Neuroscience 100

Lesson 6: Memory

What is Alzheimer's ?

- Alzheimer's disease (AD), also known as Senile Dementia of the Alzheimer Type (SDAT) or simply Alzheimer's is the most common form of dementia. This incurable, degenerative, terminal disease was first described by a German psychiatrist and neuropathologist Alois Alzheimer in 1906 and was named after him.
- Alzheimer's disease (AD) is a slowly progressive disease of the brain that is characterized by impairment of memory and eventually by disturbances in reasoning, planning, language, and perception.
- Many scientists believe that Alzheimer's disease results from an increase in the production or accumulation of a specific protein (beta-amyloid protein) in the brain that leads to nerve cell death.

Signs & Symptoms:

- Memory loss for recent events
- Progresses into dementia → almost total memory loss
- Inability to converse, loss of language ability
- Affective/personality disturbance (fatuous, hostile)
- Death from opportunistic infections, etc.

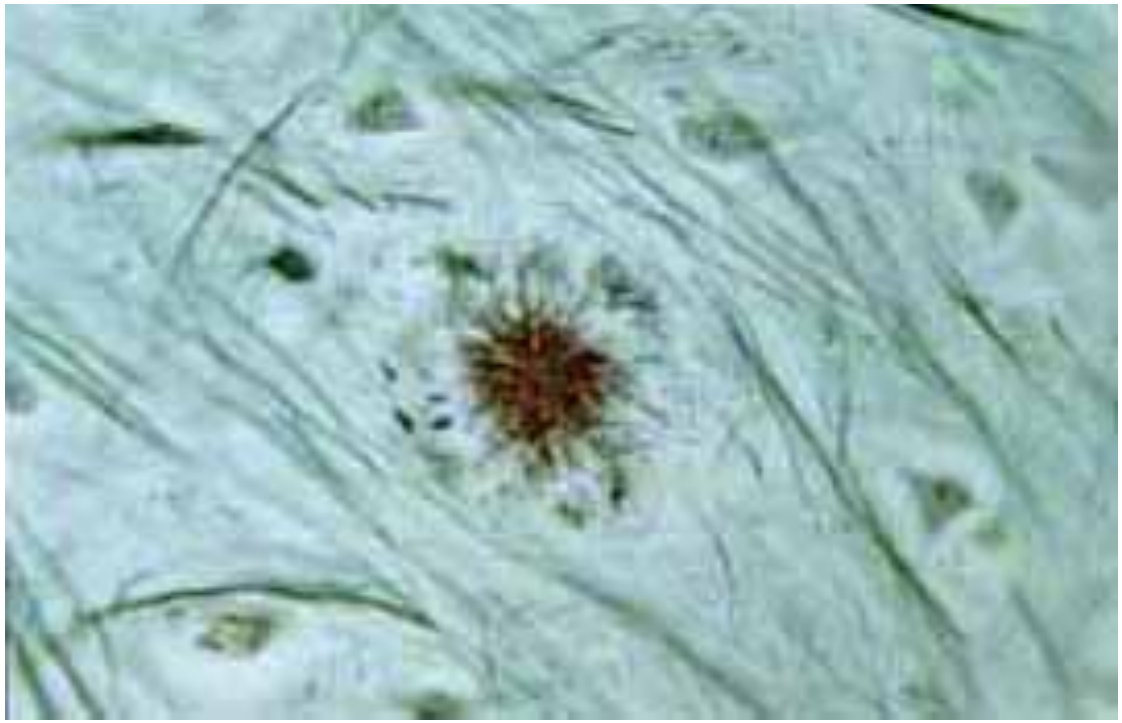
Confirmation of Diagnosis:

- Neuronal (amyloid, β amyloid, Aβ amyloid) plaques
- Neurofibrillary tangles
- Brain Atrophy

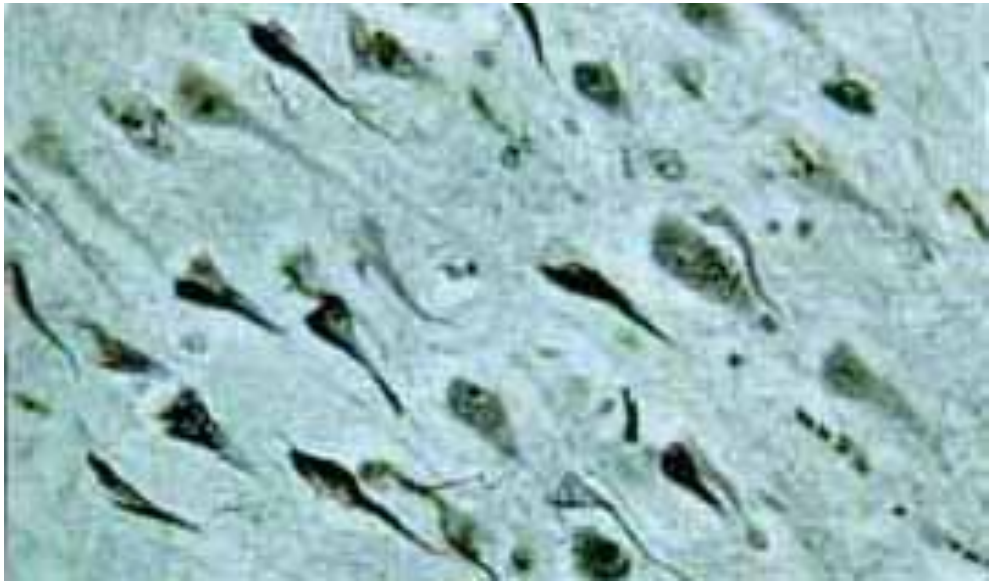
Statistics of Alzheimer's disease

- Generally, it is diagnosed in people over 65 years of age, although the less-prevalent early onset of Alzheimer's can occur much earlier.
- In 2006, there were 26.6 million sufferers worldwide.
- Alzheimer's is predicted to affect 1 in 85 people globally by 2050.

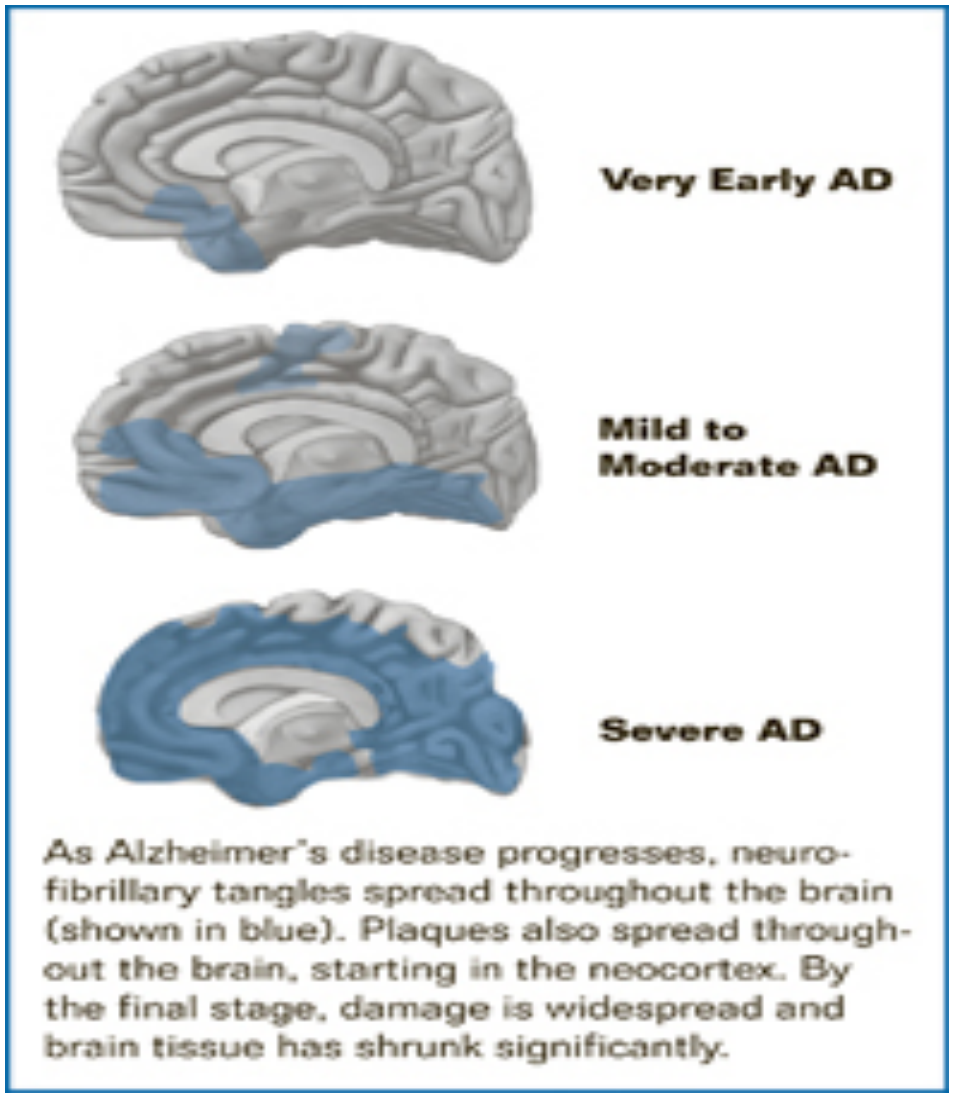
Neuronal Plaques in Alzheimer's Disease



Neurofibrillary Tangles in Alzheimer's Disease



Stages of Alzheimer's Disease



As Alzheimer's disease progresses, neurofibrillary tangles spread throughout the brain (shown in blue). Plaques also spread throughout the brain, starting in the neocortex. By the final stage, damage is widespread and brain tissue has shrunk significantly.

Working / Short Term Memory

Sunglasses
Chair
Dress
Earrings
Boots
Bed
Counter
Shower
Floor
Shoes
Desk

Visualize what you did last night

What is the average of the following numbers?

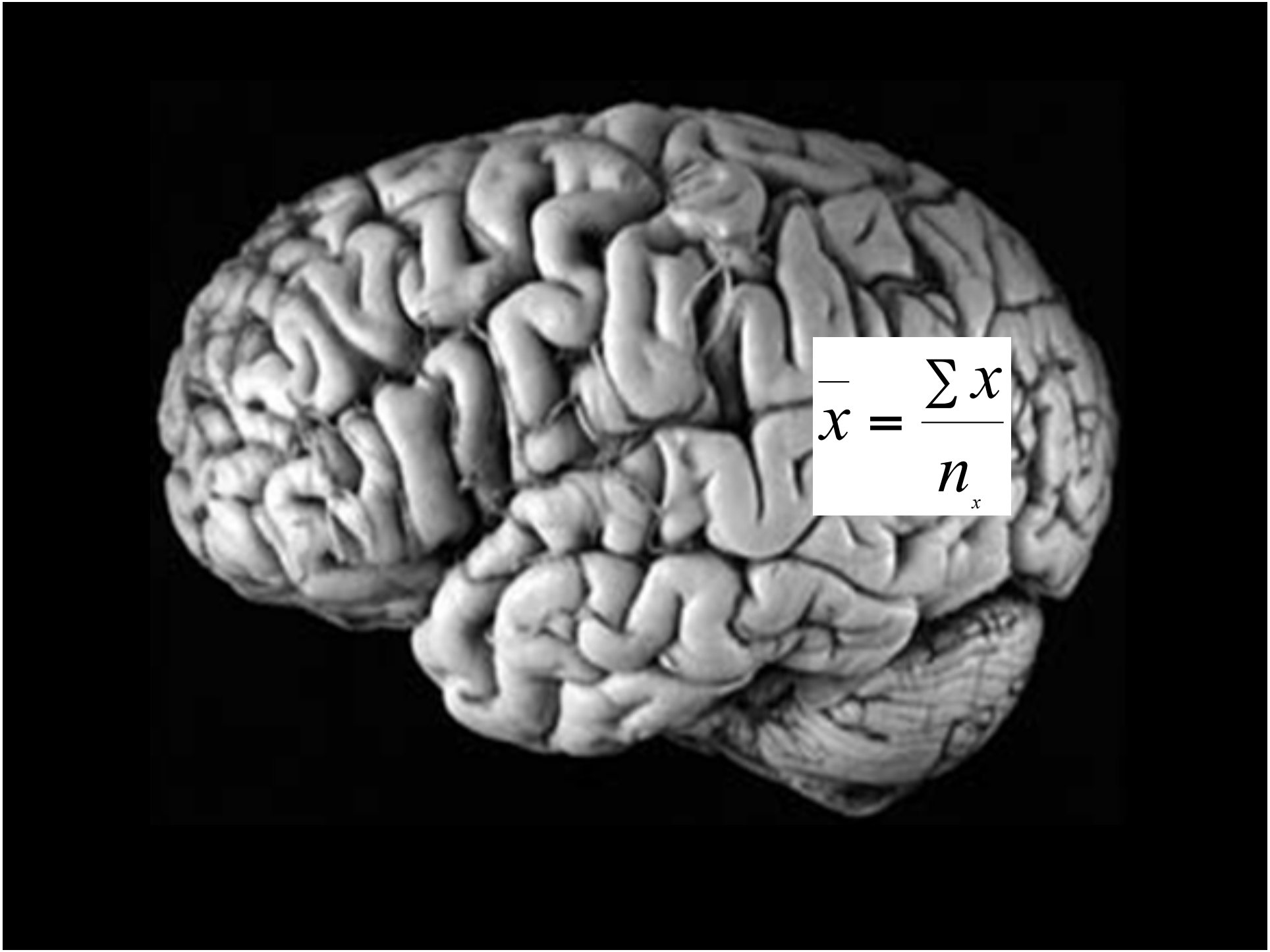
1

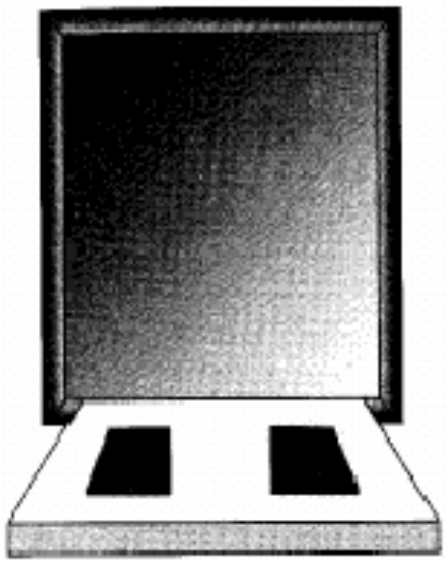
3

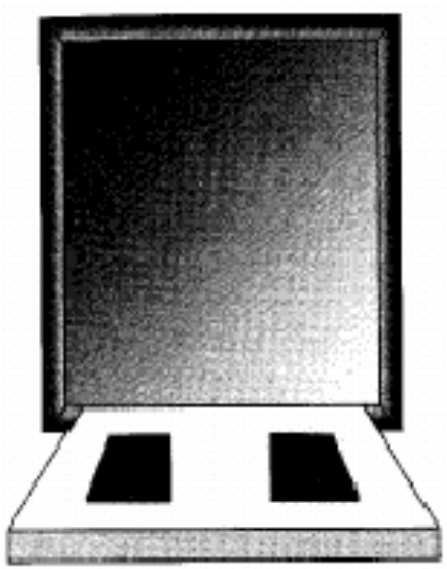
6

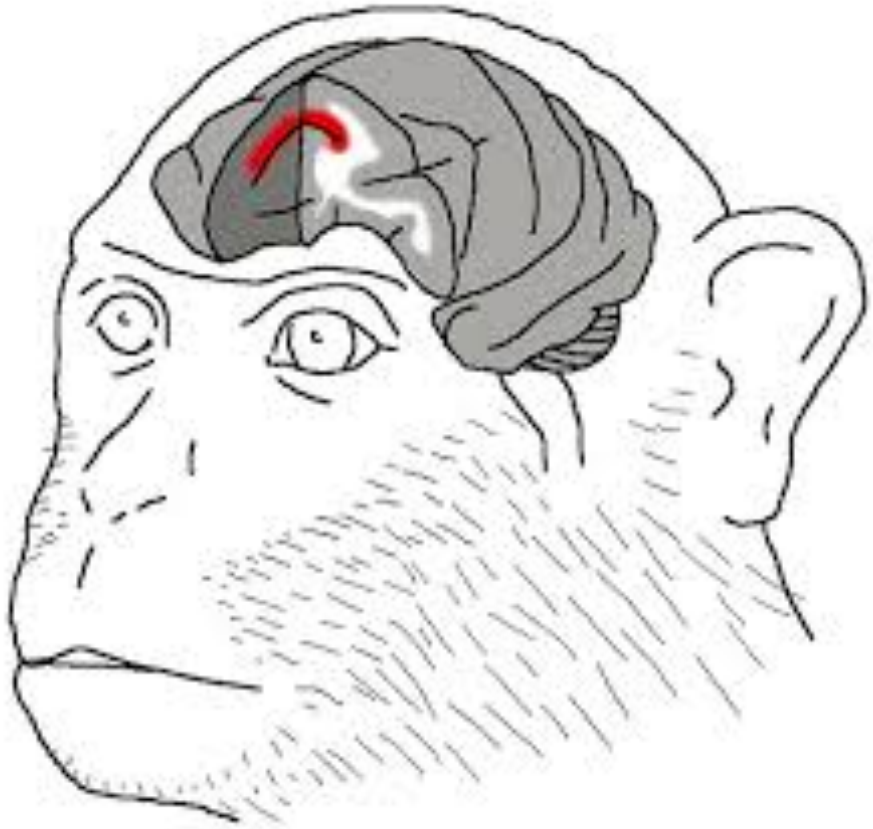
9

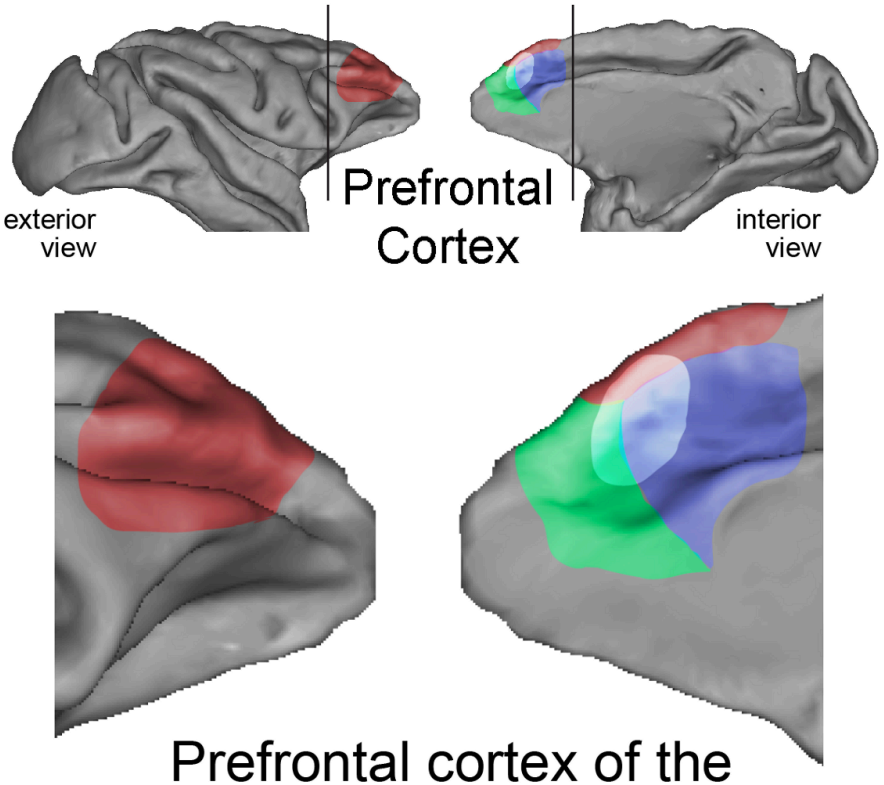
11


$\overline{x} = \frac{\sum x}{n_x}$

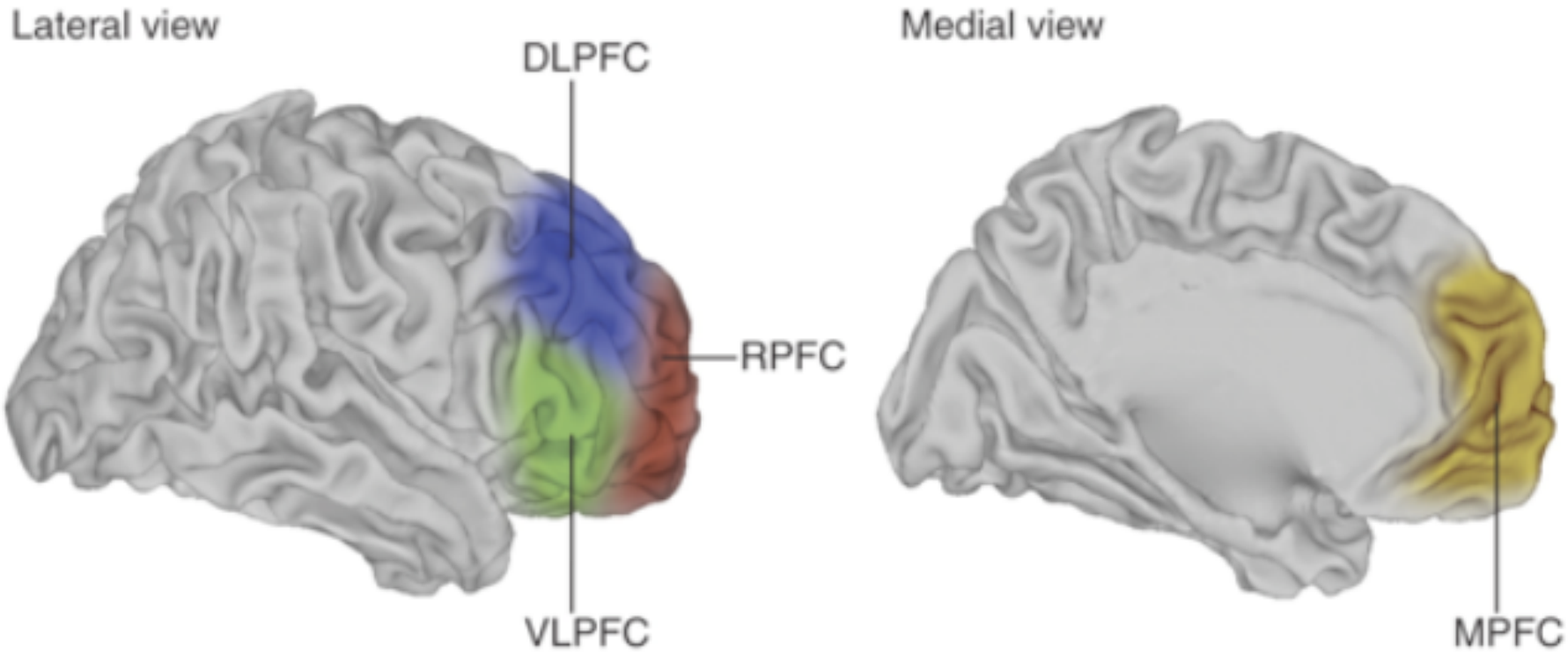


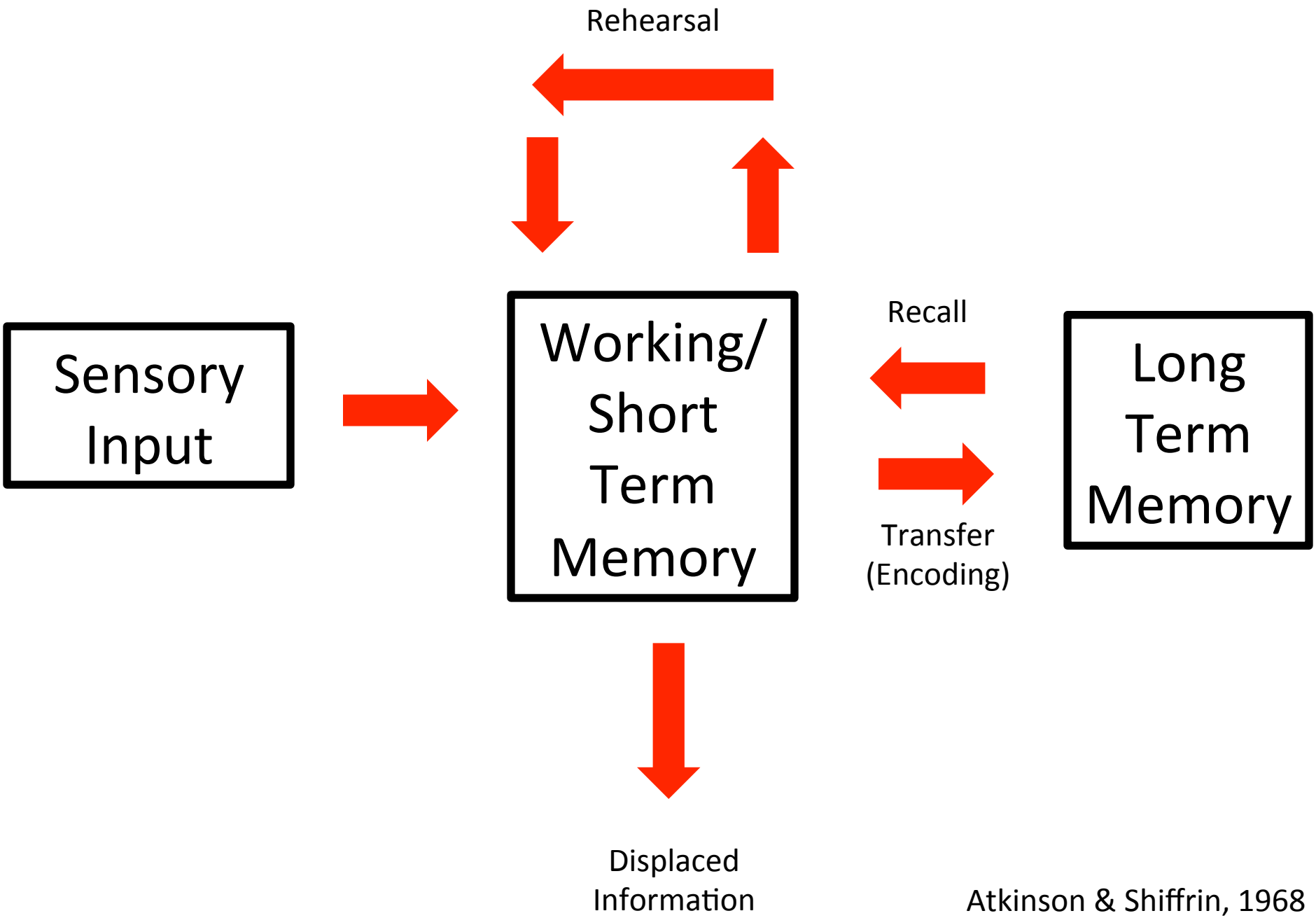






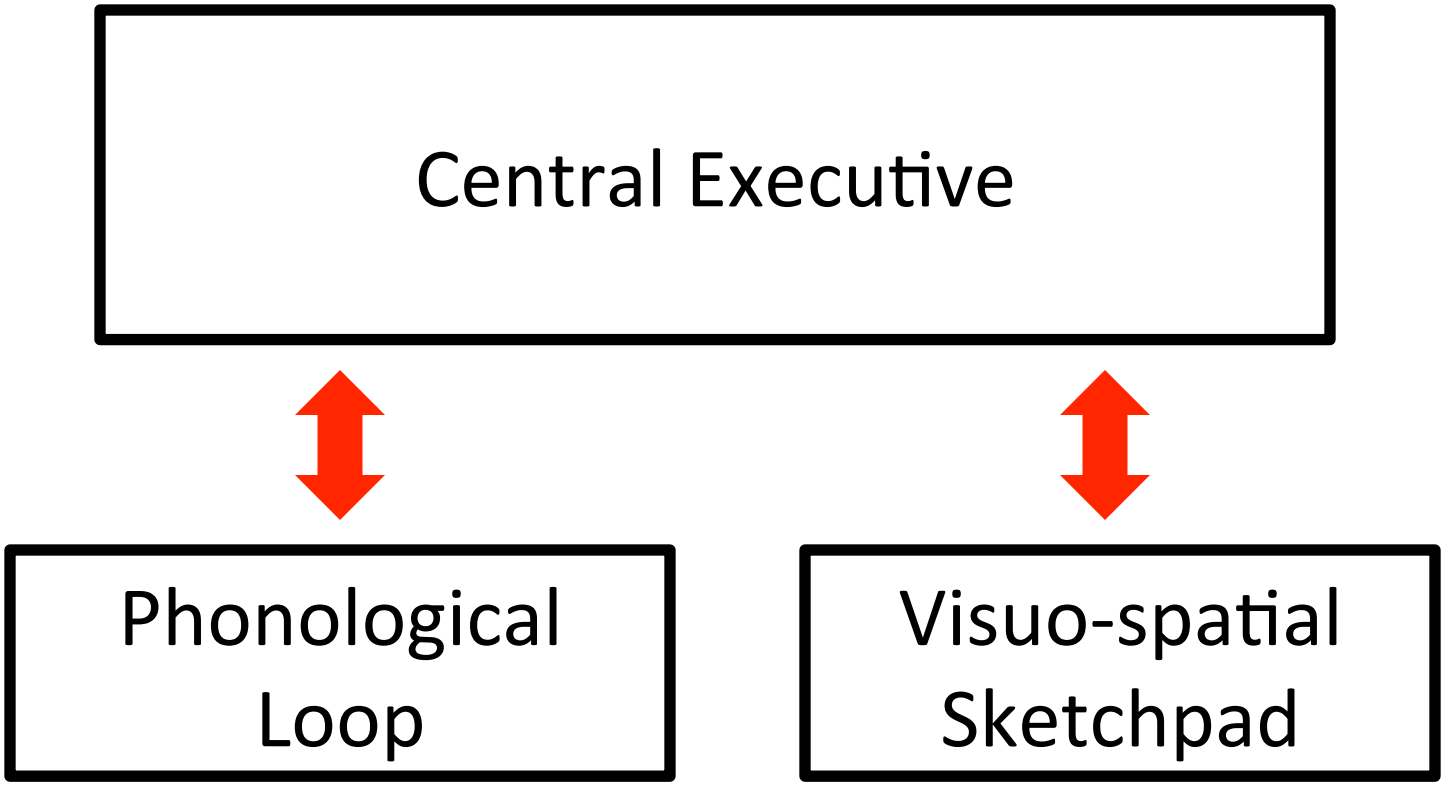
Prefrontal cortex of the
macaque monkey brain


Lateral view
DLPFC
RPFC
VLPFC
Medial view
MPFC



Atkinson & Shiffrin, 1968

Working Memory



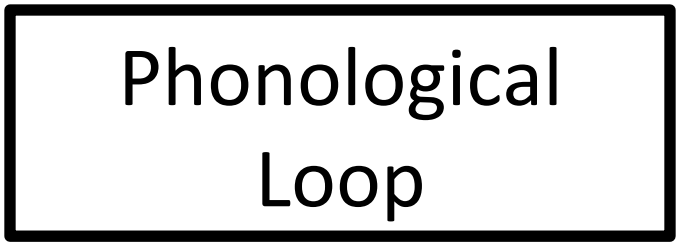
Baddeley & Hitch, 1974

maintains visual and spatial memories

Visuo-spatial Sketchpad

Baddeley & Hitch, 1974

maintains auditory memories



Baddeley & Hitch, 1974

add / delete items from working memory
selecting from items
recall from long term memory
transfer to long term memory

Baddeley & Hitch, 1974

The model defines important features:

1) Manipulation – requires central executive

2) Rehearsal – independent of central executive

3) The model is modality specific

What was that list
of words?

Sunglasses
Chair
Dress
Earrings
Boots
Bed
Counter
Shower
Floor
Shoes
Desk

control of working memory
setting goals and planning
task switching
stimulus response selection (inhibition)

Updating Working Memory

The “n” back task

Target = 4

3

5

1

9

4

1

3

2

8

5

0

6

7

9

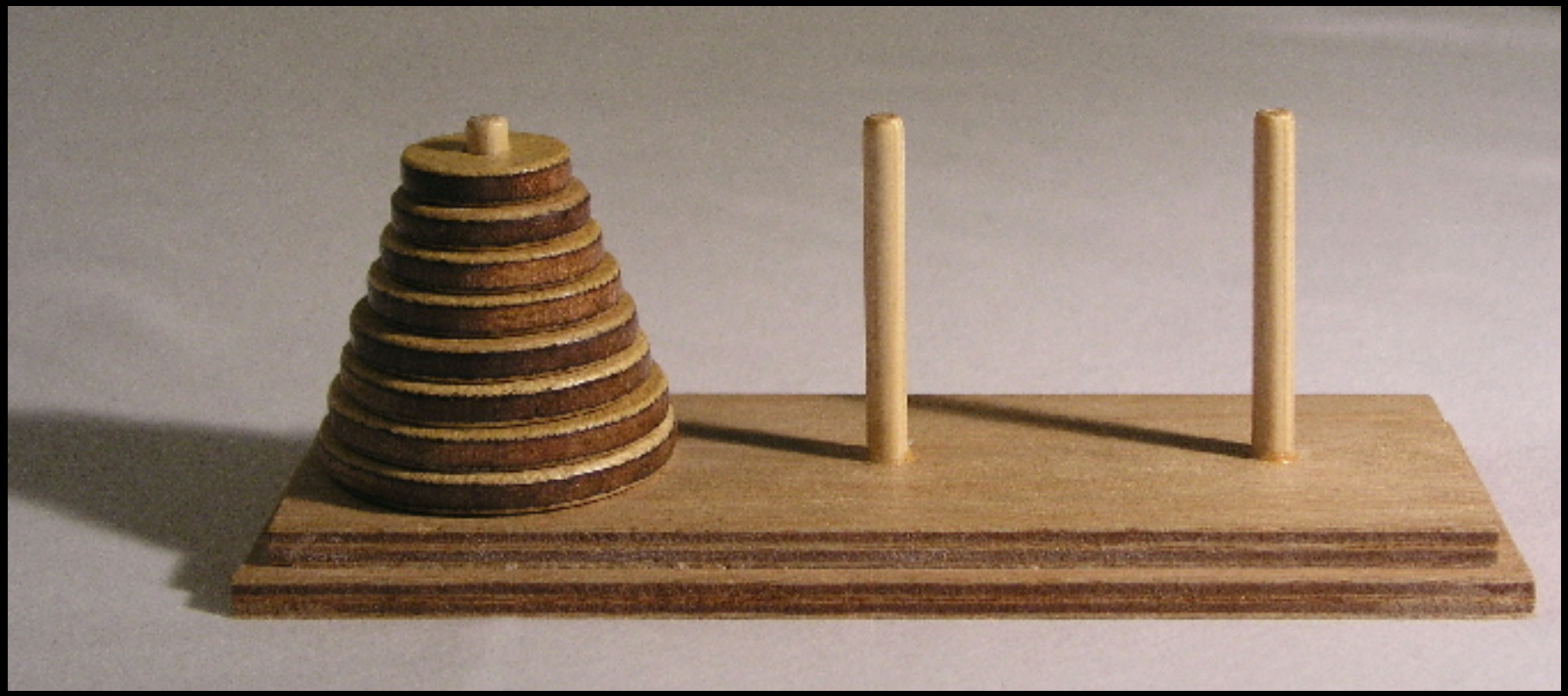
2

4

9

Setting Goals and Planning

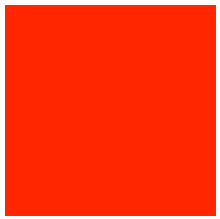
The Towers of Hanoi

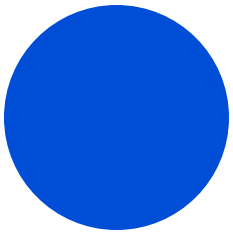


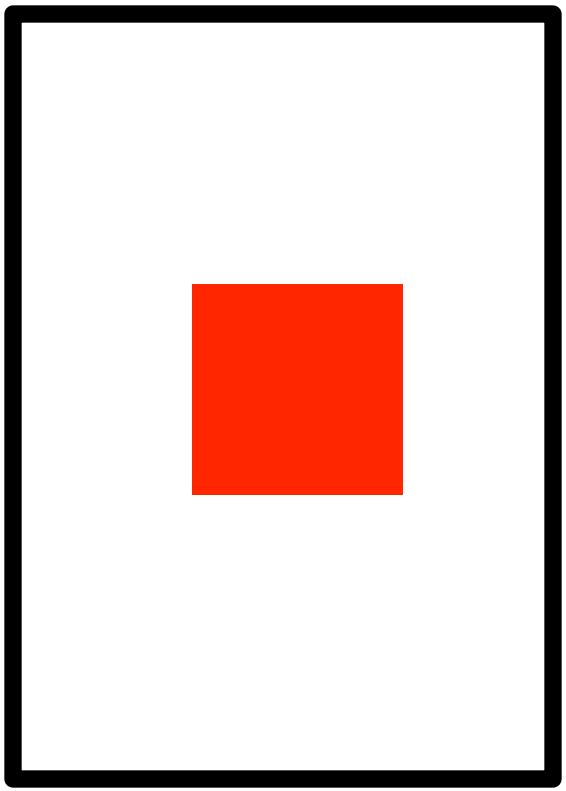
Task Switching

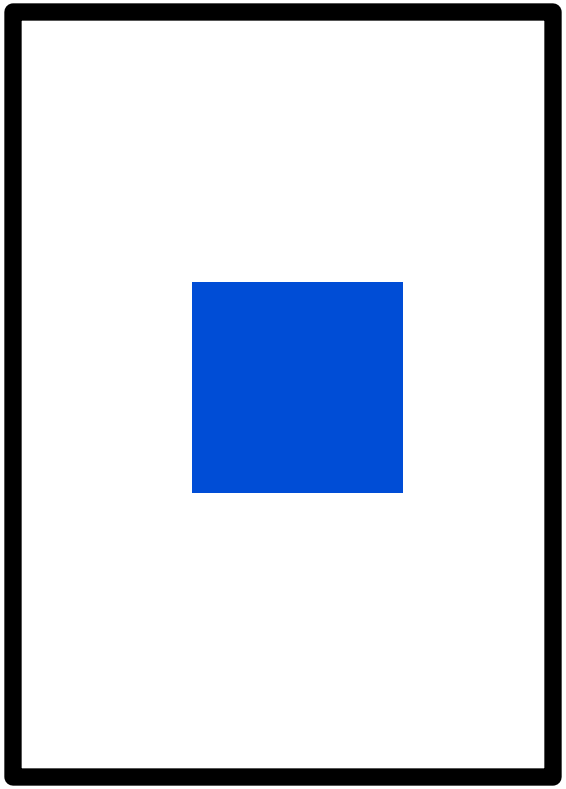
The Wisconsin Card Sort Task

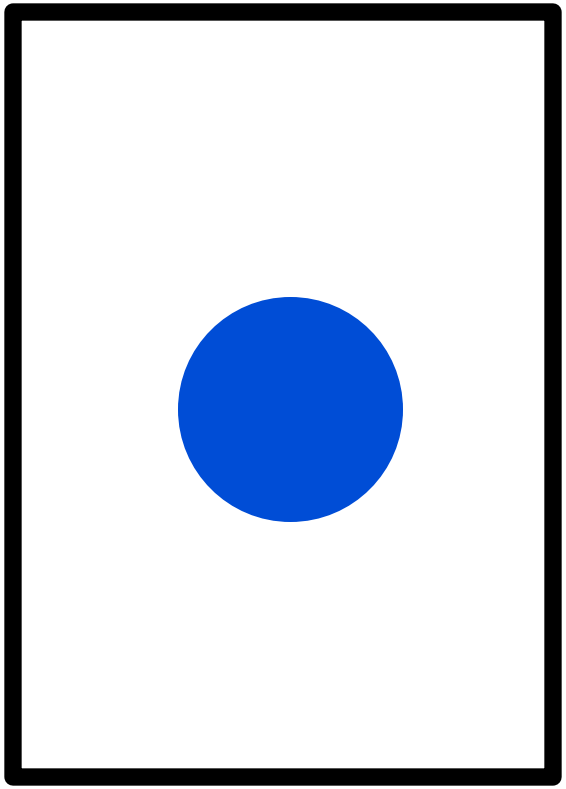
Rule: Shape

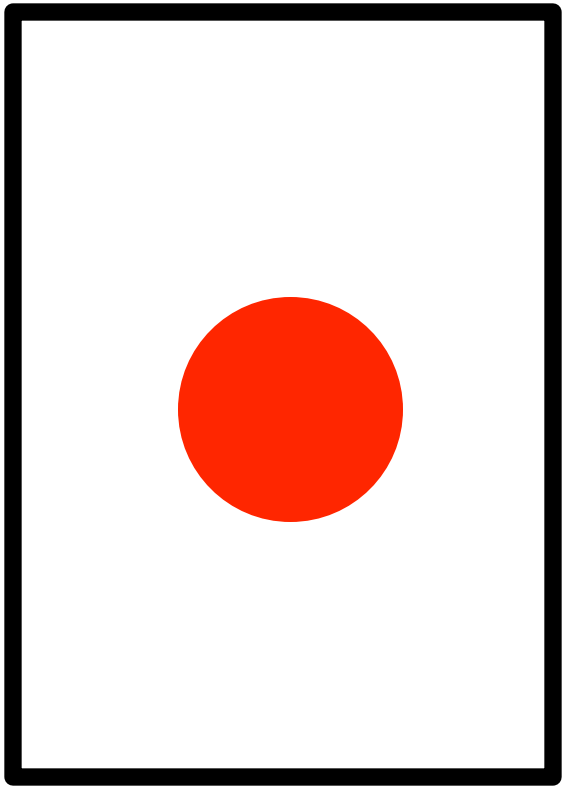


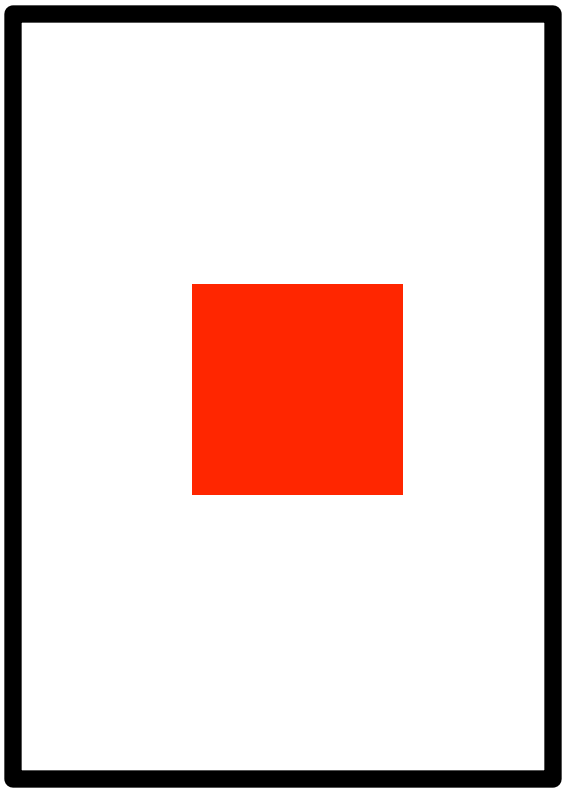


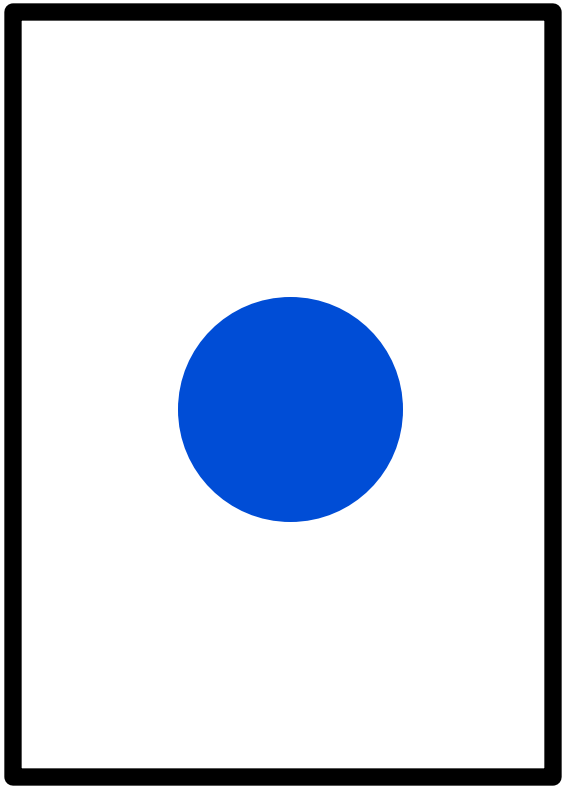


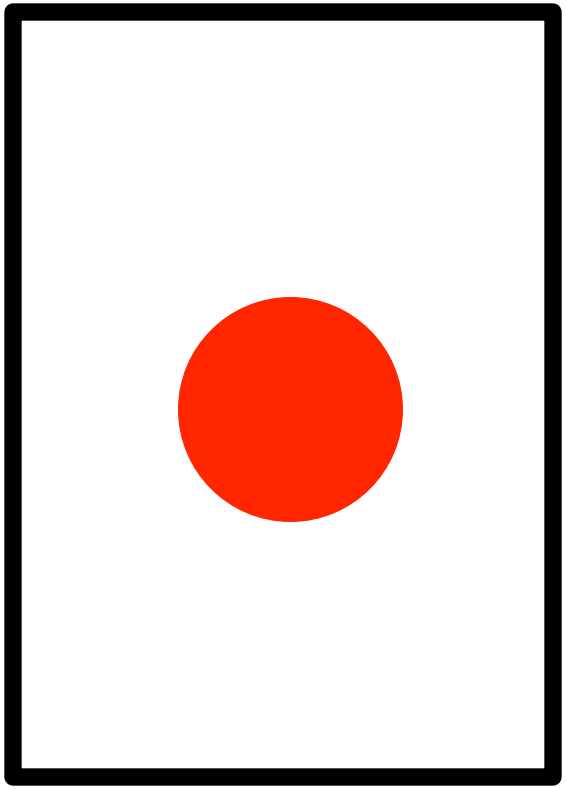




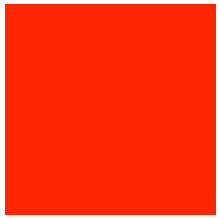


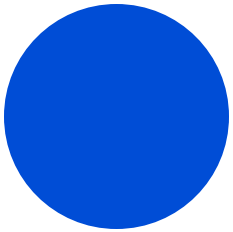


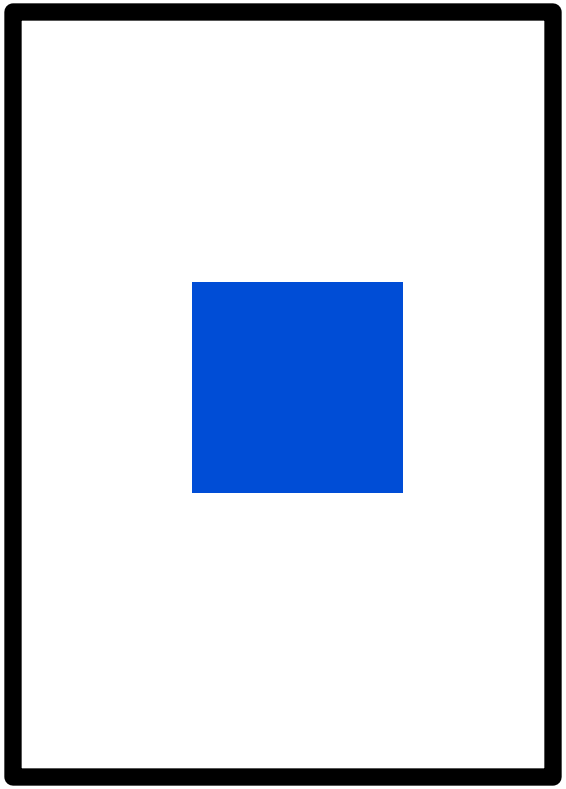


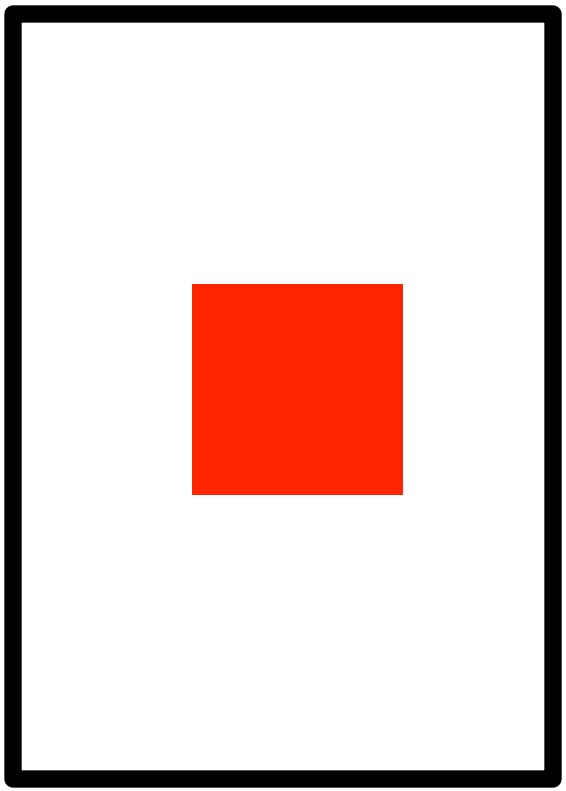


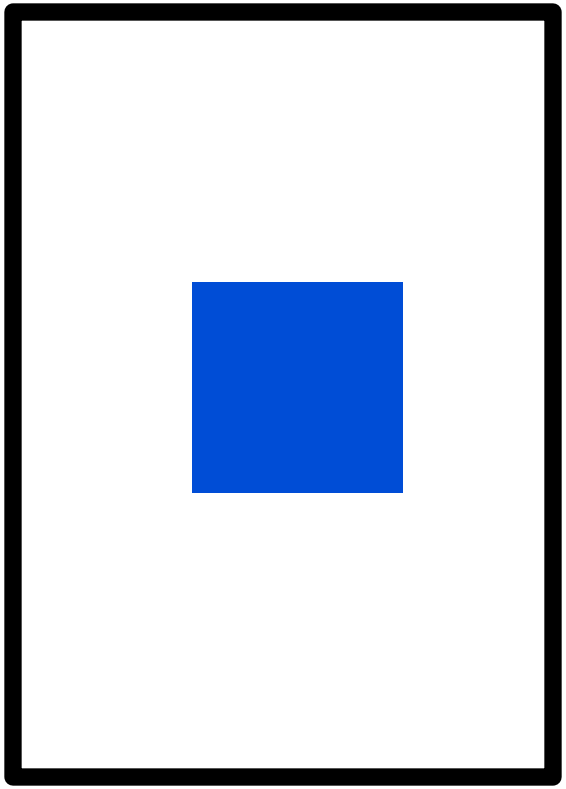
Rule: Colour

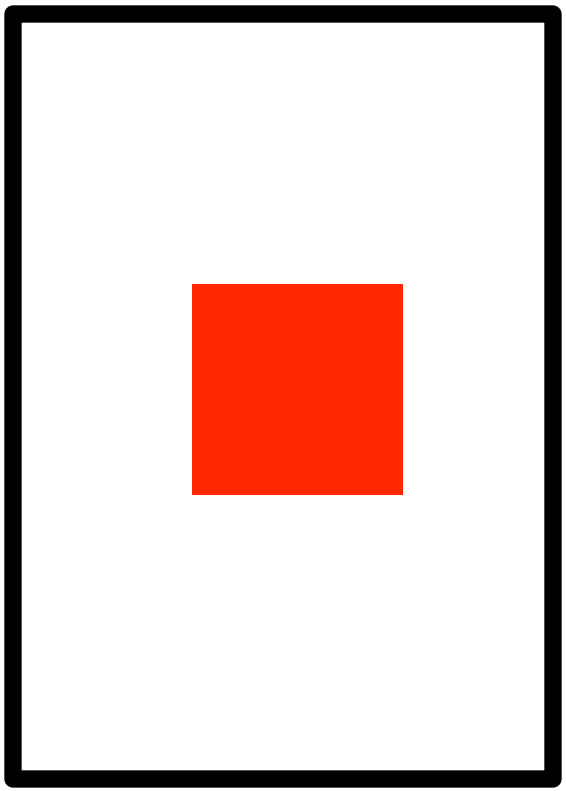


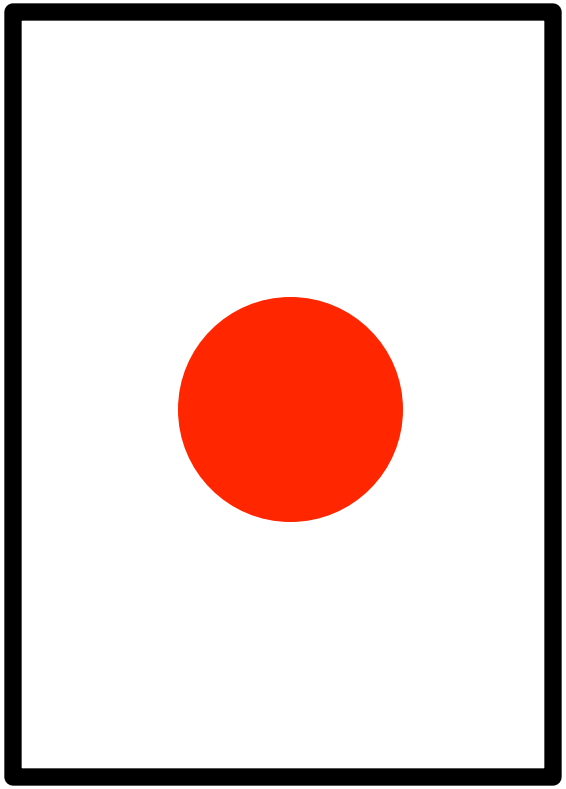


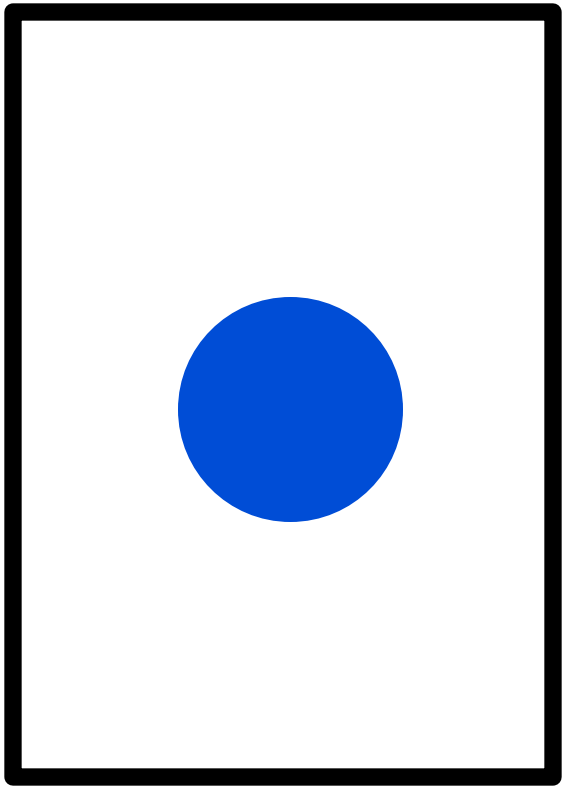


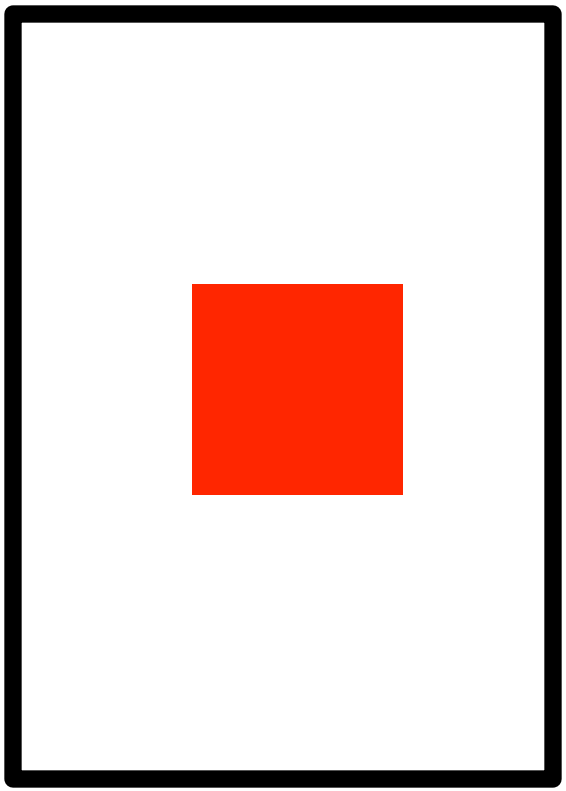


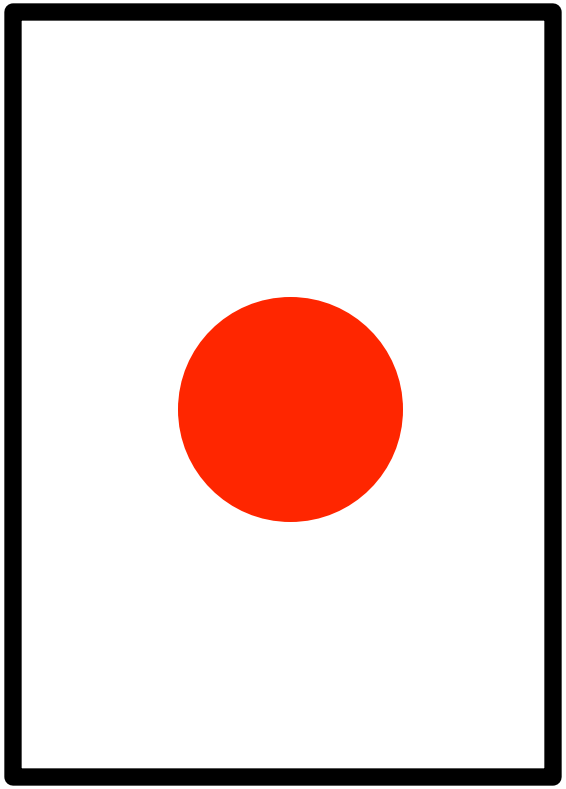




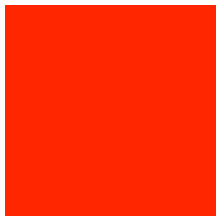


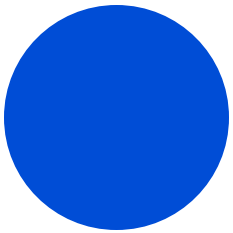


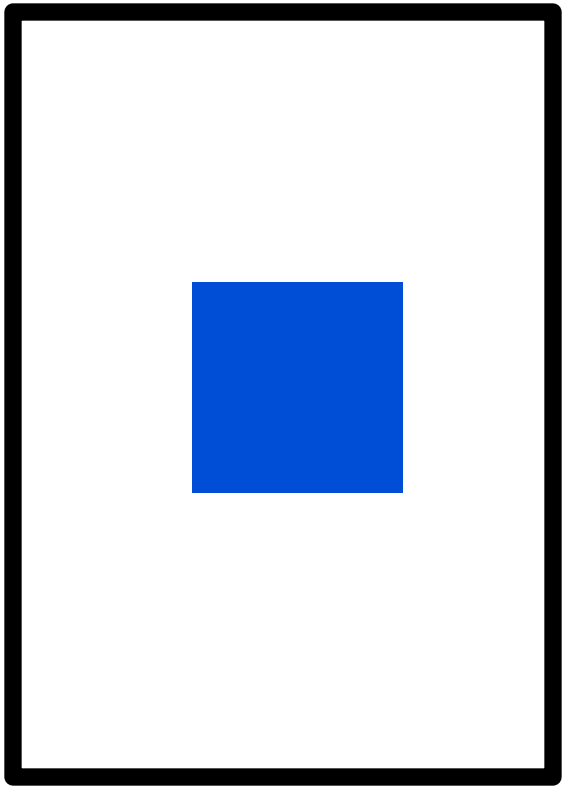


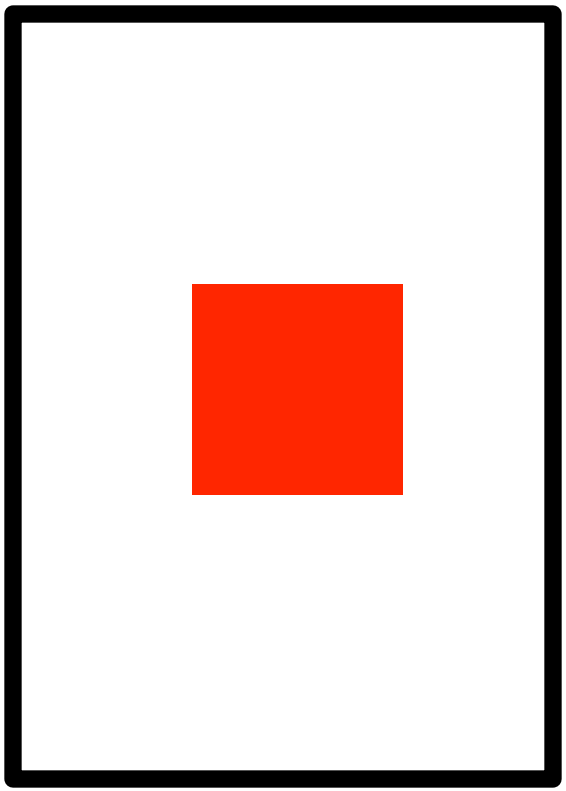


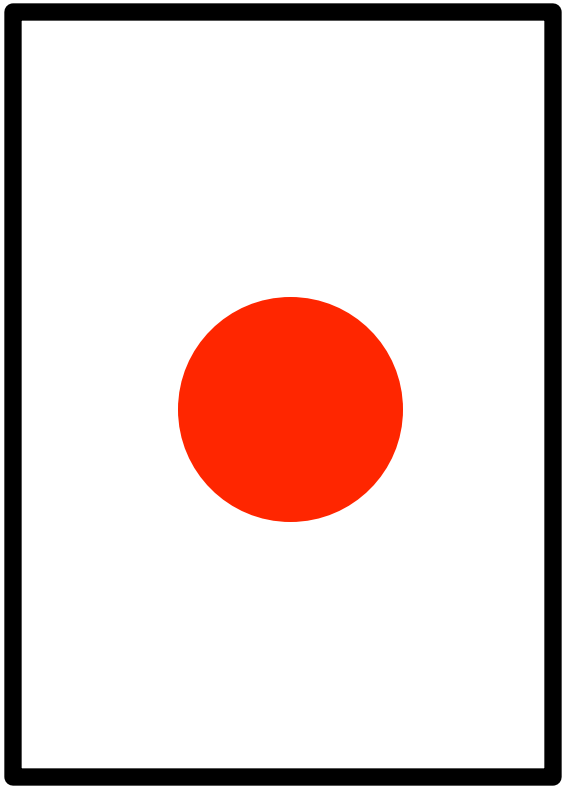
Rule: Shape

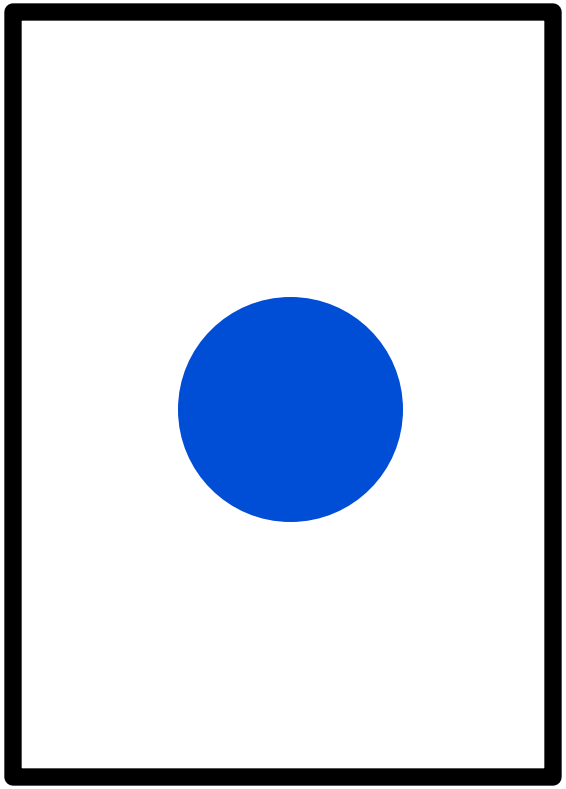


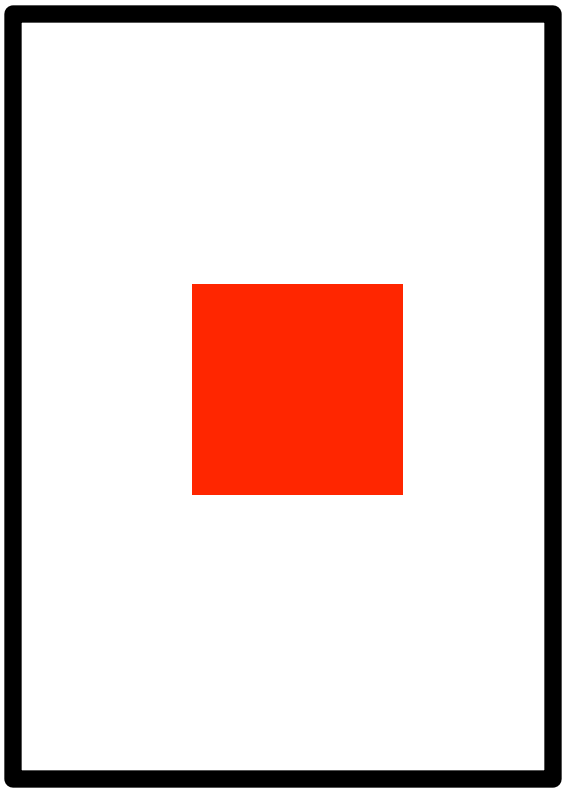












Stimulus Response Selection

The Stroop Task

Recite the colour of the words you see

Green

Red

Yellow

Blue

Red

Green

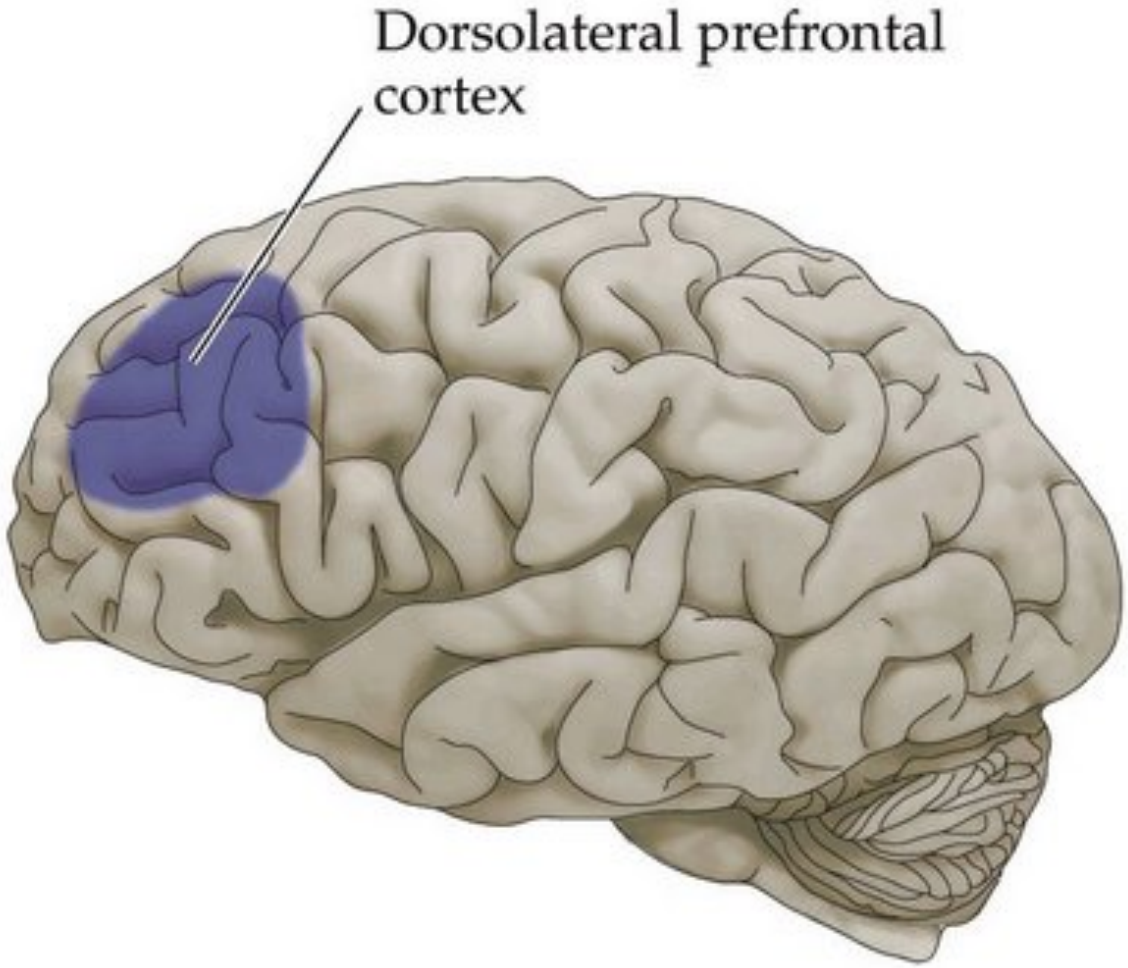
Blue

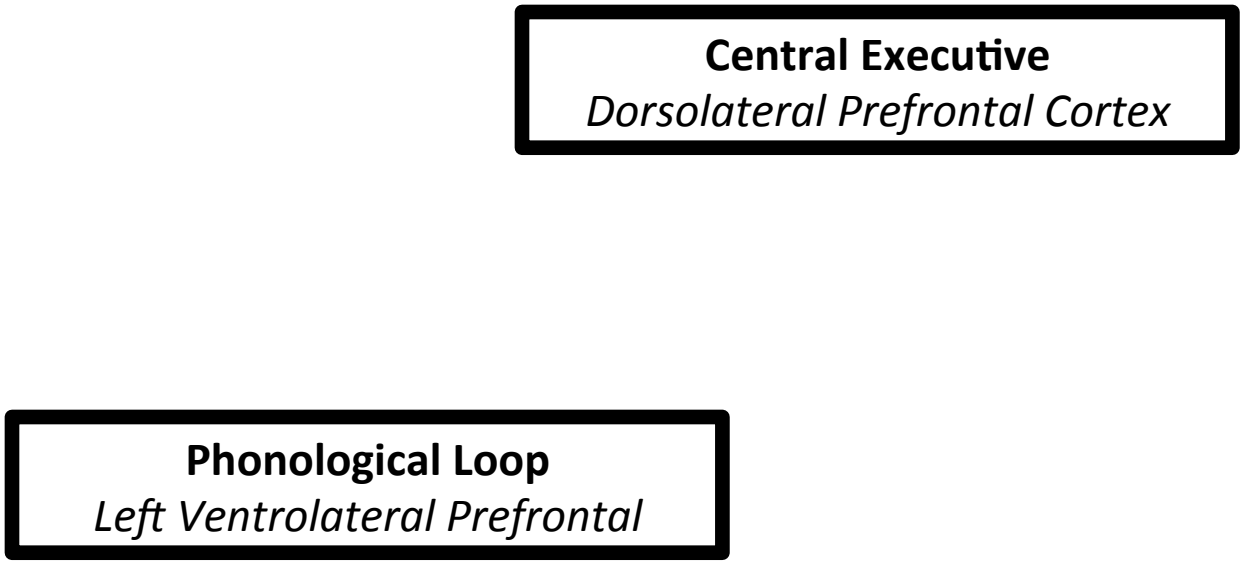
Green

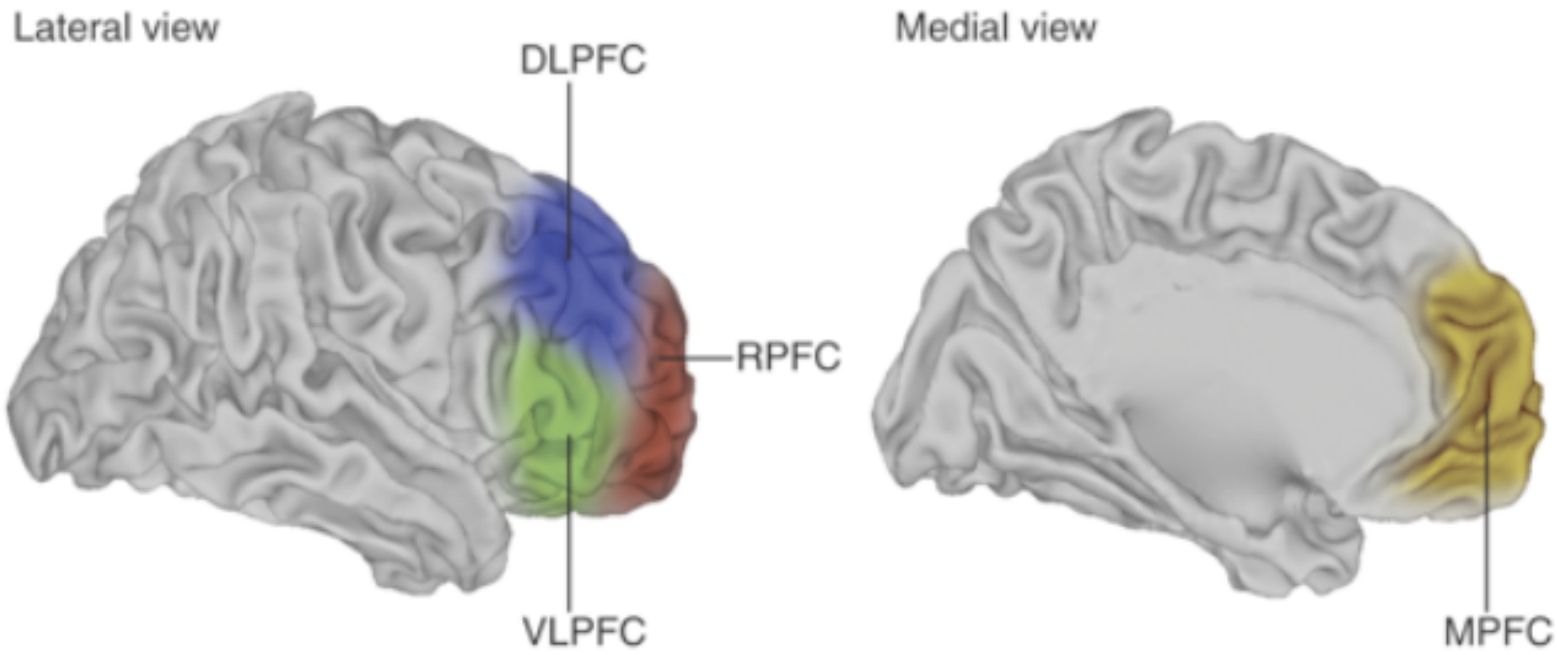
Yellow

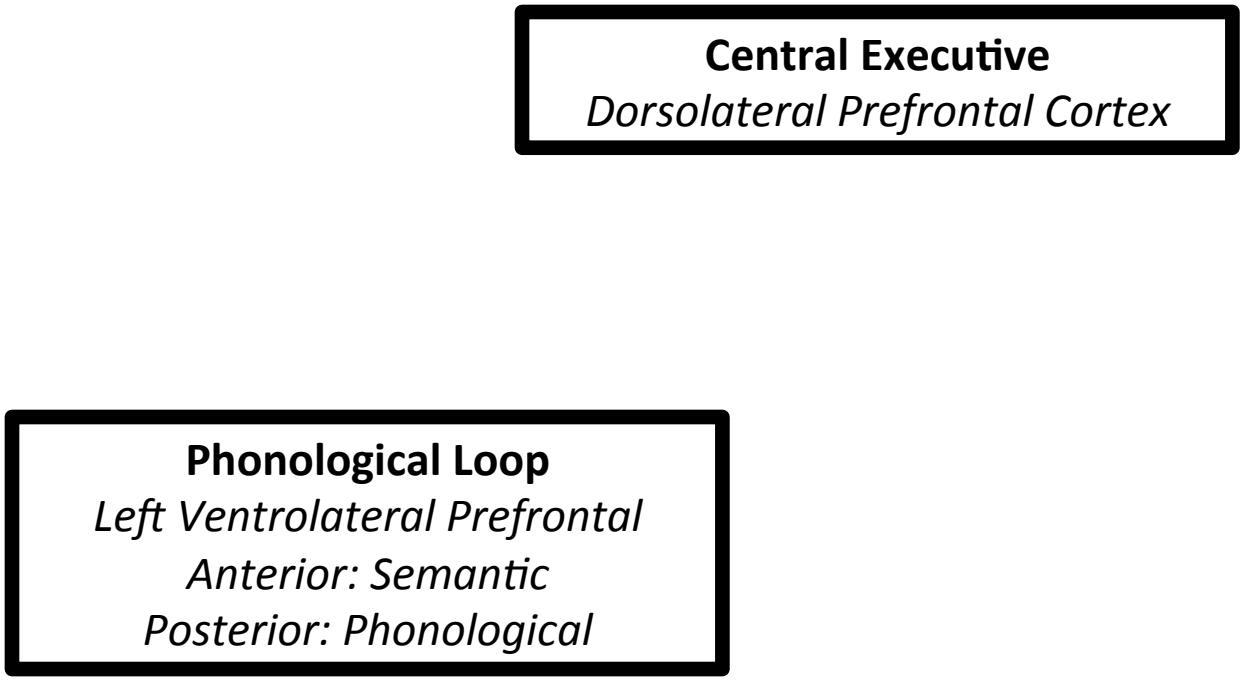
Central Executive

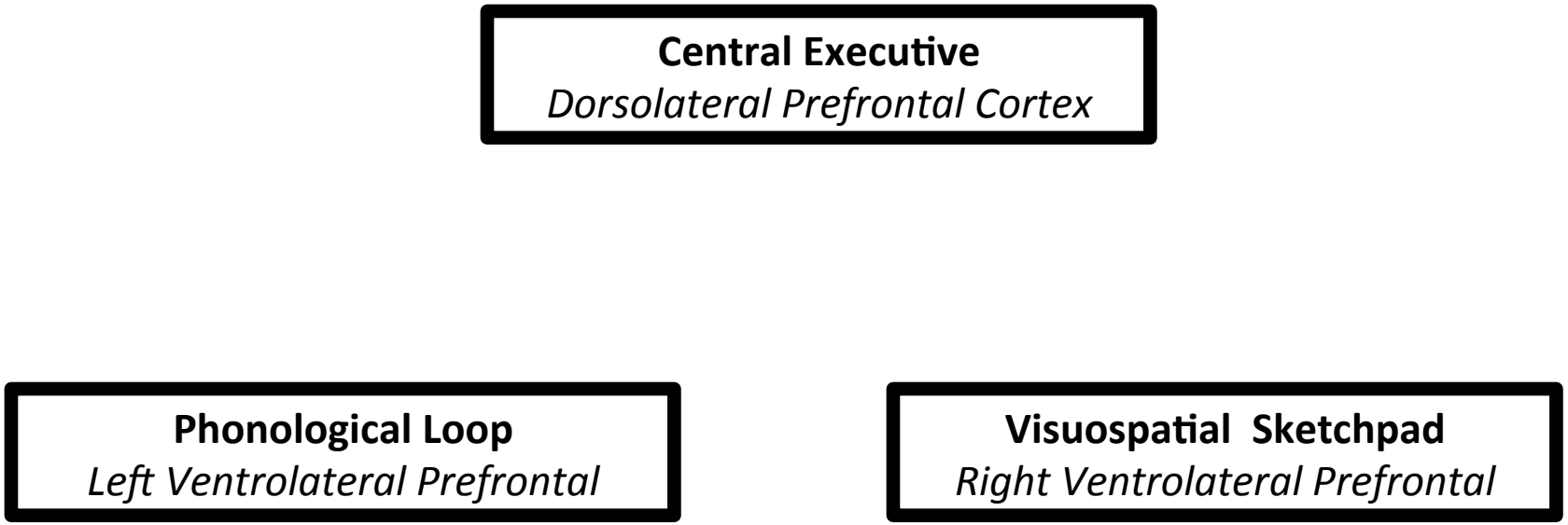
Dorsolateral Prefrontal Cortex


Dorsolateral prefrontal
cortex


Central Executive
Dorsolateral Prefrontal Cortex
Phonological Loop
Left Ventrolateral Prefrontal


Lateral view
DLPFC
RPFC
VLPFC
Medial view
MPFC


Central Executive
Dorsolateral Prefrontal Cortex
Phonological Loop
Left Ventrolateral Prefrontal
Anterior: Semantic
Posterior: Phonological

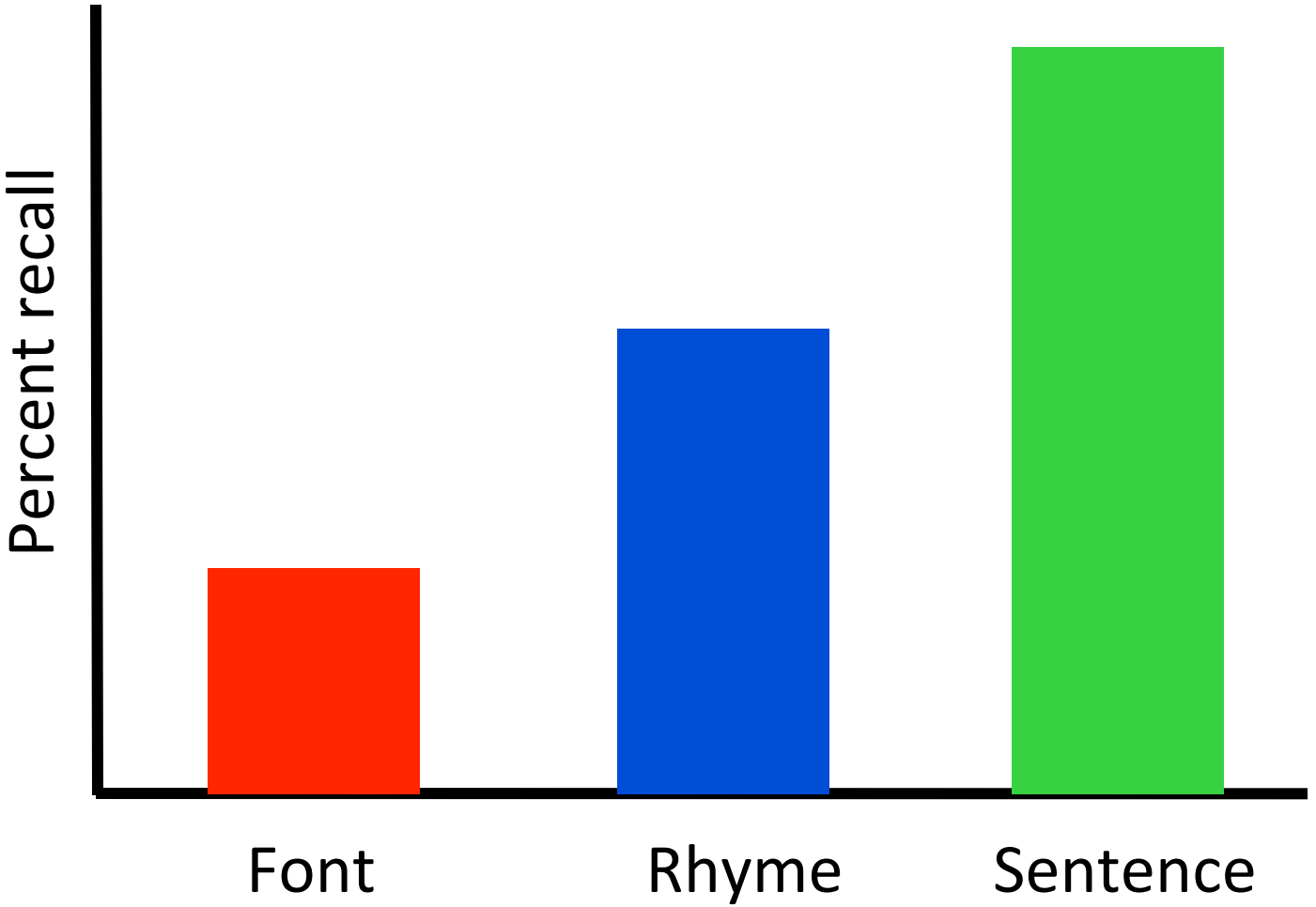

Central Executive
Dorsolateral Prefrontal Cortex
Phonological Loop
Left Ventrolateral Prefrontal
Visuospatial Sketchpad
Right Ventrolateral Prefrontal

Helping Memory:
What Makes It Stick In Your Head

Rehearsal

(well, sort of
ACTIVE REHEARSAL)

Depth of Processing



Think of meeting someone at a party...

Do you have a better chance of remembering their name if you are introduced or if you have a conversation?

Relevance to Self…

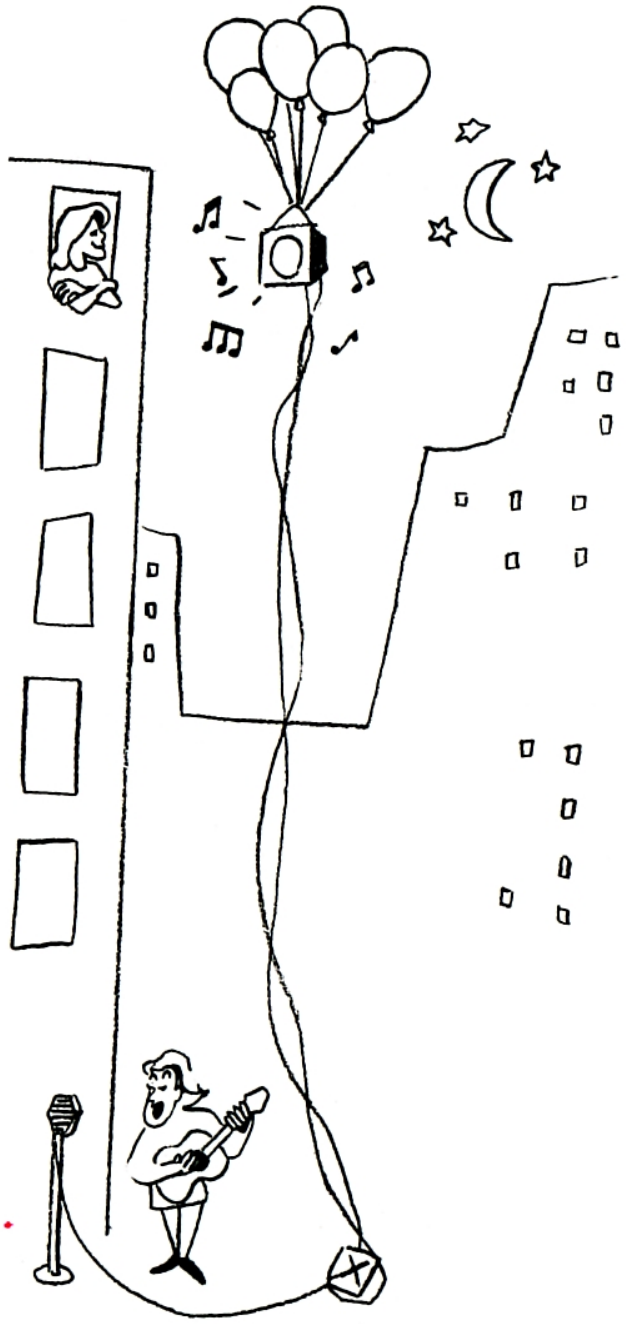
Accuracy 

RT 

Brain 

Context

If the balloons popped, the sound wouldn't be able to carry, since everything would be too far away from the correct floor. A closed window would also prevent the sound from carrying, since most buildings tend to be well-insulated. Since the whole operation depends on a steady flow of electricity, a break in the middle of the wire would also cause problems. Of course, the fellow could shout, but the human voice is not loud enough to carry that far. An additional problem is that a string could break on the instrument. Then there could be no accompaniment to the message. It is clear that the best situation would involve less distance. Then there would be fewer potential problems. With face-to-face contact, the least number of things could go wrong.



(b)

If the balloons popped, the sound wouldn't be able to carry, since everything would be too far away from the correct floor. A closed window would also prevent the sound from carrying, since most buildings tend to be well-insulated. Since the whole operation depends on a steady flow of electricity, a break in the middle of the wire would also cause problems. Of course, the fellow could shout, but the human voice is not loud enough to carry that far. An additional problem is that a string could break on the instrument. Then there could be no accompaniment to the message. It is clear that the best situation would involve less distance. Then there would be fewer potential problems. With face-to-face contact, the least number of things could go wrong.

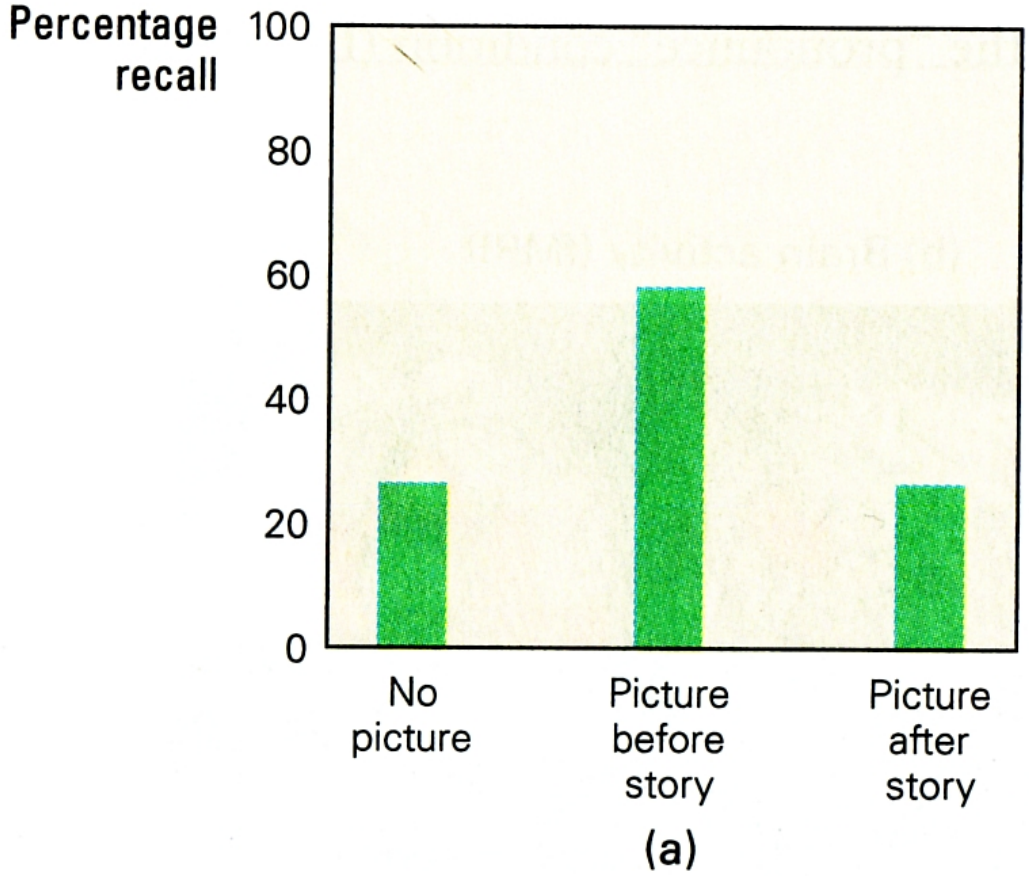


Figure 3.3 The effects of organization on memory An experimenter read aloud to participants a paragraph describing a scene. (a) Participants who heard the paragraph alone recalled few items; but participants who saw the picture in (b) and then heard the paragraph recalled more items. Participants who saw the picture only after hearing the paragraph performed no better than those who had never seen the picture. (a) Data from and (b) adapted from Bransford and Johnson, 1972.

Interference

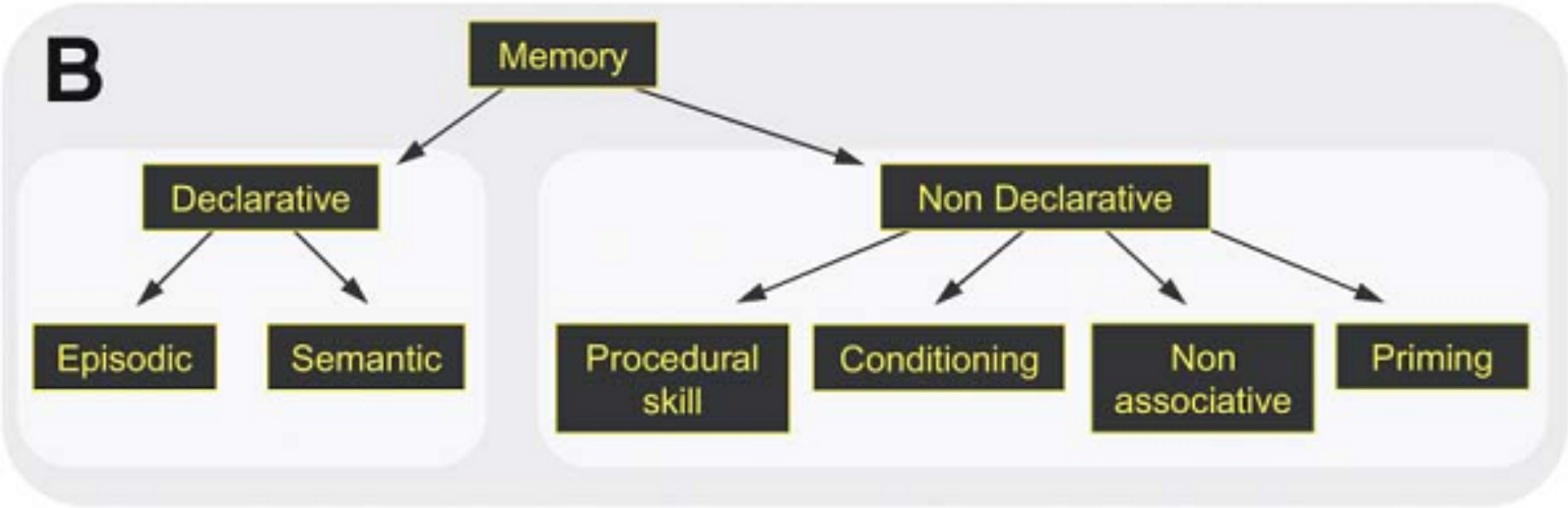
Proactive

Previously acquired information interferes with new learning

Retroactive

Acquisition of new information disrupts old memories

Long Term Memory


B
Memory
Declarative
Non Declarative
Episodic
Semantic
Procedural skill
Conditioning
Non associative
Priming

Episodic Memories

- “I remember”
- Tagged with spatial and temporal context
- Learned in a single exposure

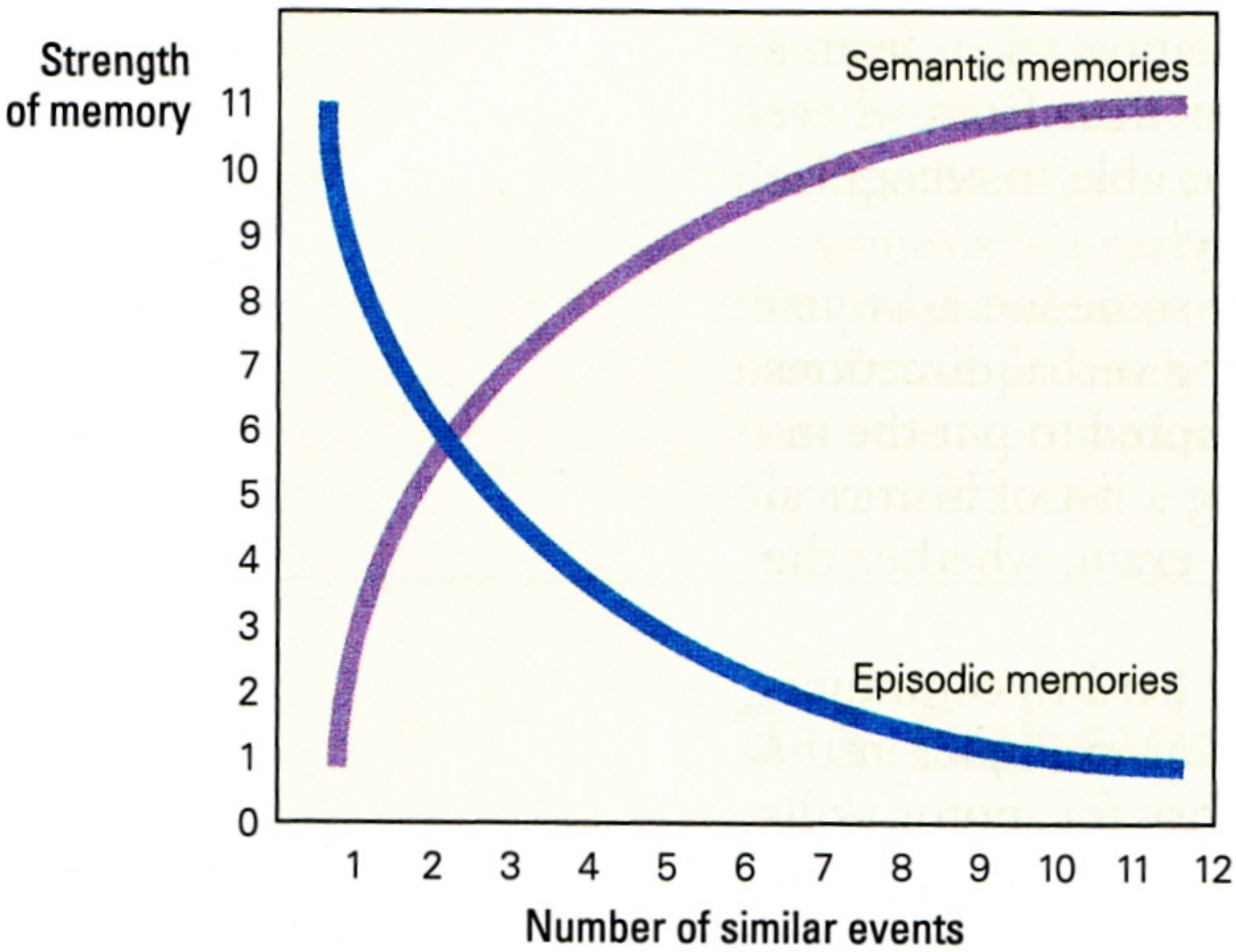
Semantic Memories

- “I know”
- Does not have to have spatial and temporal context
- Learned in a single exposure, but strengthened with repetition

Episodic and Semantic Memories

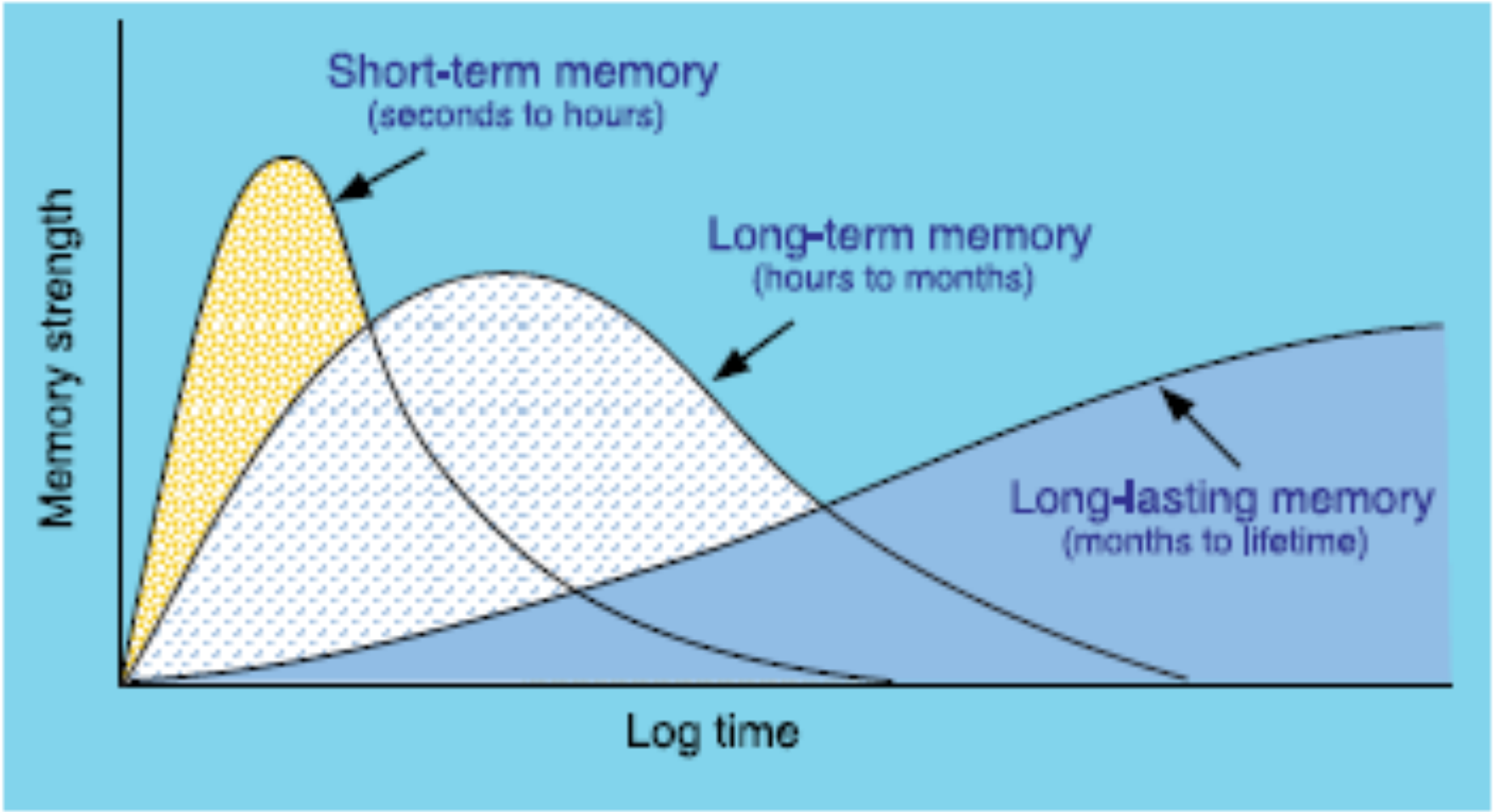
- Can be communicated flexibly in a format other than they were acquired

- Consciously accessible


Strength of memory
11
10
9
8
7
6
5
4
3
2
1
0
Semantic memories
Episodic memories
1
2
3
4
5
6
7
8
9
10
11
12
Number of similar events

Trace Levels

- Sensory Trace (< 1 s)
- Short Term Trace (develops within seconds or minutes and last for hours)
- Long Term Trace
- Long Lasting Trace


Short-term memory
(seconds to hours)
Long-term memory
(hours to months)
Long-lasting memory
(months to lifetime)
Memory strength
Log time

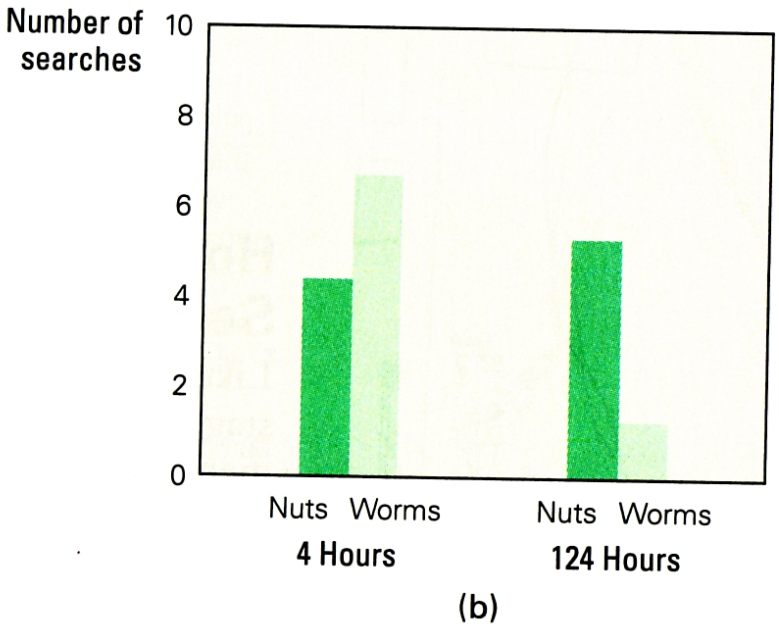
Stages of Memory Formation

1. Encoding
2. Consolidation
3. Retention
4. Retrieval

Do animals have episodic memories?

Figure 3.2 Episodic memory in birds (a) Scrub jays were allowed to cache worms and nuts in the compartments of sand-filled ice-cube trays. (b) Some time later, the birds were allowed to recover food from the trays. If the delay was 4 hours, the birds tended to recover buried worms (their favorite food). But if the delay was 124 hours, during which time the worms would have rotted, the birds tended to recover the nuts instead. This suggests that the birds remembered what they had buried where, and how long ago—an "episodic-like" memory. (a) Adapted from Griffiths et al., 1999; (b) adapted from Roberts, 2002.

(a)



(b)

Episodic-like memory in a gorilla: A review and new findings ☆

Bennett L. Schwartz [a,*], Megan L. Hoffman [b], Siân Evans [c]

[a] *Florida International University, USA*
[b] *Georgia State University, USA*
[c] *DuMond Conservancy for Primates and Tropical Forests, USA*

Received 28 February 2005

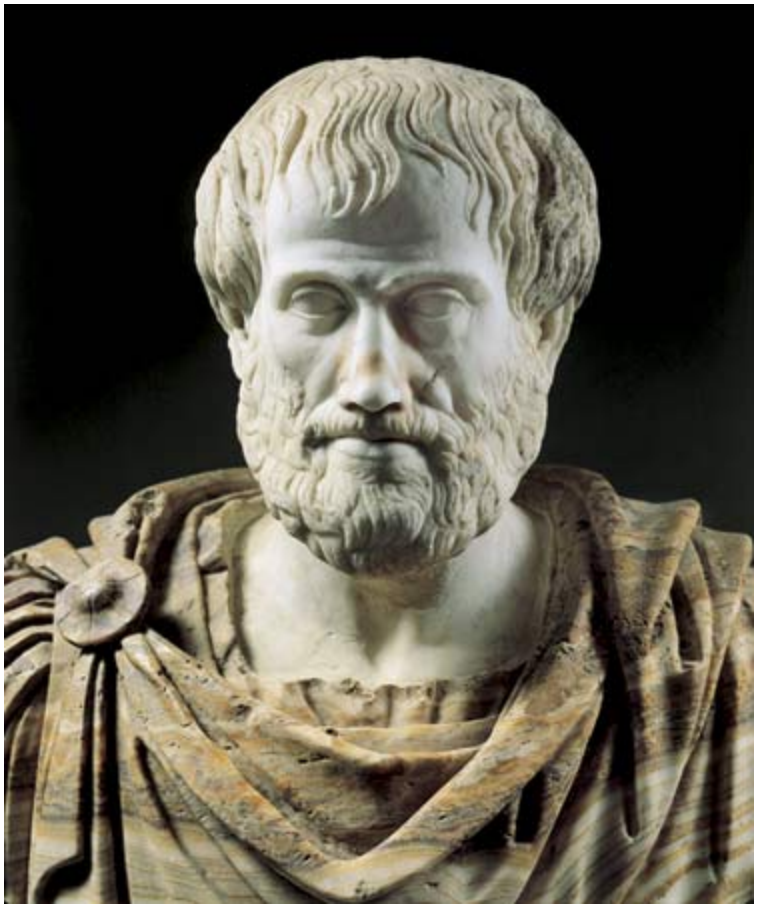
We describe two new studies with King, an adult male western lowland gorilla. We show that King can remember the order of past events (Experiment 1) and that King can remember where events occurred (Experiment 2). We conclude by discussing alternate explanations of our findings and speculate on future directions.

Table 1
King's percent correct (Schwartz et al., 2002)

	Percent correct			
	5-min RI		24-h RI	
	"What"	"Who"	"What"	"Who"
Experiment 1	70%		82%	
Experiment 2	55%	82%	73%	87%

20% is chance baseline for "what" questions; 50% is chance baseline for "who" questions.

Models for Episodic and Semantic Memory



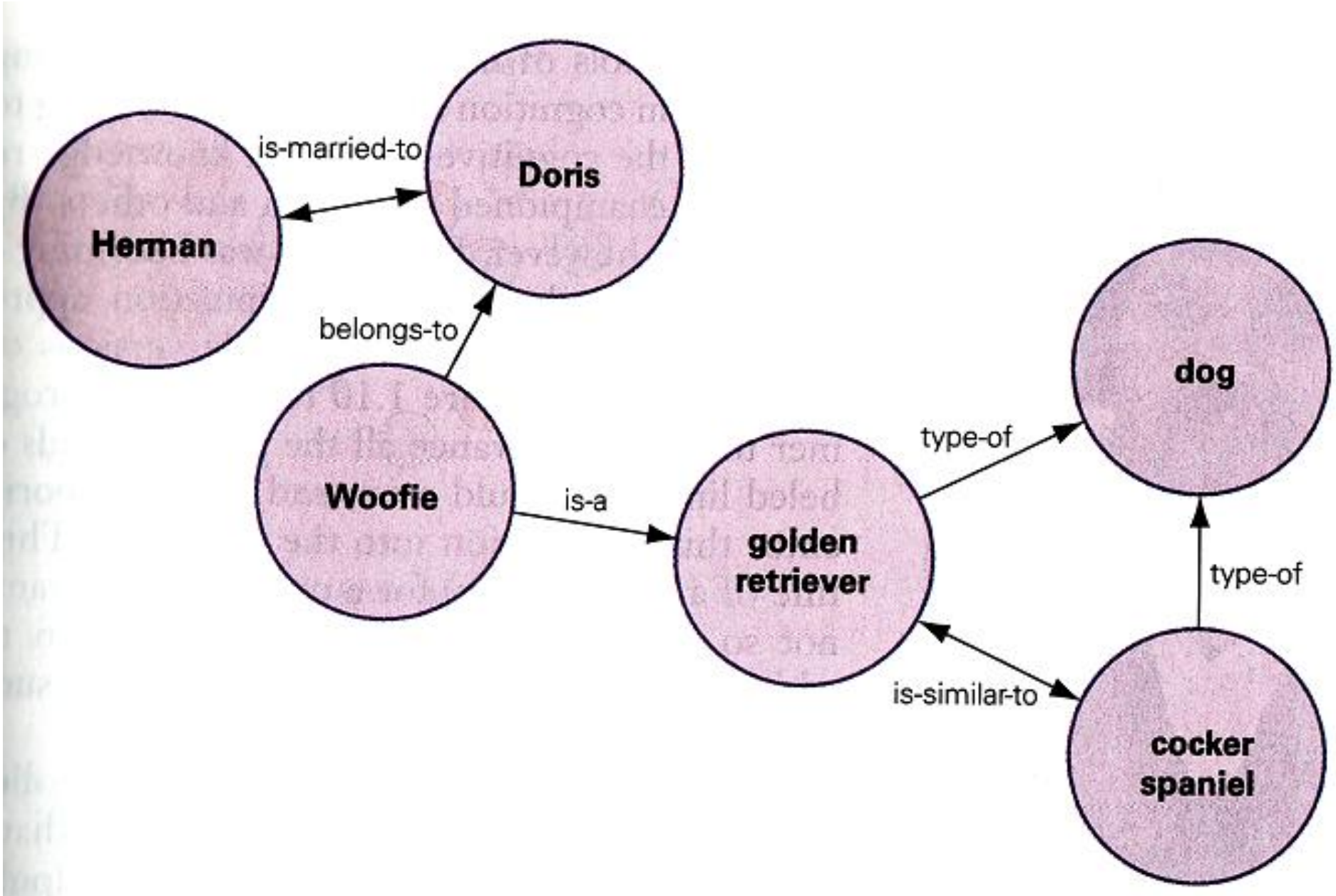
Aristotle

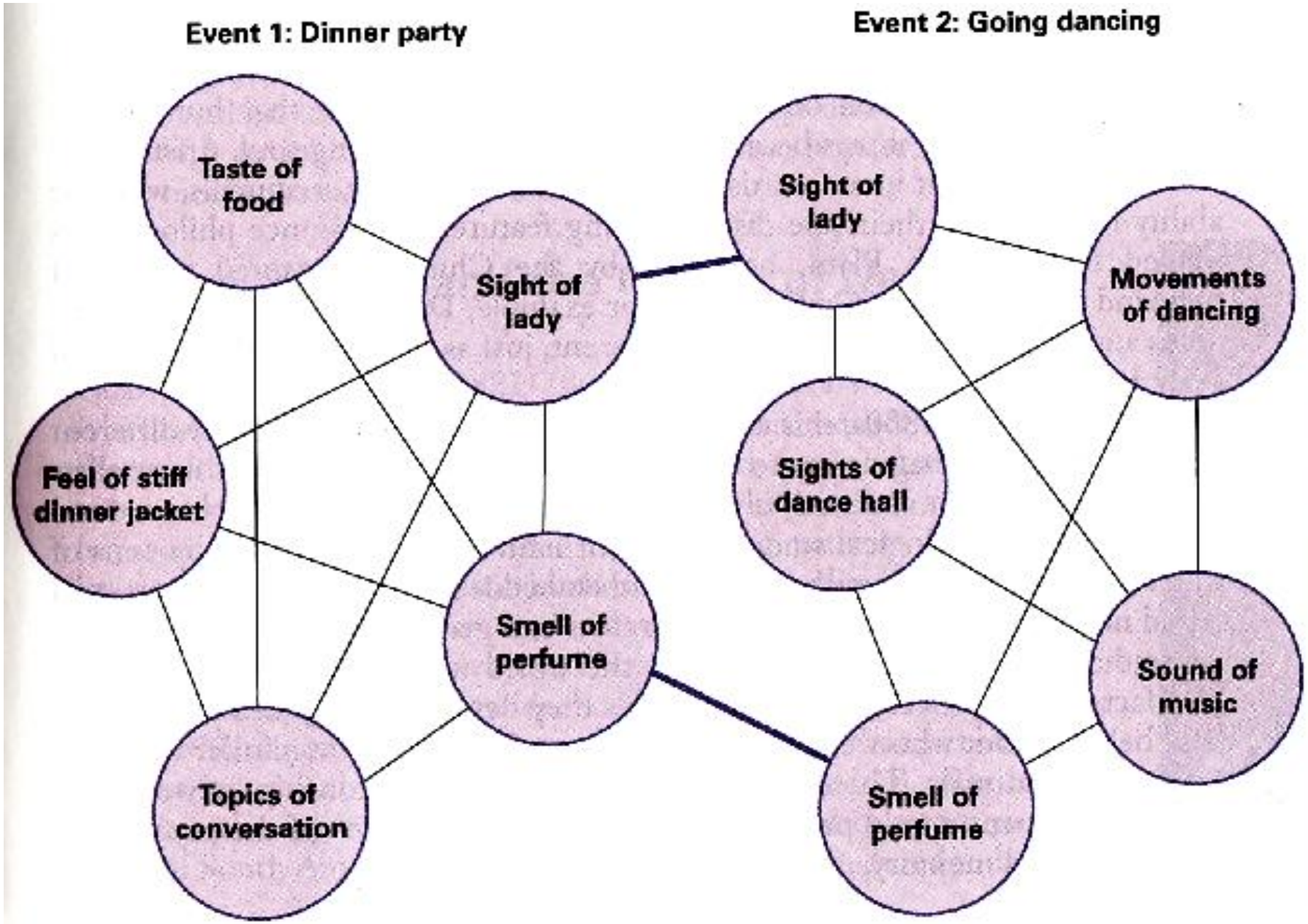
Associationism

- Linkages between events or ideas

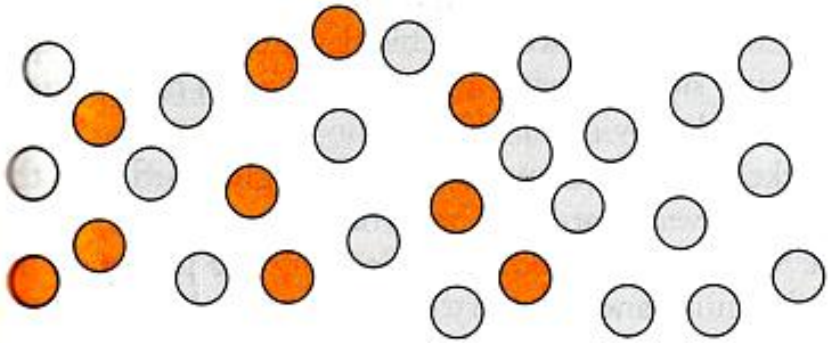
Three Principles

- Contiguity
- Frequency
- Similarity

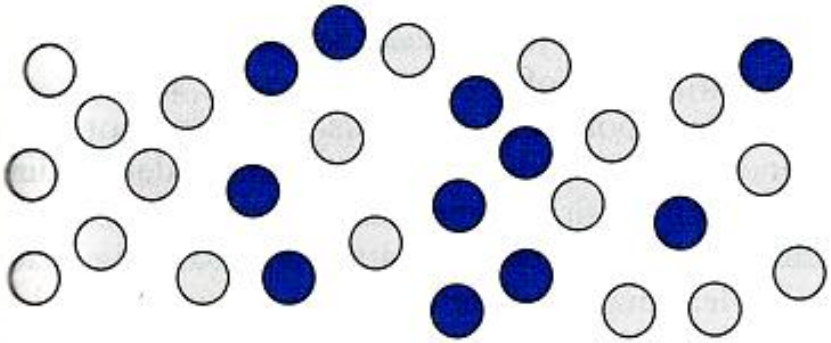

Herman
is-married-to
Doris
belongs-to
Woofie
is-a
golden retriever
type-of
dog
type-of
is-similar-to
cocker spaniel


Event 1: Dinner party
Event 2: Going dancing
Taste of food
Sight of lady
Feel of stiff dinner jacket
Smell of perfume
Topics of conversation
Sight of lady
Movements of dancing
Sights of dance hall
Sound of music
Smell of perfume

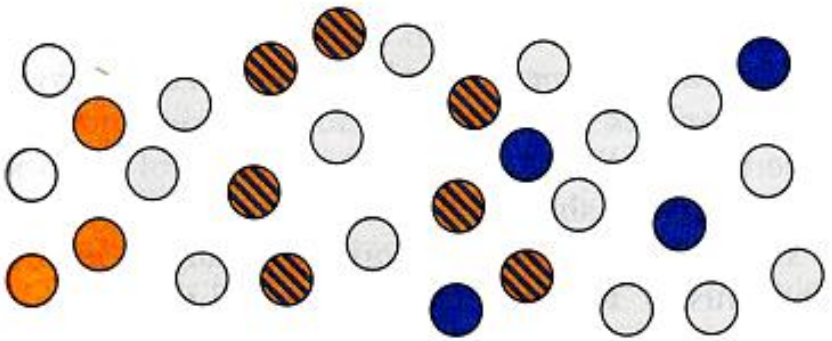
(a) "Golden retriever"



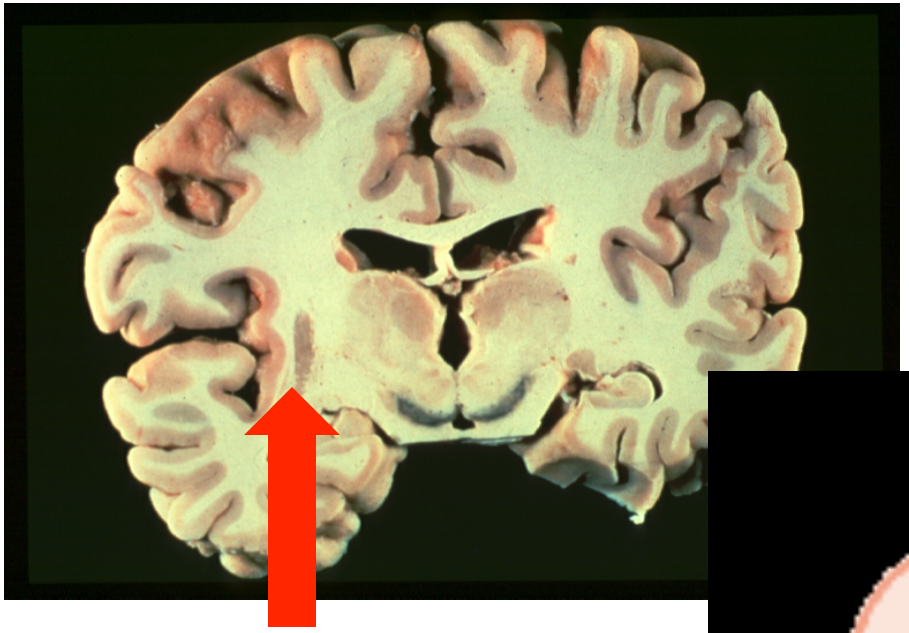
(b) "Cocker spaniel"

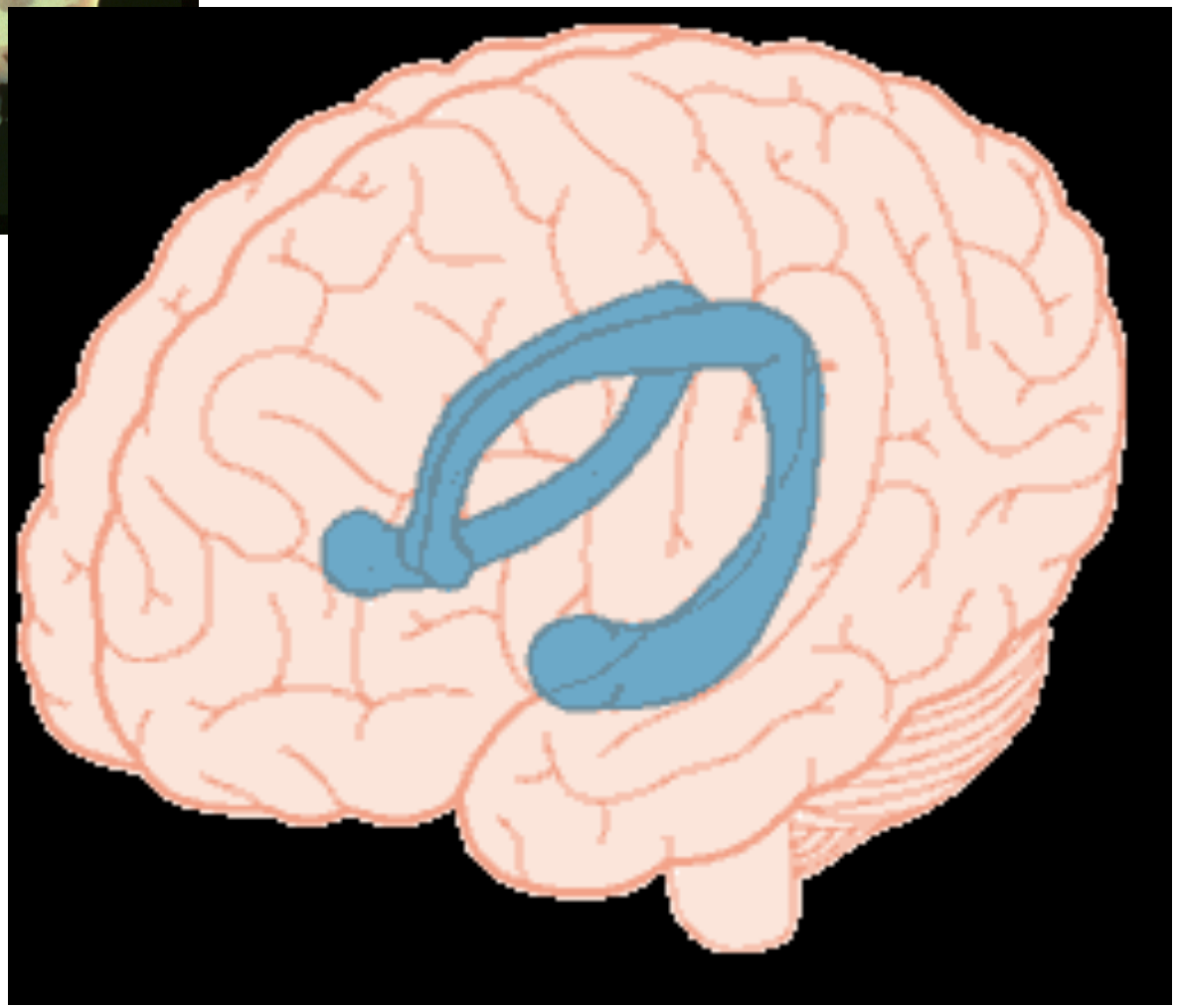


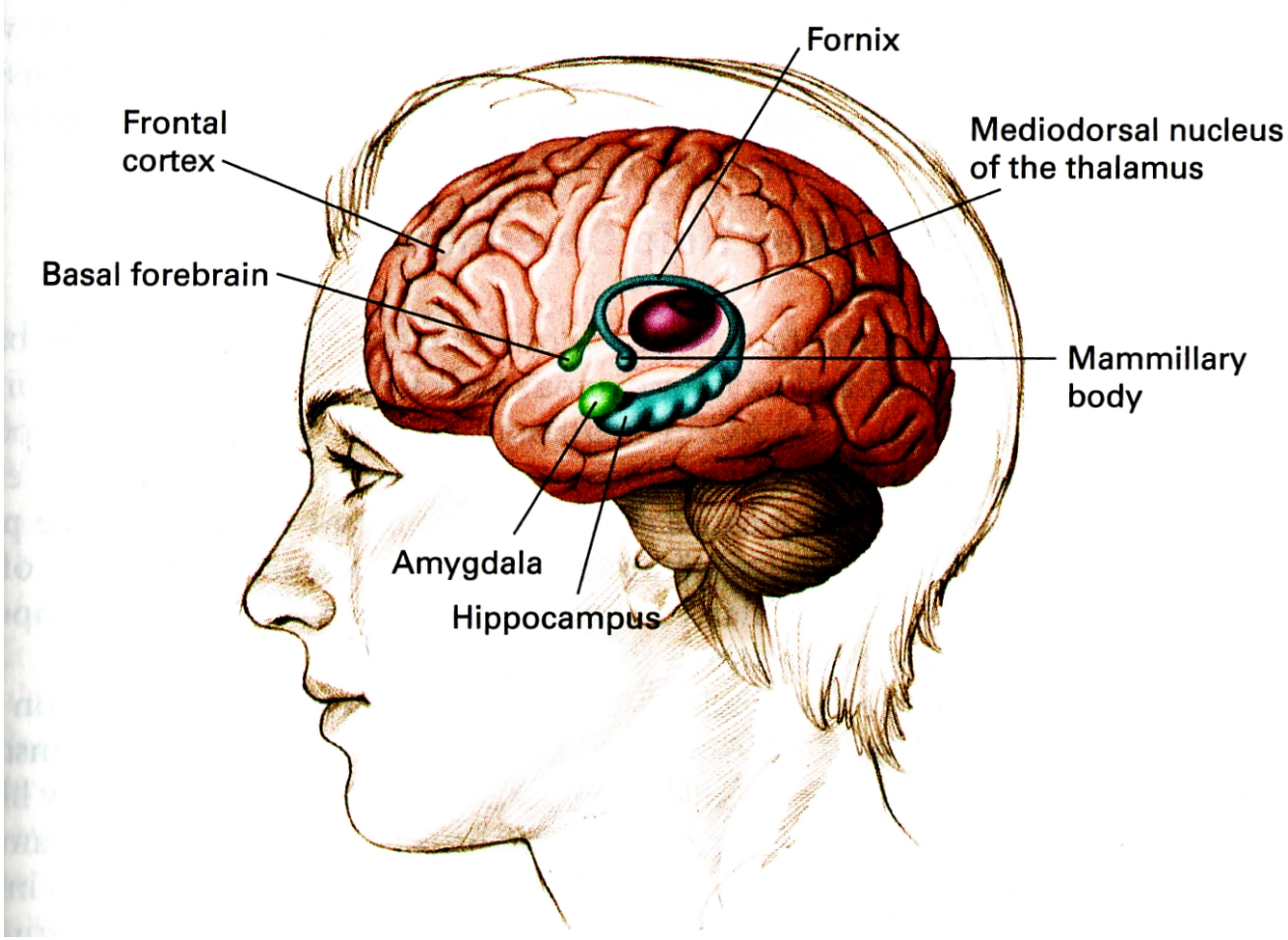
(c) "Dog"



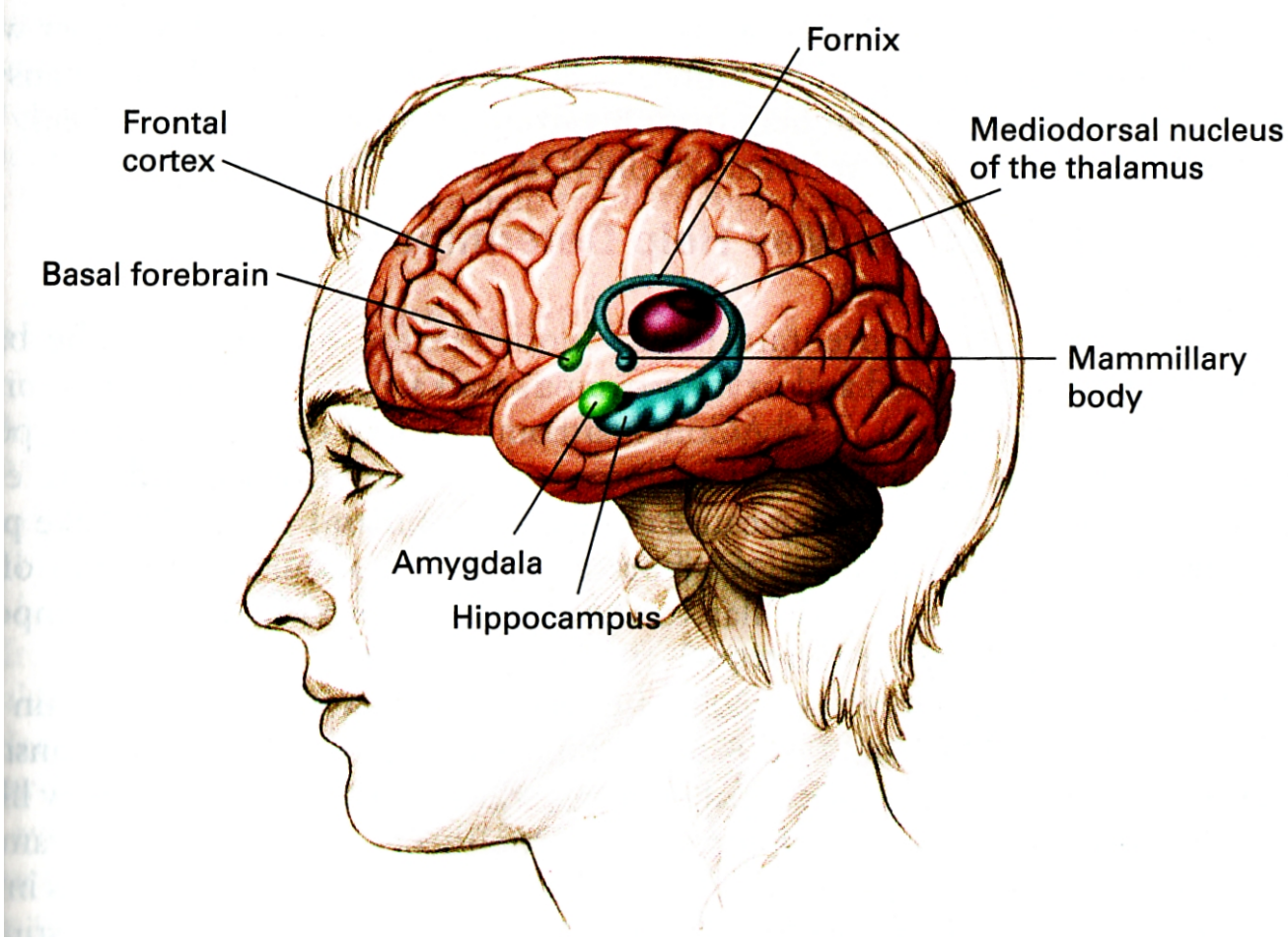
Neuroanatomy of Semantic and Episodic Memories



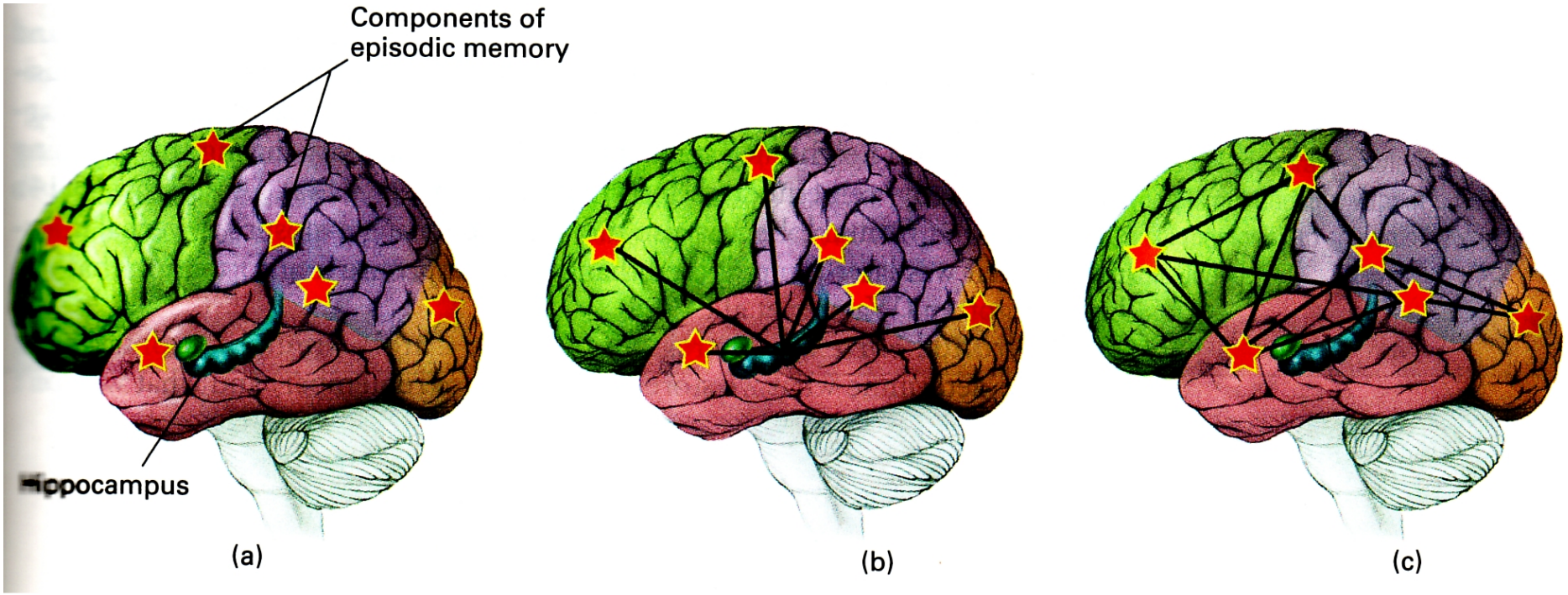




Basal Forebrain: signals that new information needs to be encoded



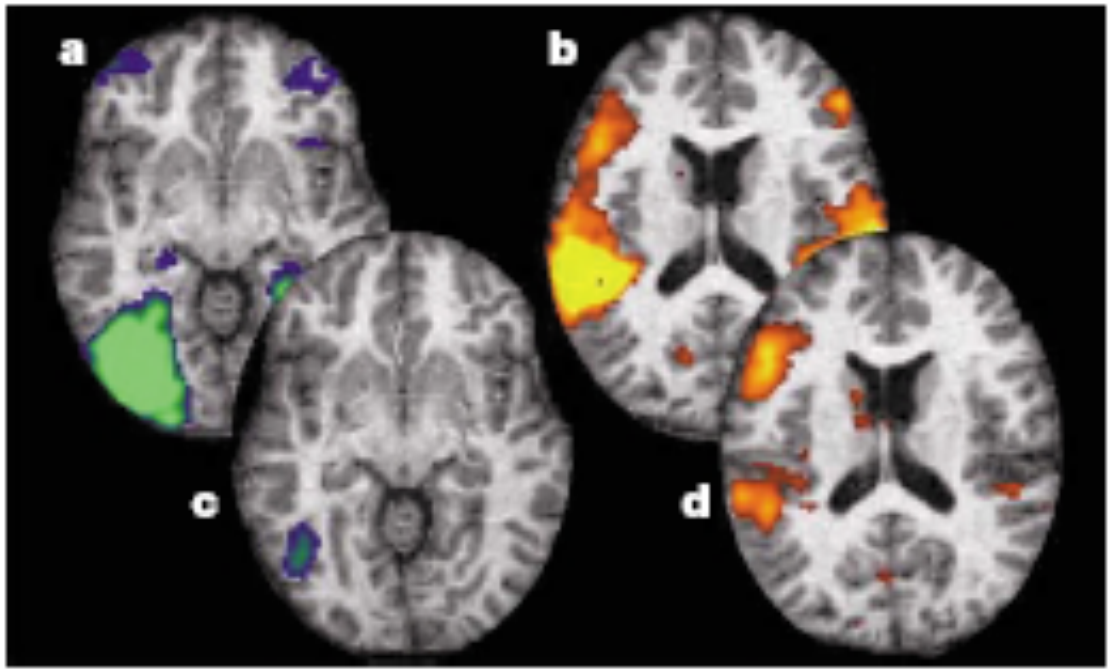
Hippocampus helps make links between information and encode new information

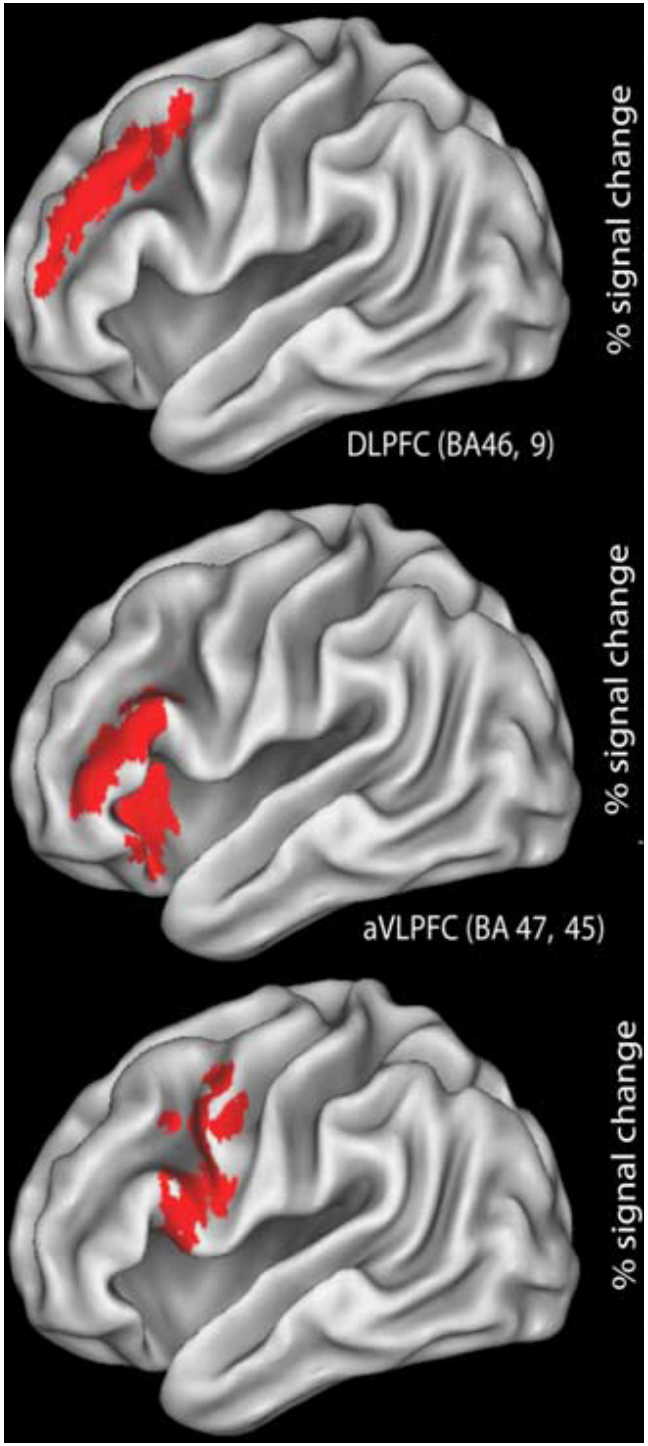

Components of
episodic memory
Hippocampus
(a)
(b)
(c)

Pictures Sounds

Perception

Recall



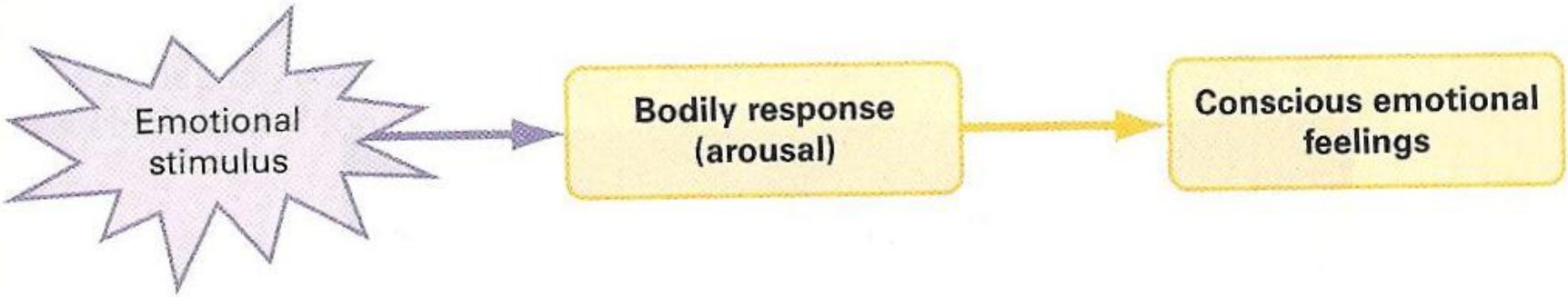


Relationships btw Episodic Memory Items

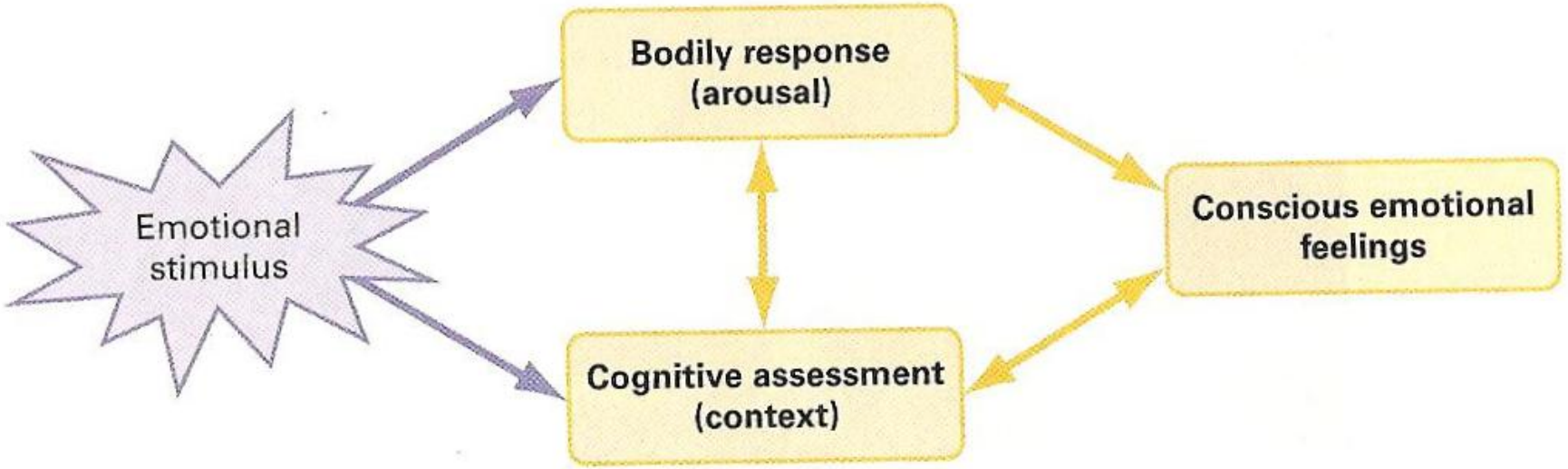
Encoding of Individual Items

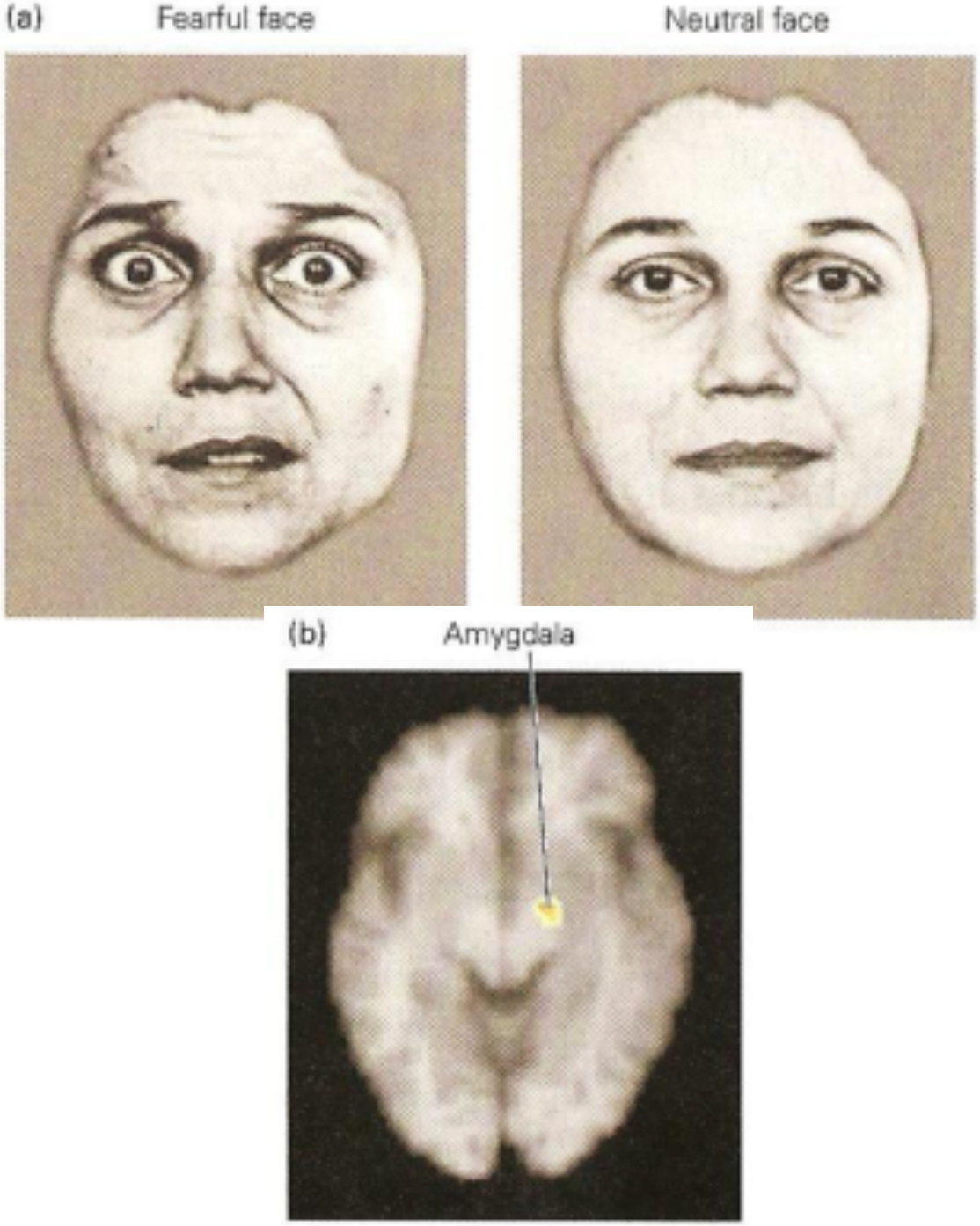
Emotion and Memory

(a) **James-Lange theory**



(b) **Modern emotional theory**




(a)
Fearful face
Neutral face
(b)
Amygdala

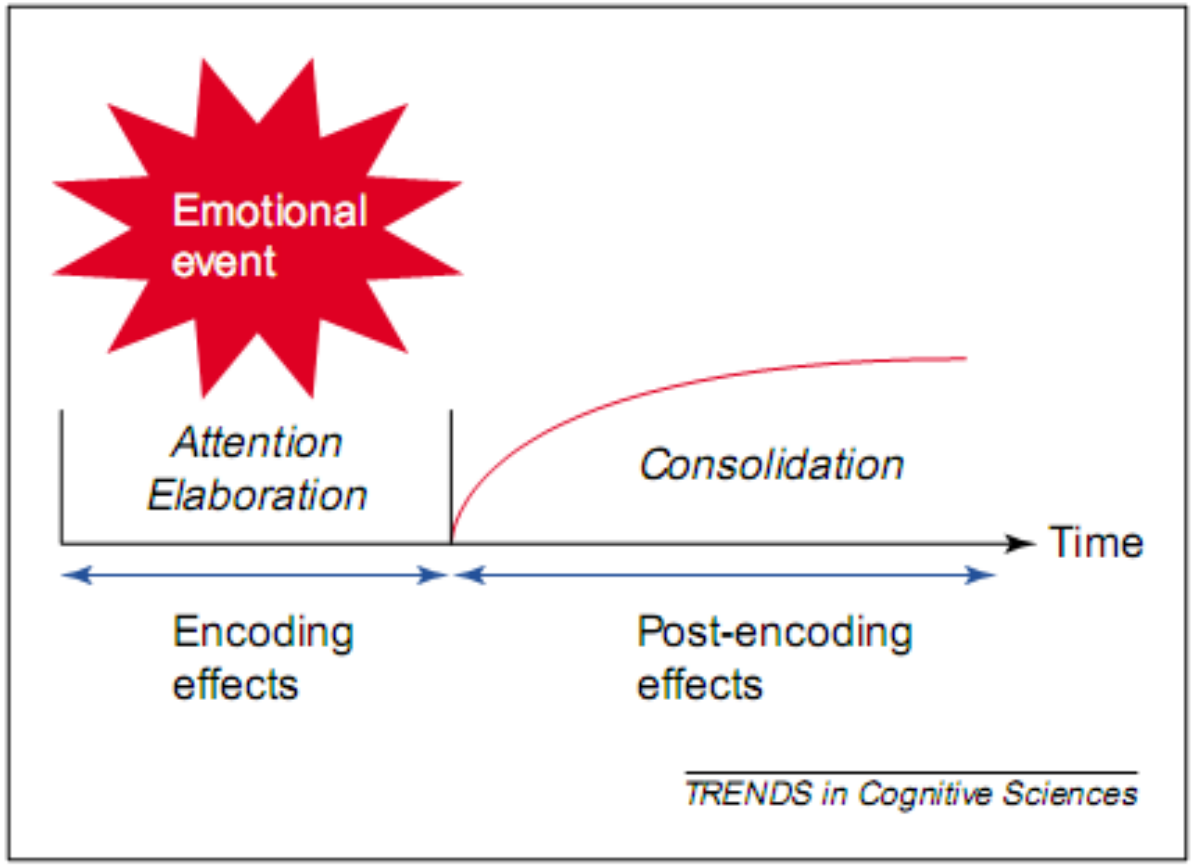
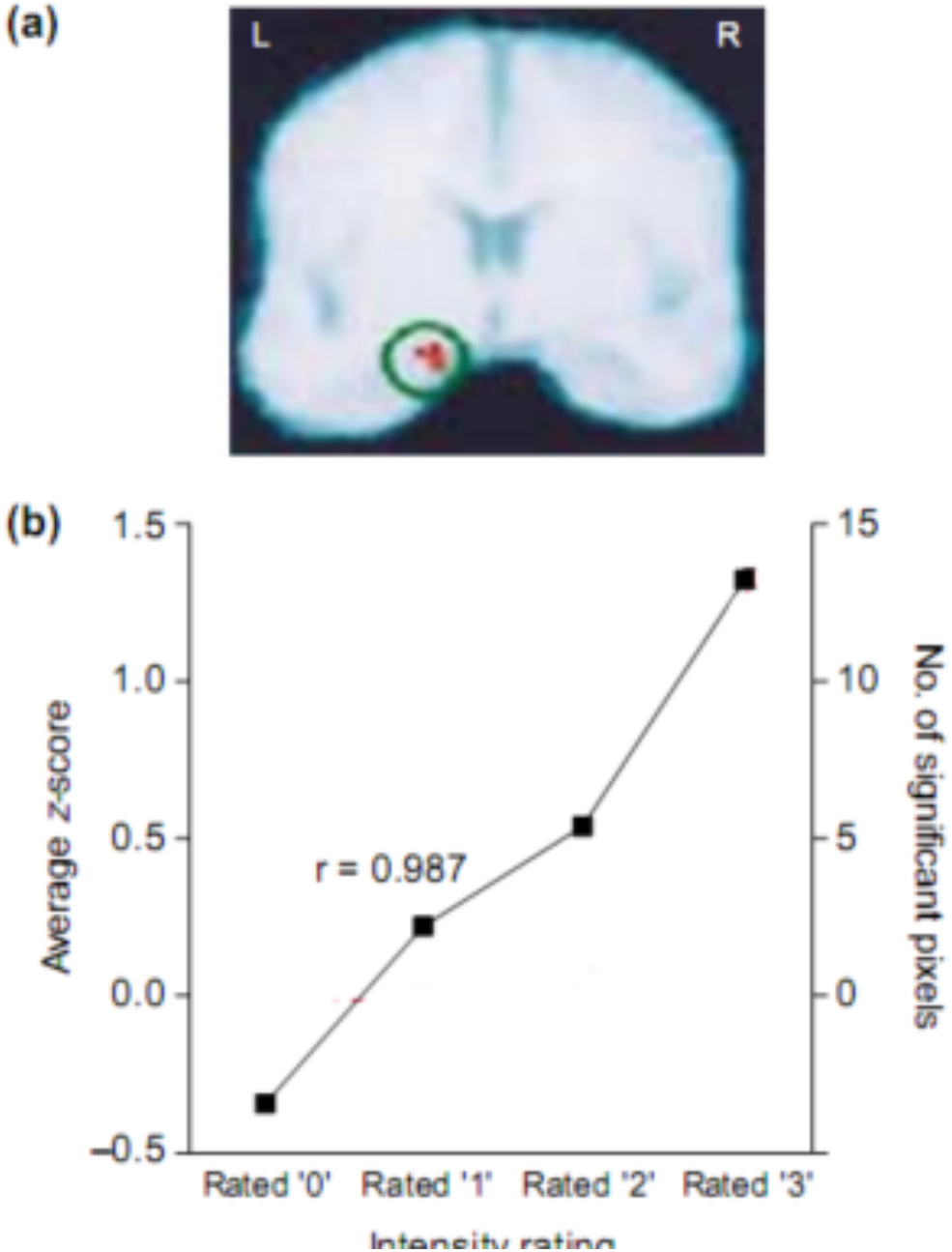


Fig. 1. Encoding and post-encoding effects of emotion. Encoding processes create the initial memory representation. After the event, post-encoding processes, primarily consolidation, continue to influence the memory representation. Consolidation is thought to continue for an extended period; therefore, the observed effects of emotion on memory should increase with time until consolidation is complete.

(1) The amygdala is the primary orchestrator of processes of emotional memory, without which emotional effects on memory cannot occur.

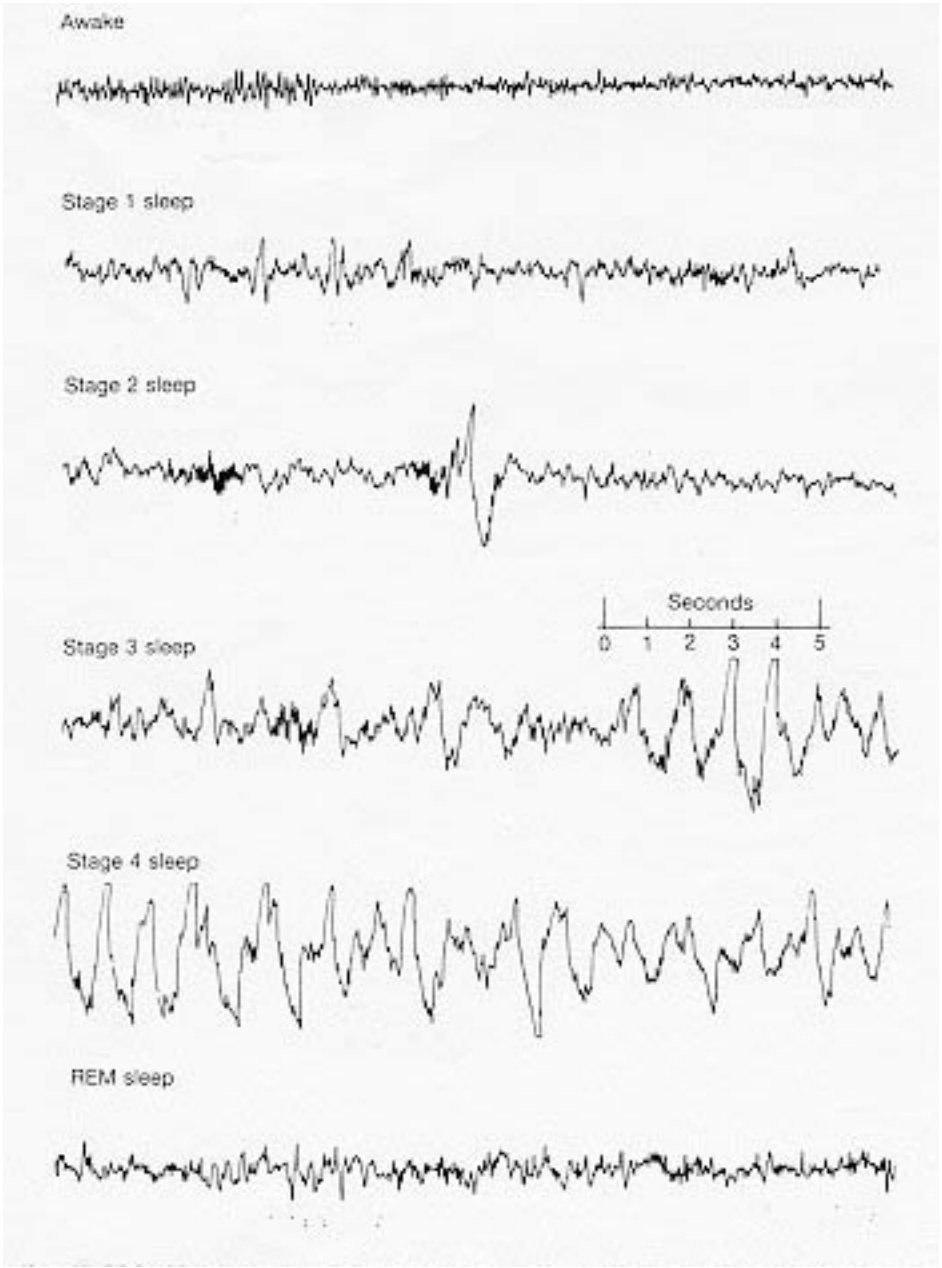
(2) The amygdala can affect explicit memory by modulating or enhancing the activity of other brain regions involved in memory.

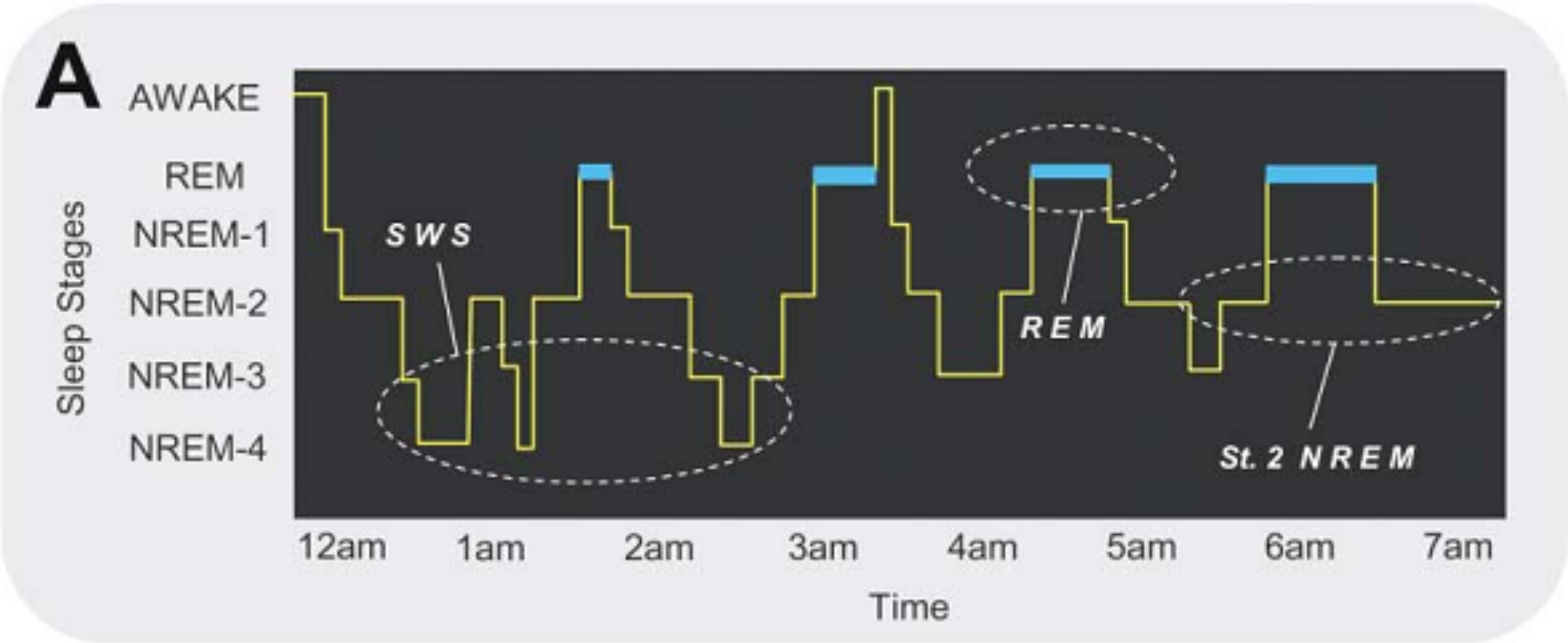

(a)
L
R
(b)
1.5
1.0
0.5
0.0
–0.5
Average z-score
15
10
5
0
No. of significant pixels
r = 0.987
Rated '0'
Rated '1'
Rated '2'
Rated '3'
Intensity rating

Sleep and Memory

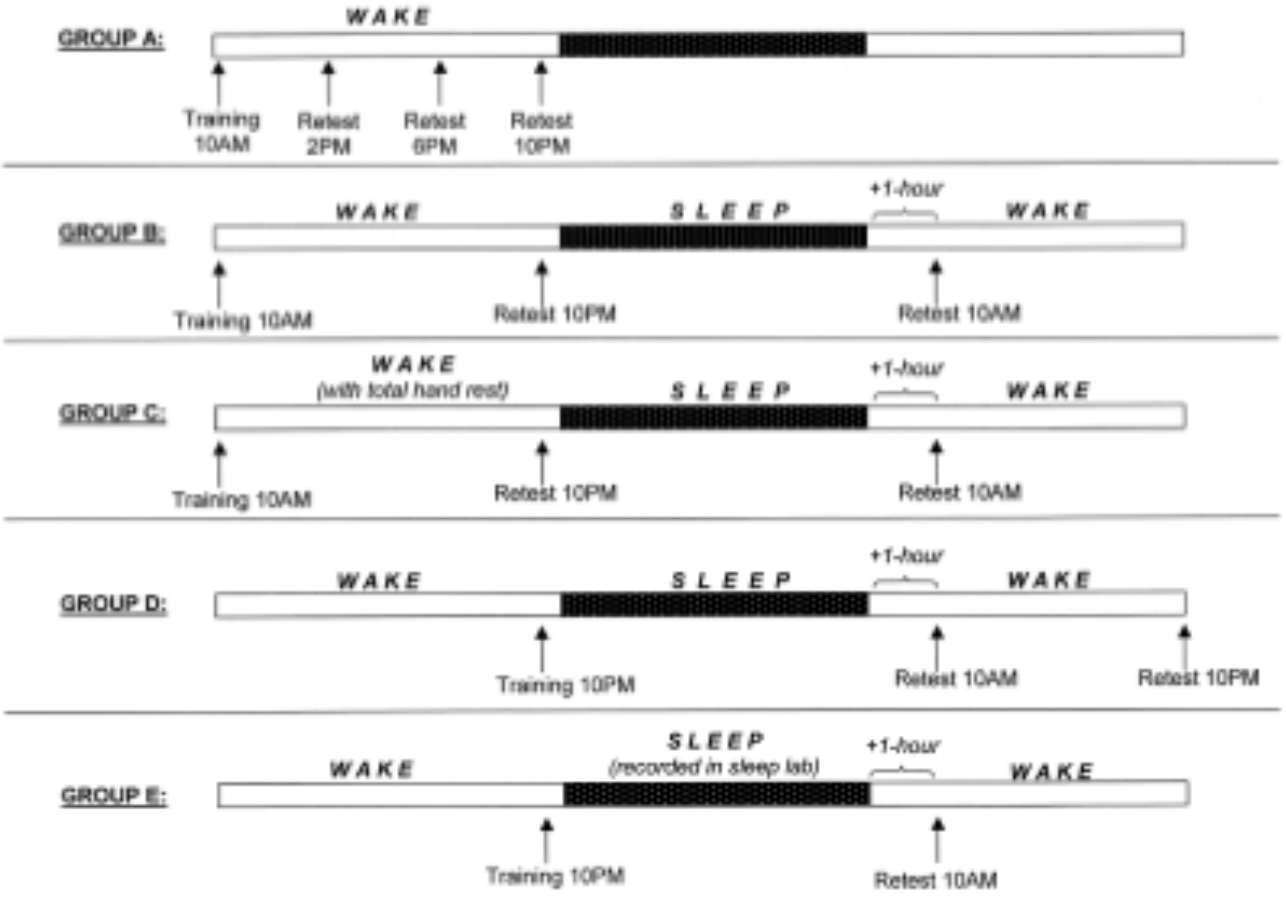
Stages of Sleep

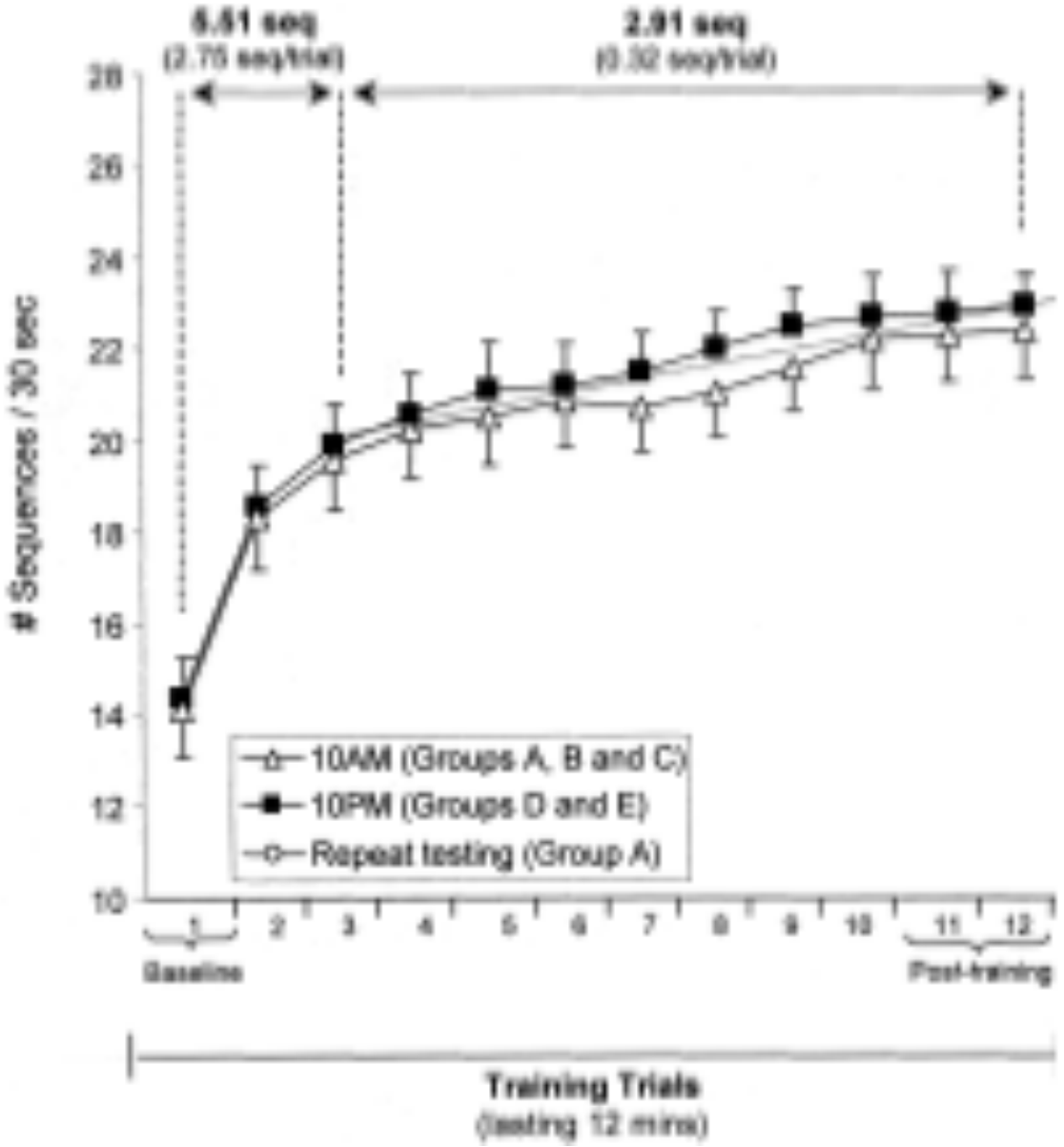
Stage 1	Light Sleep
Stage 2	Eye movements stop, change in brain activity
Stages 3 and 4	Deep Sleep
REM	Rapid Eye Movement

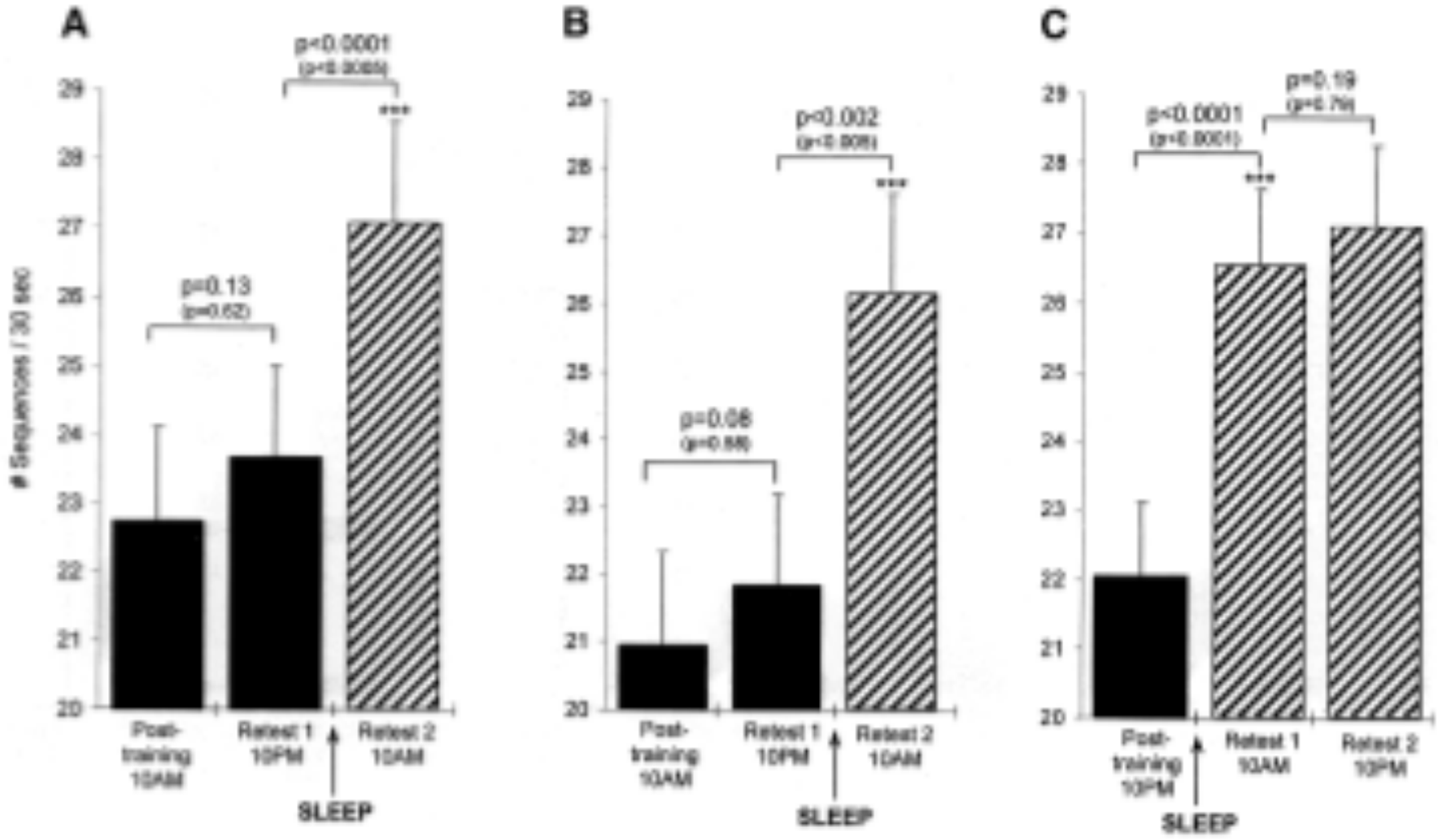

Awake
Stage 1 sleep
Stage 2 sleep
Seconds
0 1 2 3 4 5
Stage 3 sleep
Stage 4 sleep
REM sleep

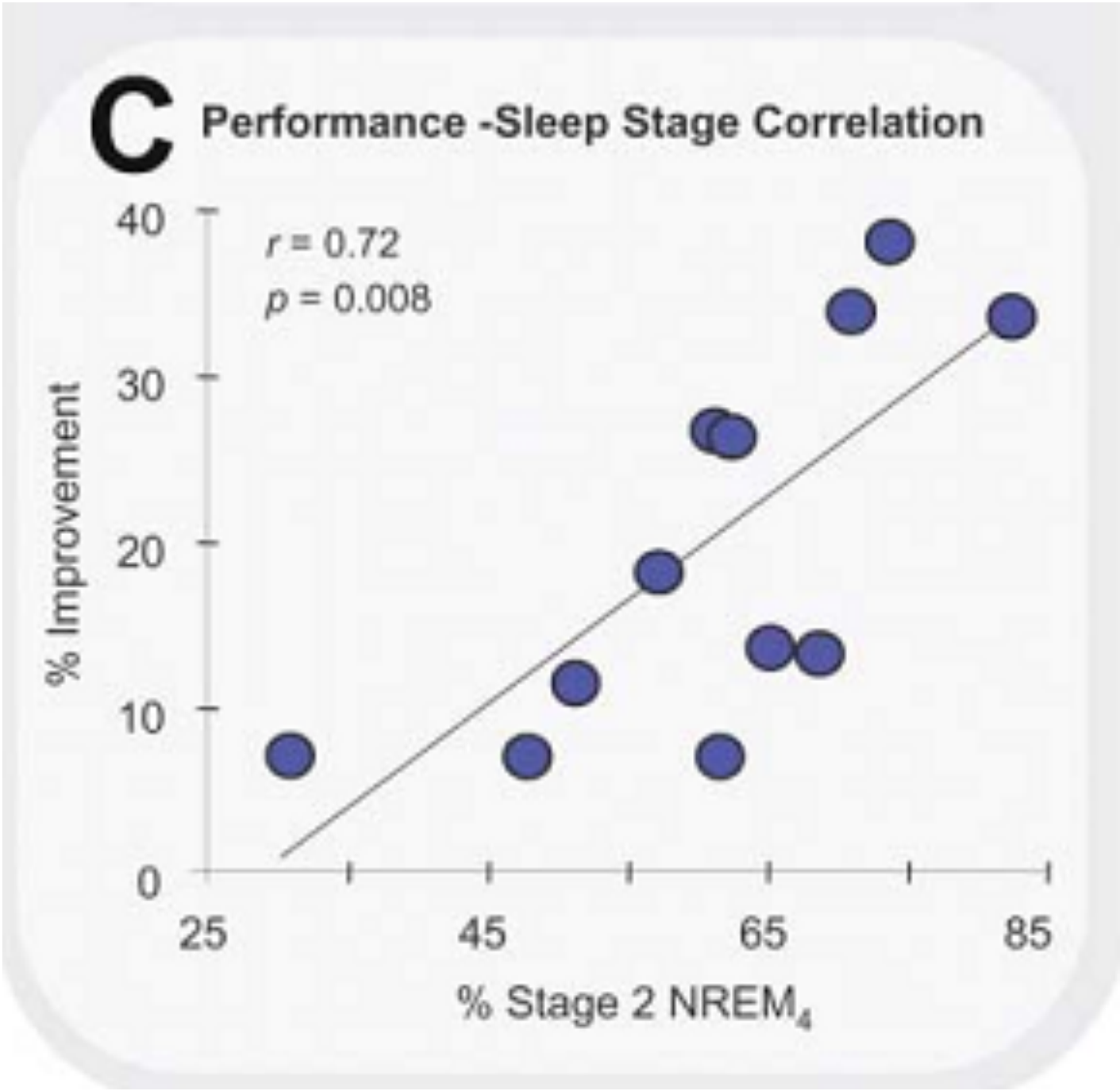

A
AWAKE
REM
NREM-1
NREM-2
NREM-3
NREM-4
Sleep Stages
SWS
REM
St. 2 NREM
12am
1am
2am
3am
4am
5am
6am
7am
Time

Practice With Sleep Makes Perfect: Sleep-Dependent Motor Skill Learning


GROUP A:
WAKE
Training 10AM
Retest 2PM
Retest 6PM
Retest 10PM
GROUP B:
WAKE
SLEEP
+1-hour
WAKE
Training 10AM
Retest 10PM
Retest 10AM
GROUP C:
WAKE
(with total hand rest)
SLEEP
+1-hour
WAKE
Training 10AM
Retest 10PM
Retest 10AM
GROUP D:
WAKE
SLEEP
+1-hour
WAKE
Training 10PM
Retest 10AM
Retest 10PM
GROUP E:
WAKE
SLEEP
(recorded in sleep lab)
+1-hour
WAKE
Training 10PM
Retest 10AM


5.51 seq
(2.75 seq/trial)
2.91 seq
(0.32 seq/trial)
Sequences / 30 sec
28
26
24
22
20
18
16
14
12
10
10AM (Groups A, B and C)
10PM (Groups D and E)
Repeat testing (Group A)
1
2
3
4
5
6
7
8
9
10
11
12
Baseline
Post-training
Training Trials
(testing 12 mins)


A
B
C
Sequences / 30 sec
p<0.0001
(p<0.0001)
***
p=0.13
(p=0.62)
p=0.002
(p<0.005)
***
p=0.08
(p=0.55)
p<0.0001
(p<0.0001)
***
p=0.19
(p=0.76)
Post-training 10AM
Retest 1 10PM
Retest 2 10AM
SLEEP
Post-training 10AM
Retest 1 10PM
Retest 2 10AM
SLEEP
Post-training 10PM
Retest 1 10AM
Retest 2 10PM
SLEEP
Group B
Group C
Group D


C
Performance -Sleep Stage Correlation
r = 0.72
p = 0.008
% Improvement
40
30
20
10
0
25
45
65
85
% Stage 2 NREM4

A deficit in the ability to form new human memories without sleep

Seung-Schik Yoo[1], Peter T Hu[2], Ninad Gujar[2], Ferenc A Jolesz[1] & Matthew P Walker[2]

Evidence indicates that sleep after learning is critical for the subsequent consolidation of human memory. Whether sleep before learning is equally essential for the initial formation of new memories, however, remains an open question. We report that a single night of sleep deprivation produces a significant deficit in hippocampal activity during episodic memory encoding, resulting in worse subsequent retention. Furthermore, these hippocampal impairments instantiate a different pattern of functional connectivity in basic alertness networks of the brainstem and thalamus. We also find that unique prefrontal regions predict the success of encoding for sleep-deprived individuals relative to those who have slept normally. These results demonstrate that an absence of prior sleep substantially compromises the neural and behavioral capacity for committing new experiences to memory. It therefore appears that sleep before learning is critical in preparing the human brain for next-day memory formation—a worrying finding considering society's increasing erosion of sleep time.

Table 1 Memory performance

	Hits
Sleep control	
Mean	0.86
s.d.	0.019
Sleep deprivation	
Mean	0.74
s.d.	0.044
P	0.029*

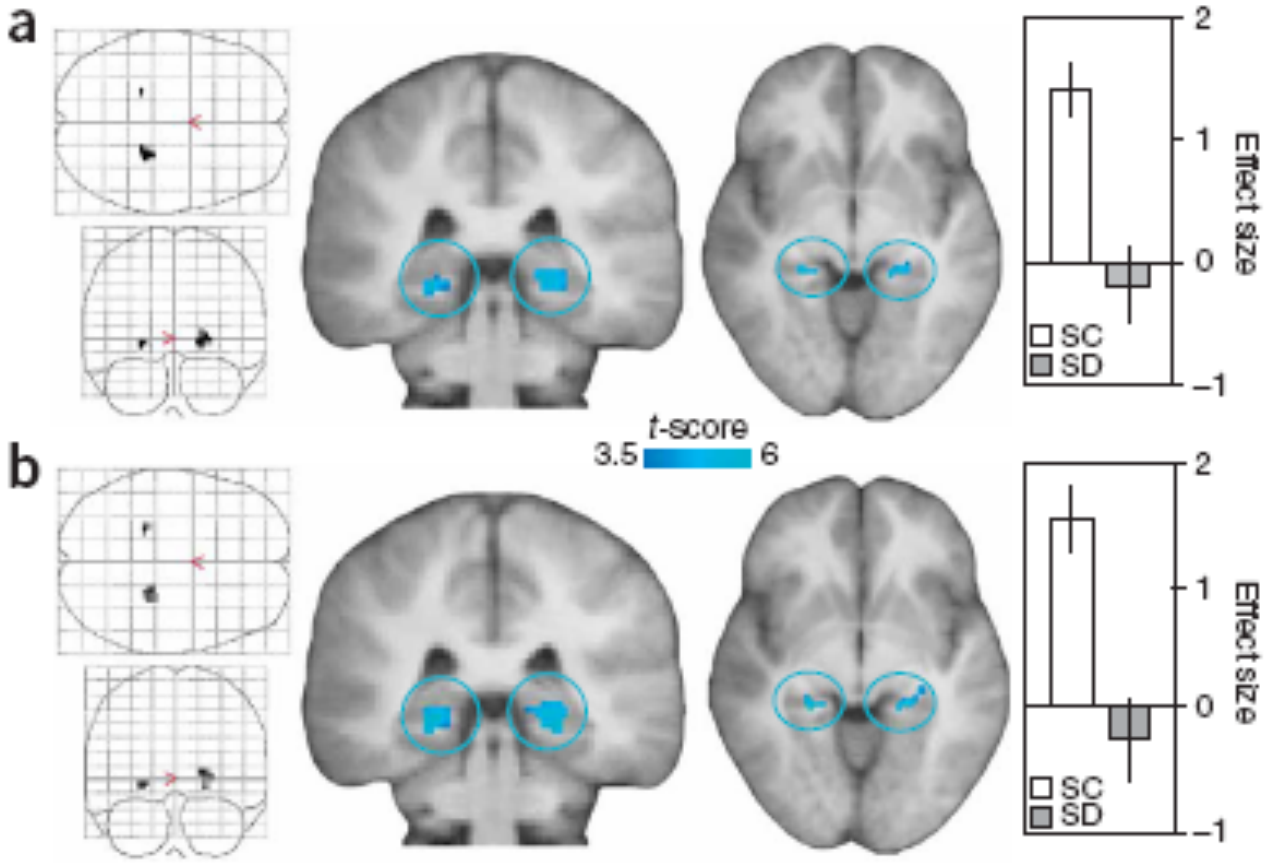


Figure 2 fMRI group-level encoding differences. (**a**,**b**) Statistical activation maps showing regions of significantly reduced activation in the sleep deprivation (SD) group relative to the sleep control (SC) group in bilateral posterior hippocampal regions for all encoding trials (peak MNI space coordinates (*x*, *y*, *z*); left peak: −27, −33, 0; *Z* score = 3.53; right peak: 24, −36, −3; *Z* score = 3.52) (**a**) and hit trials (left peak: −21, −30, 6; *Z* score =

The Amnesias

Anterograde Amnesia

Definition:

Inability to form new memories

Neural Issue:

Typically, damage to the hippocampus

Retrograde Amnesia

Definition:

Loss of old memories

Neural Issue:

Unclear… prefrontal damage, loss of neural connections, ???

Source Amnesia

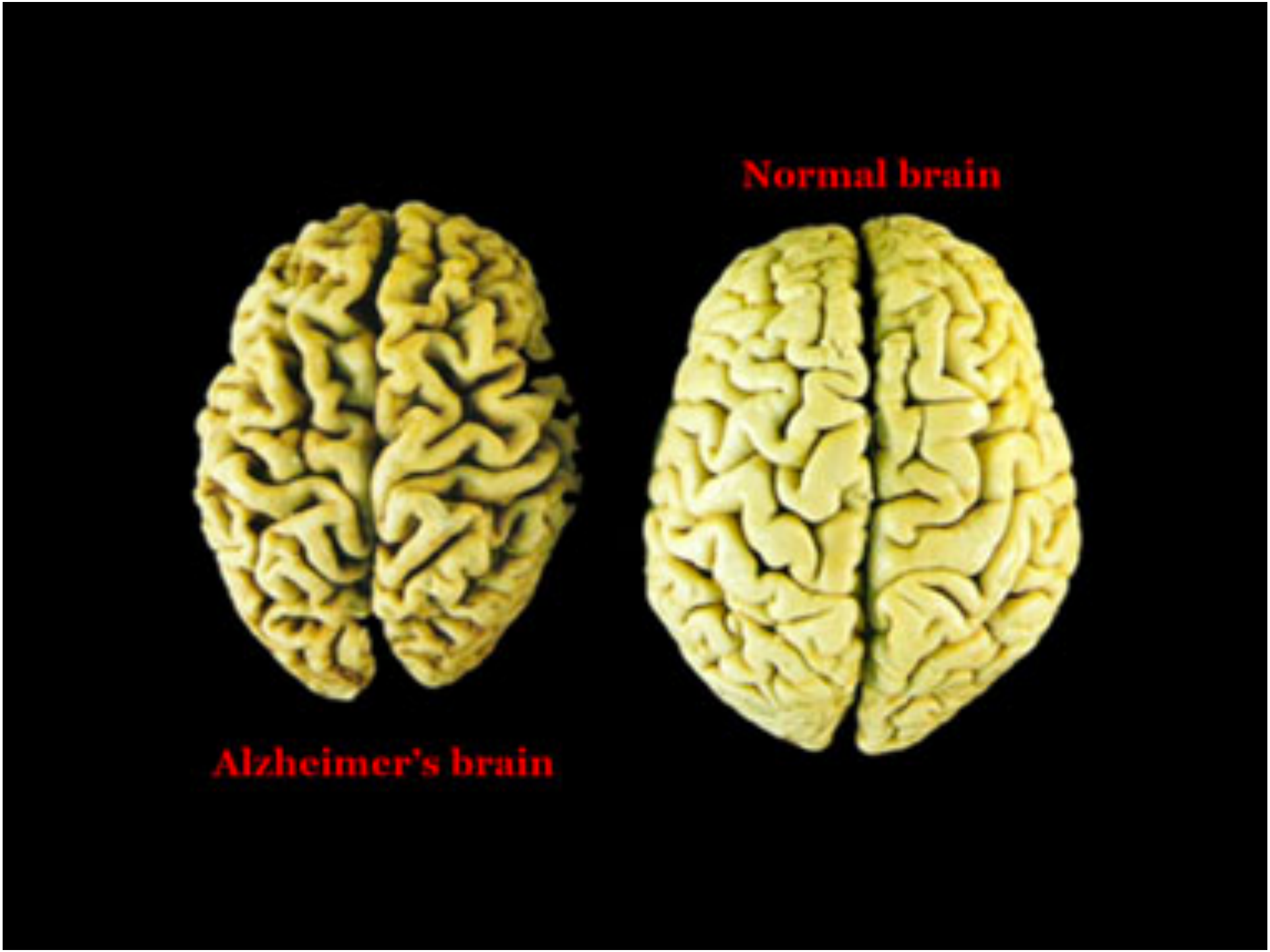
- Definition:
  - Remembering the photograph, not the event

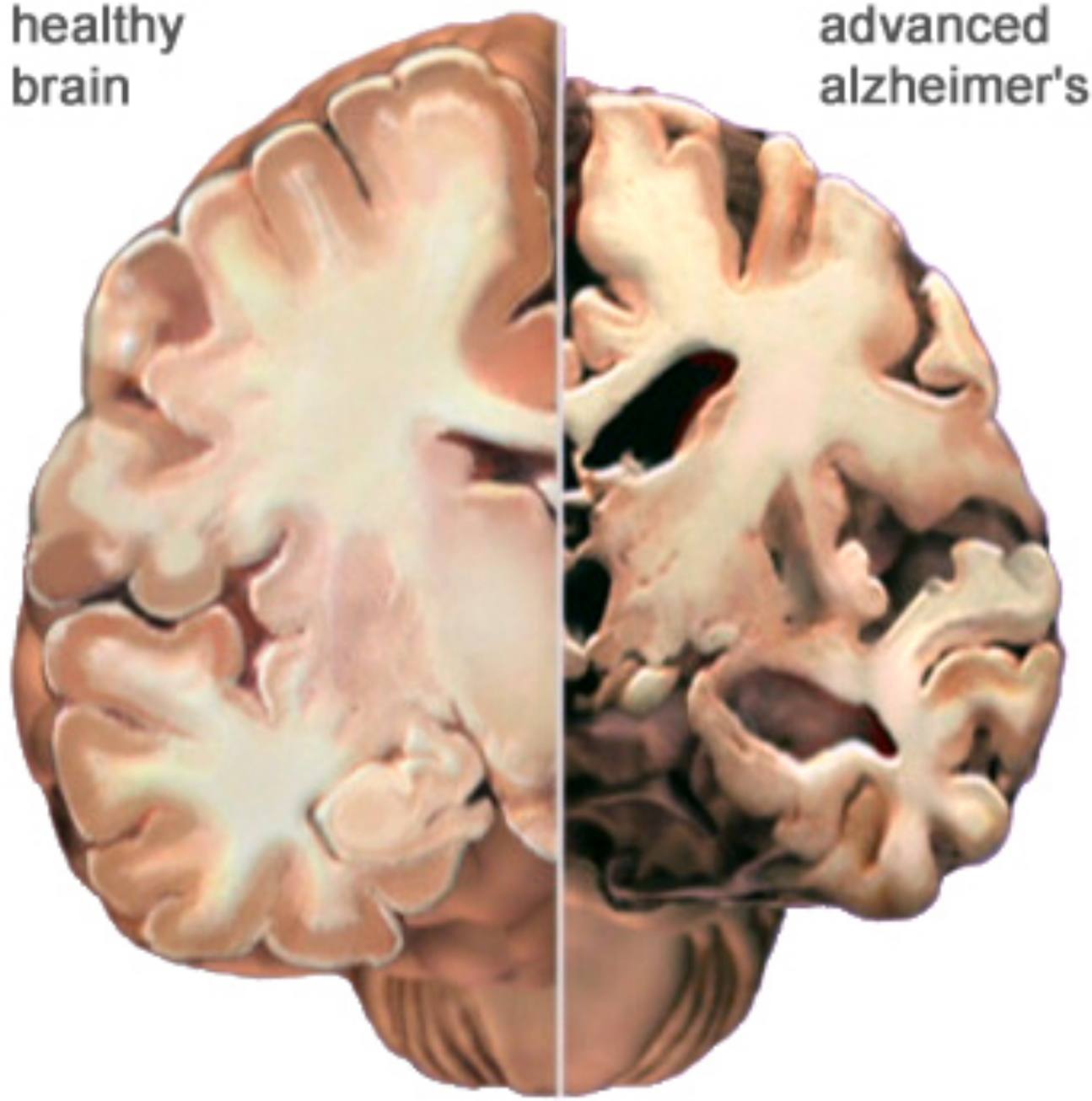
- Neural Issue:
  - Partial loss of memory – linkage by the hippocampus?

Cryptomnesia: the Plagiarists Excuse

- Definition:
- Thinking your current thoughts and ideas are original

- Neural Issue:
- Partial loss of memory – linkage by the hippocampus?


Normal brain
Alzheimer's brain


healthy
brain
advanced
alzheimer's

Brain Atrophy in Advanced Alzheimer's Disease