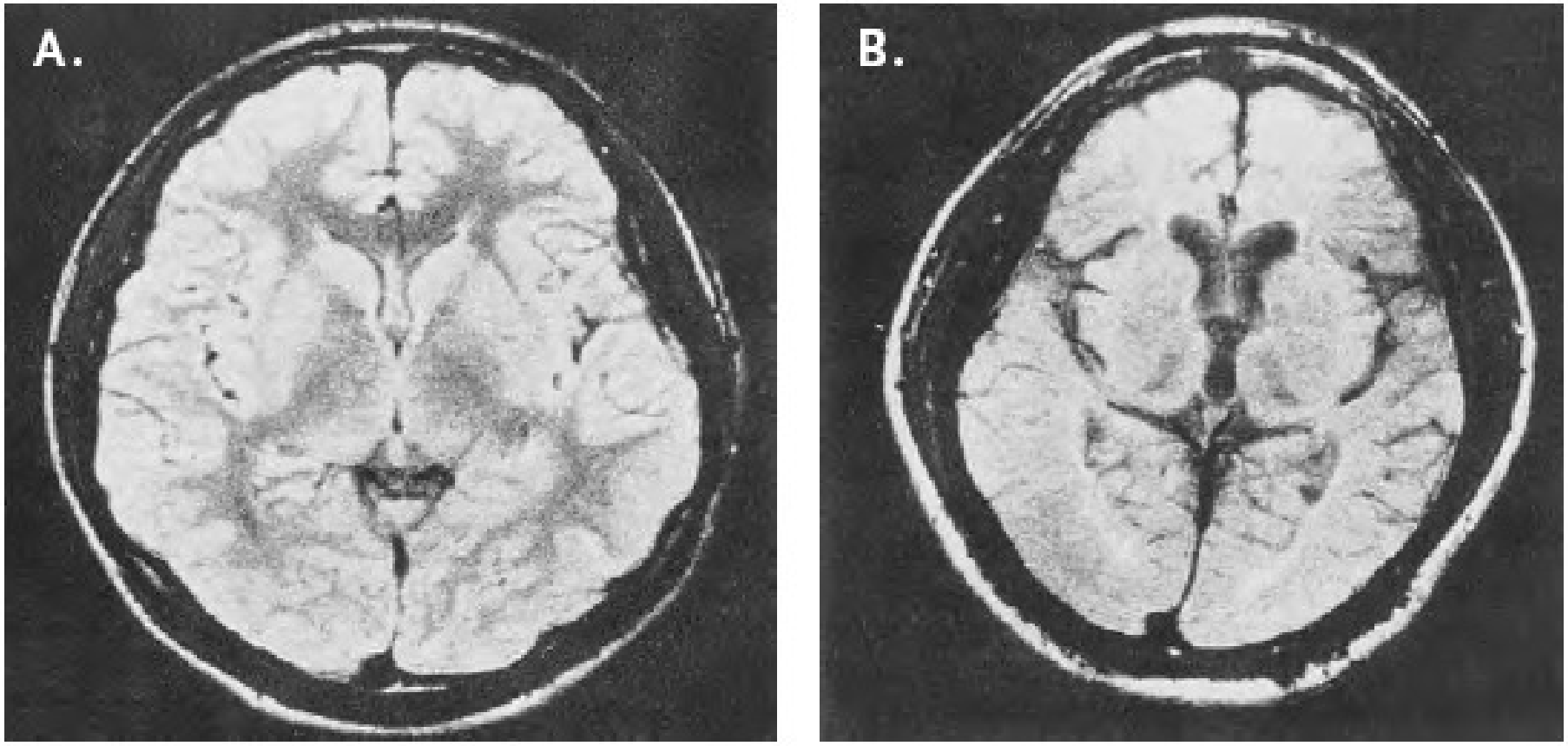
Dangers of VSA

- Cardiac sensitization to catecholamines is a recognized risk during exposure to halogenated hydrocarbons that can lead to serious arrhythmia and death.

- Mechanistically, halogenated solvents can interact with repolarizing cardiac hERG K^+ channels and other outward rectifying K^+ currents, as well as with Ca^{2+} and Na^+ channels, which can alter action potential shape and electrical impulse conduction, which may facilitate arrhythmogenesis (potentiated by catecholamines).

Dangers of VSA

FIGURE 1. Brain Atrophy in a Toulene Abuser



Compared with the brain of an individual with no history of inhalant abuse (A), that of a chronic toluene abuser (B) is smaller and fills less of the space inside the skull (the white outer circle in each image). Courtesy of Neil Rosenberg, M.D., *NIDA Research Report* (NIH 05-3818).

Dangers of VSA

Other hazards:-

- Violent, bizarre or aggressive behaviour
- Suffocation
- Burns sustained when gasses have been ignited.

Clinical presentations of VSA:-

- Drunk, dazed or dizzy appearance
- Perioral eczema or “glue sniffers rash”
- Oesophagitis and gastritis; vomit with unusual odour.

Dangers of VSA

Other symptoms:-

- Dyspnoea and a non-productive cough

- Sleep disturbances and irritability

- Slow, slurred speech, ataxia, loss of coordination, confusion, delusions, visual/ auditory hallucinations, memory loss.

Detection of inhalant abuse

Chronic heavy inhalant abusers may be identifiable because of poor hygiene and grooming, frequent episodes of intoxication, loss of appetite, weight loss, and a conspicuous odour of the inhalant (exhaled or spilled onto clothing).

Detection of inhalant abuse

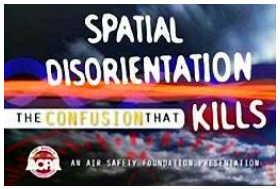
Additional clues include:-

- Red or runny eyes and/or nose
- Stained clothing, flecks of paint or glitter on the face and perioral rash

- Correction fluid on fingernails
- Sitting with a pen or marker near the nose
- Finding products of abuse stored in unusual locations - large cache of potential inhalants
- Deviation from normal behaviour - indicator of potential dysfunction in the adolescent.

What are the effects of sniffing?

- Mainly **disorientation** caused by the toxic effects of the chemicals.



- Due to solvent lipophilicity - **effects take hold quickly** as substance enters bloodstream directly through the lungs. Effects appear within minutes of inhalation.

- Cortical centres initially affected → **euphoric 'high'; slurred speech; ataxia** (similar to alcohol effects). User experiences disorientation, altered perception or hallucinations, general feeling of confidence.

What are the effects of sniffing?

- **Nausea, vomiting,** tinnitus, sneezing, flushing and coughing may occur. Also, dangerous delusions - imagined ability to fly or swim, leading to deaths.

- **Initial effects of sniffing usually last for 15-45 min.,-** user needs to continue sniffing to maintain the desired effect.

- **User will feel drowsy** for the next 2 hrs as the effects wear off; headache is a common after effect.

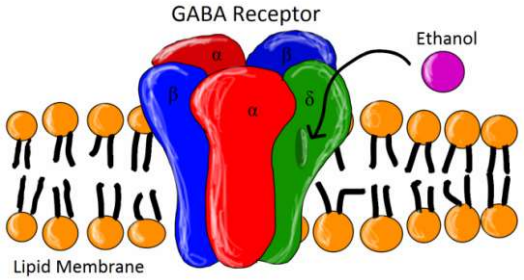
Dependence

- The dependence potential of solvents has not been fully evaluated.

- Withdrawal symptoms can occur:- hallucinations, nausea, excessive sweating, hand tremors, muscle cramps, headaches, chills and ***delirium tremens***. Inhalant abuse can lead to abuse of other substances.
- Solvents do not produce the powerful reinforcing effects of heroin or amphetamine, but do exert strong **psychological effects** and a means of escaping reality.

Mode of action

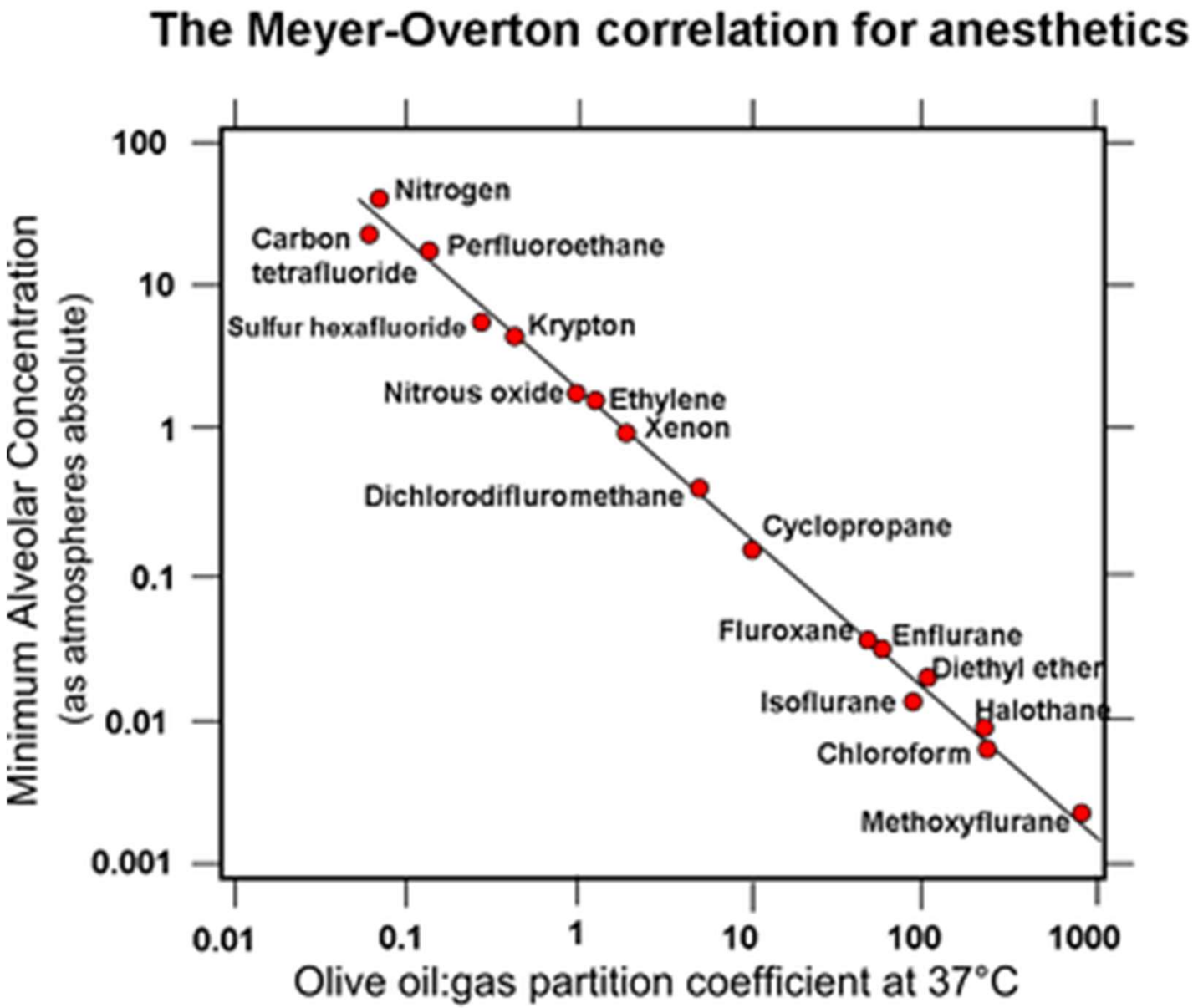
- Volatile solvents (like ethanol) are best regarded as **CNS depressants** and, their mode of action is analogous to that of other volatile inhalational general anaesthetic agents, like **ether, chloroform, halothane, isoflurane.**



Effects of volatile solvents are primarily on:-

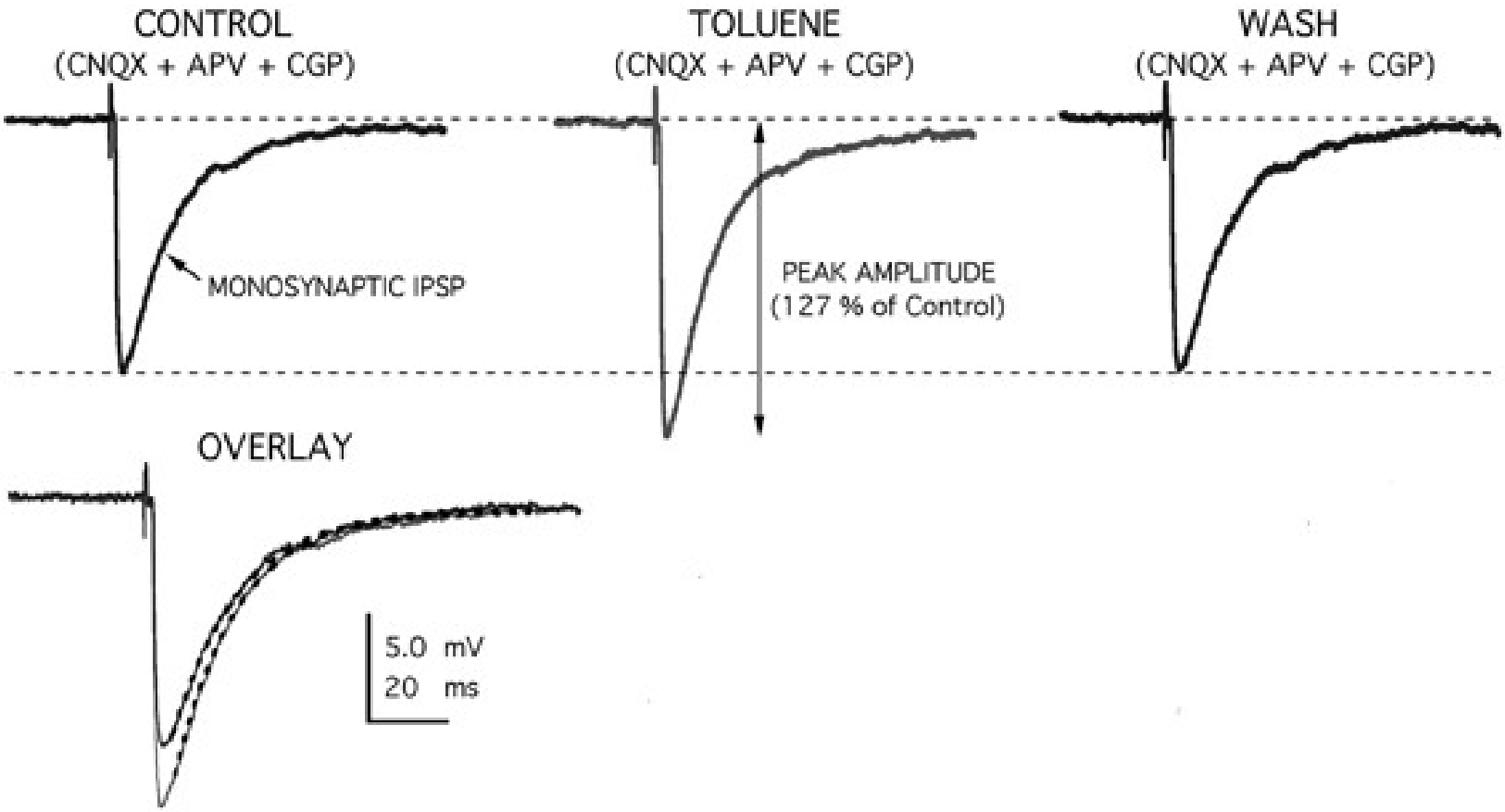
- **$GABA_A$Rs** (potentiation) and **NMDARs** (inhibition); also **glycine (+), $5HT_3$ (+)** and **nicotinic ACh Rs(-).**

Mode of action



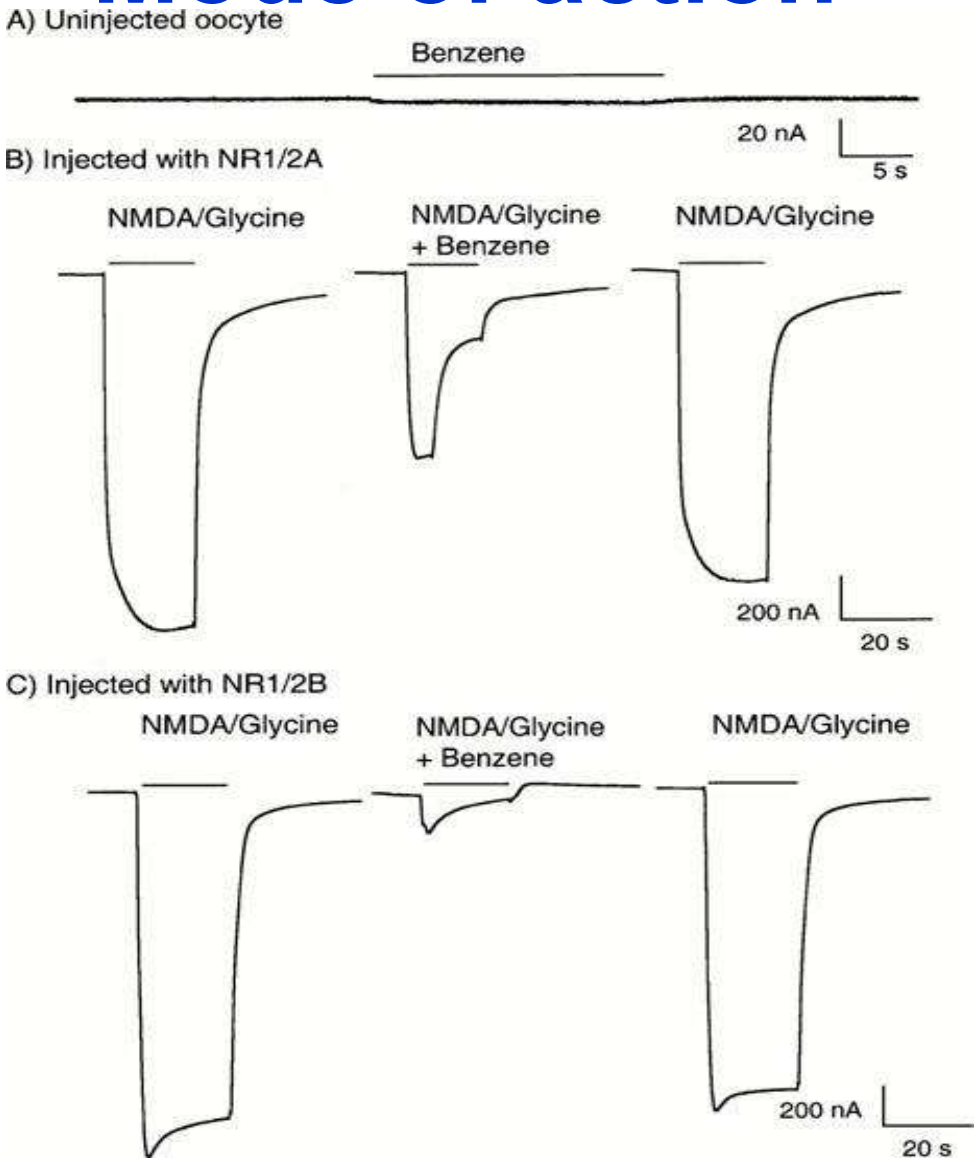
MAC ∝ to 1/potency

Mode of action



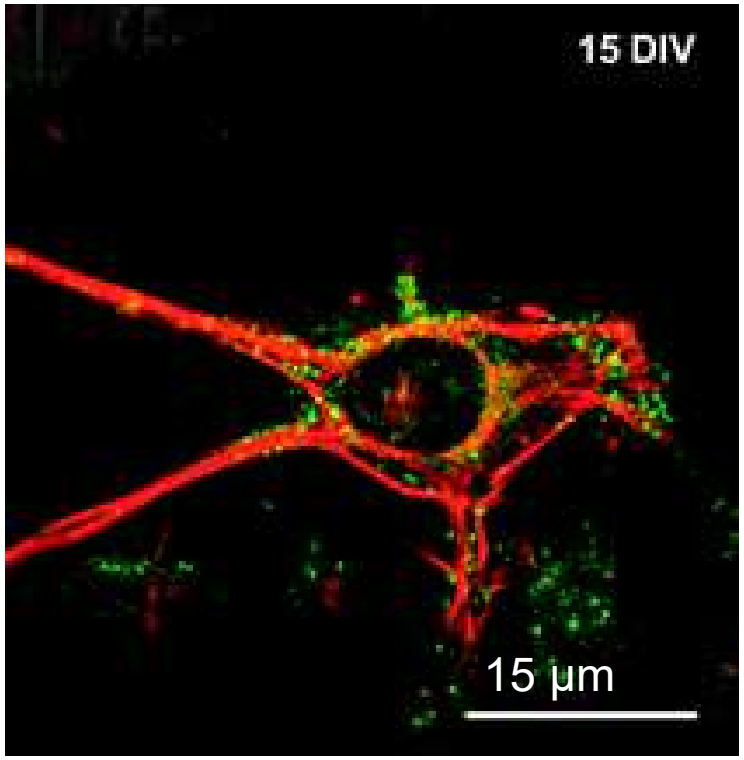
Toluene (1 mM) enhanced GABA-mediated IPSPs recorded from CA1 pyramidal neurones (top recordings) and this effect recovered following washout of the inhalant. IPSP response amplitude was measured from prestimulus baseline to peak negativity, as indicated by the arrows. An increased IPSP amplitude was clearly evident in the overlay of control and toluene recordings (left, middle).

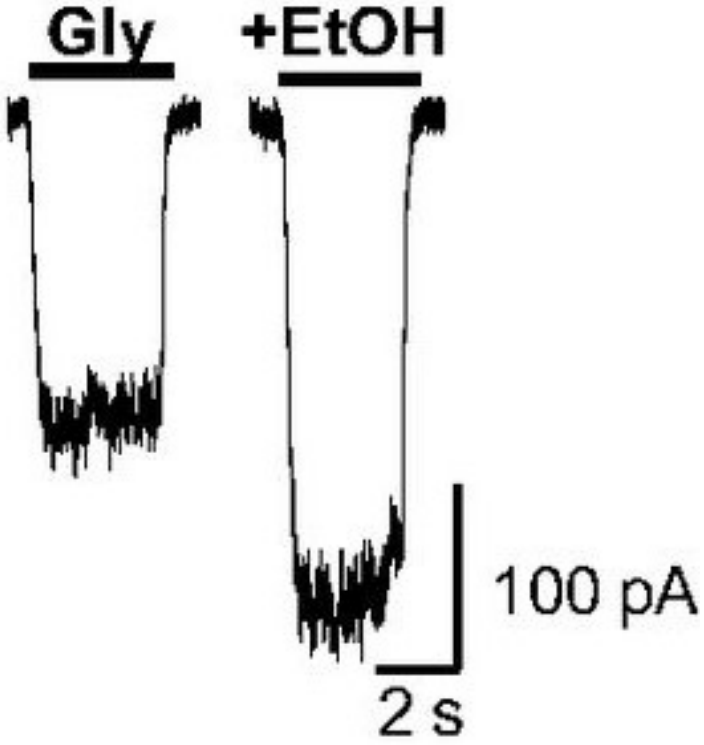
Mode of action



Effects of **11 mM benzene** on membrane currents in uninjected (A) and NMDA-induced currents in **NR1/2A and NR1/2B injected eggs** (B and C, respectively). Oocytes held at −80 mV in extracellular recording medium were exposed for 20 s .

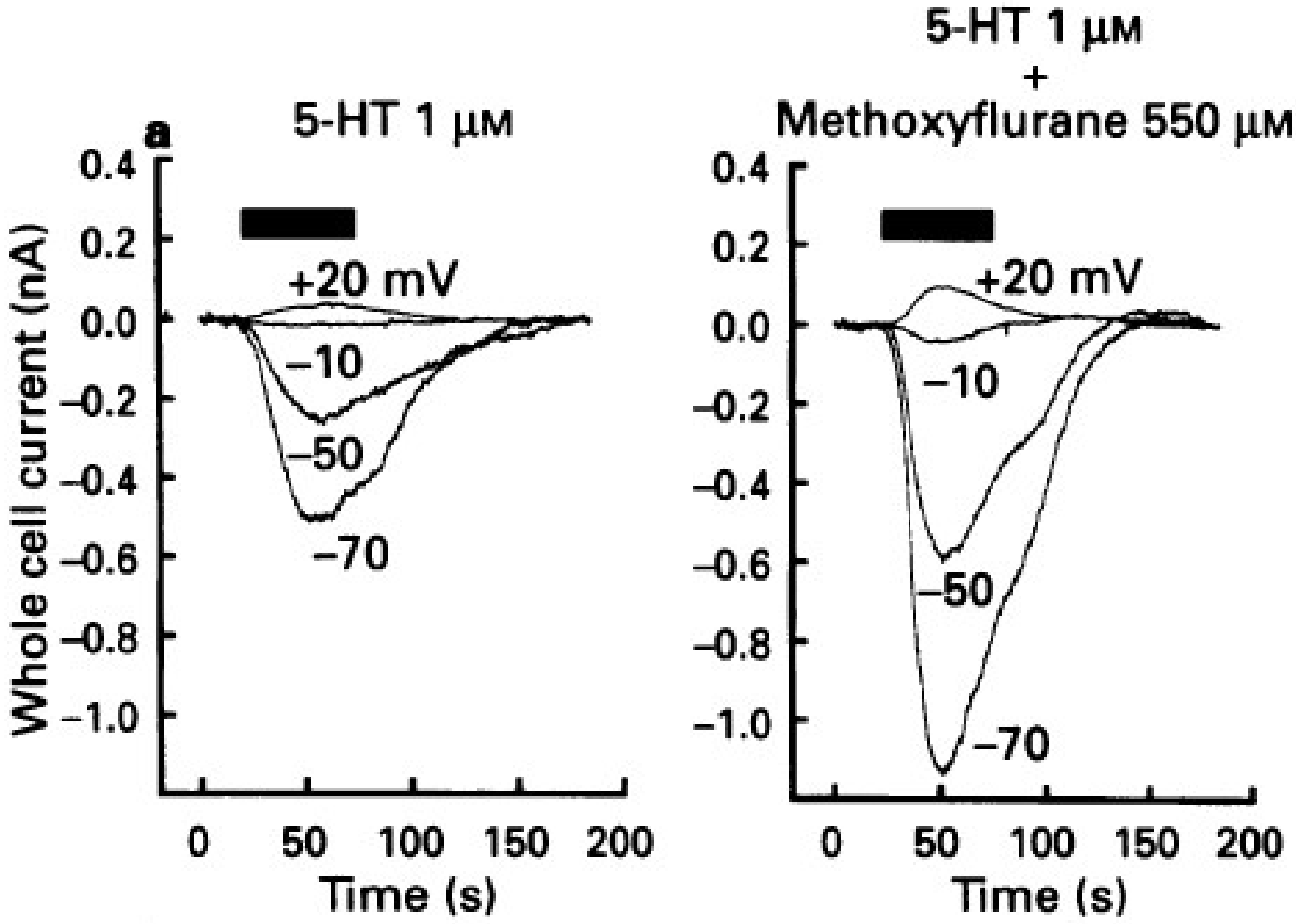
Mode of action





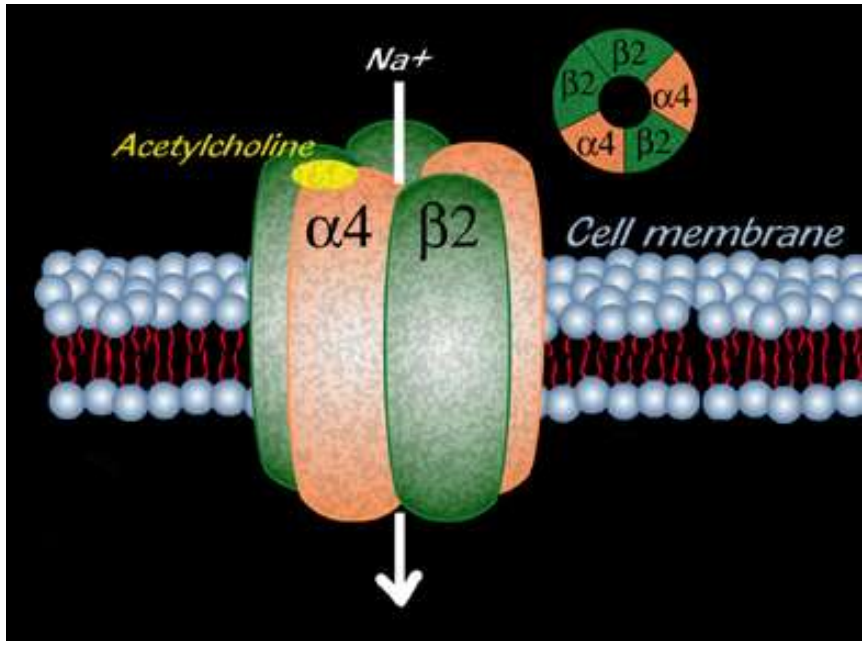
Effect of ethanol on Cl^- current activated by exogenous glycine (15 µM) in a cultured mouse spinal cord neurone. Potentiation of glycine-evoked current in the presence of **ethanol (100 mM)** compared with the control.

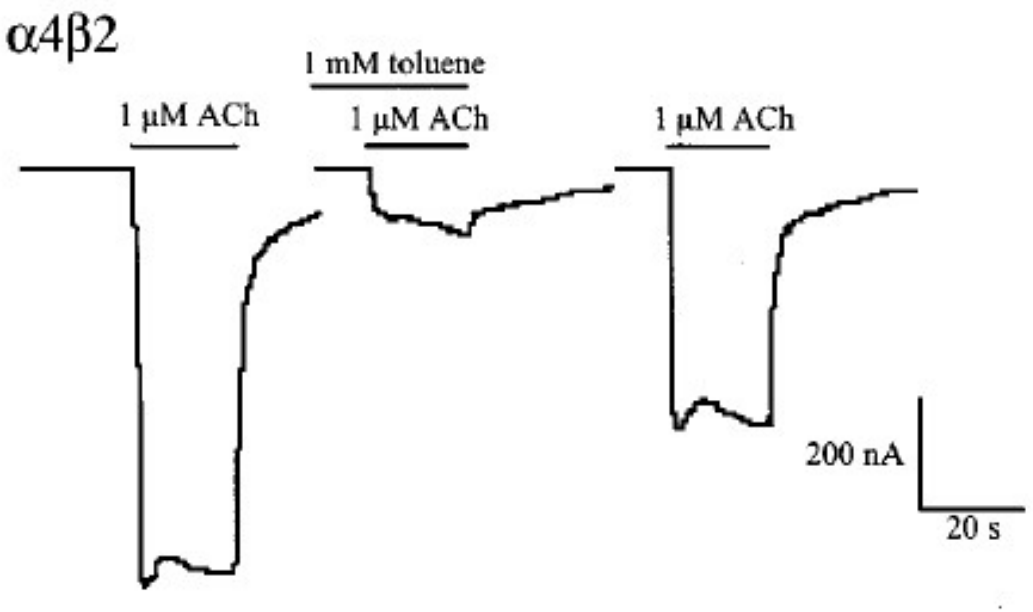
Mode of action



Effect of membrane potential on control and **methoxyflurane**-potentiated Cl^- currents activated by 1 µM 5-HT in mouse N1E-115 neuroblastoma cells which naturally express 5-HT_3 receptors. The methoxyflurane concentration was 550 µM.

Mode of action





Effect of toluene on α4β2 nAChRs expressed in a *Xenopus* oocyte. Trace shows response to ACh (1 μM) with and without **toluene (1 mM)** and after washout. The oocyte was voltage clamped at -80 mV.

Is VSA illegal?

VSA itself is not illegal **nor is possession of solvents.**

Criminalization of the user is probably not a meaningful deterrent for the prevention of inhalant abuse.

Is VSA illegal?

Under the Intoxicating Substances (Supply) Act of 1985, it was an offence for a person to supply, or offer to supply, any volatile substance to someone under the age of 18 years if there was reasonable cause to believe that the substance is, or it's fumes were, likely to be inhaled for the purpose of intoxication. Each offence against the Act carried a fine of up to £5000, or a six-month prison sentence, or both, but there was little evidence of any substantial prosecutions under this Act. **The ISSA 1985 has now been replaced by the Psychoactive Substances Act 2016.**

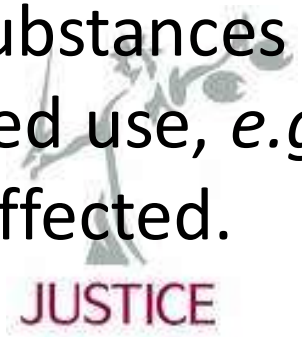
Is VSA illegal?

In May 2016, the ISSA 1985 was replaced by the Psychoactive Substances Act 2016 intended to ban 'designer' psychoactive substances ('legal highs'), in the UK and to prevent supply of these previously unregulated, frequently harmful substances for human consumption. The Act also now includes other intoxicants *e.g.* N_2O. Additionally, it will affect conventional retailers responsible for suppling products that contain potentially psychoactive substances, *e.g.* solvents and butane gas. The new Act is thus intended to cover psychoactive substances that aren't covered by the existing Misuse of Drugs Act 1971.

Is VSA illegal?

For the purpose of the Act, a new or existing substance **(New Psychoactive Substance: NPS)** that produces a psychoactive effect to be covered by the new legislation, is something that can affect a person's mental functioning or emotional state by stimulating or depressing their (central) nervous system.

The Act specifically applies to substances which are supplied for human consumption for their psychoactive effect unless they are exempt (food, medicine and controlled drugs, alcohol, nicotine and tobacco products, caffeine). Substances that are sold by a retailer for their intended use, *e.g.* cleaning, gardening, industrial use, are not affected.



Is VSA illegal?

All substances that were covered by the ISSA 1985 will now be covered by this Act. These will include the following:

- solvent-based glues
- correction fluids/thinners
- marker pens
- any kind of aerosols
- anti-freeze
- nail varnish/nail varnish remover
- nitrous oxide*

Is VSA illegal?

***Nitrous oxide (N_2O)** has presented a particular problem in recent years as a 'legal high'. People inhale the gas from small refill canisters in order to obtain a recreational 'high' or dispense the gas from larger canisters into balloons, which are then used to inhale the gas. Retailers are thus advised to pay particular attention to the potential for abuse of N_2O, particularly where customers are trying to purchase in bulk or in unusually large volumes.

Interestingly, so-called **'poppers' (amyl nitrite and butyl nitrite)** commonly used as a party drug, will not be banned under the new legislation, as they are regarded not to directly stimulate or depress the CNS.

Is VSA illegal?

Nitrous oxide (N_2O): In **November 2023**, the UK law was updated to make possession of nitrous oxide illegal if it is, or is likely to be, wrongfully inhaled, by classifying it as a Class C drug under the *Misuse of Drugs Act 1971*. It is therefore now a criminal offence in the UK to be found in possession of the drug where its intended use is to be inhaled 'to get high'. Repeat illegal users of nitrous oxide now could face up to 2 years in prison and dealers up to 14 years. It will continue to be lawful for catering purposes and in maternity wards when used as pain relief during labour.

JUSTICE

Is VSA illegal?

Under the Cigarette Lighter Refill (Safety) Regulations of 1999, it is however, still an offence, to supply any cigarette lighter refill canister containing butane, or a substance with butane as a constituent part, to any person under the age of 18 years. The maximum penalty for a breach of the Regulations by the retailer, is currently a six-month prison sentence, a fine of up to £5000, or both. Once again, this law has been hard to enforce and only a handful of prosecutions are brought per year.

JUSTICE

Prevention

- **Limiting the availability of inhalants** is impractical because they comprise a large group of products that are universally available and licit, and have legitimate uses.

- **Restricting some product availability** results in a shift to the use of other products or creates a black market for restricted products.

Prevention

- **Education** is considered the most effective preventive strategy if initiated before the usual age of experimentation (particularly in areas where inhalant abuse is prevalent).

- **Harm minimization approach** - adopted during the 1980s – accepted that people were unlikely to stop inhaling solvents, -sought to reduce harm and danger associated with their use - e.g. use of smaller plastic bags for ‘sniffing’ - not spraying aerosols directly into the mouth - avoiding sniffing alone or in potentially dangerous areas.

Prevention

- **The Department of Health** (1992,1994), launched campaigns to raise public awareness of VSA -led to the fall in the number of reported deaths after 1992.

- **Harm minimization approach** has now been criticized: Simple message nowadays is – **"VSA is too dangerous, don't do it".**

SOLVENT ABUSE CAN KILL INSTANTLY

- **Provision of education in schools** about dangers of VSA is strongly encouraged. VSA awareness also raised by charity work: **Re-solv.**

RESOLV™

Prevention

- **Manufacturers:** strong pressure to change their formulations, and to restrict the size of cigarette lighter refills - response has been limited.

- **Adding warning labels** to products liable to abuse may allow children to identify sniffable substances easily.

- **Retailers:** increasing awareness of retailers to problems of VSA and how to recognize potential solvent abusers.

Treatment

- **Treatment of inhalant users** is difficult because of the many pharmacological, clinical, cultural and demographic factors that make this type of substance abuse unique.

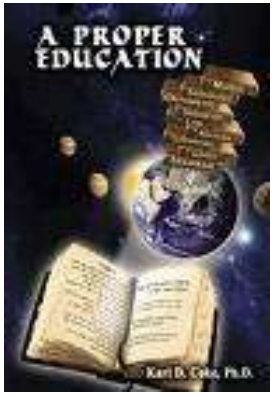
- **Treatment requires general counselling** rather than specific substance abuse treatment - may be most effective when conducted by reformed inhalant abusers.

Treatment

Recommendations

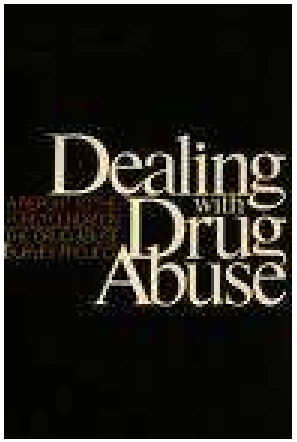
- **Encourage health care providers** to increase their awareness of inhalant abuse complications, particularly CNS damage and sudden sniffing death syndrome.

- **Promote education about hazards** posed by substance abuse to children, adolescents, parents, teachers, media representatives and vendors of volatile substances.



Treatment

Recommendations



- **Include information on inhalant abuse** in substance abuse prevention curricula in primary and secondary schools; particularly in communities where inhalant abuse is endemic.

- **Further research effort needed** to identify and evaluate prevention and treatment approaches specific for this type of substance abuse.

HAZARD CREW

THE REALITY IS...

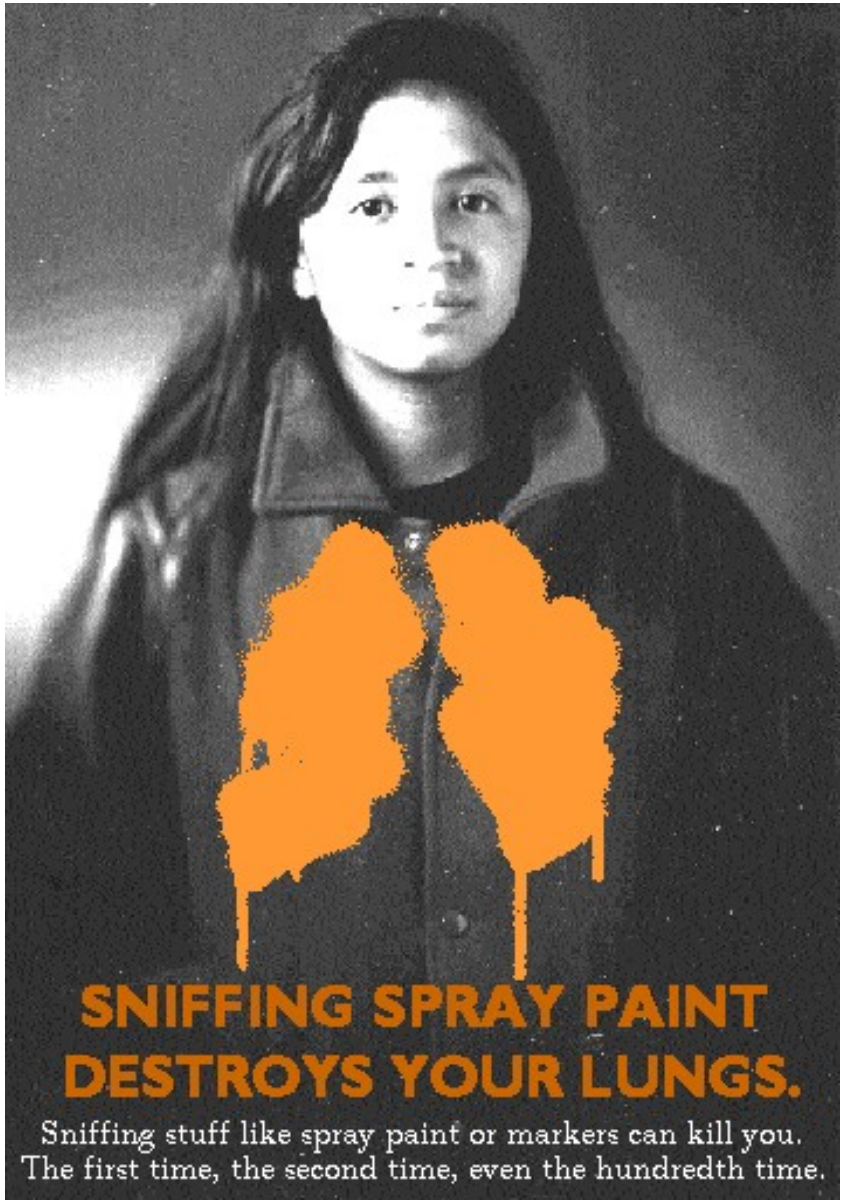
Michael aged 15, was a well like teenager who would have done anything to help his family and friends. He died one Monday evening after experimenting for the first time with air freshener bought in a local shop. Michael's family miss him loads and are left without their only son and brother.

Danielle aged 16, collapsed at a friend's house after inhaling an aerosol can. She died a short time later in hospital. She is missed by her family and her father said: "The family had no idea she was abusing solvents. All kids know what is going on, but it is the parents who do not know."

Ricky aged 12, died after inhaling petrol in the back of a car. A relative said that the family was devastated. "They just don't know what day it is," he said. "They will be living with this for the rest of their lives."

WWW.SNIFFING.ORG.UK

Re-Solv


SNIFFING SPRAY PAINT
DESTROYS YOUR LUNGS.
Sniffing stuff like spray paint or markers can kill you.
The first time, the second time, even the hundredth time.


EXTRA-STRENGTH
HEART
FINISHER
PLUS CONVULSIONS


Fast-acting
Brain Remover
NOW WITH CANCER