

Drugs in the workplace
:psychopharmacological aspects
of the use of medicines.

Dr. Ian Hindmarch
Emeritus Professor of Human
Psychopharmacology,
University of Surrey, UK.

ian@psychopharma.co.uk

www.psychopharma.co.uk

Drugs in the workplace.

- Use, possession & trading in illicit drugs leads to criminal prosecution of the individual and a legal liability on behalf of the owner of the premises.
- The same liability does not exist in law, where prescribed or OTC drugs are concerned.

**HEALTH & SAFETY ISSUES re USE OF DRUGS
IN THE WORKPLACE ARE IDENTICAL
IRRESPECTIVE OF LICIT or ILLICIT
STATUS OF SUBSTANCE.**

*Effects of Prescribed and Over-the-
Counter Drugs on Workplace Performance*

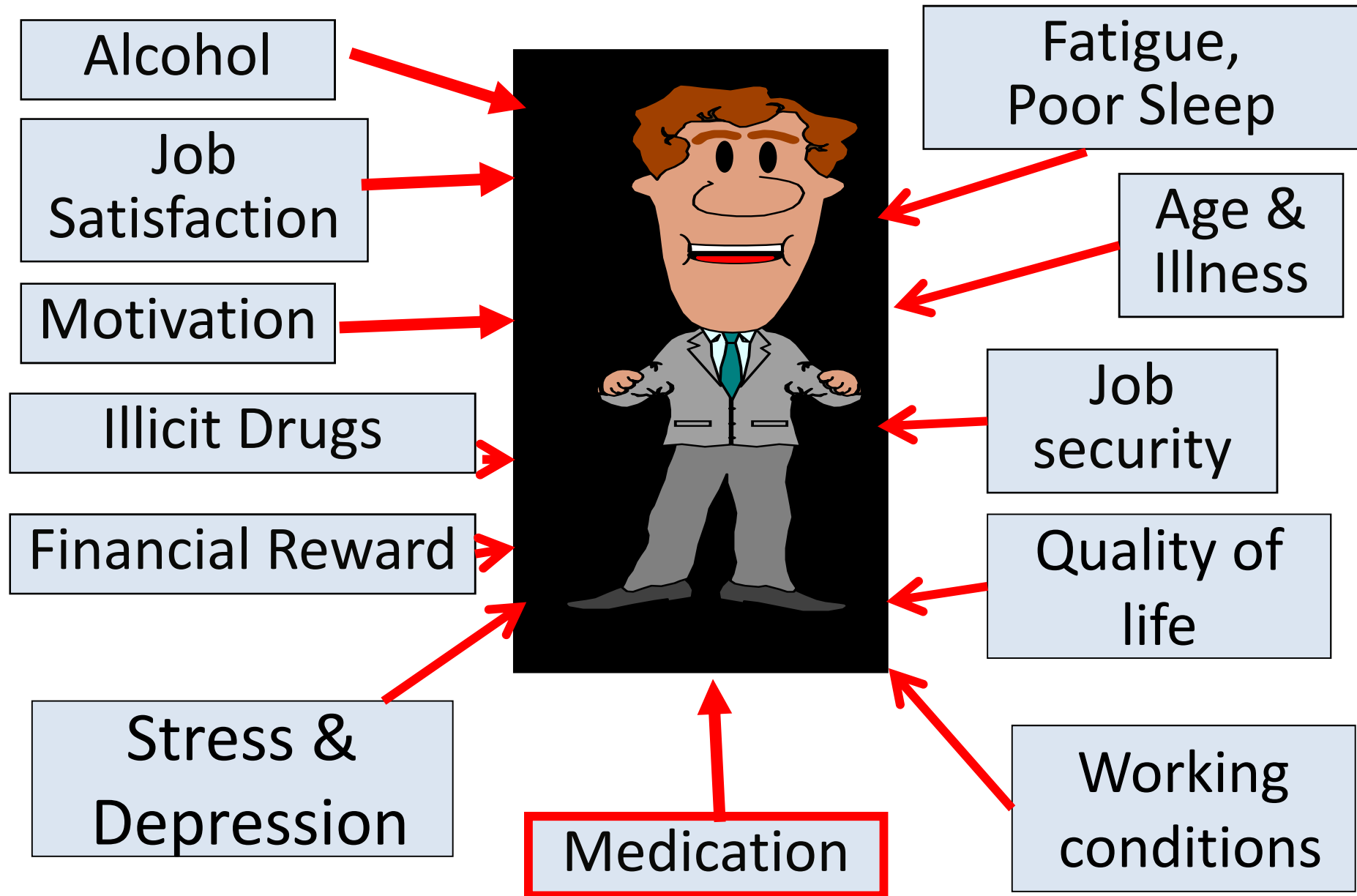
Ian Hindmarch

In Ghodse, H.(editor)

Addiction at work: tackling drug use and misuse in the workplace.

[2005] CHAPTER 7 pages 69-85; Gower, ALDERSHOT.

Some Factors Affecting Workers' Performance.



**ALL OF FACTORS AFFECTING WORKERS'
SAFE PERFORMANCE DIRECTLY INFLUENCED BY
ANY IMPAIRMENT OF COGNITION.
i.e. HOW INFORMATION IS ORGANISED.**

Henry HEAD 1861-1940

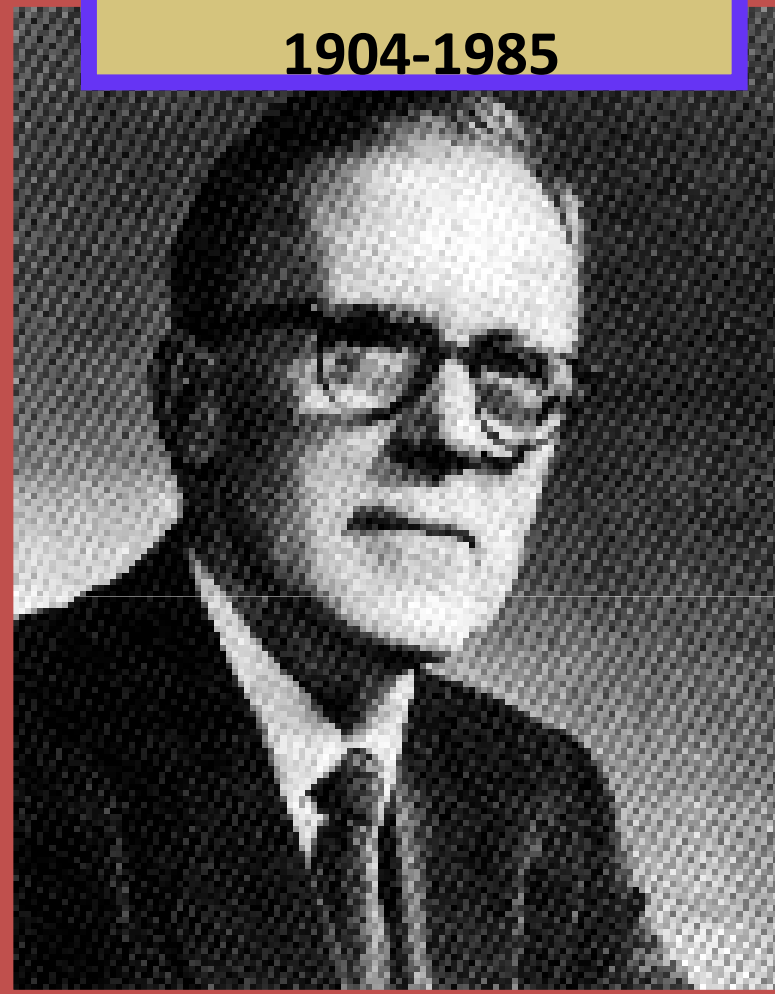
SCHEMA (-ATA) mental structures that represent
aspects of the environment
used to organise current information and to
structure experience to assist understanding

Egon Brunswik
1903-1955



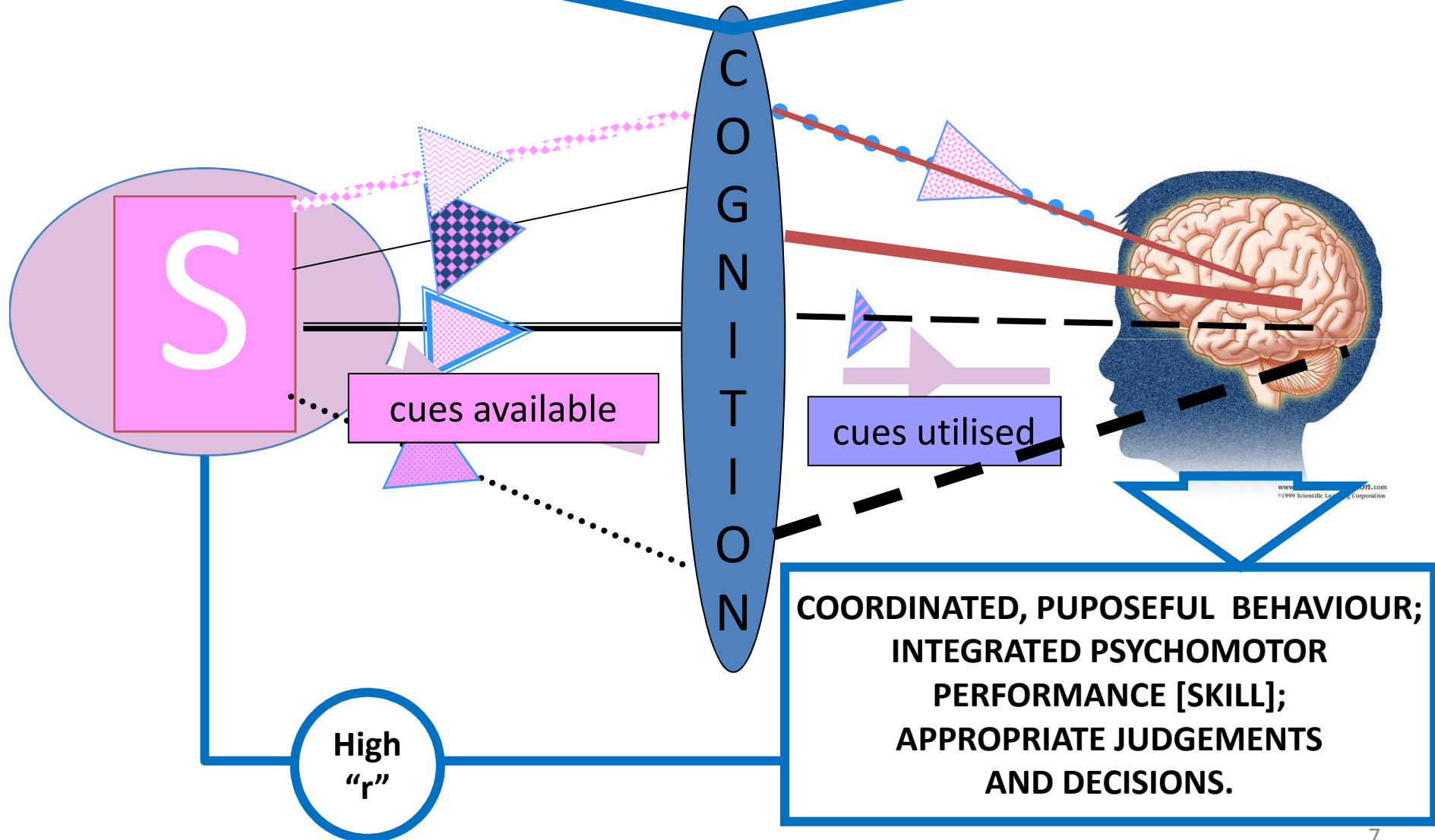
**'LENS MODEL' FOR COGNITIVE
PROCESSING OF INFORMATION.**

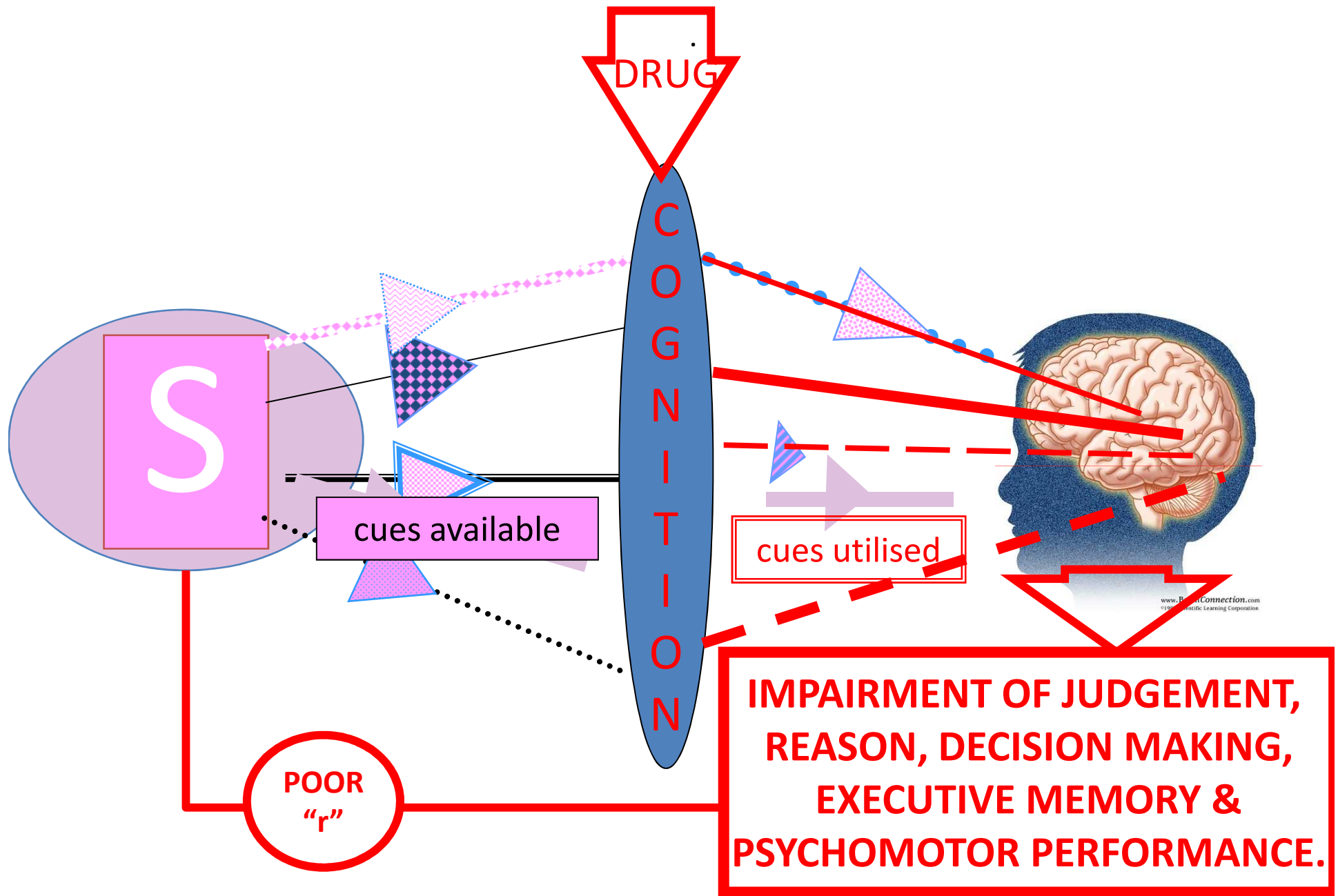
Donald O. Hebb
1904-1985



**COGNITIVE COMPETENCE
INITIATES NEURAL GROWTH**

**ORGANISATION INFLUENCED BY GENETIC PREDISPOSITIONS [40%]
and PRIOR EXPERIENCES, HABITS AND EXPECTATIONS [60%]**





NB. Era of the 'brainless mind' ended at the Royal Society 's 2006 meeting on ***'Mental Processes in the Human Brain'***.

DRUGS WITH A **DIRECT** NEUROPHARMACOLOGICAL ACTION ON THE BRAIN WILL HAVE A **DIRECT** EFFECT ON **COGNITION** and **PSYCHOMOTOR ABILITY**.

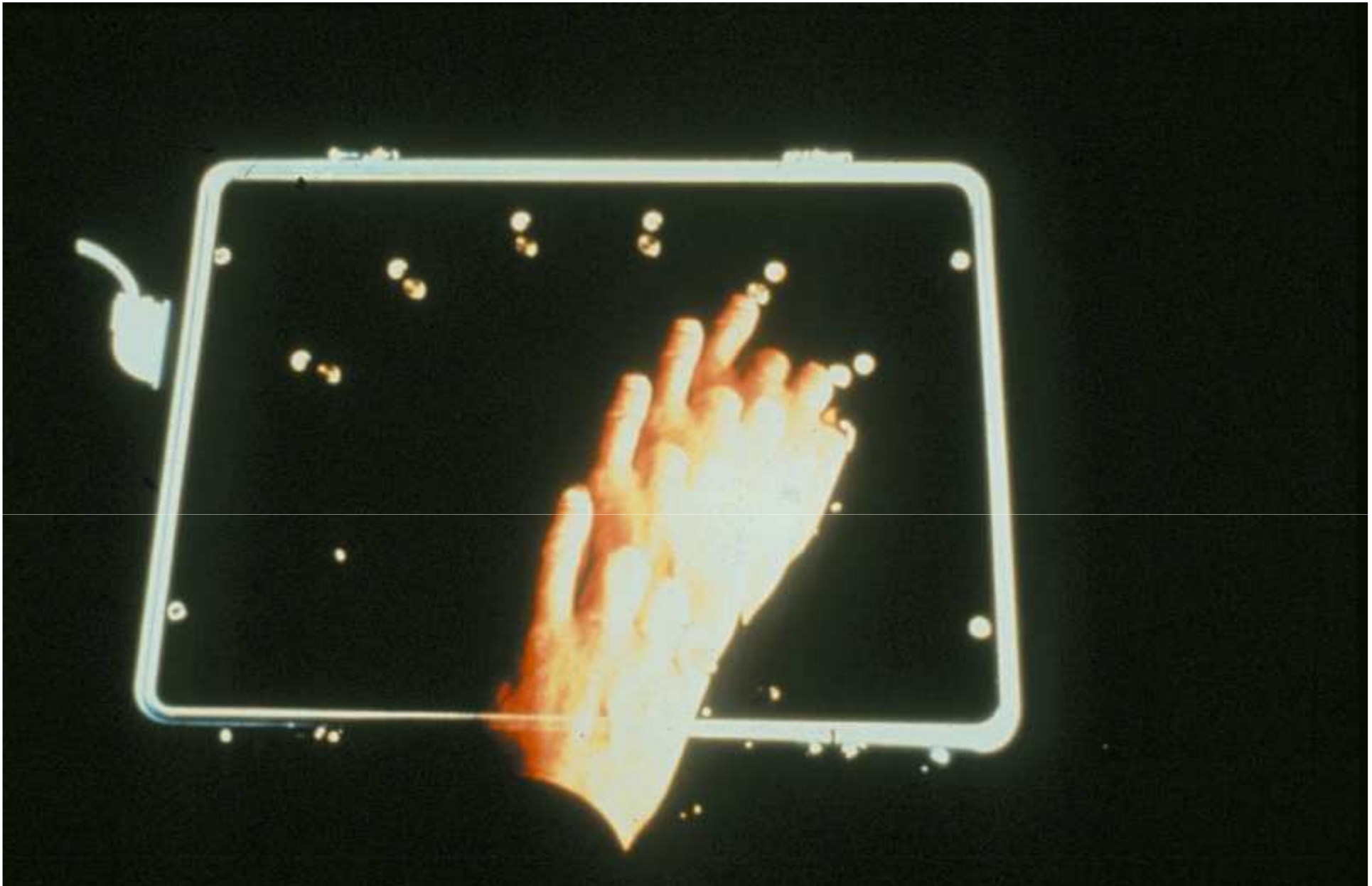
DRUGS WITH DIRECT NEUROPHARMACOLOGICAL ACTIVITY IN THE BRAIN INCLUDE:
ANTIHISTAMINES.
ANTIDEPRESSANTS.
DRUGS FOR ANXIETY SPECTRUM DISORDERS.
HYPNOTICS.

HOW ARE DRUG EFFECTS ON COGNITION MEASURED?

- BY ASKING PATIENT[VARs etc]
NOT RELIABLE as individual not aware of compromised function.
- PET, NMRI'S, etc {FMRI'S}
RELIABLE, but only receptor sites 'lit-up'.
- EEG,EPs, P300,CNVs, etc
RELIABLE, but need validating.
- PSYCHOMETRIC TESTS
MOST RELIABLE



**COGNITIVE and PSYCHOMOTOR FUNCTION
Measured objectively via PSYCHOMETRIC TESTS.**



LEEDS PSYCHOMOTOR TESTER; CRT,MRT,RRT.¹²



**I.BRAKE REACTION TIME MEASURED
DURING ON- THE- ROAD CAR DRIVING .**



II. BRAKE REACTION TIME MEASURED DURING ON- THE- ROAD CAR DRIVING .

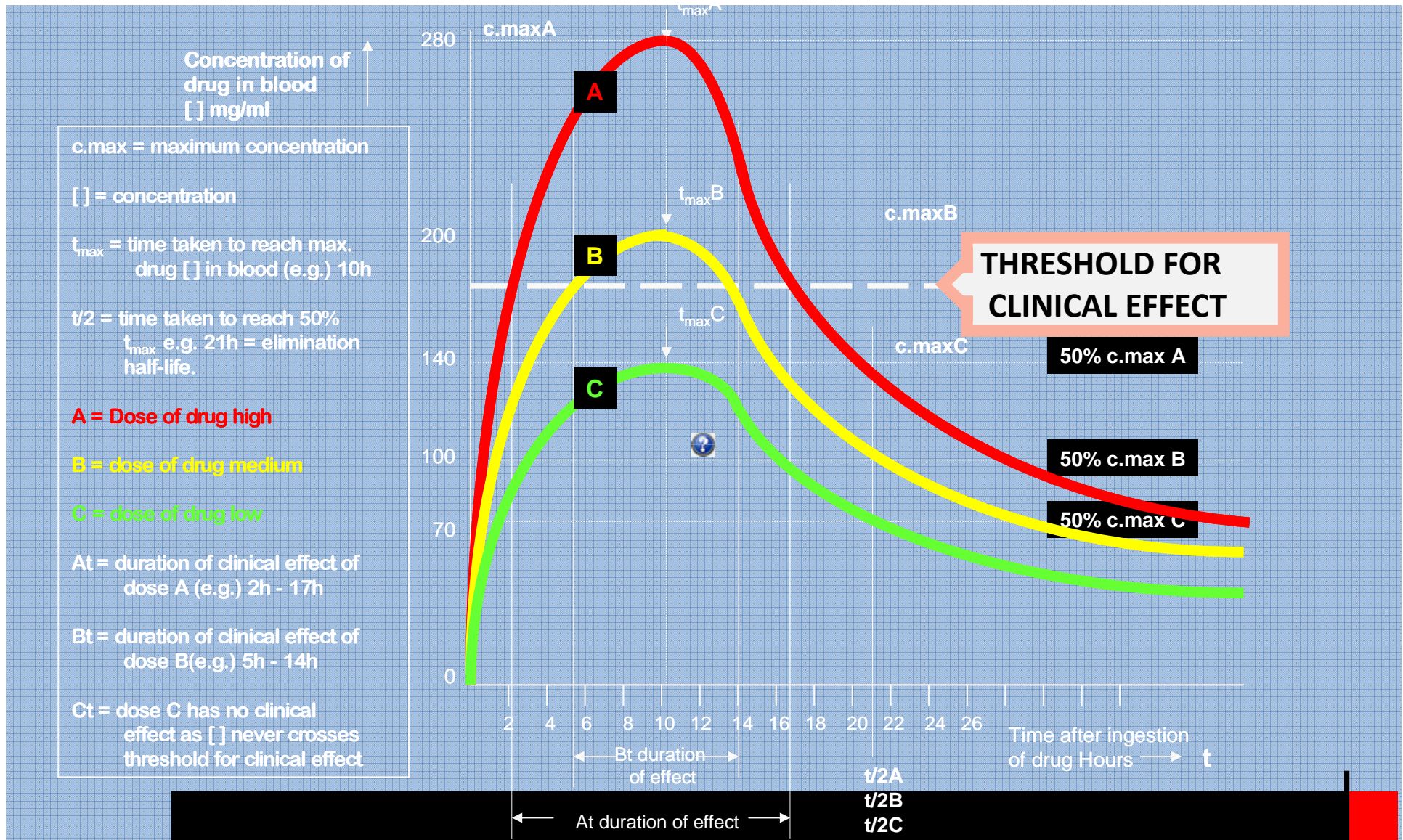
COGNITIVE FUNCTION

STROOP TEST

COGNITIVE FUNCTION

EXECUTIVE MEMORY
&
SHORT TERM STORAGE

AN IMPORTANT CAVEAT



HALF-LIFE & DURATION OF ACTION ARE **NOT** THE SAME .

**PSYCHOACTIVE MEDICATIONS IN THE WORKPLACE
INCLUDE:**

ANTIHISTAMINES.

ANTIDEPRESSANTS.

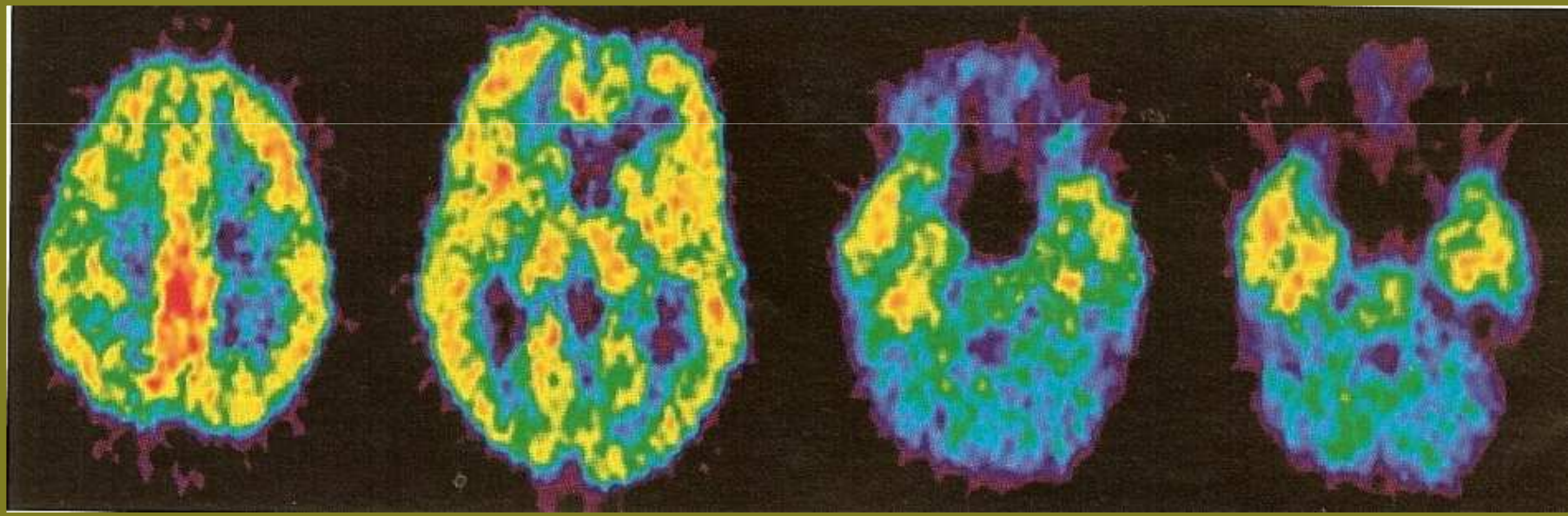
DRUGS FOR ANXIETY SPECTRUM DISORDERS.

HYPNOTICS.

WHY IS HISTAMINE SUCH AN IMPORTANT NEUROTRANSMITTER ?

**PLAYS CRUCIAL ROLE IN MAINTAINING AWARENESS
AND REGULATING CIRCADIAN CYCLICITY**

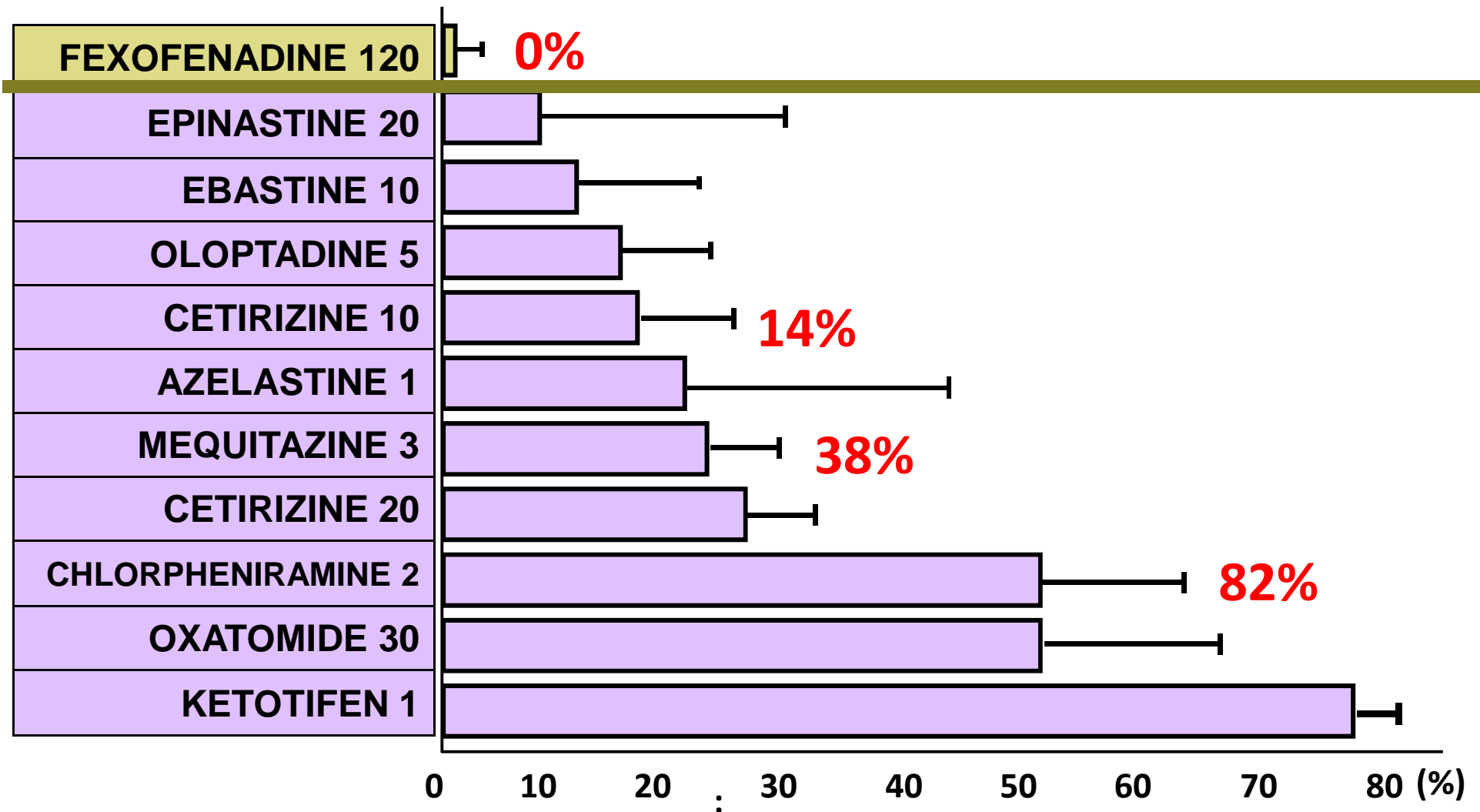
[Monnier et al.,1970 Tashiro et al. 2002]



Histamine-1 Receptors shown to be widely distributed in brain via PET scans & C11-doxepin [Yanai & Tashiro,2007: Pharm .Ther.113 1-15]

OCCUPANCY of CNS H-1RECEPTORS from PET STUDIES

% IMPAIRMENT OF PSYCHOMETRIC TESTS.



[Yanai K, 2007 J. Jap.Pediatric Soc. 48 (10) :1435]

Daily dose [8mg]chlorpheniramine causes COGNITIVE IMPAIRMENT \equiv 360ml of whisky.

Yanai et al 2002 : Br J Clin Pharm 53 : 296; Tagawa, et al 2000 : Jpn J Pharml 83 : 253,



She tried
to kill me .

... **crushed
promethazine
tablets**

... **became
drowsy and
fell asleep...**

The London Times, March 16th 2001

IMPAIRMENT AND ANTIHISTAMINES : SAFETY CRITICAL JOBS

TRAIN DRIVING SIMULATOR PERFORMANCE IMPAIRED BY KETOTIFEN 1mg

Minami et al 2007 (*Pharma Medica* 25,11)

AIR CRASHES IN PAST 6 years
ANTIHISTAMINES 100+; ANTIDEPRESSANTS 67+; CANNABIS 43
National Transportation Safety Board 2007; (USA.)

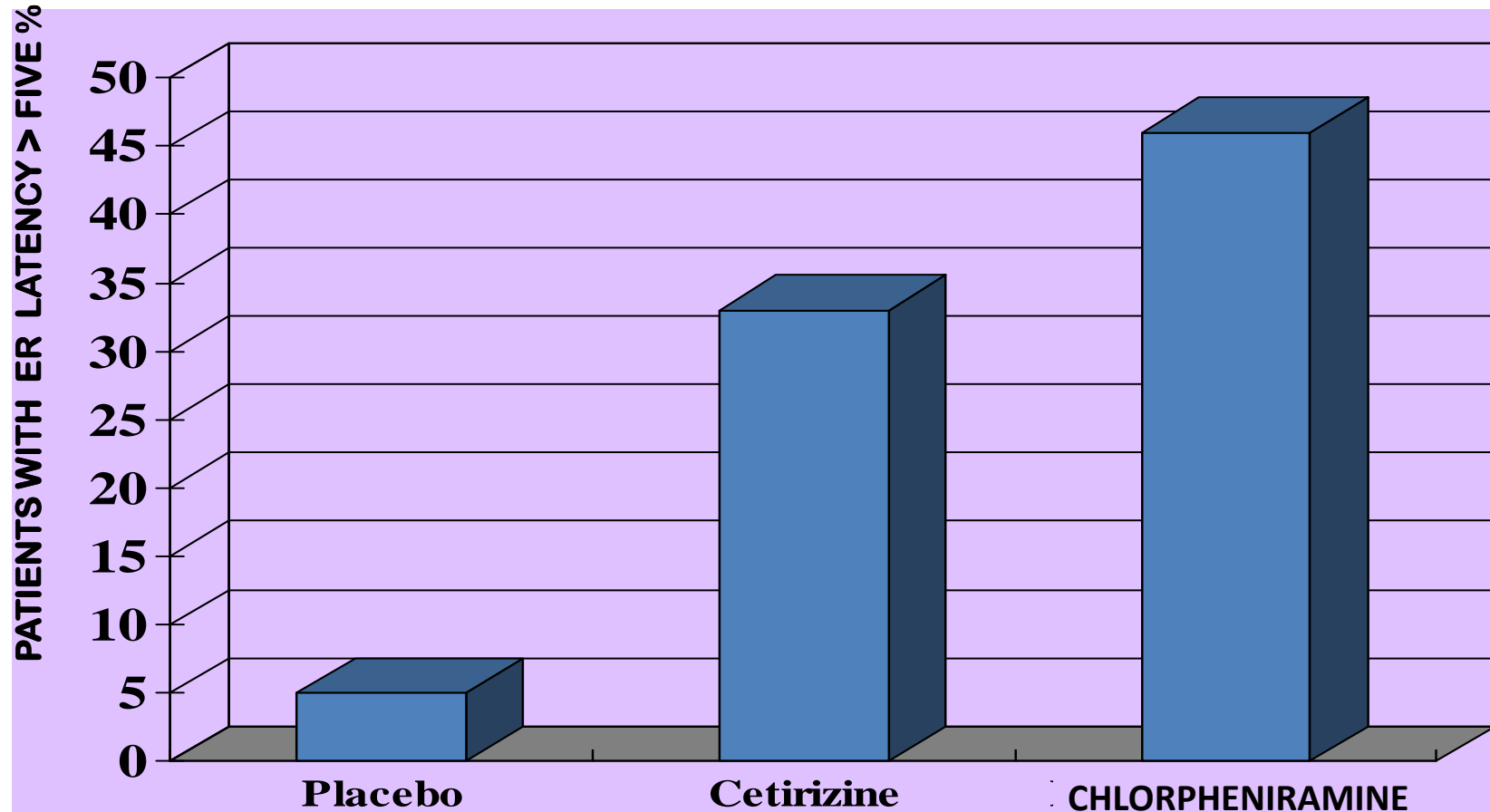
CHLORPHENIRAMINE, DIPHENHYDRAMINE, PROMETHAZINE, DOXYLAMINE, PHENIRAMINE FOUND IN FATAL AIR CRASHES

Sen et al 2007 (*Aviat Space Environ Med*78,514)

CETIRIZINE NOT FREE OF CNS
IMPAIRMENT AT RECOMMENDED DOSES
NOT APPROVED FOR AIR CREW
Nicholson +Turner,1998



IMPAIRMENT OF P300 EVOKED RESPONSE IN 7-14 y.o] WITH ALLERGIC RHINITIS [Ng et al.,2004 *Paediatrics* 113,116]



- IMPAIRMENT NOT REFLECTED IN SCHOOLCHILDREN'S SUBJECTIVE RATINGS OF TIREDNESS.

ALLERGIC RHINITIS ON EXAM DAY ☹
40% INCREASED RISK OF DROPPING EXAM GRADE

USING CHLORPHENIRAMINE ON EXAM DAY ☹
70% INCREASED RISK OF DROPPING EXAM GRADE.

Seasonal allergic rhinitis is associated with a detrimental effect on examination performance in UK teenagers: case-control study.

Walker et al.2007; J Allergy Clin Immunol 120,381

**HOWEVER; NO DATA OR RESULTS FROM ANY OTHER
ANTIHISTAMINES USED TO TREAT CHILDREN.**

PSYCHOACTIVE MEDICATIONS IN THE WORKPLACE

INCLUDE:

ANTIHISTAMINES.

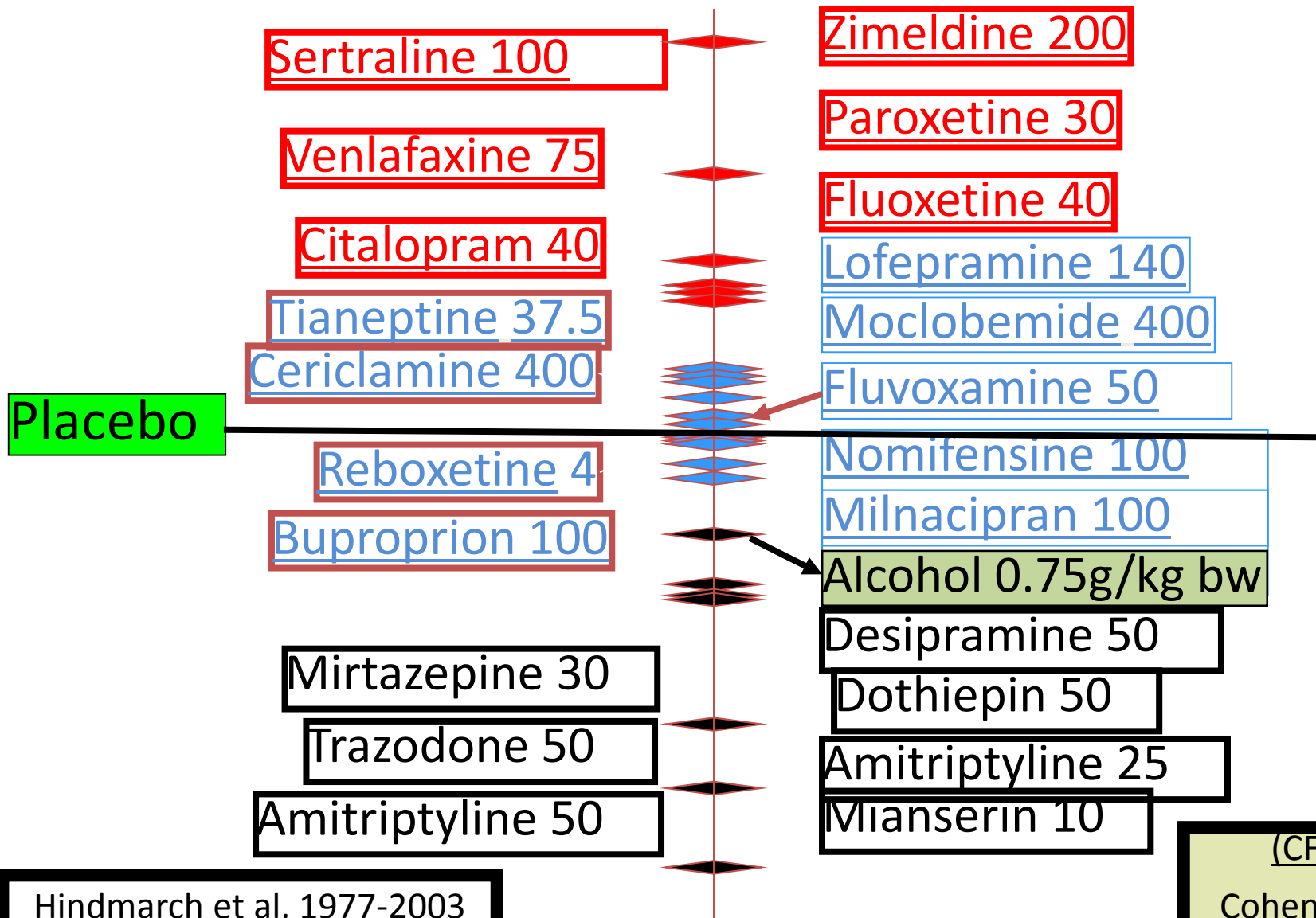
ANTIDEPRESSANTS.

DRUGS FOR ANXIETY SPECTRUM DISORDERS.

HYPNOTICS.

ACTIVATING, NEUTRAL, SEDATING,

COGNITIVE TOXICITY OF ANTIDEPRESSANTS (mg)

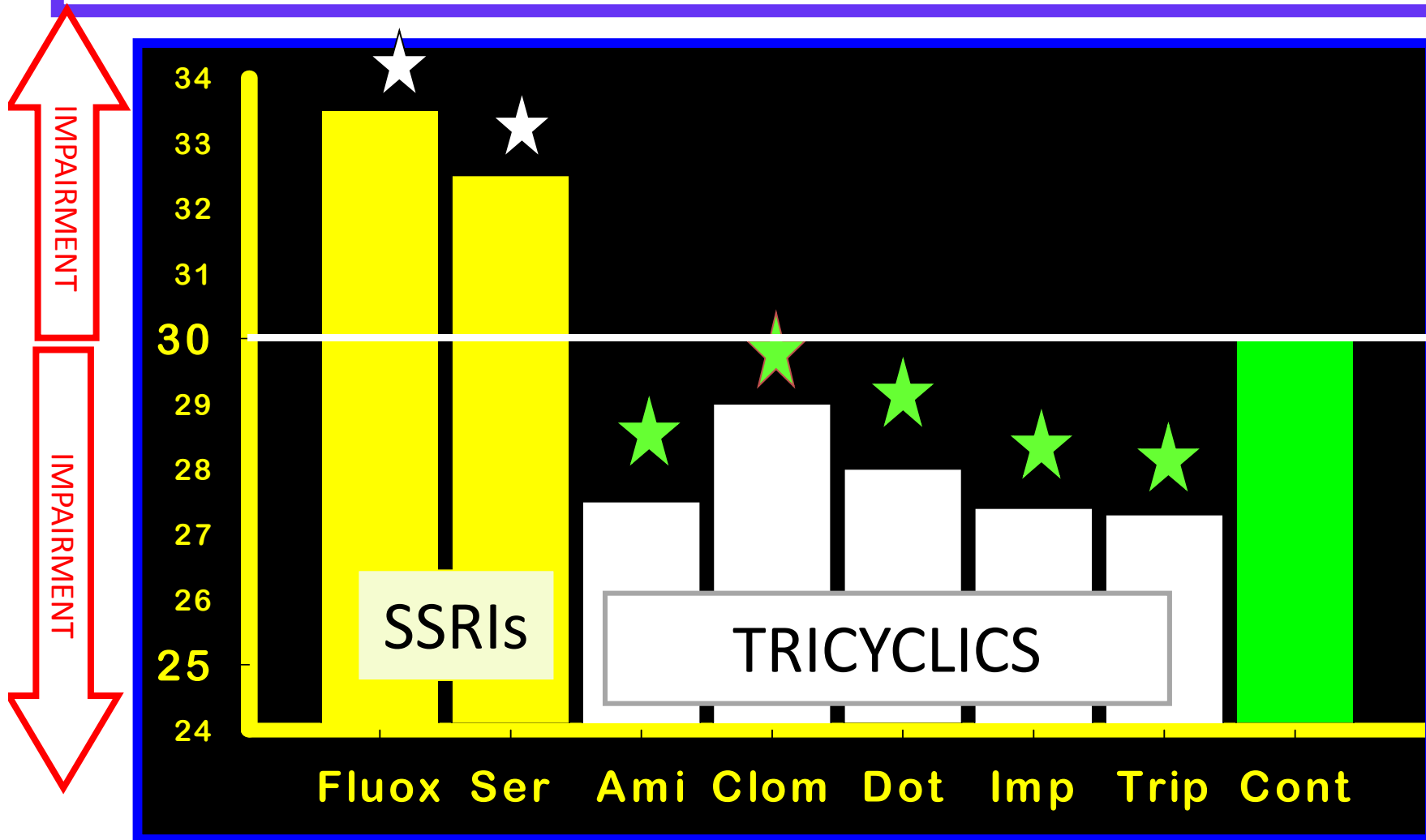


Placebo

Hindmarch et al, 1977-2003

(CFF)-
Cohen's "d"₇

**COGNITIVE IMPAIRMENT [Δ CFF] IN PATIENTS WITH MDD
MEDICATED FOR >3 months v. UNTREATED PATIENTS [Hale et al.1995]**



ACTIVATING ANTIDEPRESSANTS CAUSE COGNITIVE IMPAIRMENT.

- ❖ directly by causing ‘errors of commission’.
- ❖ indirectly via syndrome of activation and “jitteriness”
increased anxiety Ξ impaired cognition.

**PSYCHOACTIVE MEDICATIONS IN THE WORKPLACE
INCLUDE:**

ANTIHISTAMINES.
ANTIDEPRESSANTS.

DRUGS FOR ANXIETY SPECTRUM DISORDERS.
HYPNOTICS.

HOW CAN BETWEEN-DRUG COMPARISONS OF COGNITIVE IMPAIRMENT BE MADE?



PROPORTIONAL IMPAIRMENT RATIO[PIR]

$$\text{PIR} = \frac{a}{a+b} \text{ divided by } \frac{c}{c+d}$$

	Impairment	No- Impairment
Specific medication.	a	b
All other medications in database.	c	d

SHAMSI & HINDMARCH (2000) Hum.Psych.15,3-30

FLUVOXAMINE	0.03	0.08
PAROXETINE	0.14	0.44
ESCITALOPRAM	0.21	0.67
MOCLOBEMIDE	0.23	
VENLAFAXINE	0.31	
FLUOXETINE	0.46	1.63
SERTRALINE	0.53	5.33
CLOMIPRAMINE	0.79	
MIRTAZEPINE	1.25	
NEFAZODONE	1.36	
AMITRIPTYLINE	1.81	
MIANSERIN	2.62	

PROPORTIONAL IMPAIRMENT RATIOS (PIRs) : DRUGS USED IN SOCIAL ANXIETY DISORDER.

OBJECTIVE IMPAIRMENT OF COGNITIVE AND PSYCHOMOTOR FUNCTION.

PIRs for SSRIs

{TOTAL OF 28 DRUGS}

Hindmarch,2009; Int. J. Clin. Practice.

PSYCHOACTIVE MEDICATIONS IN THE WORKPLACE

INCLUDE:

ANTIHISTAMINES.

ANTIDEPRESSANTS.

DRUGS FOR ANXIETY SPECTRUM DISORDERS.

HYPNOTICS.

BEHAVIOURAL TOXICITY OF HYPNOTICS: PROPORTIONAL IMPAIRMENT RATIOS(PIR)

DRUG	Min dose (mg)	Max dose (mg)	t max (h)	t/2 (h)	PIR
Nitrazepam	2.5	10	2	25	0.6
Zolpidem	2.5	20	1.8	2	0.9
Temazepam	7.5	60	1.6	10	1.0
Zaleplon	10	20	1	1	1.0
Zopiclone	2.5	10	1.0	5	1.5
Flunitrazepam	1.0	2	1.2	15	2.6

**important lessons from psychiatry;
medico-legal implications of
prescribing a drug known to
impair cognition may be far reaching.**

[Lane & O'Hanlon, 1999; *German J. Psychiatry*]