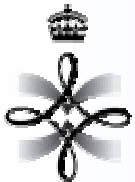


Measurement and Interpretation of the Central Effects of Drugs: Implications to Behavioural and Forensic Toxicology

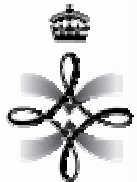
Julia Boyle

University of Surrey, UK



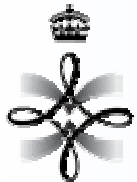


What is 'Behavioural Toxicity'?



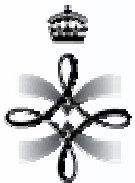


- Extent to which CNS side effects interfere with everyday activities
- Counter-therapeutic
- Of particular concern - car driving ability



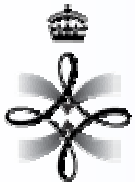


- **CERTIFIED project**
 - High priority benzodiazepines, alcohol
 - Medium priority amphetamine, opiates, cocaine, cannabis
 - Low priority methadone, antihistamines, antidepressants
- **IMMORTAL project**
 - Continuing investigation into medicinal drugs and driving





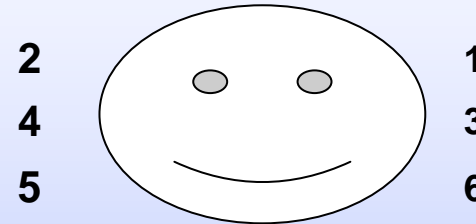
How do we obtain reliable data on impairment?





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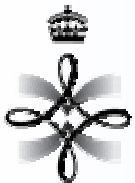
- FIT
 - Neurological tests



- Gymkhana

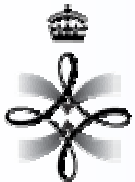


- City Driving





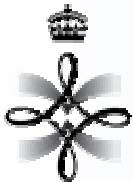
- Correlation to driving ability?
- Subjective assessment
- Time consuming / expensive





Standard Deviation of Lateral Position and Car Following

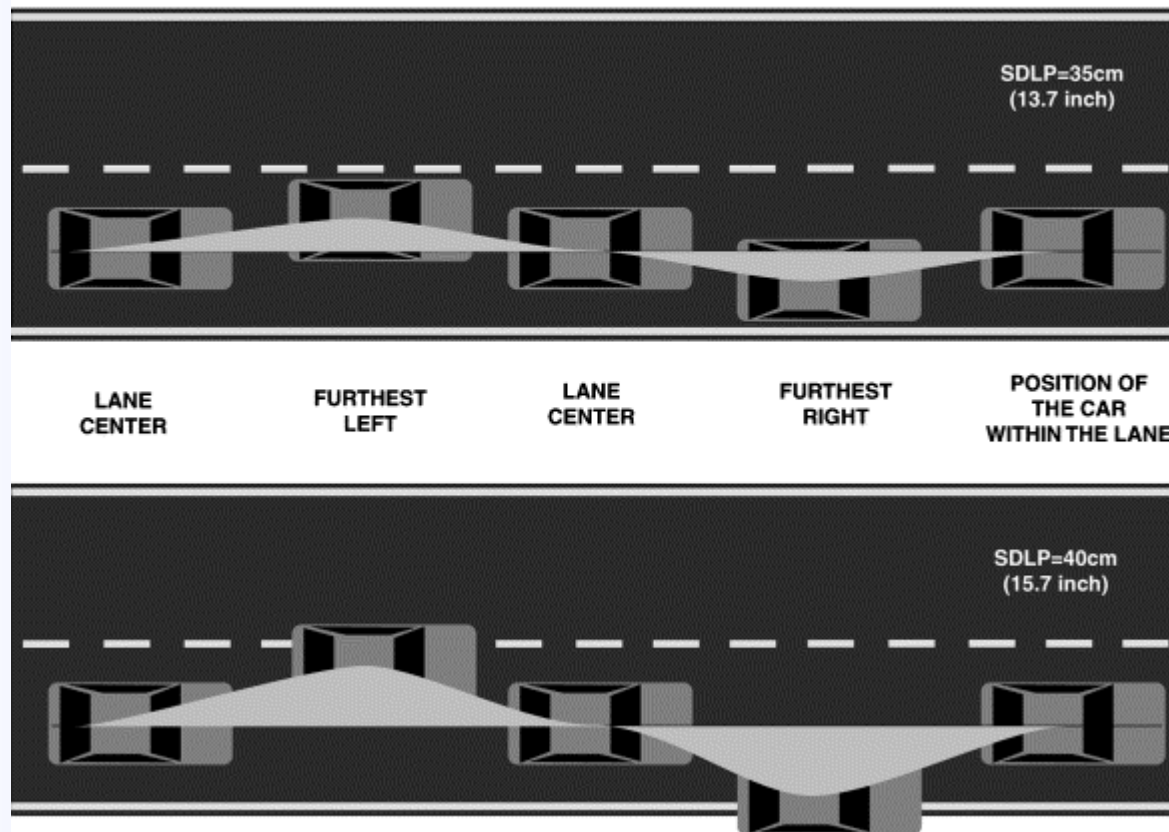
**Experimental Psychopharmacology Unit,
Brain & Behaviour Institute
Maastricht University**





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CALCULATION AND MEANING OF THE "WEAVING INDEX" (SDLP)



Strong correlation ($r = 0.99$) to BAC (O'Hanlon & Volkerts, 1986, *Acta Psychiatrica Scand.* **74**, 95-105)



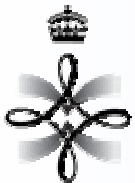
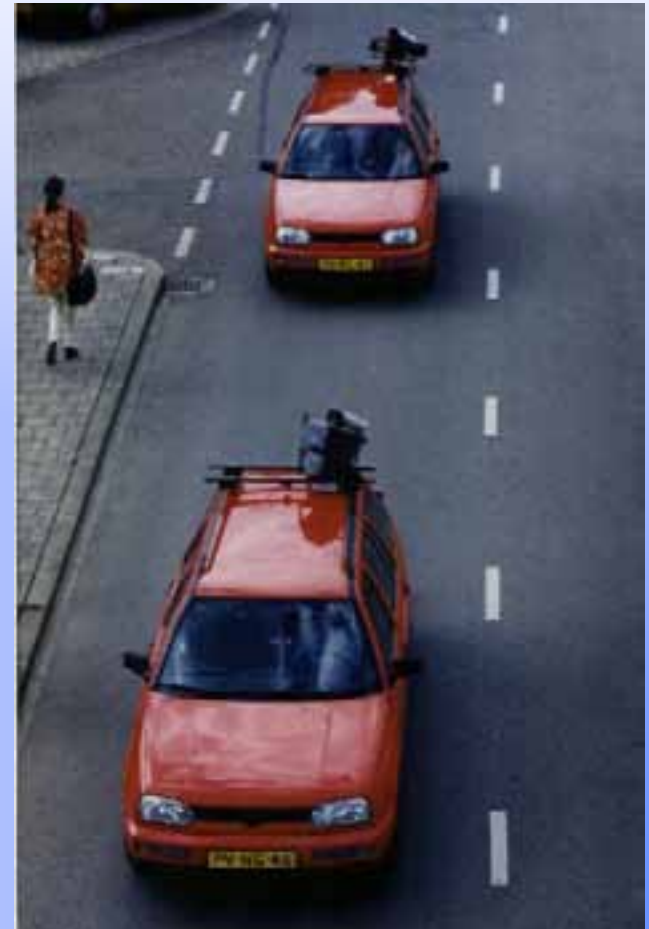
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- Follow a lead car
- Car handling
- Vehicle separation
- Relative speed

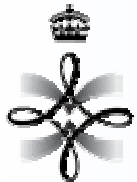


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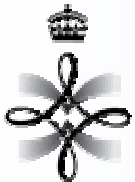


- Environmental factors
- Expensive
- Time consuming
- Driving skills?
 - Readiness to brake sensitive and reliable





On-the-road Brake Reaction Time

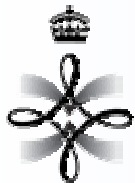


UniS Brake Reaction Time (BRT)



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- Parallels the car following task



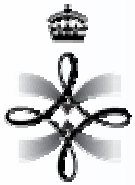
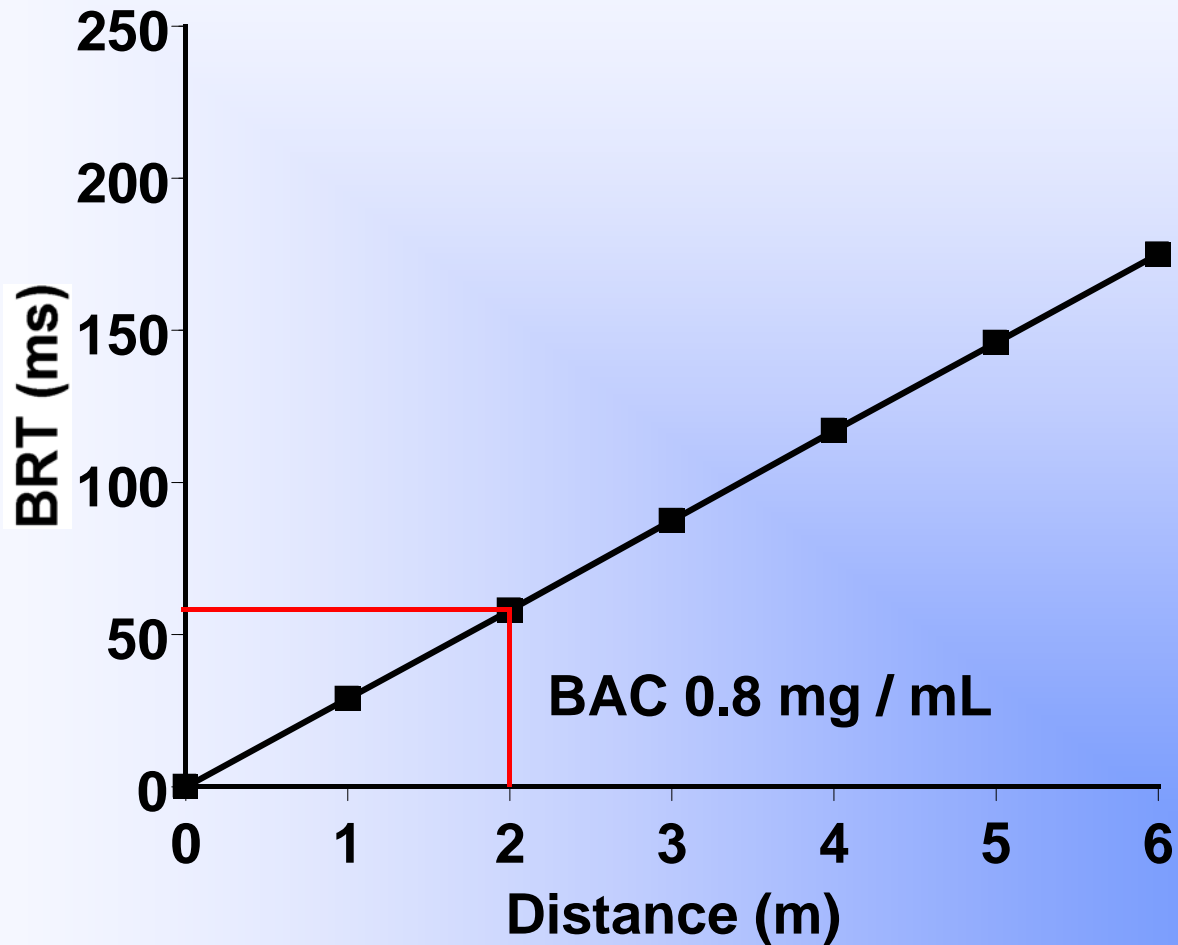
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BRT Correlates with Stopping Distance

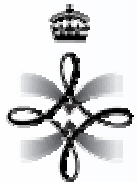


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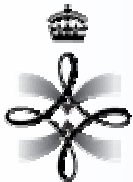


Psychometric Tests





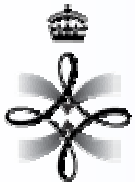
- Controlled and objective performance measures
- Battery to assess all aspects of cognition and psychomotor performance
- Sensitive, reliable and good correlation with everyday tasks





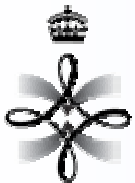
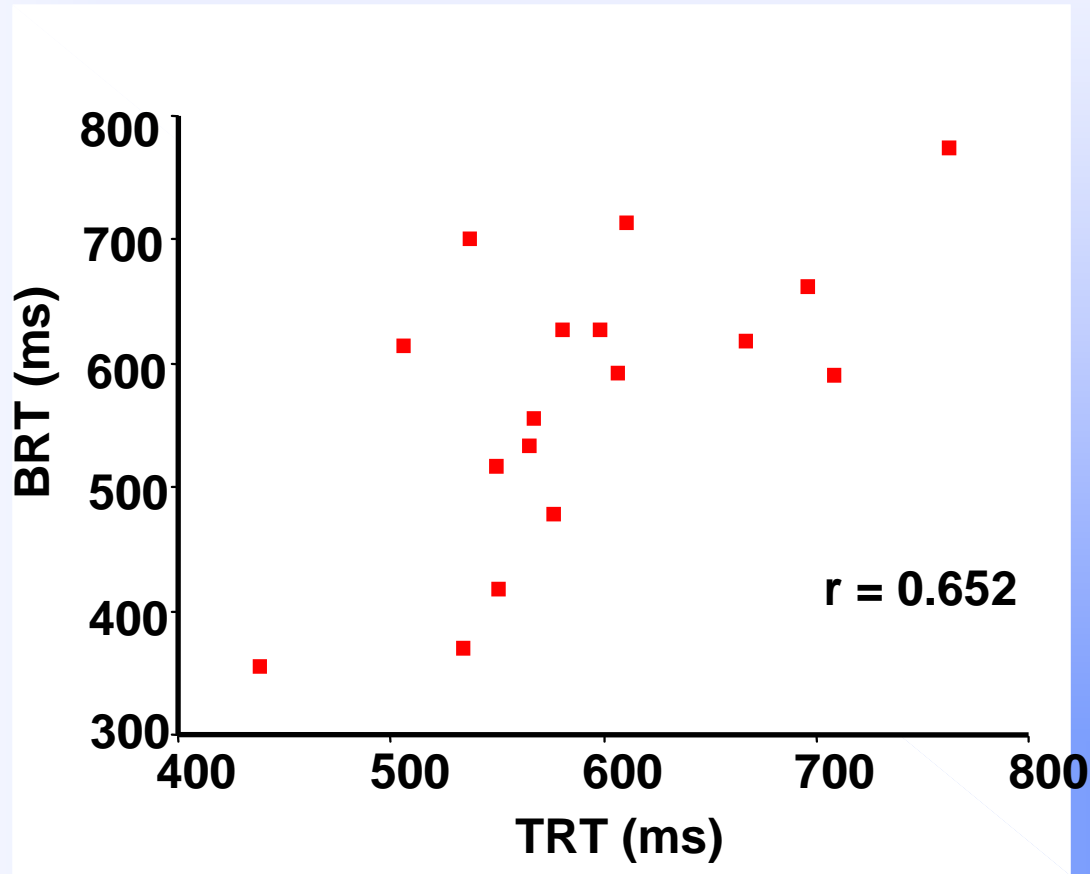
- Tracking tasks
 - Sensitive & correlation with SDLP
- Executive function tasks
 - Stroop

BLUE	BLUE
GREEN	GREEN
- Sensori-motor tasks
 - DSST and choice reaction time



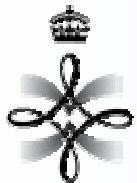


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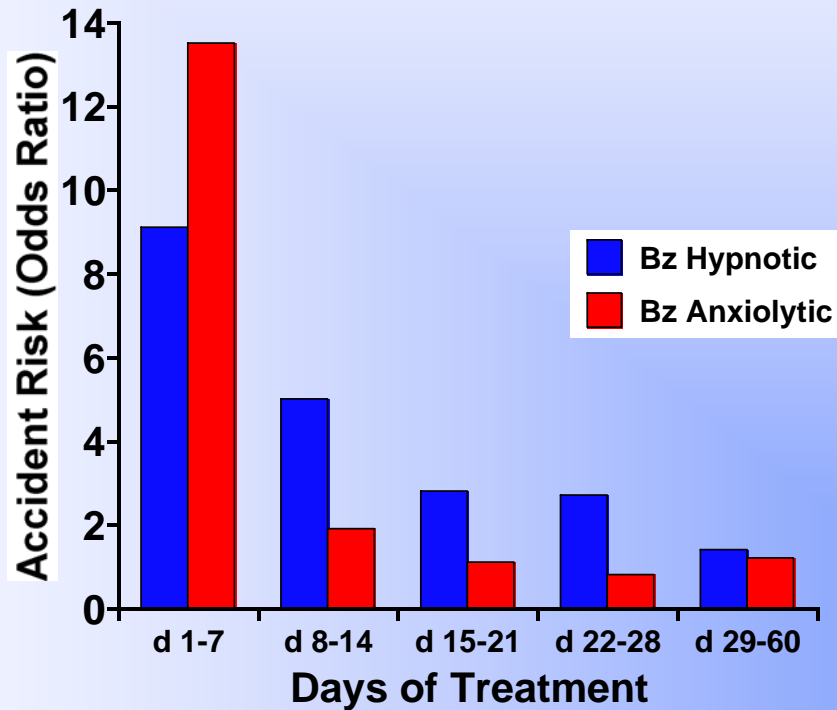


High Priority Psychoactive Drugs: Hypnotics / Anxiolytics

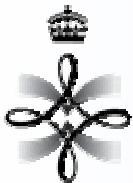




- Risk of road accident greatest with Bz

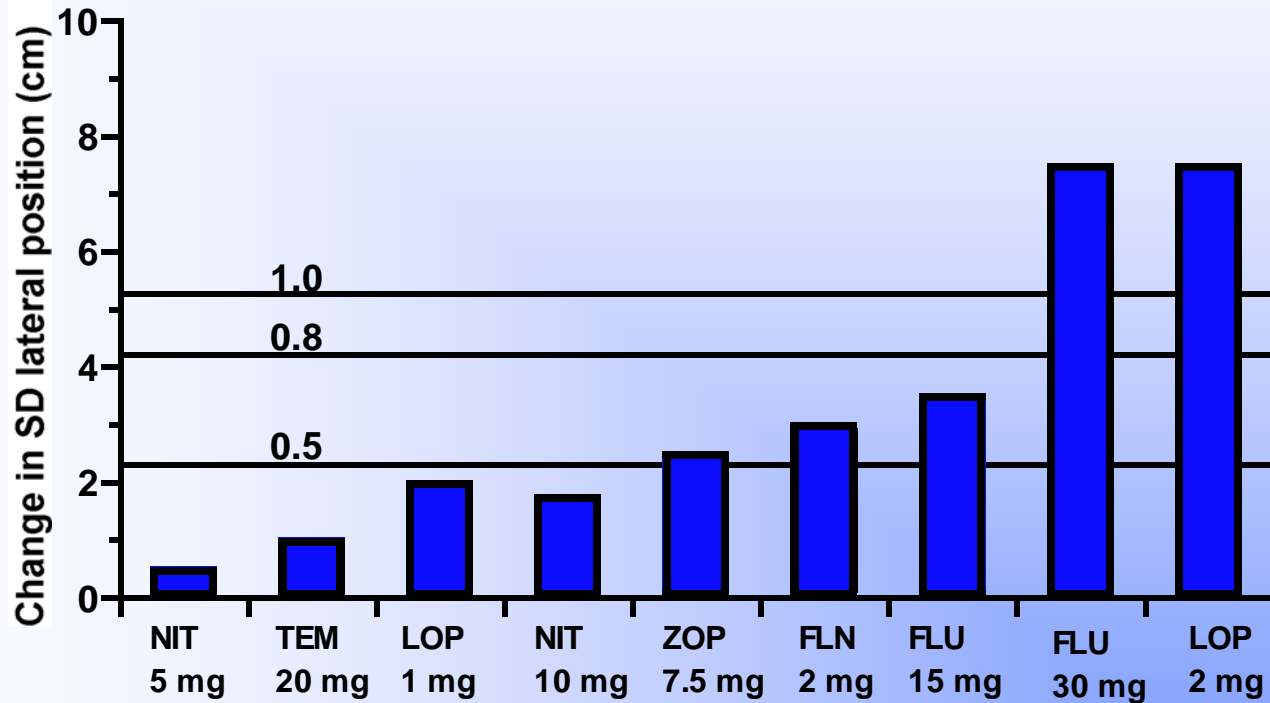


Neutel, 1995, *Annals of Epidemiol.*, 5, 239-244

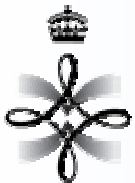




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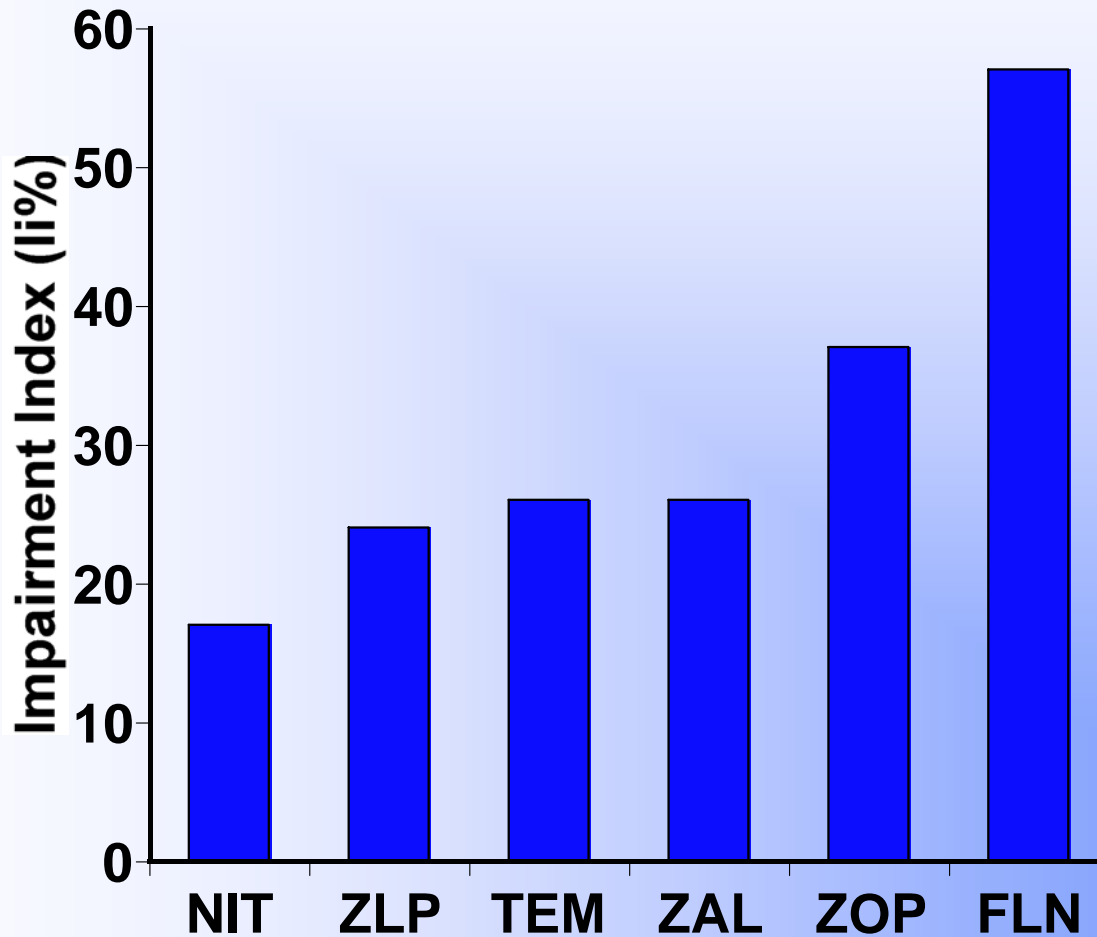


O'Hanlon & Volkerts (1986), Acta Psychiatr. Scand. 74, 95-104

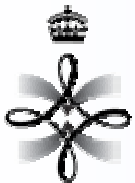




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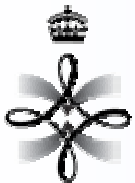


li% = No. of tests imp / total no. of tests



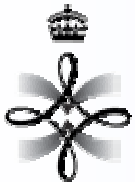


- PK important for drug selection
 - Hypnotics rapid absorption, short $t_{1/2}$
 - Anxiolytics slower absorption preferable
- Gender differences
- Increased impairment with increasing age



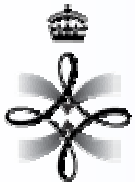


Low Priority Psychoactive Drugs: Antidepressants & Antihistamines



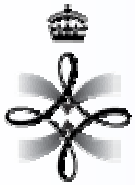
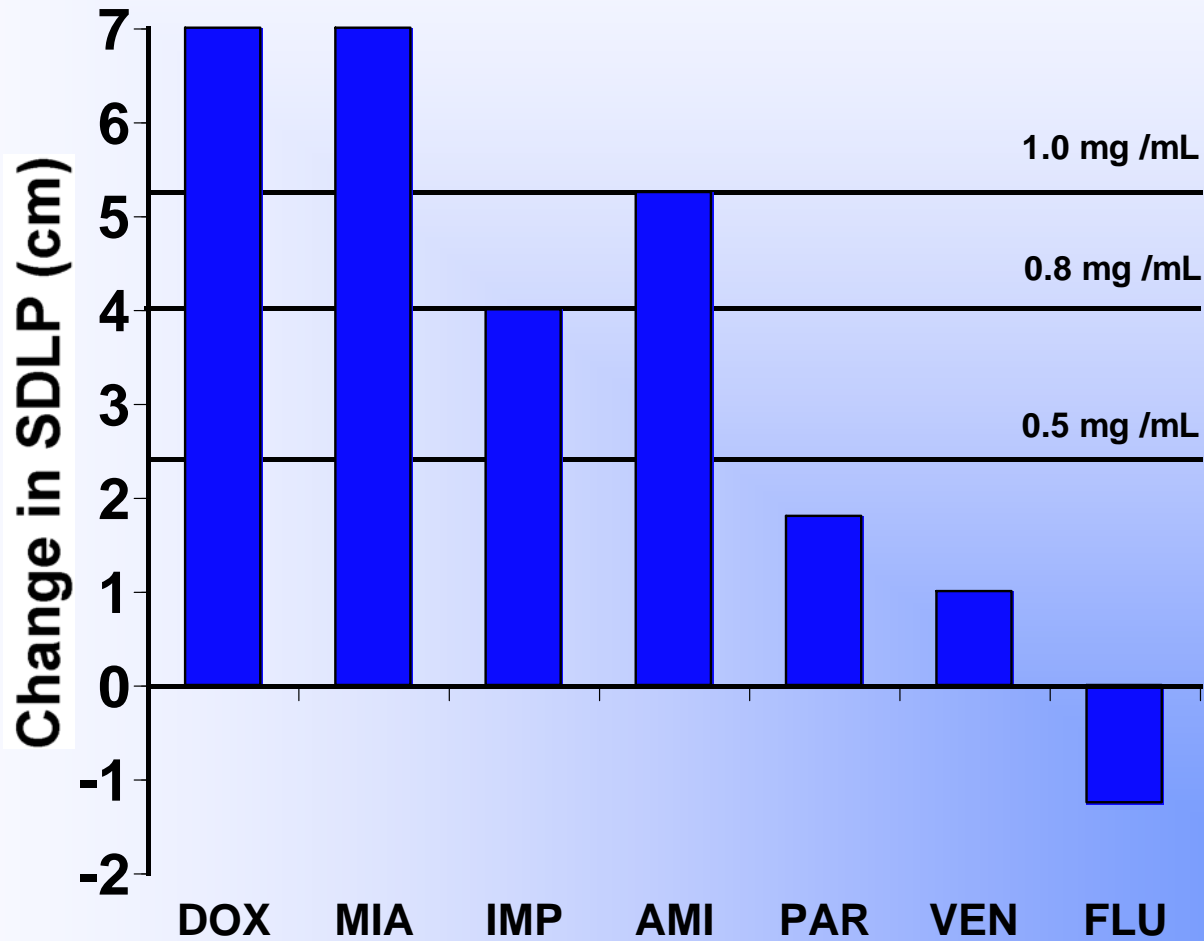


- TCA and SSRIs similar efficacy but greater accident risk with TCAs
- Impairment linked to anticholinergic and antihistaminergic action
- Elderly especially more sensitive to anticholinergic effects
- Accident risk increased in elderly patients (OR 2.1)



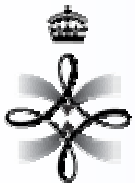
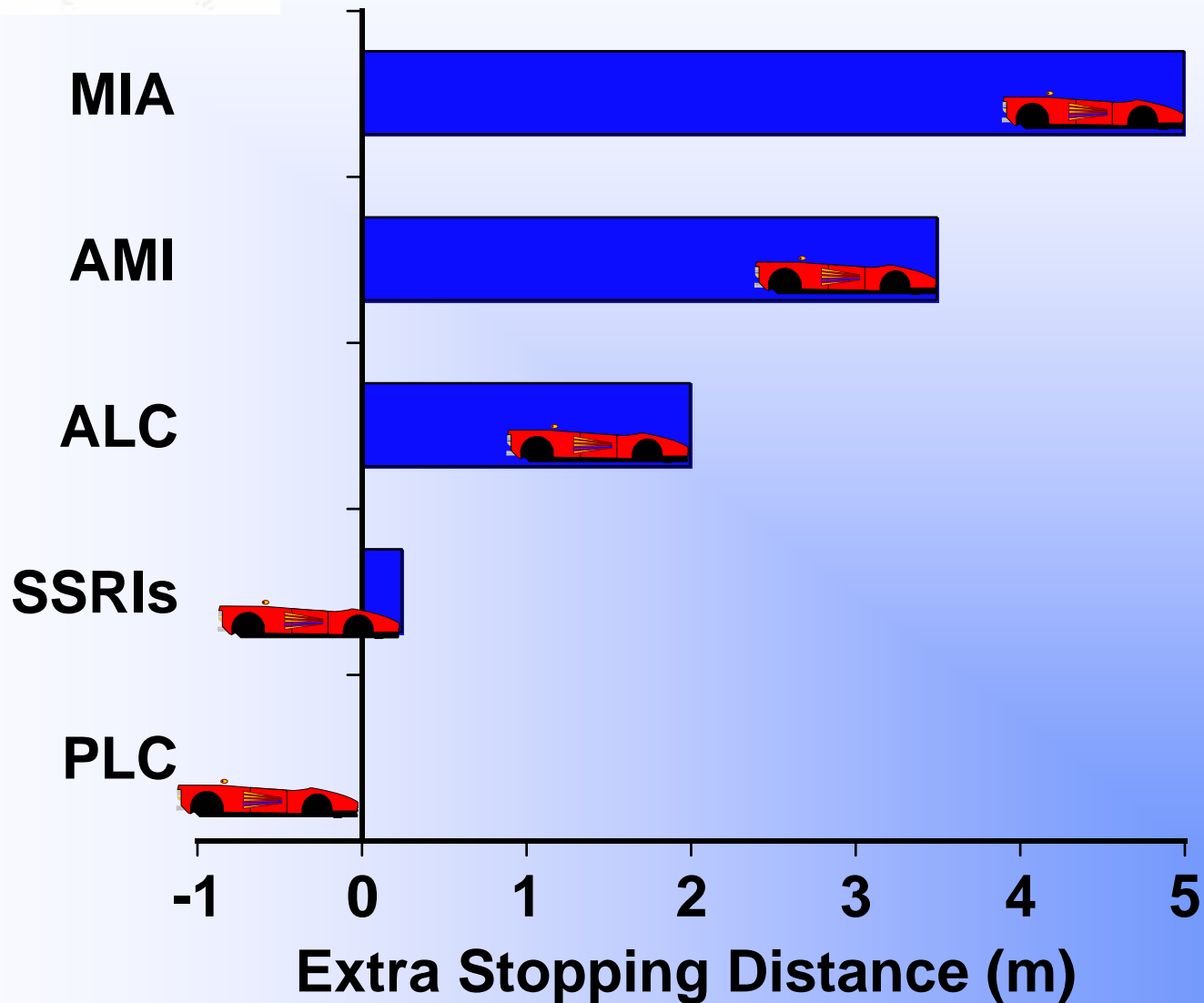


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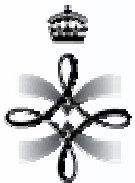
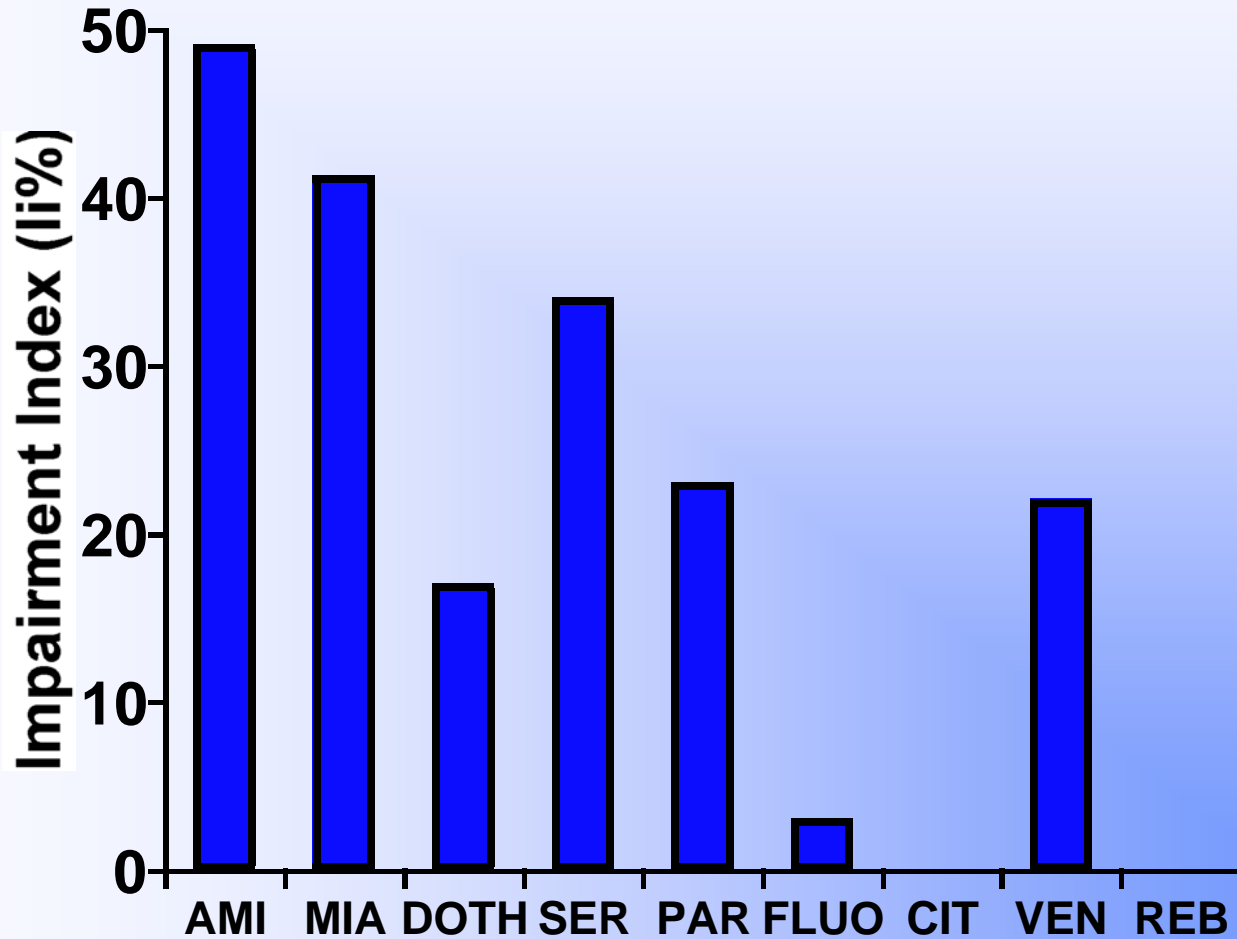


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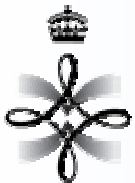
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- Evidence of increased accident risk particularly for first generation AHs
- Of concern as many available OTC

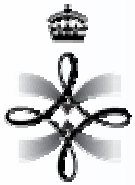
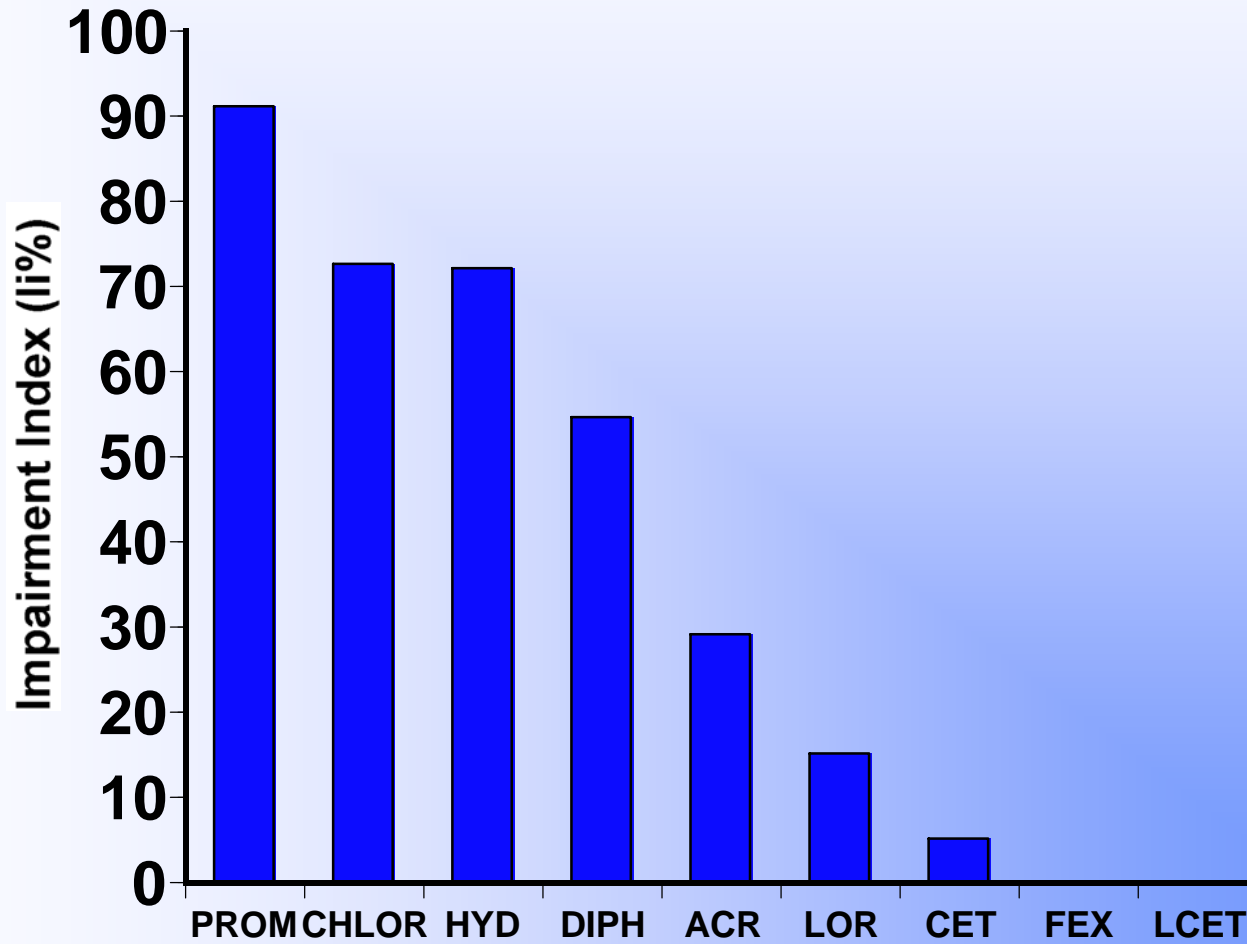
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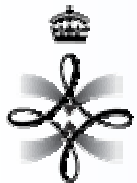
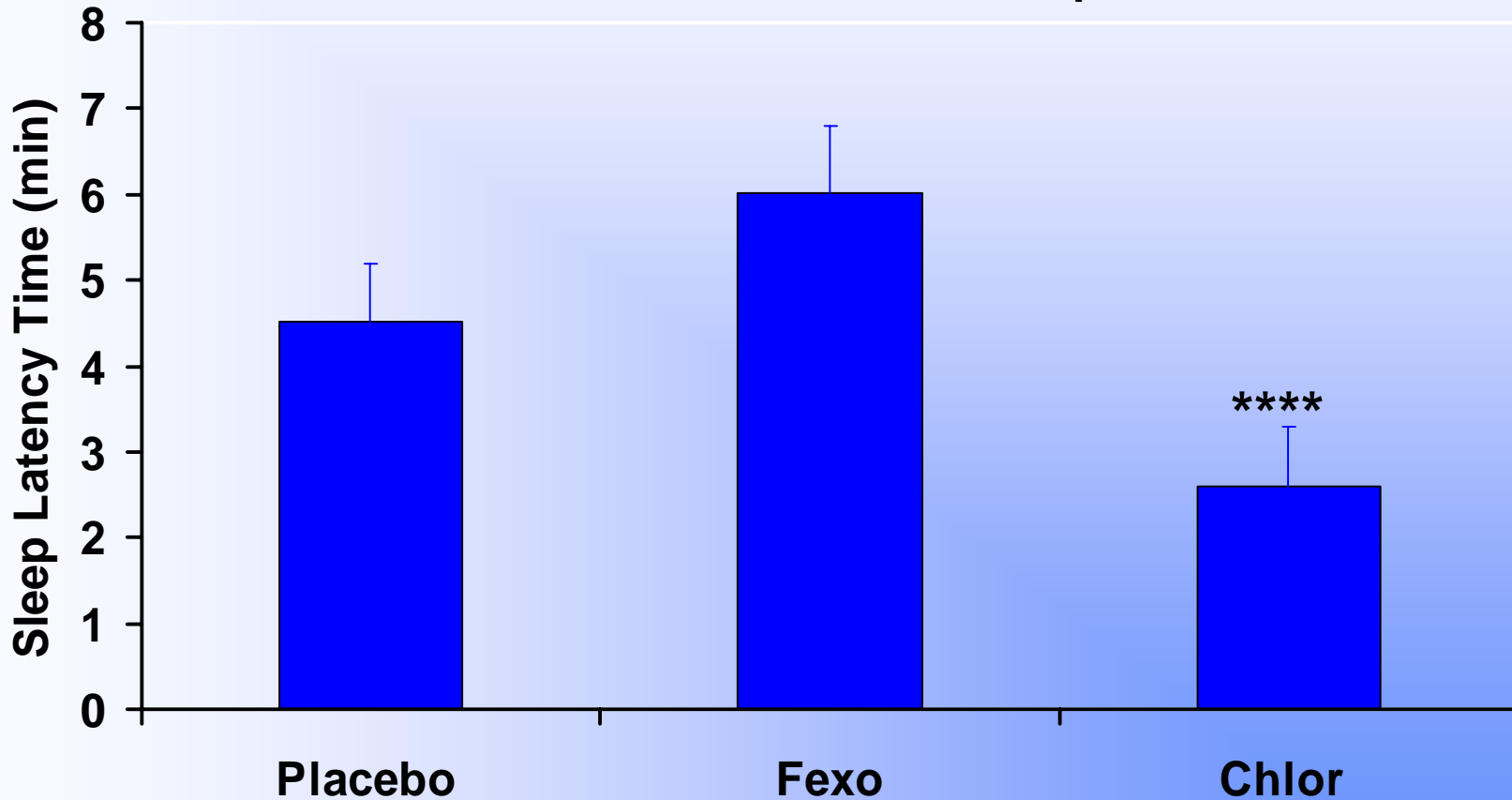
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Ease of falling asleep
10.5 h post dose

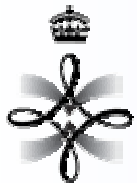
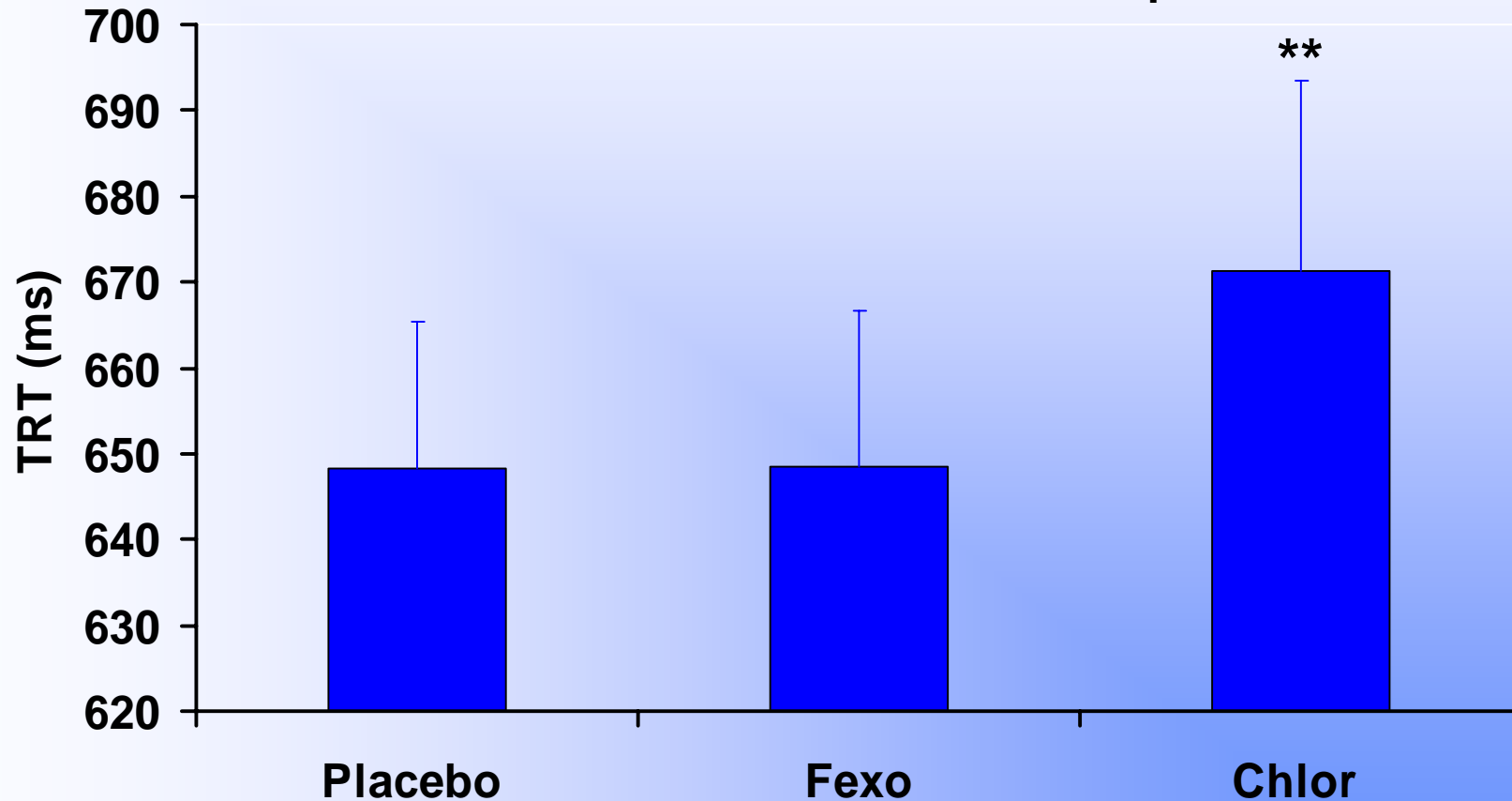


UniS Antihistamines: Japanese



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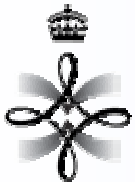
Change in reaction
time 8 h post dose



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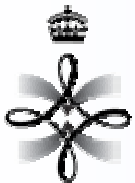
2002

Can experimental data on impairment be applied?





- Care needed to interpret and apply data
 - Epidemiology studies (Barbone et al., 1998)
 - Impairment due to disease or medication?
- Consider acceptable risk – pilot vs driver

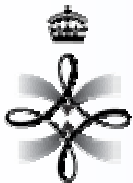




- Investment to establish acceptable impairment limits



- Need co-ordinated multidisciplinary approach





- Psychoactive medication associated with impaired performance
- Reliable impairment data from discrete tests
- Application of impairment data needs multidisciplinary approach

