



Nicotine Reduction Workshop

Role of nicotine in smoking behaviour

Derek Mariner



Introduction



- **“Nicotine itself is not especially hazardous ... if nicotine could be provided in a form that is acceptable and effective as a cigarette substitute, millions of lives could be saved.”**

Harm reduction in nicotine addiction: helping people who can't quit, a report by the Tobacco Advisory Group of the Royal College of Physicians, 2007

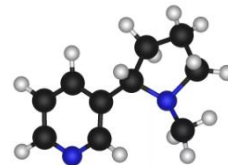
- **Nicotine inhaled from smoking tobacco is highly addictive. But it is primarily the toxins and carcinogens in tobacco smoke – not the nicotine – that cause illness and death.**

"Tobacco harm reduction approaches to smoking, UK National Institute for Health and Care Excellence, public health guidance 45, July 2013

- **“People smoke for the nicotine, but die from the tar.”**

Professor Michael Russell, British Medical Journal, 1976

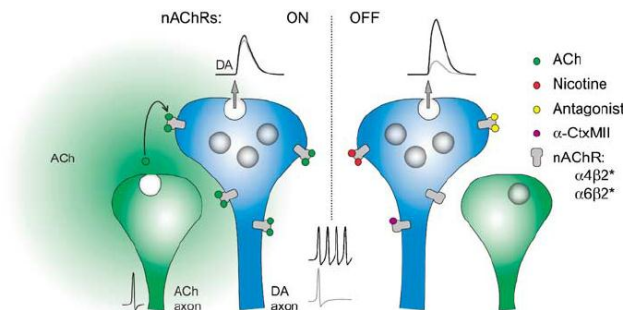
- **Nicotine at all concentrations has the potential to cause addiction. www.bat.com**



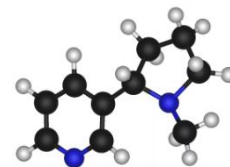
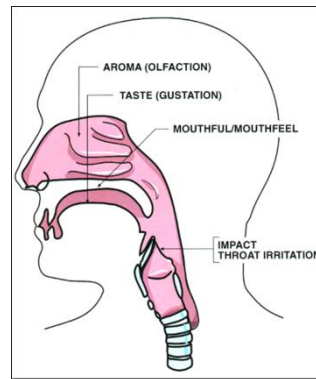


Smoke effects

- Pharmacological (nicotine)
 - binds to nicotinic cholinergic receptors facilitating neurotransmitter release: dopamine, glutamate, and gamma aminobutyric acid
 - induces stimulation and pleasure, and reduces stress and anxiety
- Sensory (smoke and nicotine)
 - Gustation, olfaction, flavour
 - Common chemical sense (trigeminal): irritation, mouthfeel/full, impact



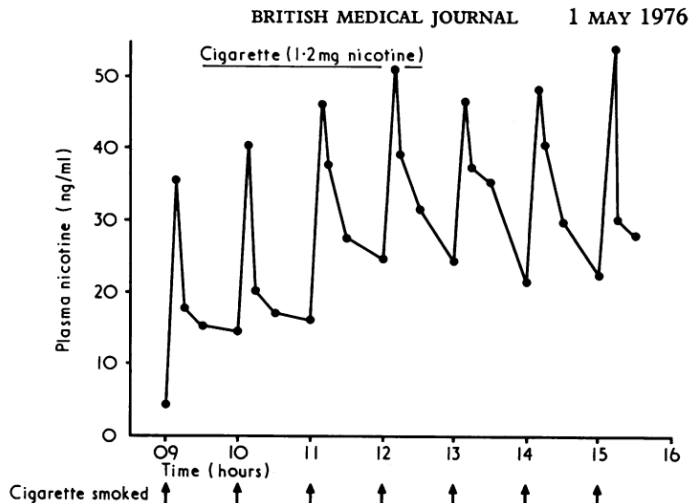
R Exley and SJ Cragg, British Journal of Pharmacology (2008) 153, S283–S297





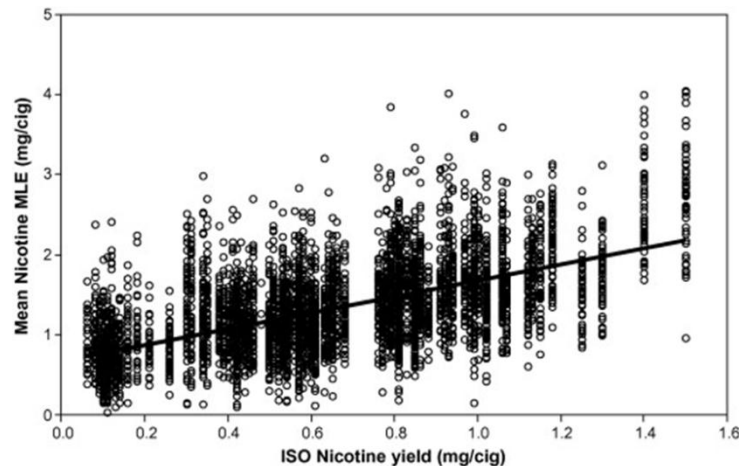
Nicotine uptake

- Plasma nicotine peaks after each cigarette



Russell et al, BMJ, 1976, 1, 1043-1046

- Behaviour varies widely



Mariner et al, Reg Toxicol Pharmacol, 2011, 61, S39-S50



Compensation



- The extent to which smokers change their behaviour when switching to a cigarette with different tar and nicotine yield
 - Review by Scherer (1999) concluded that compensation is partial
 - NIH NCI Monograph 13 (2001) concluded that compensation is complete
- Potential mechanisms
 - Puff number ✓
 - Puff volume ✓
 - Inhalation pattern ✗
 - Ventilation blocking ⇄
 - Cigarette consumption ✗



Role of nicotine in compensation

- Early studies (70s): Difficult to separate nicotine effects from tar effects
- Low tar/medium nicotine
 - Stepney et al (1981) concluded that tar yield was more important than nicotine yield, possibly due to sensory mechanisms
 - BAT sensory panels rejected the products as unbalanced – mouthfeel too low and irritation too high
- Denicotinised tobacco
 - Hasenfratz et al (1993) “reduction in tar yield appeared to be more important than a reduction in nicotine yield”
- Constant tar/varying nicotine (similar to the proposed regulatory approach)
 - Dixon et al (2003) No significant effect on puffing parameters, no evidence of compensation, significant reduction in “impact”
 - Benowitz et al (2004) found a reduction in nicotine exposure, no increase in CO or NNK exposure

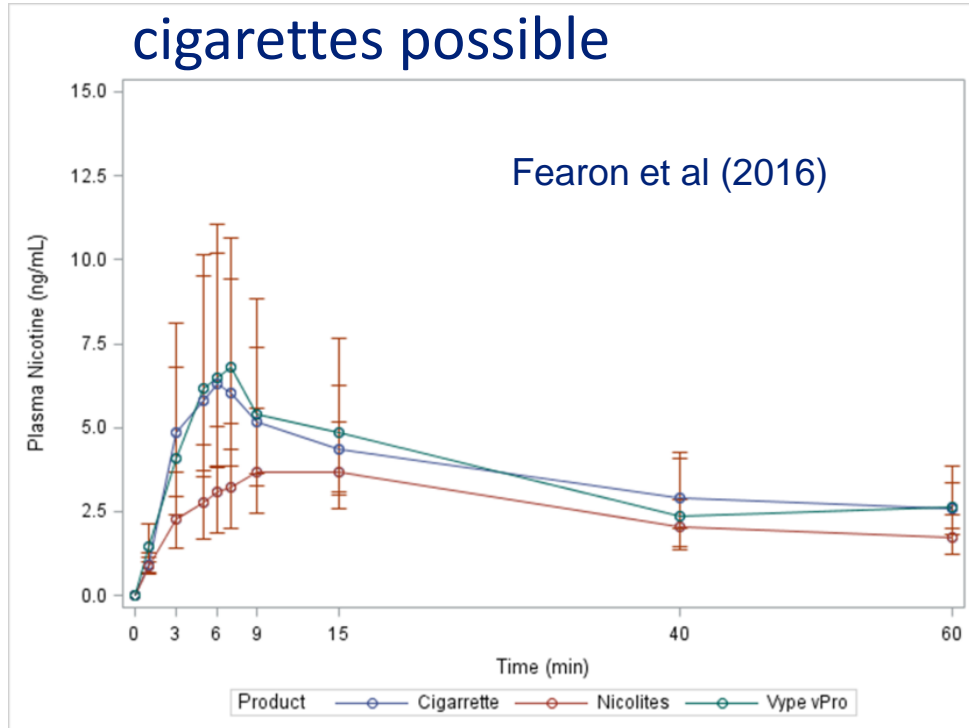


Non-nicotine factors

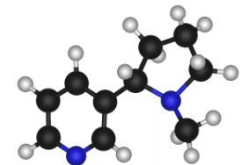
- Requires that nicotine and non-nicotine factors can be decoupled eg using IV administration of nicotine (Jed Rose, 2005)
 - IV nicotine provides limited subjective satisfaction, but some craving relief
 - IV nicotine plus denicotinised cigarettes provide increased satisfaction and craving relief (increased in subjects with higher FTND scores)
 - IV nicotine had only small effect on ad libitum smoking behaviour
- Concluded that sensory and behavioural /motor cues are important

Does appropriate e-cigarette regulation provide an opportunity to reduce smoking prevalence?

- Similar nicotine uptake to cigarettes possible



- Provide many of sensory and behavioural cues from cigarette smoking
- Use appears to be associated with an increase in successful quit attempts (Beard et al (2016))





References



- Harm reduction in nicotine addiction: Helping people who can't quit. A report by the Tobacco Advisory Group of the Royal College of Physicians, London, RCP, 2007
- Tobacco harm reduction approaches to smoking, UK National Institute for Health and Care Excellence, Public Health Guidance 45, July 2013
- Exley R and Cragg SJ, British Journal of Pharmacology (2008) 153, S283–S297
- Russell M et al (1976) BMJ 1: 1043-1046
- Mariner DC et al (2011) Reg Toxicol Pharmacol, 61: S39–S50
- Scherer G (1999) Psychopharmacology 145:1-20
- NIH NCI Monograph 13 (2001)
- Stepney R et al (1981) BMJ 283:1292-1296
- Hasenfratz M et al (1993) Psychopharmacology, 112:253-258
- Dixon M et al (2003) Psychopharmacology, 170: 434-442
- Benowitz N et al (2004) Nic Tob Res 6: 708-709
- Rose J (2005) Psychopharmacology doi 10.1007/s00213-005-0250-x
- Fearon I et al (2016) poster at Global Forum on Nicotine, Warsaw, June 2016
- Beard E et al (2016) BMJ 354:i4645

Thank you

www.bat-science.com



@BAT_Sci