



## Training and plasticity of working memory and attention



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### WM training improves WM and attention

- Underlying mechanisms
- Summary of evidence

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### Outline

- Models of WM and attention
- WM and attention in ADHD
- WM training
  - Effects on WM and attention
  - Neural correlates

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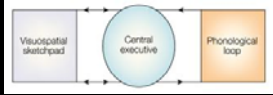
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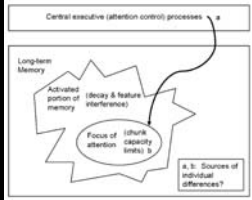
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# Working memory models



Alan Baddeley



Nelson Cowan

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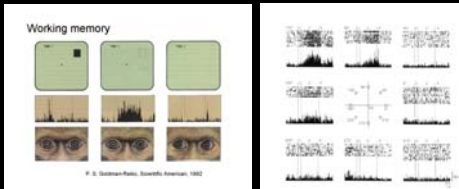
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# Neurophysiology of WM




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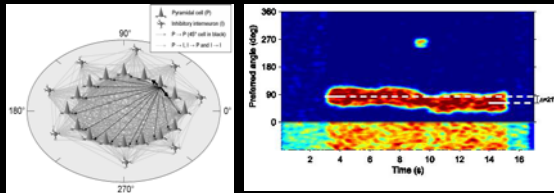
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# A working memory model



Compte et al. (2000)  
 Constantinidis, Wang (2004)  
 Edin et al. (2007) JOCN  
 Edin et al. (2009) PNAS

Sustained activity in WM tasks  
 Spatial code

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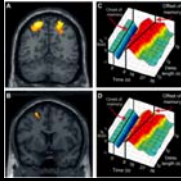
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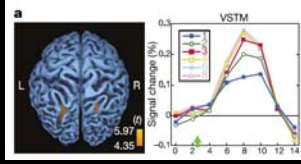
# Storage and sustained activity in humans

Sustained delay activity



Rowe and Passingham (2000) Science

Storage related activity



Todd and Marois (2004) Science

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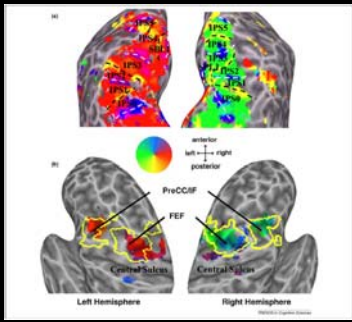
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# Spatially selective areas



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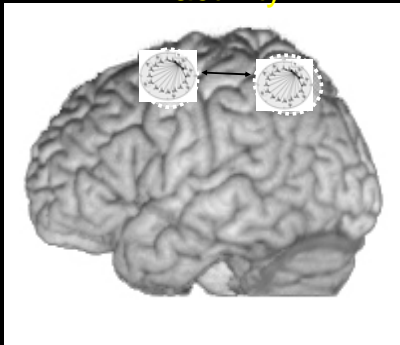
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# Spatial maps with sustained activity



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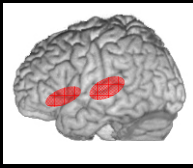
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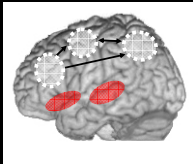
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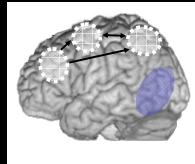
## WM networks



Verbal STM



Verbal WM



Visuospatial WM and STM

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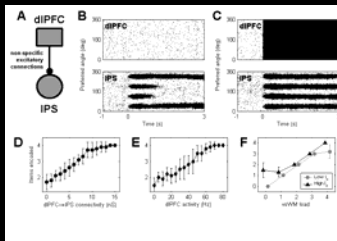
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## Prefrontal boosting



$$v = g([G^+ + G^-(p-1)]v + \mu_{\lambda})$$

- V = frequency
- G+ = effective connectivity from neurones coding for the same item
- G- = effective connectivity from neurones not coding for the same item (negative)
- p = number of maintained items
- U = external input

Edin et al. 2009 PNAS

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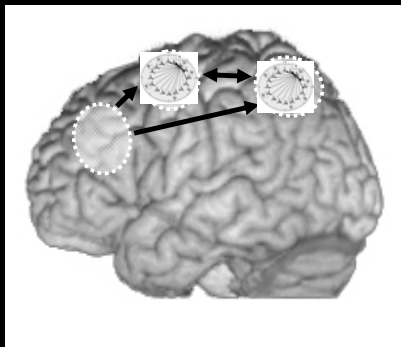
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## PFC + spatial maps in WM




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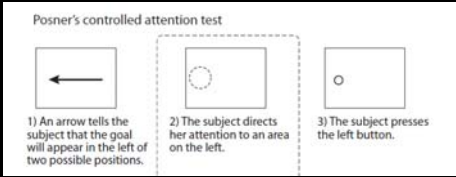
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# Attention

- The Attentional Network Task



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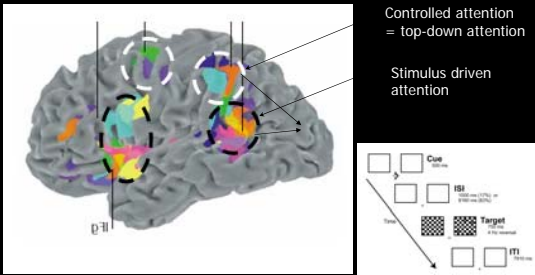
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# Attention systems



Corbetta and Shulman, 2002

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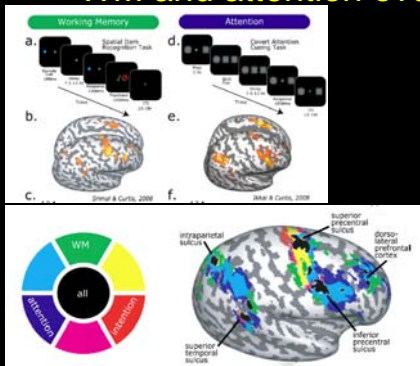
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# WM and attention overlap



Ikkai and Curtis (2010)

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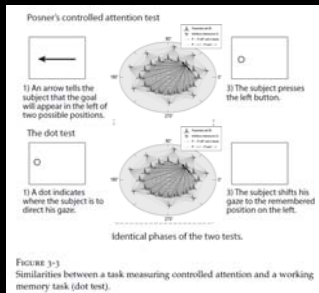
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## WM and attention mechanisms



Klingberg (2008) *The Overflowing Brain*

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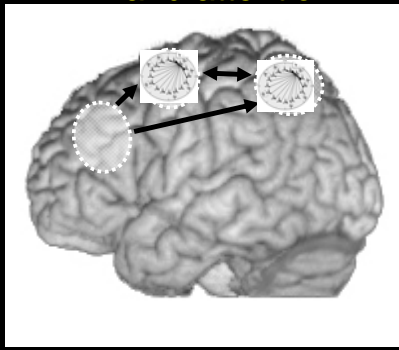
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## PFC + spatial maps in WM and attention



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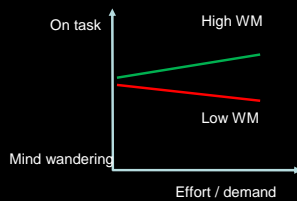
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## Inattention and WM



Kane et al., (2008) *Psychol Sci*

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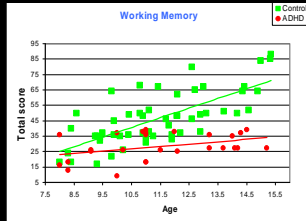
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## Clinical WM deficits

- ADHD
- Traumatic brain injury
- Stroke



Westerberg et al., 2004

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## WM deficit in ADHD

Memory Domain	Number of Studies	Number of Subjects		Standardized Mean Difference	t	95% CI	I <sup>2</sup> (95% CI)
		ADHD	NC				
Verbal Storage	16	476	847	0.47	7.8***	0.36 - 0.59	0 (0 - 52)
Verbal C.E.	13	475	557	0.56	4.1***	0.29 - 0.83	76 (58 - 86)
	12 <sub>a</sub>	464	538	0.43	4.5***	0.24 - 0.62	49 (1.5 - 73)
Spatial Storage	9	318	304	0.85	7.2***	0.62 - 1.08	45 (0 - 75)
Spatial C.E.	8	161	166	1.06	6.2***	0.72 - 1.39	56 (5 - 80)
	7 <sub>c</sub>	151	156	1.14	7.0***	0.82 - 1.46	50 (0 - 79)

ADHD = attention deficit hyperactivity disorder; NC = normal controls; C.E. = central executive.

46 studies on WM in ADHD Review by Martinussen et al. 2005

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## WM and ADHD review

Chamberlain et al. Biol. Psychiatry, 2011

	Effect size
Spatial working memory	0.9
Response inhibition	0.8
Executive planning	0.5
Attentional set-shifting	0.2

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## WM deficit (ES) span-board like tasks



	CANTAB WM	WAIS span-board
Dowson -04	1.15	-
Kempton -99	1.33	1.22
Barnett -01	1.45	1.06
Westerberg -04	-	1.34

Mean = 1.26 SD

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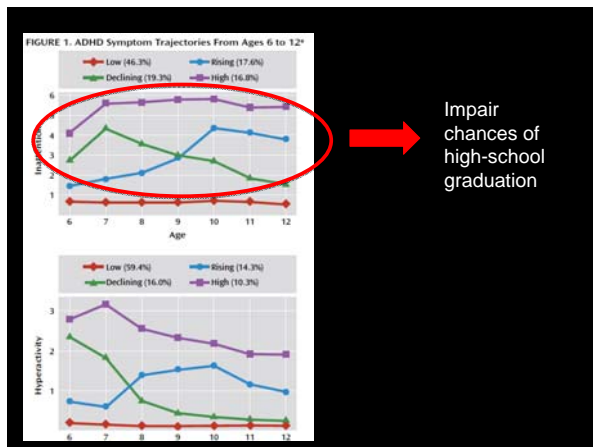
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## Inter-individual differences

WM capacity



- WM tasks
- Inattentive behavior
  - "Normal" distractability
    - Kane et al. 2007
    - Vogel et al. 2005
    - McNab and Klingberg 2008
  - ADHD inattentiveness
    - Barkeley 1997
    - Castellanos, Tannock (2002)
    - Martinussen et al. (2005)

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## Improving WM

- Teaching of rehearsal  
Butterfield et al. (1973)  
"On the theory and practice of improving short-term memory"
- Chunking and association to LTM  
Ericsson et al. (1980)  
"Acquisition of a memory skill"

Explicit

Implicit ?

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## WM training (Klingberg et al. 2005)



- Repeated performance with feedback (no strategy instruction)
- Adaptive difficulty close to capacity limit
- Mainly visuo-spatial WM tasks
- Intense and extensive
  - 35 min per day
  - 5 days/week
  - 5 weeks

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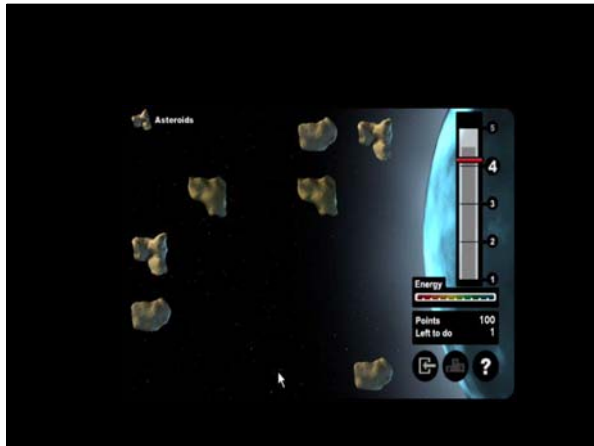
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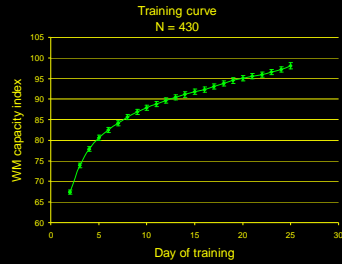
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## Improvement on trained tasks




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## Transfer from training?



WM training



- WM tasks
- Inattentive behavior
  - "Normal" distractability
  - ADHD inattentiveness
- Other cognitive tasks
  - Reasoning, problem solving
  - Inhibitory functions




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Journal of Clinical and Experimental Neuropsychology  
2002, Vol. 24, No. 6, pp. 781-791

1380-3395/02/2406-781\$16.00  
© Swets & Zeitlinger

### Training of Working Memory in Children With ADHD

Torkel Klingberg, Hans Forssberg, and Helena Westerberg  
Department of Neuropediatrics, Karolinska Institute, Stockholm, Sweden

Improvement in:

- Non-trained VSWM task (span-board)
- Problem solving (RPM)
- Response inhibition (Stroop)

• N = 14

Klingberg et al. 2002

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## Computerized Training of Working Memory in Children With ADHD—A Randomized, Controlled Trial

TORKEL KLINGBERG, M.D., Ph.D., ELISABETH FERNELI, M.D., Ph.D., PERNILLE J. OLESEN, M.Sc., MATS JOHNSON, M.D., PER GUSTAFSSON, M.D., Ph.D., KERSTIN DAHLSTRÖM, M.D., CHRISTOPHER G. GILLBERG, M.D., Ph.D., HANS FORSSBERG, M.D., Ph.D., AND HELENA WESTERBERG, L.P., Ph.D.

- 53 children (9 girls, 44 boys)
- 7-12 years of age (mean 9.9 years)
- ADHD

Klingberg et al. 2005

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## Randomized, double blind design Active control group

### Treatment

- Adaptation of difficulty level



### Control

- Easy trials (level 2)



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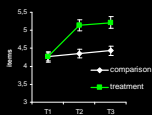
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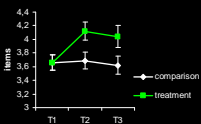
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## Transfer to working memory



### Span-board



### Digit-span

"2 8 4 7 2 9"

"9 2 7 4 8 2"

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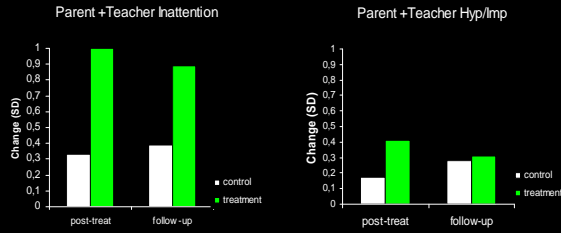
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## Inattentive symptoms (DSM-IV)



Effect size (Cohen's delta) inattention = 0.7

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## Working memory deficits can be overcome: impacts of training and medication on working memory in children with ADHD

Holmes, J, Gathercole, et al. (2009) App. Cogn. Psych.

Children with ADHD, off or on medication  
Automated working memory assessment (AWMA)

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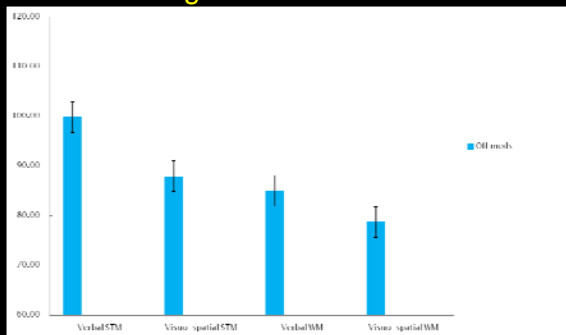
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## Training children with ADHD



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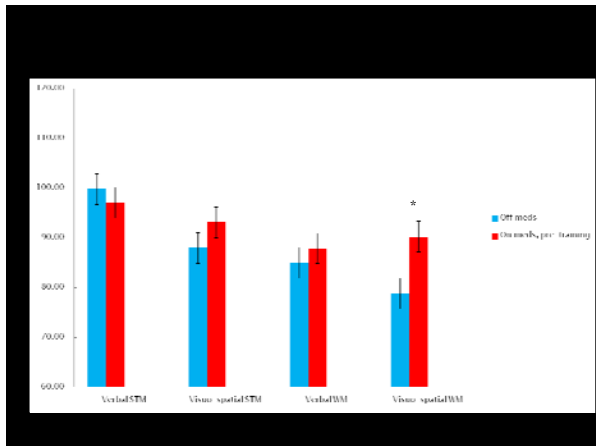
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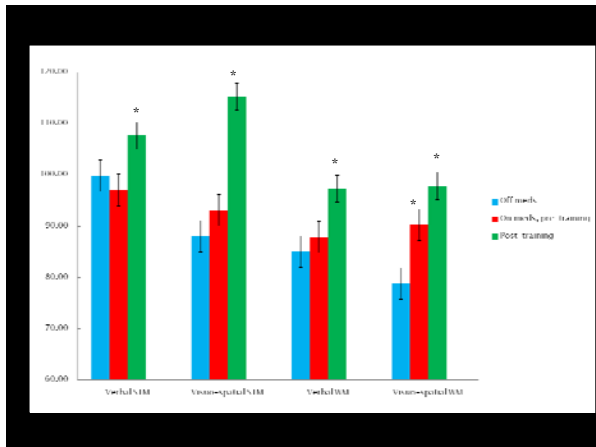
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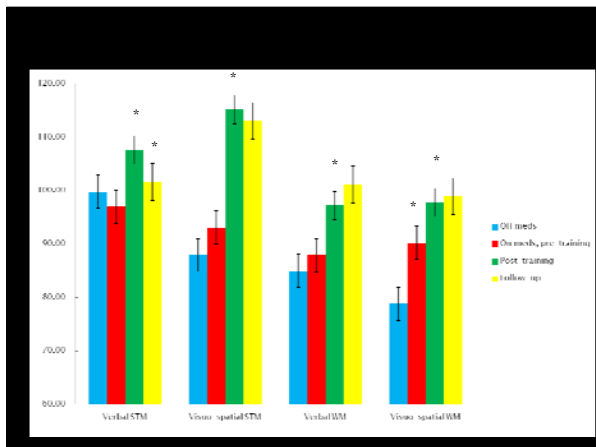
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## Adaptive training leads to sustained enhancement of poor working memory in children

Joni Holmes,<sup>1</sup> Susan E. Gathercole<sup>2</sup> and Darren L. Dunning<sup>2</sup>

<sup>1</sup> Division of Psychology, University of Northumbria, UK  
<sup>2</sup> Department of Psychology, University of York, UK

Developmental Science 2009

### Subjects

- 345, 9-10 year old children screened with WM tests
- <15th percentile included
- N = 42

Randomized, controlled, blinded design

### Intervention

- Training group, (Klingberg, 2005) (n=22)
- Control group (easy WM tasks) (n=20)
- Both groups receive 25 days of training over 5-6 weeks

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## Outcome measures

pre, post, 6 month follow-up

- Working memory (AWMA, 8 subtests)
- Instruction WM
  - “Put the blue ruler in the red folder and touch the yellow pencil”  
– Gathercole et al. (in press) Appl. Cogn. Psych.
- IQ
  - Wechsler Abbreviated Scale of Intelligence
- Mathematical reasoning
  - Wechsler Objective Number Dimensions
- Word reading
  - Wechsler Objective Reading Dimensions

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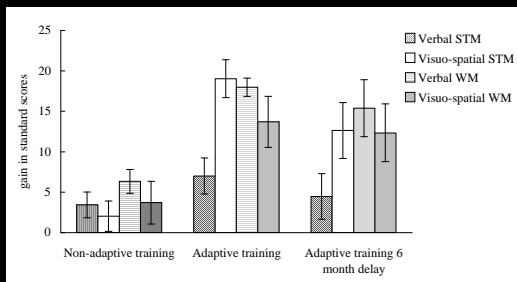
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## Transfer to WM



Holmes, Gathercole & Dunning 2009.

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## Results

	Post training	6-month followup
AWMA (verb WM+VS)	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Instruction WM	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
IQ Wech. Abbr.	<input type="checkbox"/>	<input type="checkbox"/>
Word reading	<input type="checkbox"/>	<input type="checkbox"/>
Mathematics	<input type="checkbox"/>	<input checked="" type="checkbox"/>

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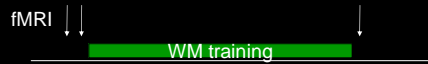
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## Neural correlates of WM training

### Experiment 1



Olesen, Westerberg, Klingberg (2004) Nature Neurosci.

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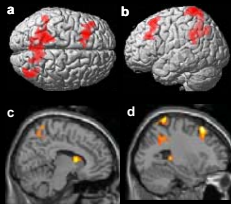
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### Experiment 2




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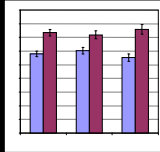
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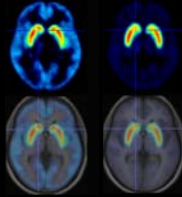
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## Dopamine and WM training

- 13 healthy, young adults
- 5 weeks of training (Klingberg et al., 2005)
- Measurement of verbal and visuospatial WM
- fMRI during performance of WM tasks
- PET of D1 and D2 binding, before and after



D1 SCH23390 D2 Raclopride



McNab et al. Science 2009

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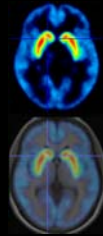
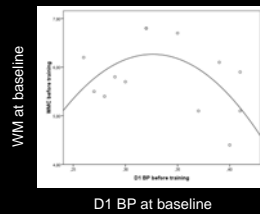
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## D1 BP vs WM at baseline

Linear model:  $y = a + \beta_1 x$   $r^2=0.09$ ;  $p = 0.33$   
Quadratic model:  $y = a + \beta_1 x + \beta_2 x^2$   $r^2=0.34$ ;  $p = 0.12$   
 $b_2$  estimate  $p = 0.08$



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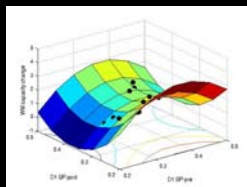
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## DA1 BP change vs WM change

Linear model:  $y_2 - y_1 = (a + \beta_1 x_2) - (a + \beta_1 x_1) = \beta_1 (x_2 - x_1)$   $r^2=0.42$ ;  $p=0.016$

Quadratic model:  $y_2 - y_1 = (a + \beta_1 x_2 + \beta_2 (x_2)^2) - (a + \beta_1 x_1 + \beta_2 (x_1)^2)$   $r^2=0.75$ ;  $p=0.001$   
 $\beta_1$  estimate  $p = 0.002$   
 $\beta_2$  estimate  $p = 0.005$



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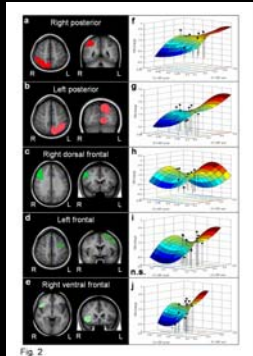
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## DA1 BP change vs WM change



McNab et al. 2009

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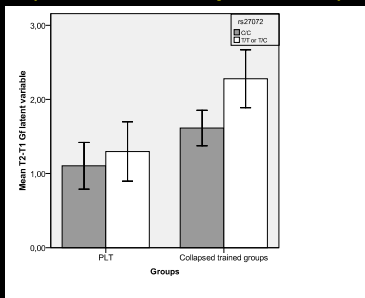
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## DAT1 and plasticity (and development?)



Söderqvist et al. (in press)

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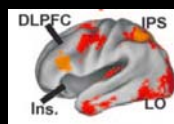
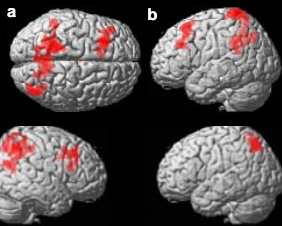
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Working memory training  
(Olesen, Westerberg, Klingberg, 2004)

Expert "concentration" meditation  
Brefczynski-Lewis, Davidson et al. 2007




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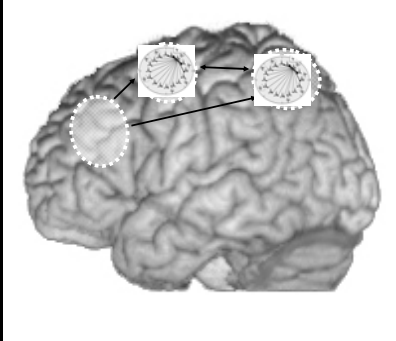
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## Plasticity of the WM and attention networks



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## Conclusions

Training of working memory:

- Improves non-trained measures of WM capacity
  - Klingberg et al. 2002, Klingberg et al. 2005, Gibson et al. 2007, Lucas et al. 2008
  - Westerberg et al. 2007, Westerberg et al. (2008), Holmes et al. (2009)
- Decreases inattentive symptoms
  - Klingberg et al. 2005, Gibson et al. 2007, Lucas et al. 2008
  - Westerberg et al. 2008, Green et al. 2009, Hardy et al. 2009
- Is associated with plasticity of parietal and prefrontal cortex, possibly including D1
  - Olesen et al. 2004; Westerberg and Klingberg 2007; McNab et al. (2009)

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