

# **Psychological assessment of cognitive deficits in the elderly**

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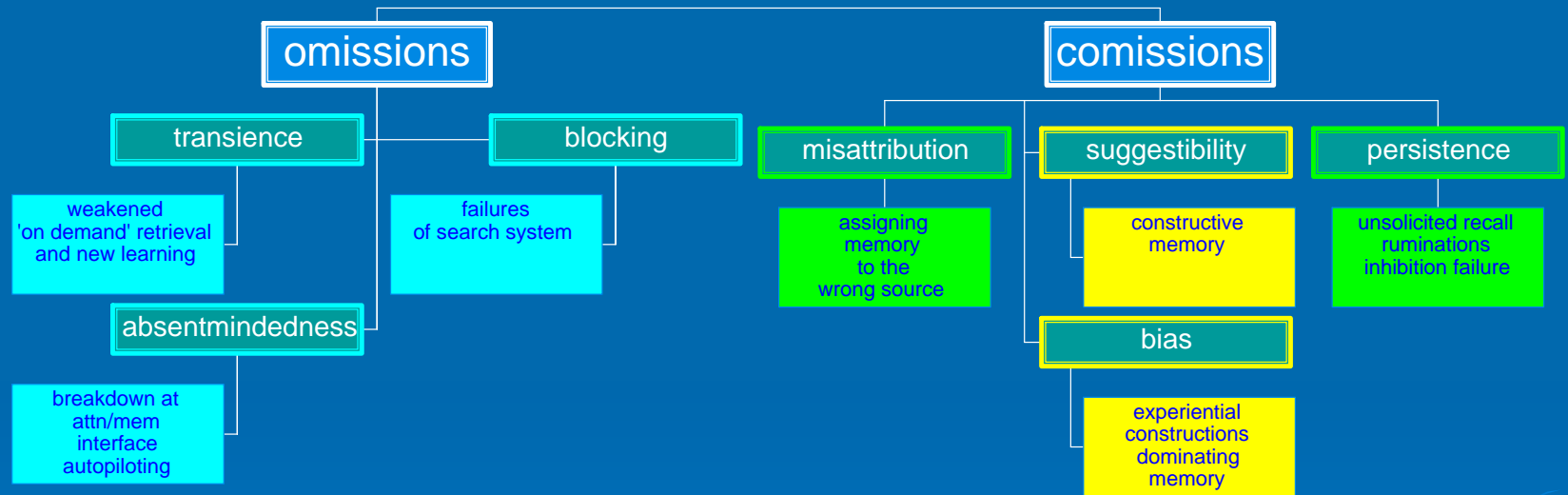
# Cognitive assessment

- Psychological models detail component cognitive processes
- Everyday cognition
  - What should we be measuring?
  - How should we be measuring?

# example: CDR battery

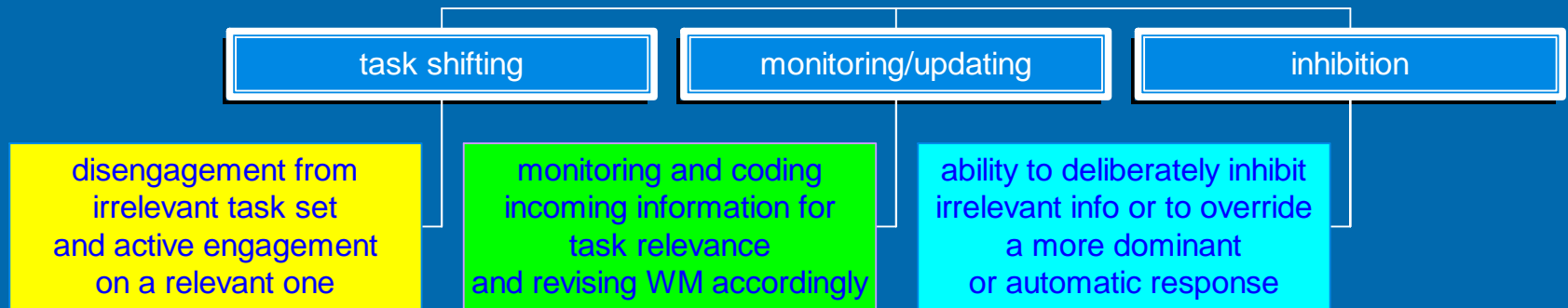
DOMAIN	TASK
Attention	RVIP
	Digit vigilance
Working memory	Spatial WM
	Numeric WM
Episodic Memory	Delayed word recognition
	Delayed picture recognition
Psychomotor and Perceptual processing	Simple RT
	Choice RT
	Critical Flicker Fusion
Speed of cognition	

# Age-related changes in memory



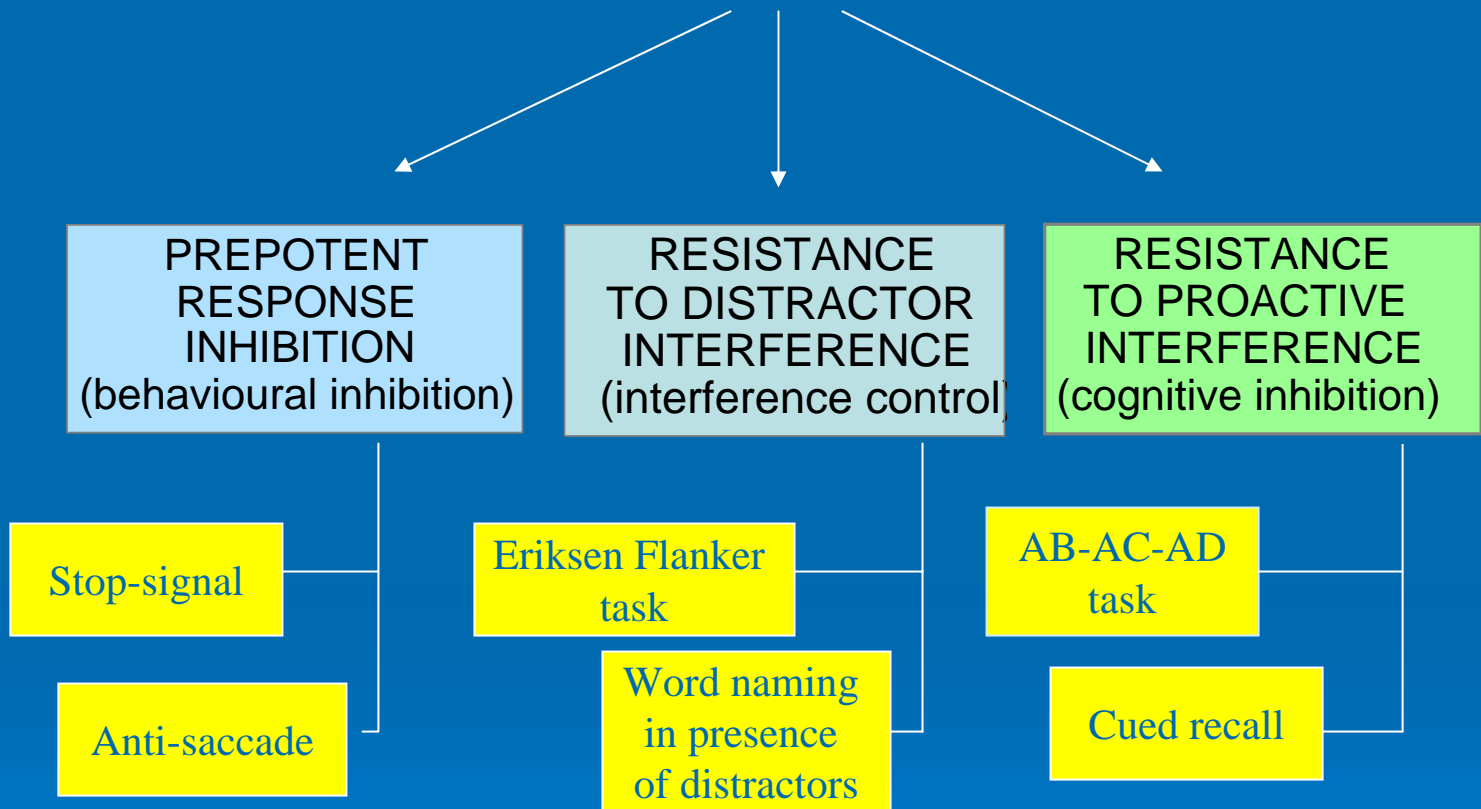
adapted from Schacter (2000)

# Age-related changes in attention



adapted from  
Miyake et al (2001)

# inhibition



# Prospective memory (PM)

- Ellis (1996) “The timely retrieval and implementation of a previously encoded intention”
- “I’ll definitely sort that paperwork on Monday when I get into work”
- “I must remember to take my medication after my evening meal”
- “I must remember to turn off the hotplate after cooking”

# Traditional paradigm

- ONGOING TASK + PM INTENTION
- ONGOING task: using assigned 'yes'/'no' buttons, decide whether letter string is a real word or a "nonword"
- Trachat
- Telephone
- History
- Descrim
- Liquid
  - 192 trials
- PM task: press a different button if any of the letter strings contain the letter "P"
  - 8 trials out of 192
  - additional processing required - attention needed

# Key measures

- Performance on the PM task: number of PM targets detected in the course of the ongoing (LDT) task
- Performance on the ongoing task: accuracy of responses and RTs to make response to letter strings
- COST to the ongoing task of maintaining a PM intention: { RT (LDT+PM) - RT (LDT) }

# Does cholinergic augmentation improve prospective memory?

- Successful PM retrieval requires attentional investment
  - Compounds that modulate attention should improve PM
- PM declines with age
  - If this decline is cholinergically-mediated, PM could benefit from procholinergic pharmacotherapies

# Standard Design

## *Design*

- Double blind placebo-controlled design
- Young adult non-smokers
- 18-35 yrs
  
- Nicotine nasal spray 1mg
- Placebo spray matched on sensory characteristics

**Ongoing Task: LEXICAL DECISION (192 trials)**

“Please decide whether each stimulus is a REAL word in English (e.g. TABLE) or a MADE-UP WORD (e.g. GATH)”

**Embedded PM task**

“Additionally, if you see  
the letter ‘p’  
then I want you to press the spacebar instead”

**Practice session**

1 block of 16 letter strings  
(no PM trials)

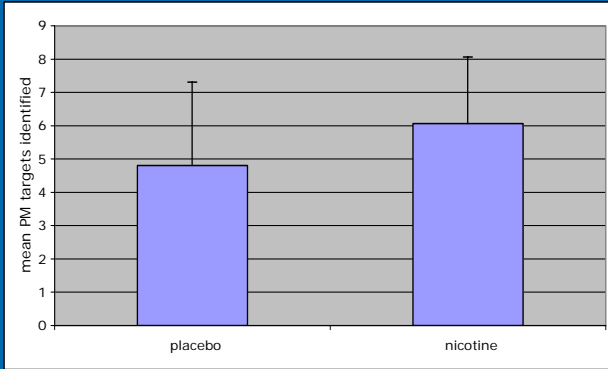
15 min (filled) delay

Intervention - eg. drug delivery/stress manipulation

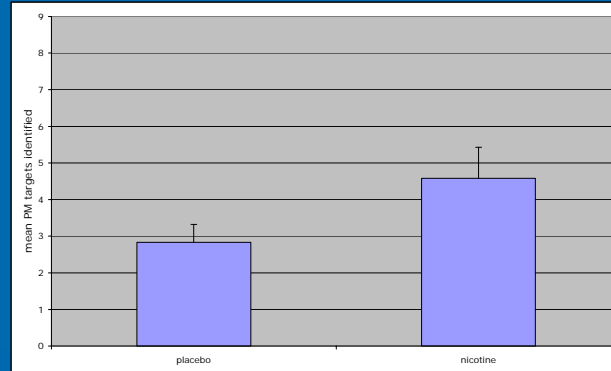
**LDT TRIALS (No reminders)**

(4 blocks of 48 trials - 8 PM targets)

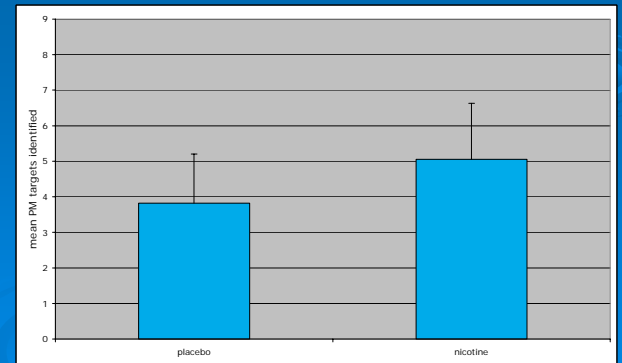
# Cholinergic augmentation and prospective memory



Rusted & Trawley, 2006



Marchant, Trawley & Rusted, 2008



Rusted et al, in press


# summary

- Nicotinic stimulation can reliably improve accuracy of prospective memory
- Procholinergic drugs have potential to enhance prospective memory
- Prospective memory function should be represented in the test batteries used to evaluate novel therapeutic compounds

- Cognitive testing: what to measure?
- Cognitive measures: how to measure?



# cognitive enhancement by losartan

- Angiotensin receptor blockers and angiotensin II receptor antagonists may have cognitive-enhancing properties
  - Modelling cognitive ageing in younger adults
  - Scopolamine 1.2 mg
- 

# cognitive enhancement by losartan

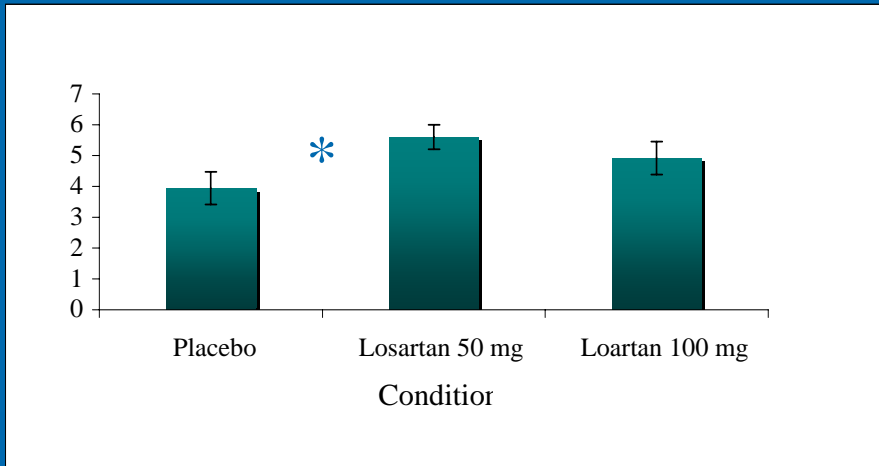
DOMAIN	TASK
Attention	Sustained attention (RVIP)
	Divided attention
	Selective attention (Stroop)
Visuo-spatial memory	Mental Rotation
	Spatial WM
	Complex figure
Memory	Immediate recall
	Delayed recall
	Prospective memory
Speed of processing	Lexical decision (LDT)
	Digit Symbol Substitution

# cognitive enhancement by losartan

## *Design*

- Double blind placebo-controlled design
- Four conditions - double dummy
  - Losartan 50 mg/Placebo (n=16)
  - Losartan 50 mg/Scopolamine 1.2 mg (n=16)
  - Placebo/Scopolamine 1.2mg (n=16)
  - Placebo/Placebo (n=16)

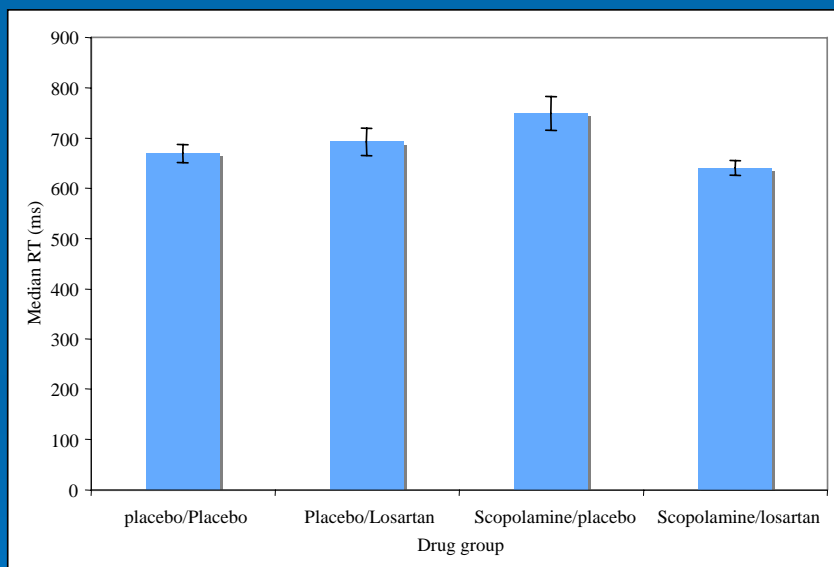
# Previous study



- Better PM accuracy following 50mg losartan [ $F(2,42)=3.11, p<.05$ ]

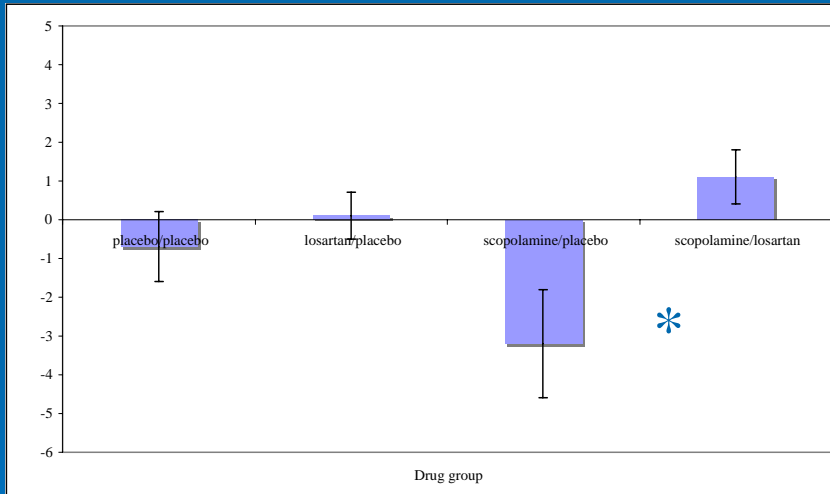
(Mechaeil et al, 2006)

# *Lexical Decision Task RT*



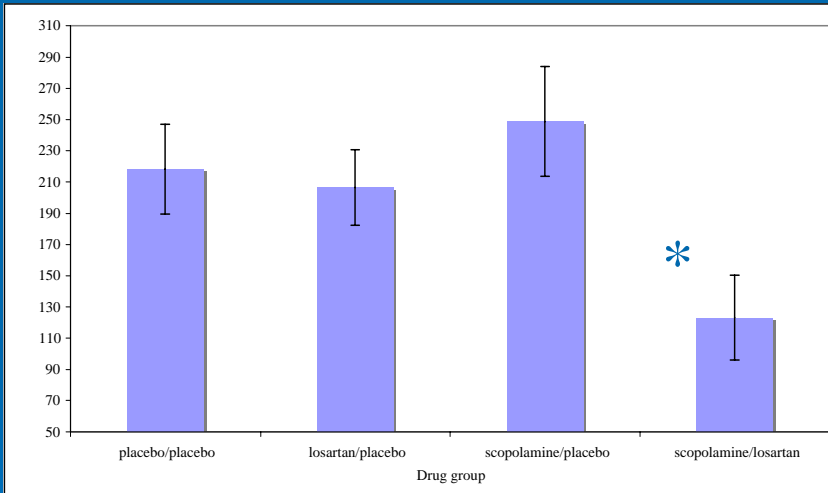
- significant group differences [ $F(3,52)=2.781, p=.05$ ]
- Bonferroni adjusted multiple comparisons - difference between scopolamine alone and scopolamine/losartan ( $p=.05$ )

# *Lexical Decision Task accuracy*



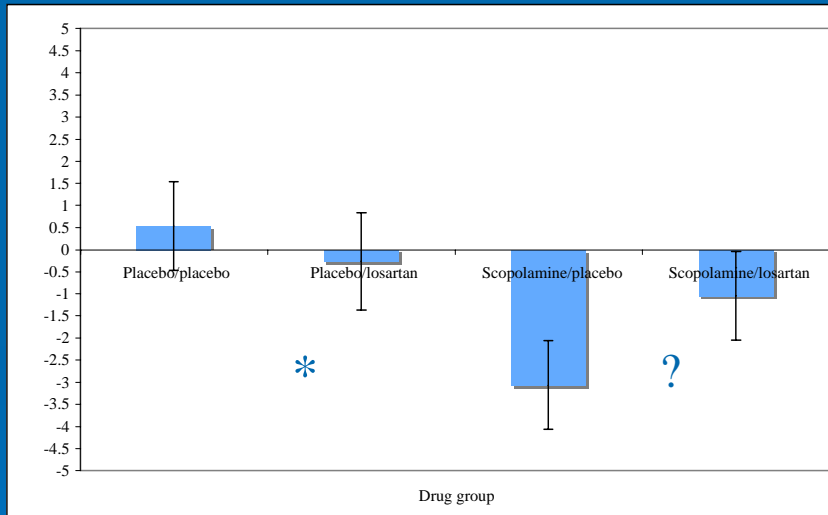
- Significant group difference for word stimuli only [F(3,55)=3.413, p=.02]
- Bonferroni adjusted multiple comparisons - difference between scopolamine alone and scopolamine/ losartan [p=.02]

# *cost of carrying a PM intention*



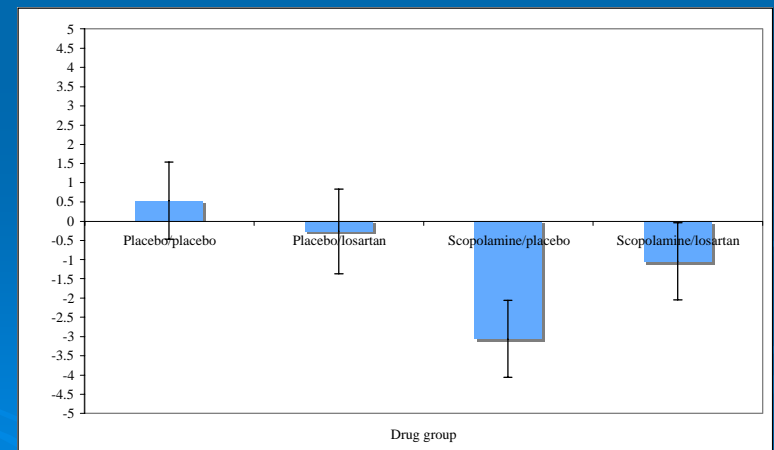
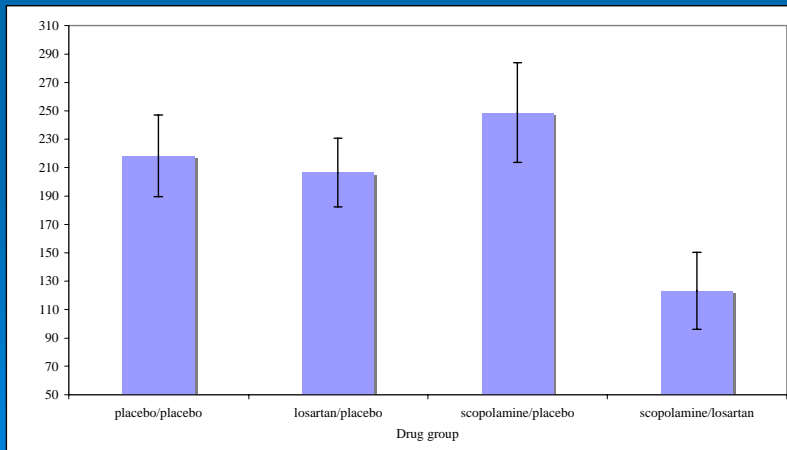
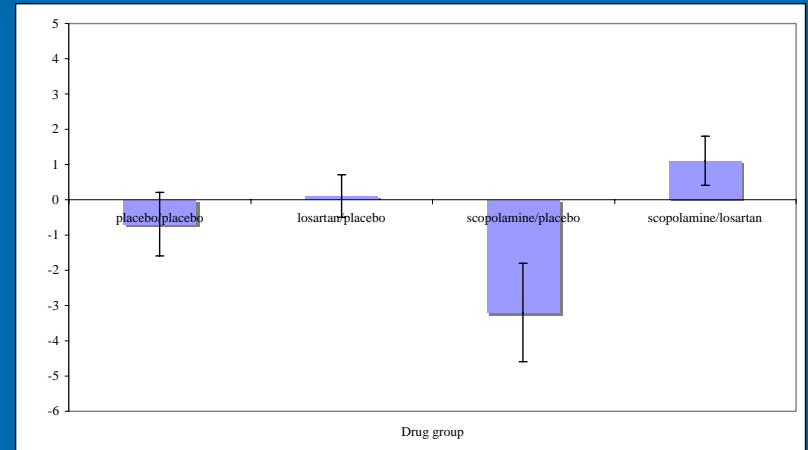
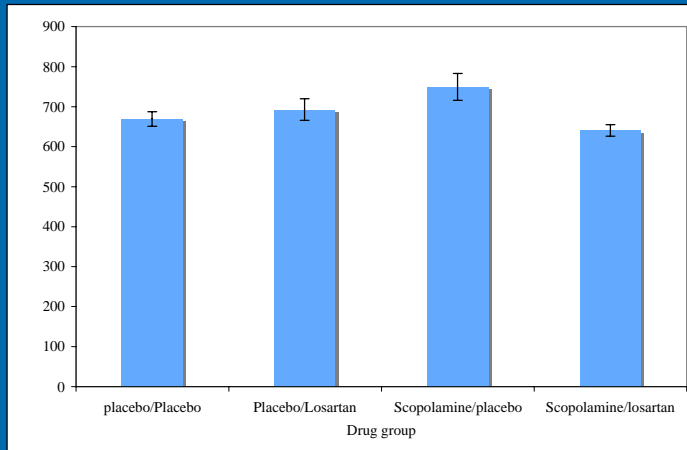
- Bonferroni adjusted comparisons - difference between scopolamine alone and scopolamine/losartan [p=.03]

# *spatial WM accuracy*



- trend towards a group difference [ $p=.07$ ]
- Bonferroni adjusted multiple comparisons - difference between the control group (placebo/placebo) and scopolamine alone [ $p =.08$ ]

# cognitive enhancement by losartan



# summary

- Losartan does have cognitive enhancing effects
- Improves performance on tasks engaging decision making and speed of processing
- Improvements are specifically associated with reversal of induced cognitive deficits / compromised systems
- These effects were not bound by cognitive domains and would have been missed with composite scores

# To conclude

- To properly profile potential cognitive enhancers, we should be using assessments that...
- ... broaden the task base and represent everyday memory needs
- ... collect the data in a way that enables a more sophisticated exploration of the profile of the compound

# Acknowledgements

## Nicotine studies

- Steve Trawley
- Natalie Marchant
  
- AB McNeil *for the gift of nasal sprays*

## Losartan studies

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- Anne Jackson
- Paul Gard
  
- BBSRC *special studentship funding to RM*