

Memory and Neuroscience

Dr Stuart Jones

Aims of the Lecture.

- Provide an overview of the Theories of Memory (Cognitive Psychology).
- Discuss how Animal Research has helped us gain an understanding of the Biological Basis of Memory.
- Examine some classic examples of Amnesic patients, exploring their deficits.

Aims of the Lecture.

- Explore how Neuroimaging has helped us further our knowledge of healthy individuals in relation to memory.
- The recent studies in Alzheimer's Disease, highlighting how Neuroimaging has helped us understand this terminal disease.

What is Memory.

- Memory refers to the persistence of learning in a state that can be revealed at a later time (Squire, 1987).
- Memory is an outcome of Learning.
 - Memory is created when something is learned.
 - May occur by single exposure to a stimuli or by repetition.
 - Persists over time.
 - Gazzaniga et al (2009).

Memory

- Subdivided into 3 major hypothetical stage.
- Encoding
 - Processing of incoming information.
 - Acquisition.
 - Consolidation.
- Storage
 - Permanent Record (results of Acquisition & Consolidation)
- Retrieval.
 - Conscious representation or execute a learned behaviour.

Memory – from Cognitive Psychology.

- Sensory Memory.
- Short Term Memory.
- Long Term Memory.

Sensory Memory

- Sensory Memory is the shortest element of memory, with a time course of milliseconds to seconds
- Ability to retain sensory information after the stimuli has ended.
 - Process of getting information from our senses to our brain.
- Not something we have conscious awareness of.
 - Gazzaniga et al (2009).

Sensory Memory

- Two most researched elements of sensory memory are.
- Echoic Memory.
 - Auditory
- Iconic Memory.
 - Vision
- What Neuroimaging techniques would be most appropriate to research sensory memory?

EEG and MEG

- Looking at Event Related Potentials (remember back to lecture on EEG and MEG).
- Mismatch Negativity (MMN) – EEG.
- Mismatch field (MMF) – MEG.
- Mismatch is caused by the presence of a deviant stimulus (e.g. a high frequency tone within a sequence of identical low frequency tones) – Gazzaniga et al, 2009.

Sams et al (1993)

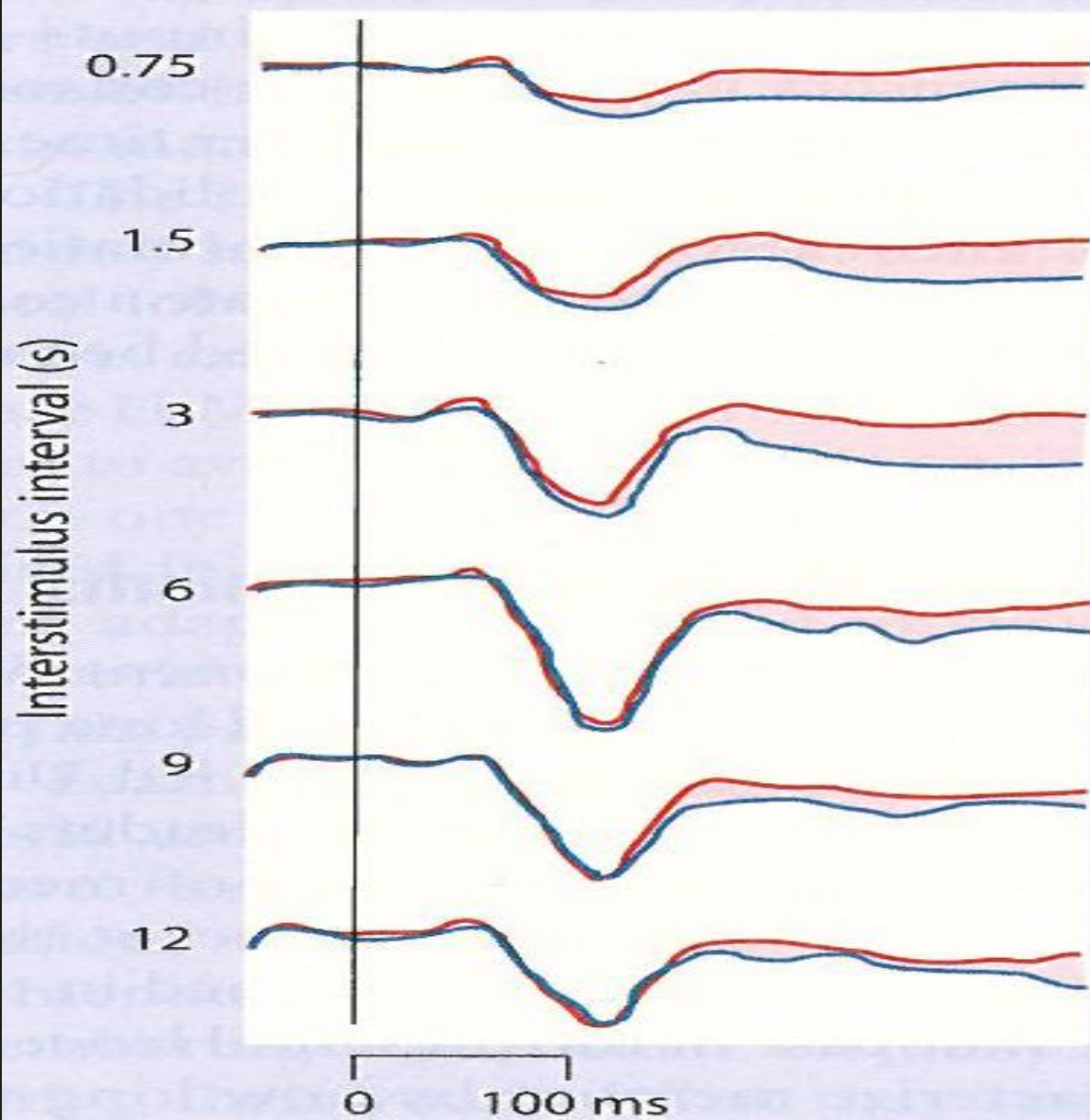
- Participants were asked to perform a reading task while in a MEG scanner.
- Instructed to pay no attention to any auditory stimuli.
- While reading two auditory stimuli were presented.
 - 1) A standard tone: A constant lower pitched tone.
 - 2) An infrequent “deviant” tone, slightly higher pitched that played at different intervals.
 - This would be a short tone and not the constant tone of the standard tone.
 - Inter-stimulus intervals.

Findings

- Standard tone evoked a consistent N100 response.
- As hypothesised, there was a change N1 potential in response to the standard tone.
 - Prominent 100 msec response to the onset of the stimuli.

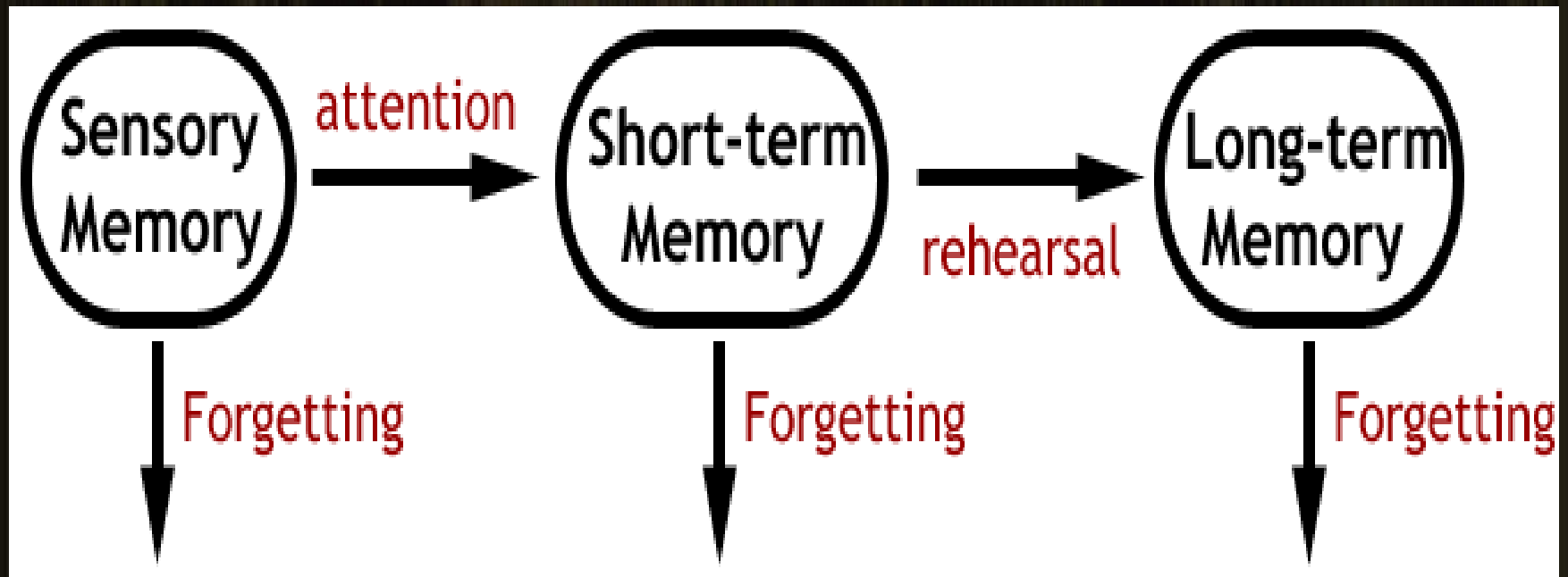
Findings

- When the second tone was added (remember this was just a short tone) with a 0.75 second delay to first tone starting an ADDITIONAL mismatch was reported.
- This pattern continued for the different inter-stimulus intervals up until 9 seconds.
- Beyond that, non significant mismatch fields were noted.
- Also location – Auditory cortex, providing further support for sensory memory.
 - Many issues with the study (paper is on moodle).



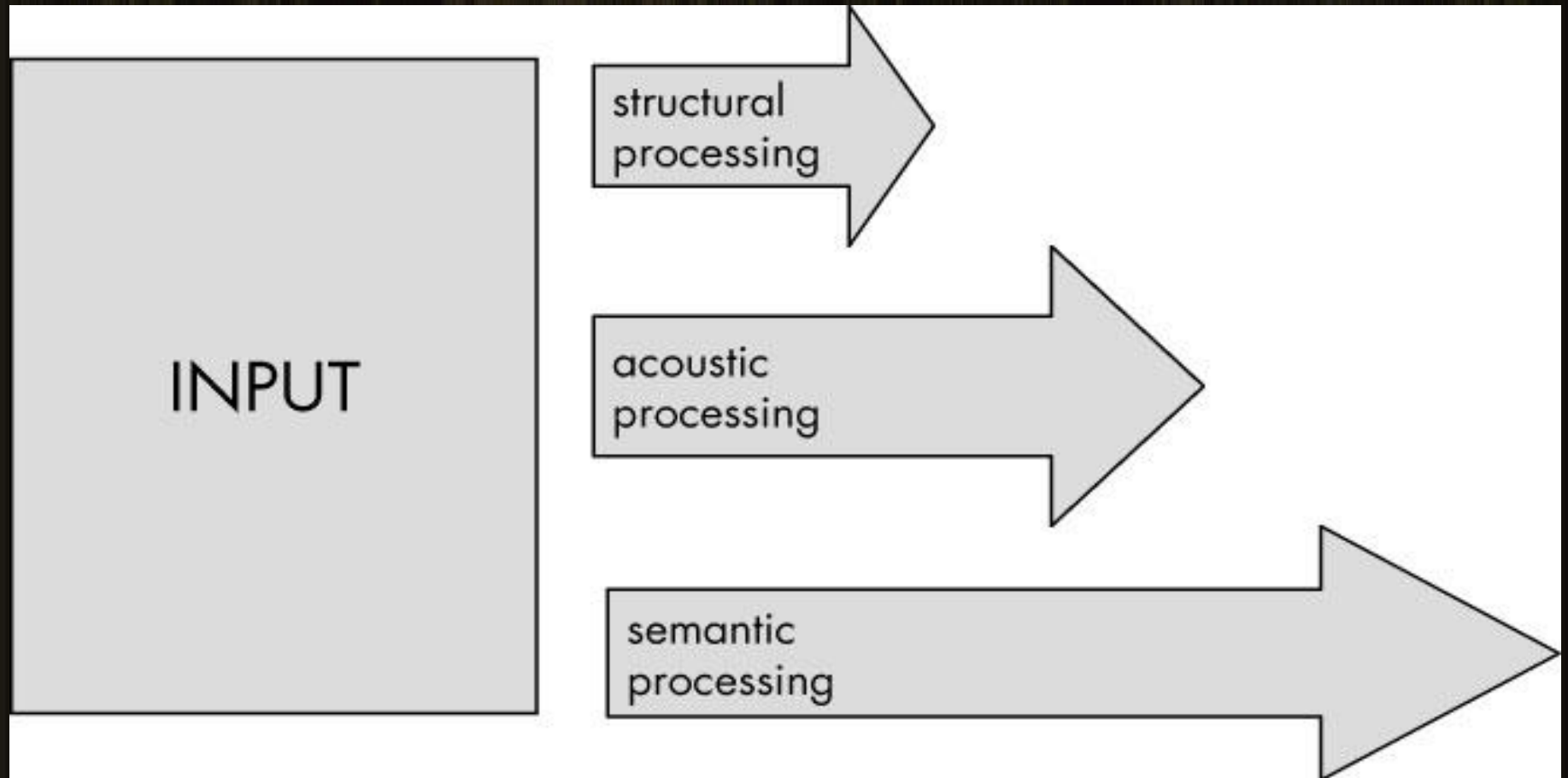
Modal Model of Memory.

- Atkinson and Shiffrin (1968).



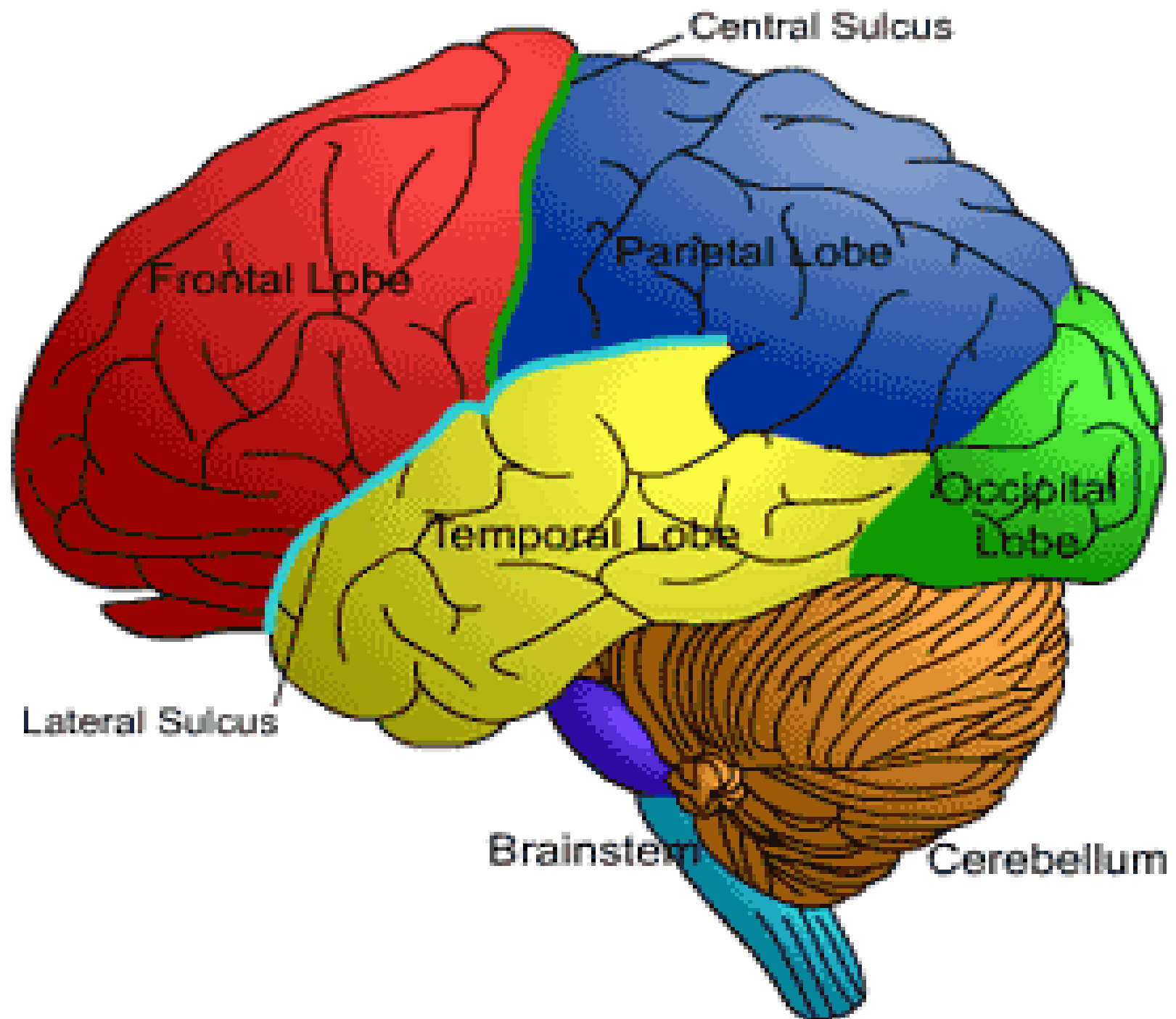
Levels of Processing Models.

- Craik and Lockhart (1972).



Neuroscience and the Memory Models.

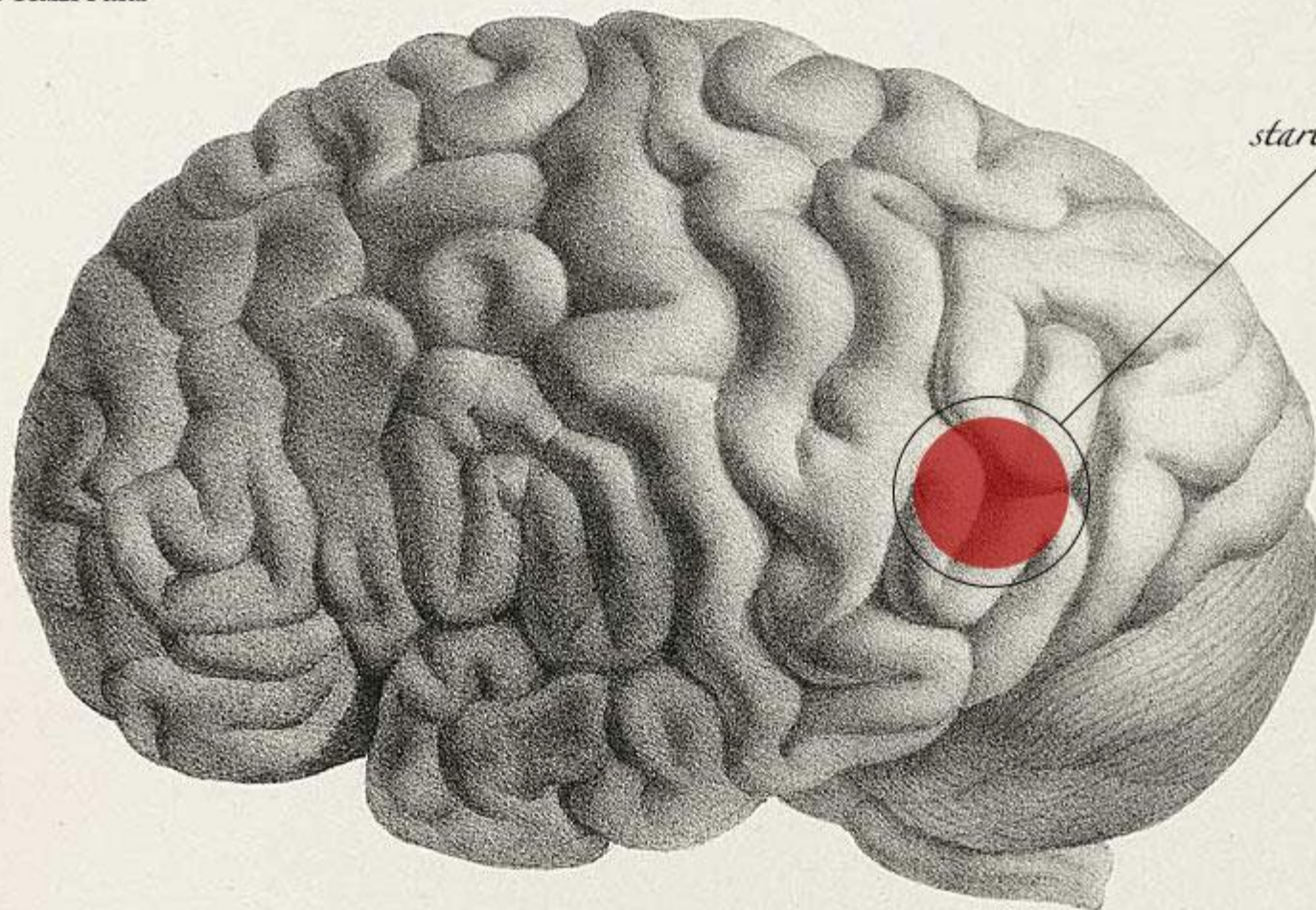
- Markowitsch et al (1999).
- E.E – tumour centred in the left angular gyrus.
- Inferior parietal cortex
- Posterior superior temporal cortex.



The inferior parietal cortex is a highly associative area, located anatomically where neural connections from vision, audition, and touch come together—a location appropriate for numerical abilities, since they are common to all sensory modalities. Lesions in this area have been shown to affect not only arithmetic but also writing.

GEORGE LAKOFF AND RAFAEL E. NÚÑEZ
WHERE MATHEMATICS COMES FROM

Pl. LXXXIII.



start here

literature
and
mathematics

spring
2008

- After tumour was removed – below normal STM, but retained LTM.
 - Normal Speech production.
 - Normal Comprehension.
 - Normal Reading.
- Issues with the Token Test.
- Why? Due to STM deficits.

- The implication of such studies (and there are many many other examples) is that the STM cannot be the gateway to LTM as Atkinson and Shiffrin insisted.
- Information from Sensory Memory can be encoded into LTM directly.
- Clear difference between STM and LTM though.

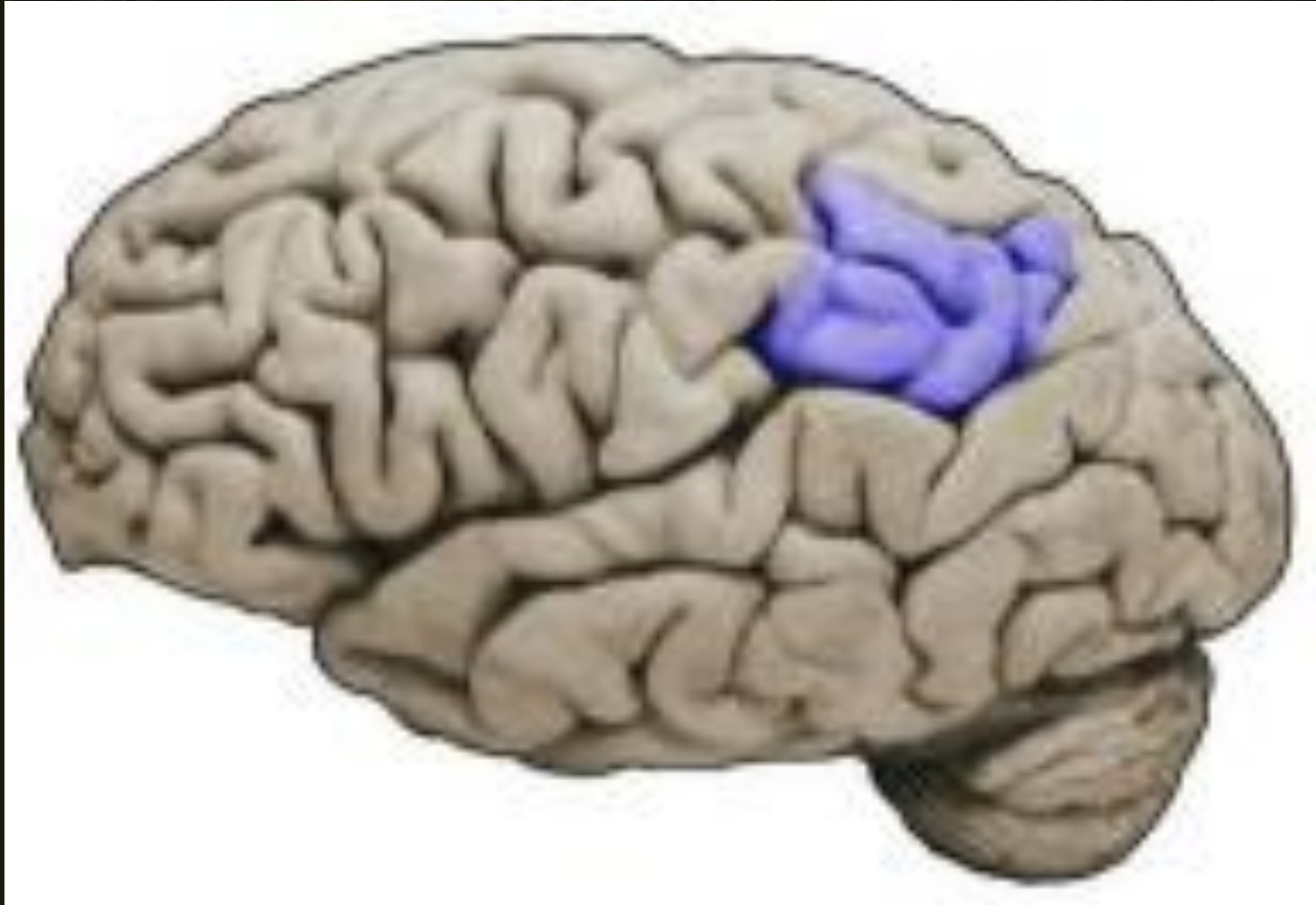
Working Memory Models.

- Baddley and Hitch (1974).
 - Central Executive Mechanism
 - Phonological Loop.
 - Visuospatial Sketchpad

Working Memory and Neuroscience.

- Lesions of left supramarginal gyrus – deficits in phonological working memory.
 - Paulesu (1993) – reduced auditory-verbal memory.
- Lateral frontal lobe and inferior parietal lobe subserves phonological working memory.
 - Close to Broca's and Wernicke's – but not associated in deficits of speech perception or production.

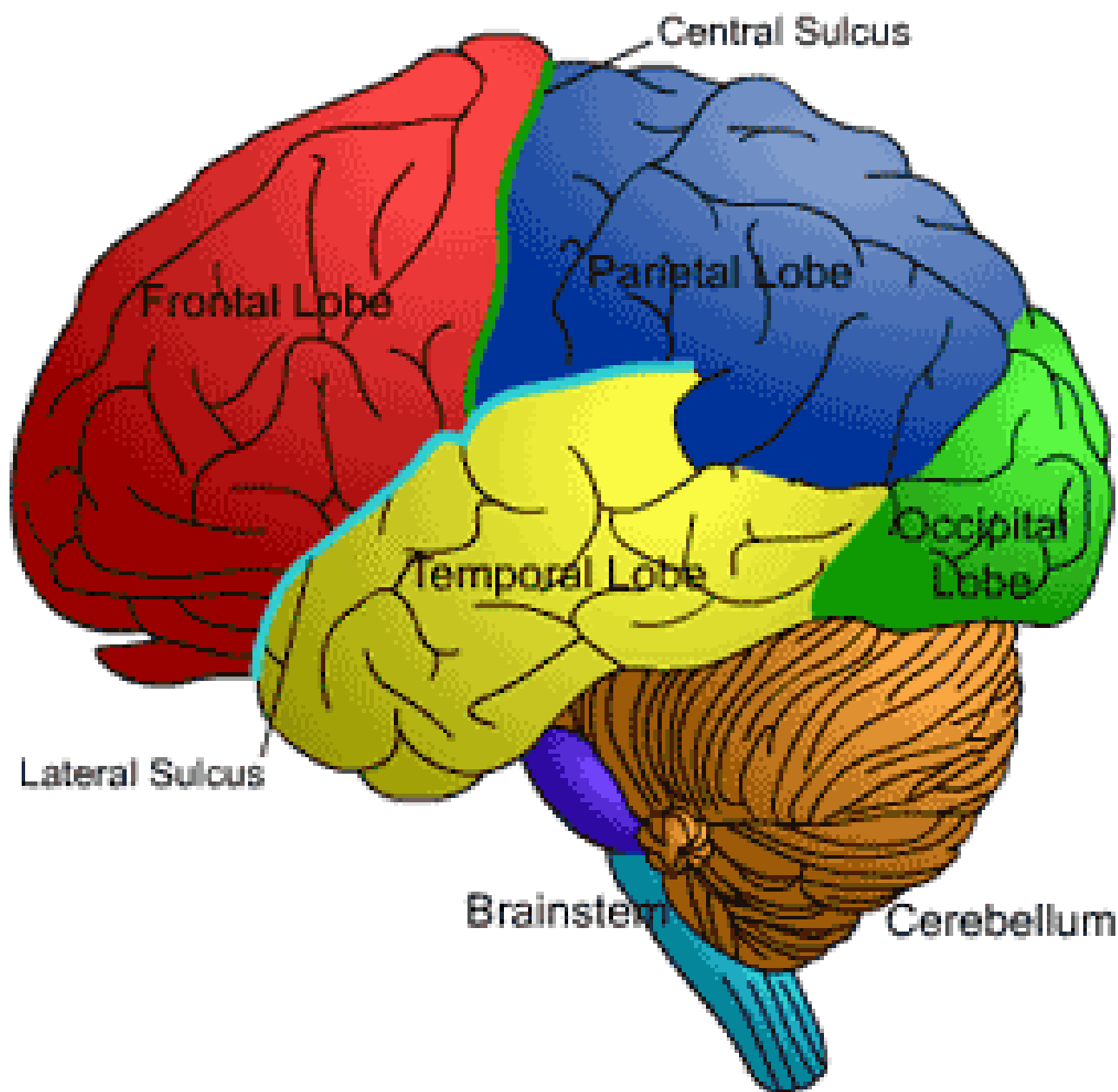
Supramarginal Gyrus



Working Memory Model.

- Visuospatial Sketch pad – Damage to parieto-occipital region of both hemisphere's.
- Right hemisphere more severe particularly with regards to STM.



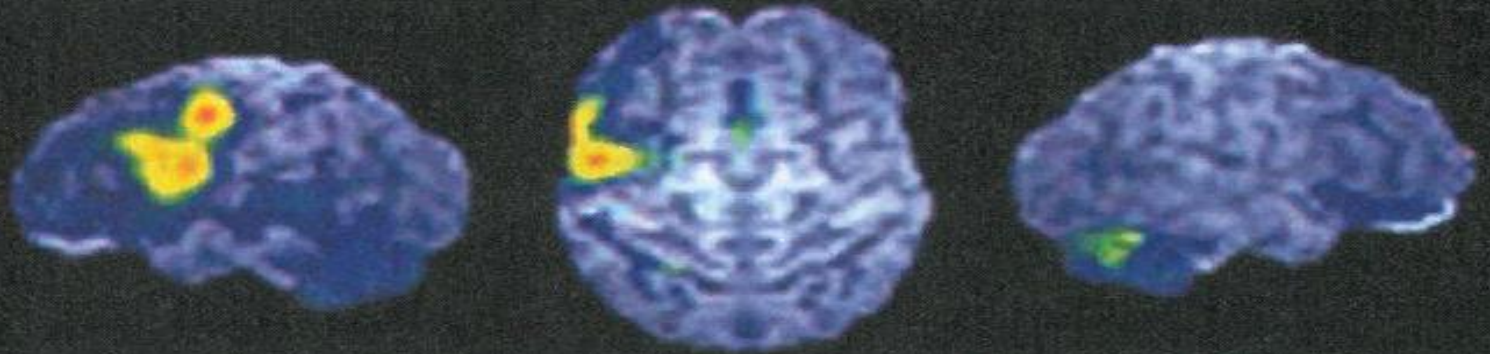


Smith et al (1996)

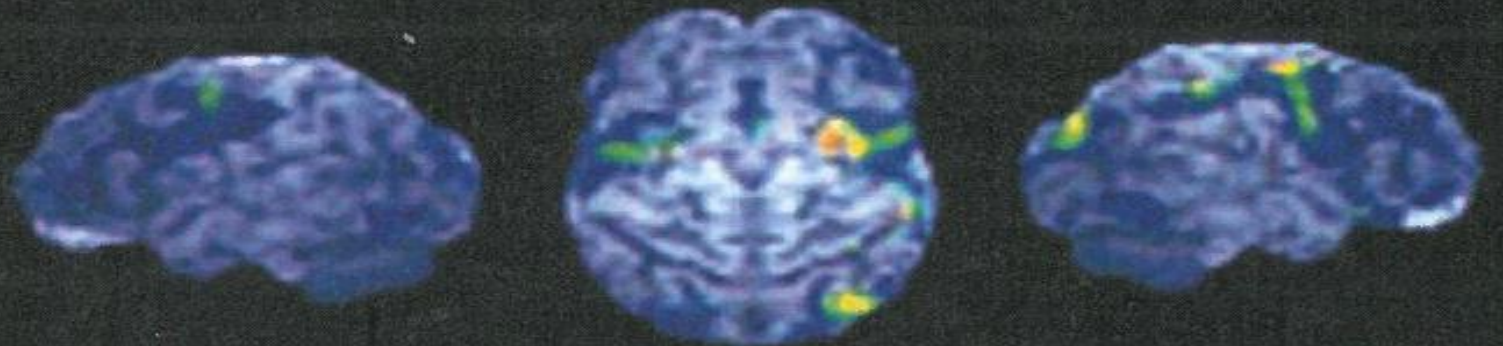
- Pet Scan Study....
- Participants presented with a randomised array of dots on computer screen (in different locations) or an array of letters on a computer screen.
 - Asked to remember the locations of the dots (spatial memory) OR
 - Asked to remember the letters on the screen (verbal memory)
 - Three second delay.
 - Then showed either a dot (in a location) or letter and asked to consider if this had been shown in the previous array.

Findings

(a) Verbal memory



(b) Spatial memory



Left lateral

Superior

Right lateral

Long Term Memory.

- Declarative Memory.
 - Memory for facts of events.
 - The capital of Wales is.....
- Non Declarative Memory.
 - Several Categories.
 - Skills, Reactions, habits, behaviours etc.
 - Fear = use of the Amygdala.
 - Classical Conditioning.

Declarative Memory.

- Episodic Memory.
 - Recall about our own lives.
 - Conscious awareness of past events.
 - Autobiographical.
- Semantic Memory.
 - Facts
 - World Knowledge
 - Language etc.

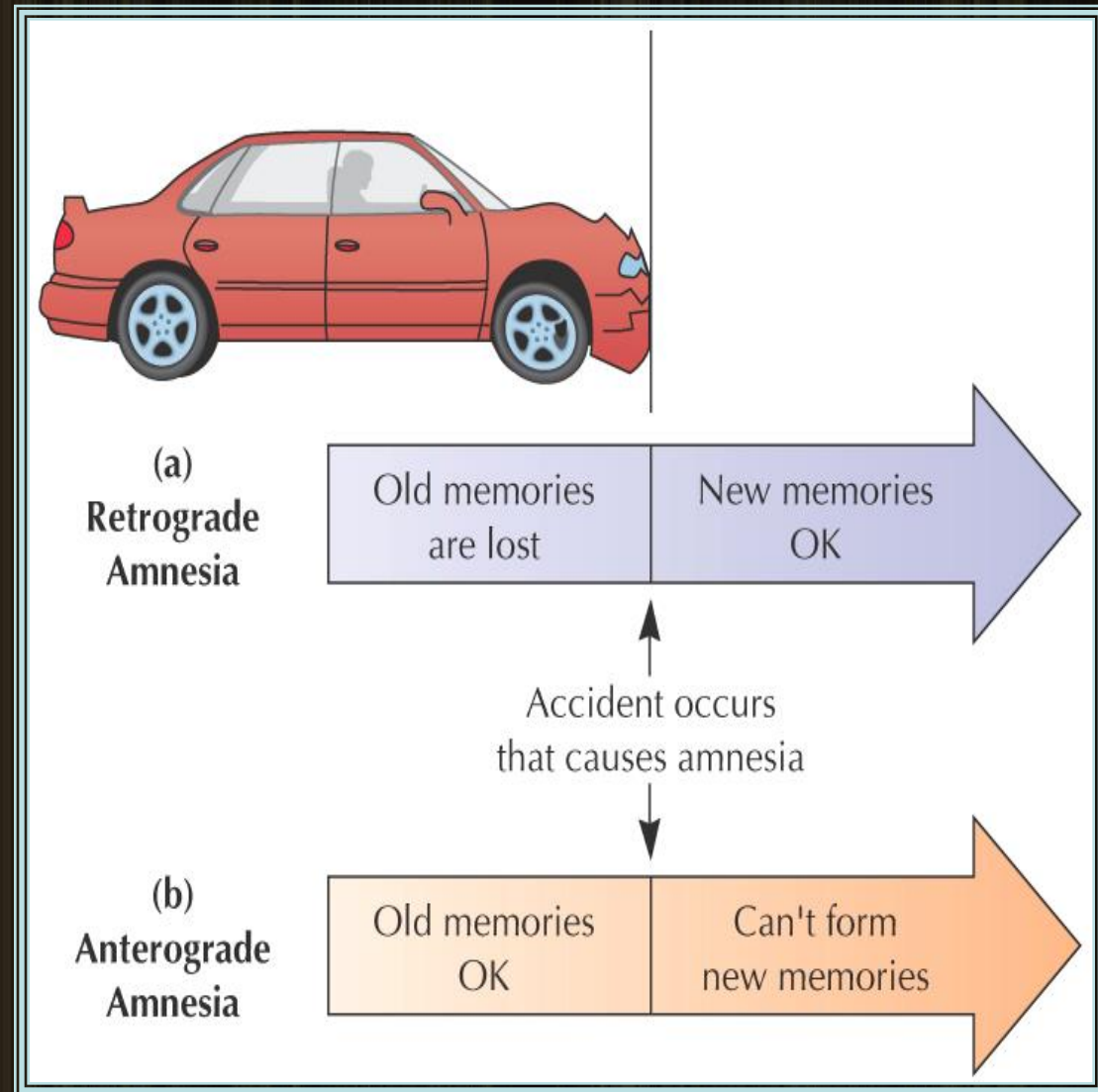
Non-declarative memory.

- Procedural Memory.
 - Motor and Cognitive Skills.
- Perceptual Representation System (PRS).
 - Perceptual Priming.
- Classical Conditioning.
 - Pavlov and his Dogs.
- Non-associative learning.
 - Simple learning (Habituation and Sensitisation).

Amnesia.

- Deficits in memory as a function of brain damage, disease or psychological trauma are known as amnesia.
- Inability to learn things.
- Loss of previous knowledge.
 - Both.

- Retrograde amnesia (old memories lost)
- Anterograde amnesia (new memories lost)



Localisation of Declarative Memories.

- Macaque Monkeys.
- Lesion of the inferotemporal cortex.....
Inferior temporal lobe.
- Can no longer perform the task even though the basic visual capacities remain intact.

Brain Surgery.

- 1940's and 1950's – attempted to treat neurological and psychiatric disease using neurosurgical procedures.
- Removal of the medial portion of temporal lobe.
 - Including Hippocampus



Scoville and Milner.

- The further posterior along the medial temporal lobe the resection was, the worse the memory loss.
- Bilateral resection of hippocampus resulted in severe amnesia.

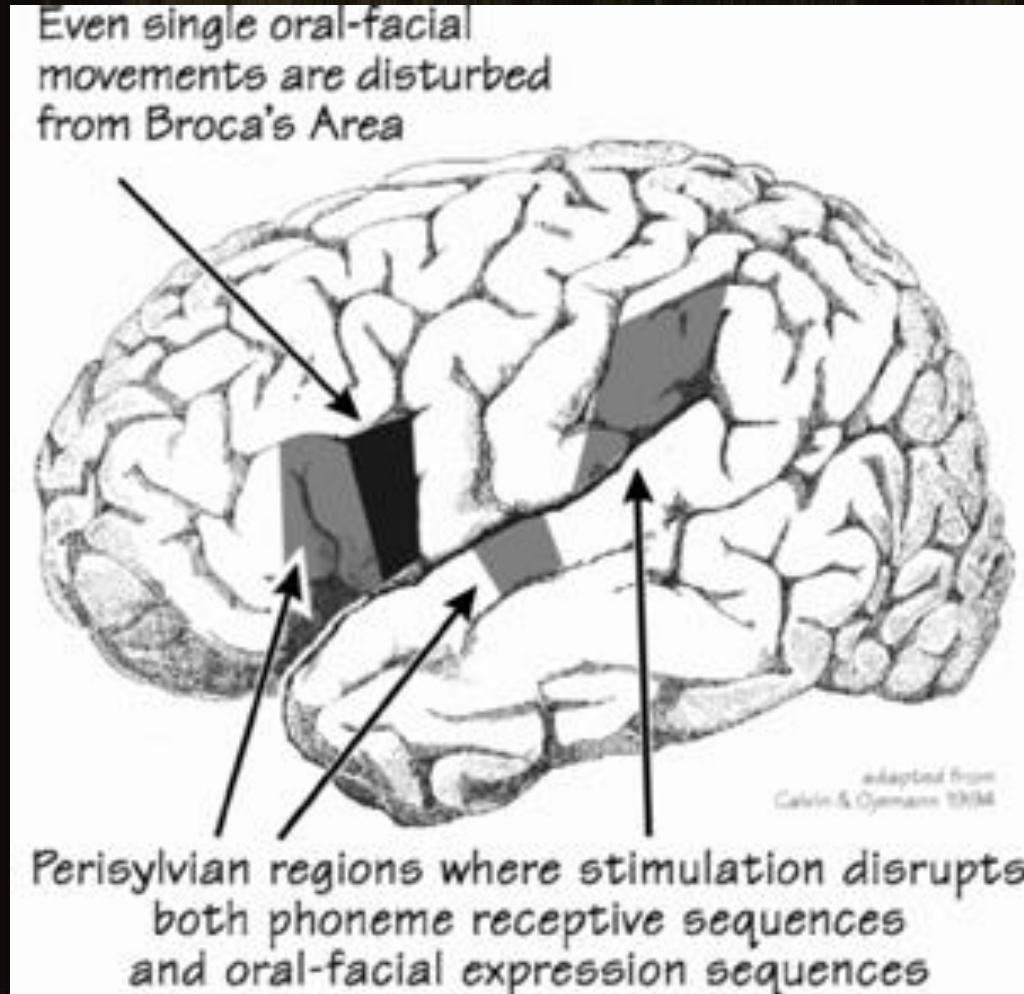
H.M.

- Suffered from severe Epilepsy
- Normal Intelligence, no psychological and mental illness.
- Bilateral medial temporal lobe resection to treat his epilepsy.
- Developed a severe and permanent inability to acquire new information.

H.M.

- Normal Short-Term memory.
- Digit span tests.
- Disrupted was the transfer of information from short term to long term memory.
- Shallice and Warrington's patient (KF) – opposite.
 - STM impaired, LTM intact.
 - Different region of the Brain Damaged

KF's Damage – Left Perisylvian Cortex



MRI on H.M.

- Corkin et al (1997).
- Half of the posterior region of H.M's hippocampus was intact.
- 5 not 8 cms of the medial temporal lobe was removed.
- Atrophied Hippocampus.

Neuroanatomy of Object-Recognition Memory

- Early animal models of amnesia involved implicit memory and assumed the hippocampus was key.
- 1970s – monkeys with bilateral medial temporal lobectomies show LTM deficits in explicit memory, the delayed nonmatching-to-sample test.
- Like H.M., performance was normal when memory needed to be held for only a few seconds (within the duration of STM).

Delayed nonmatching-to-sample task

- Monkey presented with an object
- Underneath it is food
- After a delay (where a screen is lowered in front of the monkey), the monkey is presented with 2 objects – one the same as before and a new object
- The monkey needs to be able to remember the old object to know that he now needs to look under the new object to find the food.
- If you train a monkey to do this task they can perform it to about 90% correct response rate but if the monkey has bilateral medial temporal lesions then their performance significantly worsens.

R.B.

- Ischemic Episode during heart bypass surgery.
- Anterograde Amnesia.
- Lesions restricted to his hippocampus.

Korsakoff Syndrome.

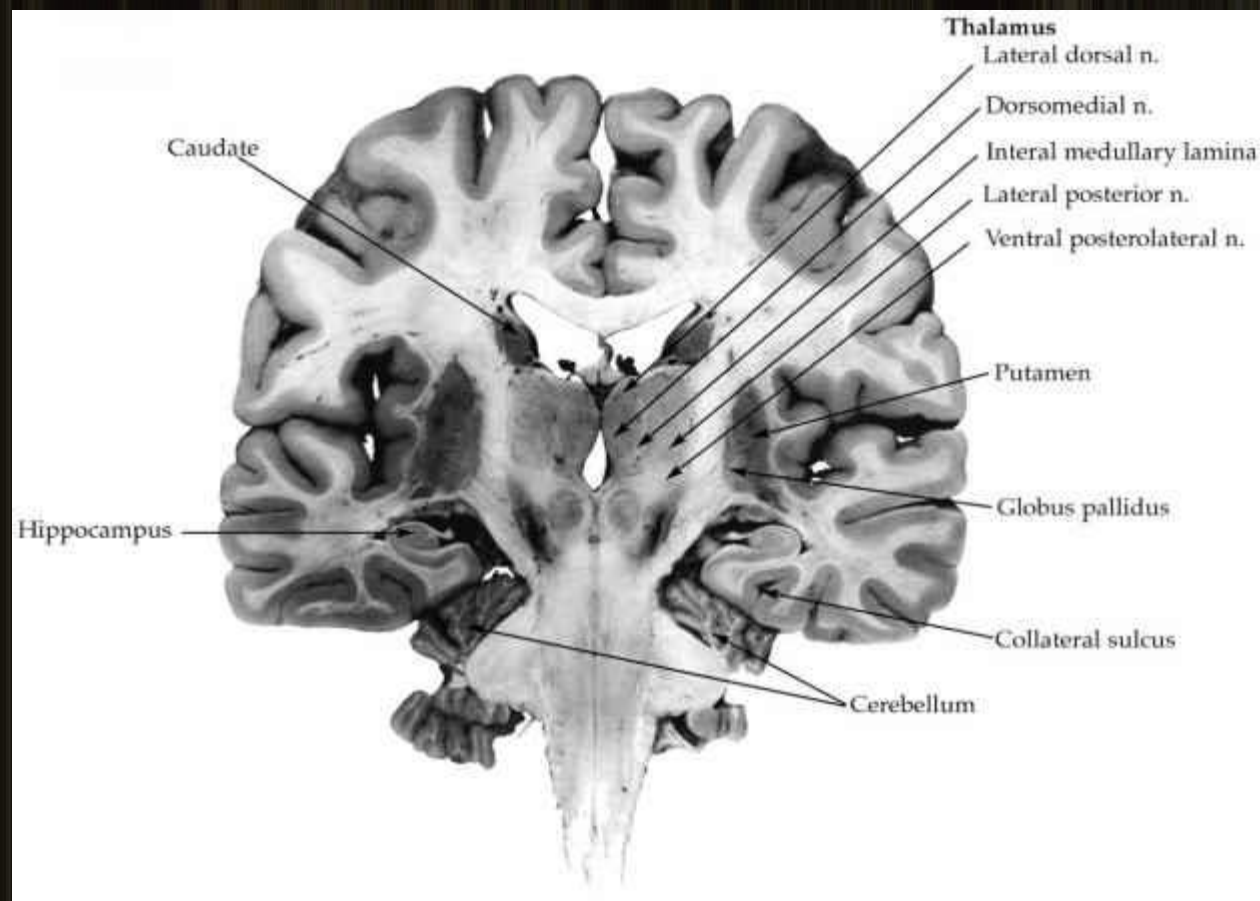
- Damage to Midline Diencephalon.
 - Interbrain
- Thalamus, Hypothalamus.
- Korsakoff Memory Loss Symptoms – Similar to damage to Medial Temporal Lobe.

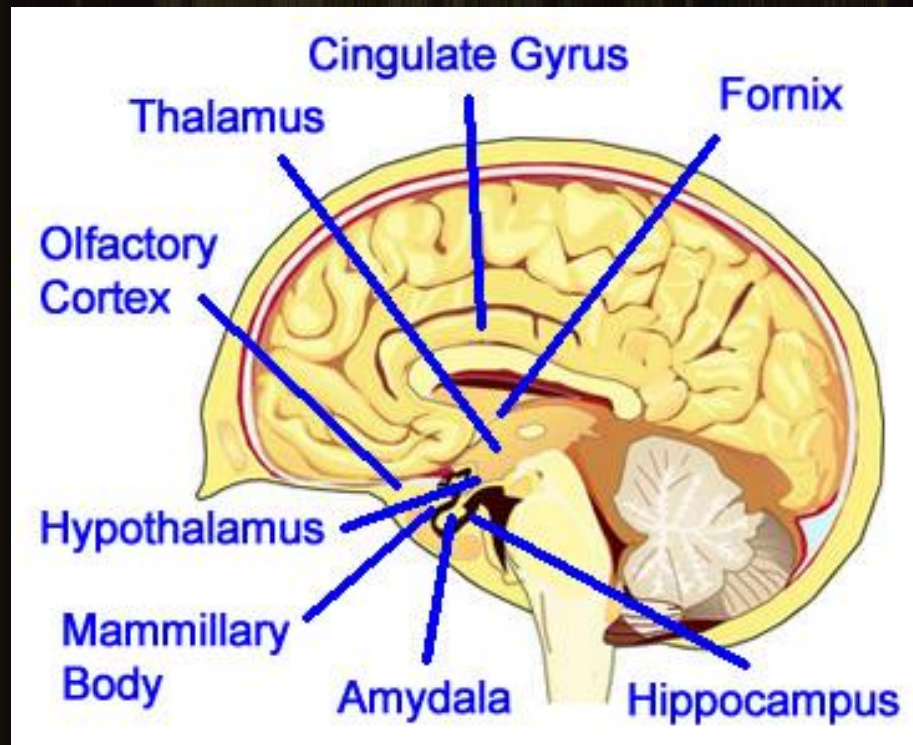
Neuroscientific Studies in Korsakoff.

- Kopelman (2015) – Review of Literature
 - Early research reported gender differences in age and frontal lobe atrophy in drinkers.
 - Women are likely to be affected at a younger age (Acker, 1985, cited in Kopelman, 2015).
 - Pitel et al (2012) – Next Slide

Pitel et al (2012).

- MRI study compared Korsakoff sufferers vs Alcholics without Korsakoff
- 11 alcoholic patients with KS, 34 alcoholic patients without KS (AL), and 25 healthy control subjects (CS).
- There were graded effects of volume deficits ($KS < AL < CS$) in the medial portion of the thalami, hypothalamus (mammillary bodies), left insula, and genu of the corpus callosum.
- Abnormalities in the left thalamic radiation were observed only in KS.





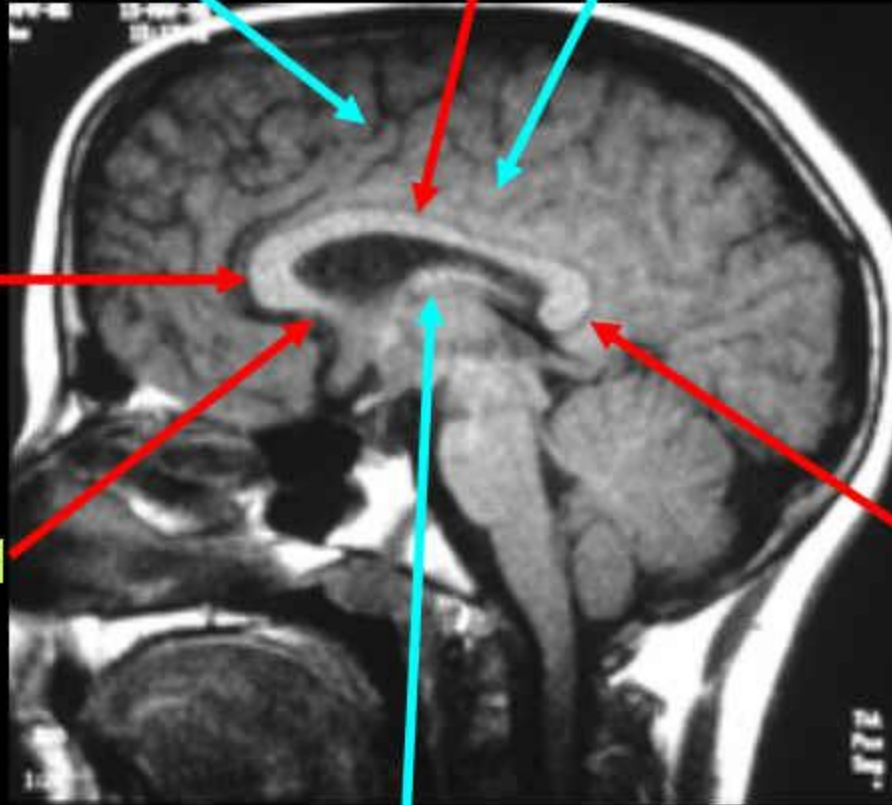
CENTRAL SULCUS **BODY** **CINGULATE GYRUS**

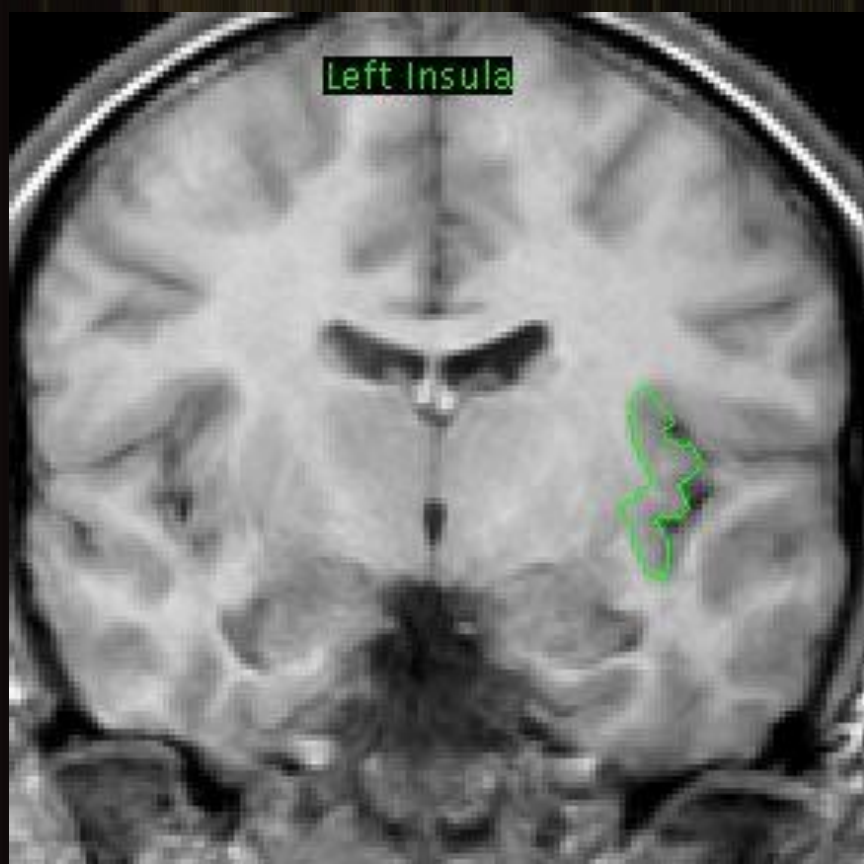
GENU

ROSTRUM

SPLENIUM

HIPPOCAMPAL COMMISSURE





Pitel et al (2012) conclusions.

- Despite significant memory deficits between the KS sufferers (KS Group) and the Alcholics without KS (AL Group) only a few cerebral were more severely damaged in KS than in AL.
 - And there was damage in these areas in the AL group compared to the Controls.
- The continuum of macrostructural damage from AL to KS is therefore restricted to key brain structures.
- Further Longitudinal investigations are required to determine whether alcoholic patients with medial thalamic volumes that are comparable to those of patients with KS are at increased risk of developing KS.

Episodic Encoding and Retrieval.

- PET and FMRI.
- Haxby et al (1996).
- Faces and Nonsense Patterns. (Pet Scans).
- Encode, Recognise and Perceptually analyse the face.

Encode the face.



Face Perception



Recognise the face.



Findings.

- Right hippocampal region activated during encoding of the face.
- But not during recognition.
- Encoding also activated the left prefrontal cortex.
- Recognition activated the right prefrontal cortex.

Wagner et al (1998), Brewer et al (1998).

- Presented participants with items and scanned brains using fMRI while encoding the information.
- Responses larger in prefrontal and medial temporal regions during encoding of stimulus that was successfully recalled.
- Left Hemisphere (Wagner et al) – Words.
- Pictures (Brewer et al) – right front cortex and in both medial temporal lobes.

Procedural Memory Encoding.

- Grafton et al (1995) – Dual Task study.
- Stimulus Reaction Time.
- Counting Task (Tone Frequency).
- Compared to participants who only had to do the SRT.

Findings.

- Implicit learning – Brain areas traditionally associated with limb movement were activated – e.g. Left Hemisphere
- Studies using TMS data supports this.
- Clear differences between brain systems involved in explicit and implicit learning and memory.

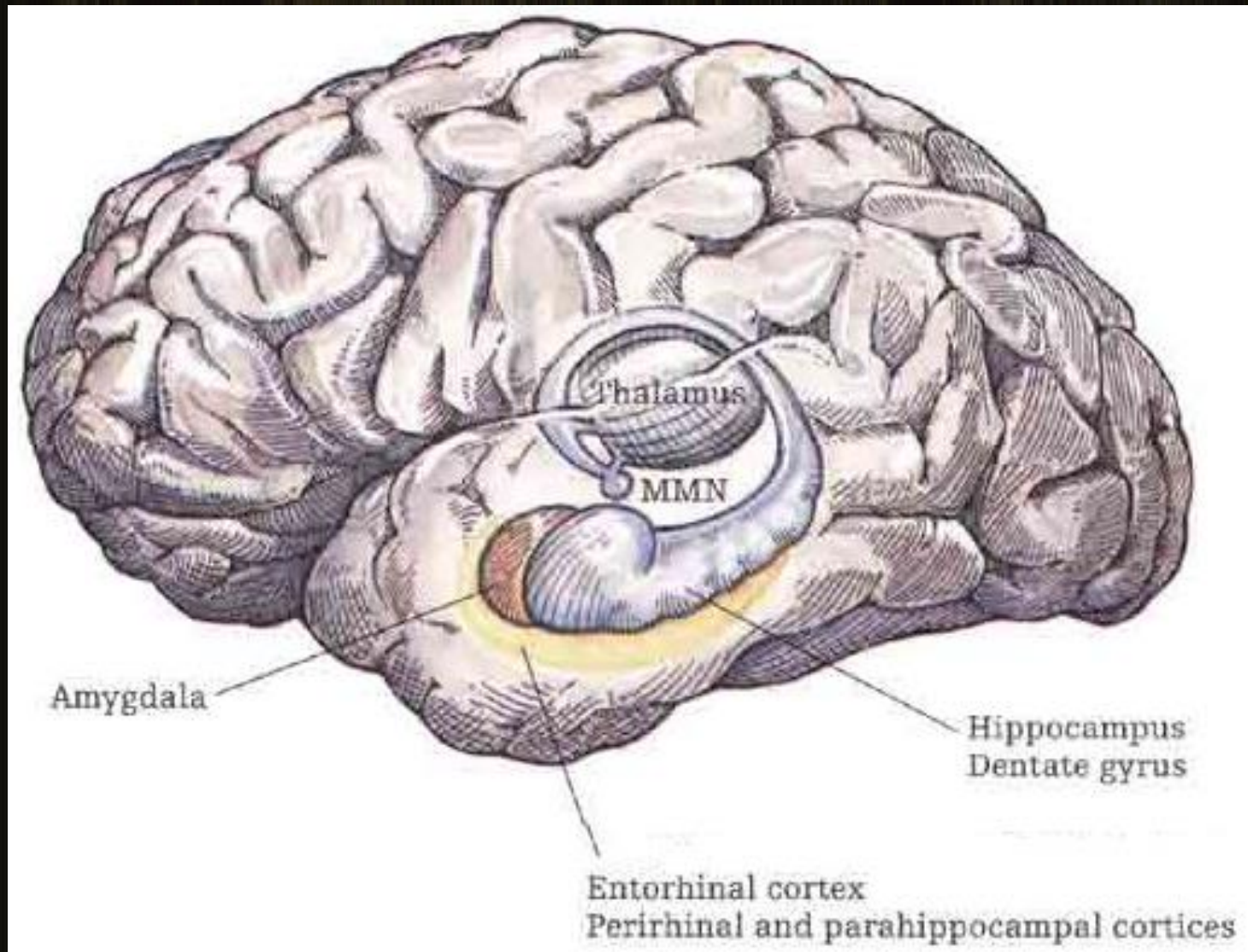
Long Term Retrieval & Familiarity.

- Montaldi et al (2006) - fMRI study.
- Showed participants a series of scenes – told not to recall them or try to remember them.
- 2 days later under fMRI conditions given a series of scenes (some shown 2 days previously, others not).
- Where asked to rate these pictures as
 - New
 - Slightly Familiar
 - Familiar
 - Very Familiar
 - Recollect from 2 days before.

Findings

- Hippocampus was activated only for pictures that the participants could recollect having seen before.
- Activation of Medial Temporal Lobe (outside hippocampus, such as the entorhinal cortex) correlated with strength of familiarity in scenes not actually recollected.

Entorhinal Cortex



Conclusions of such studies

- Medial temporal lobe supports different forms of memory....
- The different forms of memory (e.g. recollection vs familiarity) are supported by different parts of medial temporal lobe.
- Hippocampus = encoding and retrieval for episodic memories that are recollected.
- Other areas (e.g. entorhinal cortex) – Recognition based on familiarity.

Alzheimer's Disease.

- Most common form of Dementia.
- Most common symptom = The inability to acquire new memories.
- Major battle facing health practitioners due to the lack of efficacy in treatment.

Alzheimer's Disease.

- Begins with slight loss of memory and progresses to dementia.
- Research has focused on pre-dementia Alzheimer's patients, who typically show major anterograde and retrograde deficits in explicit memory tests.
 - Deficits in STM and some types of implicit memory – verbal and perceptual
 - Implicit sensorimotor memory is intact

What's happening in the brain to cause the Amnesia Seen in AD?

- Decreased acetylcholine levels due to basal forebrain degeneration thought to be involved.
- Basal forebrain strokes causing amnesia & attentional deficits suggests acetylcholine levels are critical.
- But it might not be the only factor – because AD involves many areas of the brain, such as the Medial temporal lobe and prefrontal cortex.
- So, the damage it causes is diffuse and the resulting amnesia is likely to be a consequence of acetylcholine depletion and brain damage in other areas?

Structural Imaging and AD

- Research such as Jack et al. (2002) using MRI have suggested that AD is linked to hippocampal volume.
- Through looking at ante-mortem (pre death) and post-mortem analysis of AD patients they reported that hippocampus volume decreases with progression of AD.
- Thicker hippocampi develop dementia to a lesser extent.

Bassett et al (2006).

- 95 – Asymptomatic offspring of autopsy confirmed late onset familial AD cases.
- 50-75 years of age – NOT showing symptoms.
- Aged Match controls.

Bassett et al (2006).

- Study – Comparison of fMRI activation during a paired associates memory paradigm.
 - Example of Paired Associates Test:

4 - VNR 7 - CSL 8 - RKJ
Experimenter “7”.
- Findings: At risk = More intensive and extensive activation of the frontal & temporal lobes during encoding
- Less activation in cingulum and thalamus during encoding and recall.

Bassett et al (2006).

- In most cases the sample were 10 years younger than when their parent/s developed symptoms.
- Is Neuroscience demonstrating predictive powers in terms of AD?
- More research.

Landau et al (2010).

- Predicting Alzheimer's.
- Sample 85 Participants – diagnosed with Mild Cognitive Impairment (MCI)
- Longitudinal Study.
- Number of tests – PET, MRI, Episodic Memory test.

Landau et al (2010).

- None of the 85 sample – went back to their pre MCI capacity.
- 28 – Developed Alzheimer's.
- Pet Scans and Episodic Memory tests combined – excellent at predicting which would develop AD.

Landau et al (2010).

- Concluded – Abnormal scores in both Pet and the Episodic Memory Test meant the participant was 12 times more likely to develop AD.
- Practical Issues – COST.
- Sample.

Where are memories stored?

- Each memory is stored diffusely throughout the brain structures that were involved in its formation
- Some structures have particular roles in storage of memories
 - Hippocampus – spatial location
 - Perirhinal cortex – object recognition
 - Mediodorsal nucleus – Korsakoff's symptoms
 - Basal forebrain – Alzheimer's symptoms

Where are memories stored?

- Inferotemporal Cortex

- Involved in visual perception of objects
- Stores memories of visual patterns
 - Evidence from recording of neurons in monkeys

- Amygdala

- Plays a special role in memory for the emotional significance of an experience.
 - Evidence from rats with amygdala lesions don't show typical fear response.
 - But may not store memory – instead strengthens emotional memories

Where are memories stored?

- Prefrontal cortex

- Temporal order of events and working memory
- Tasks involving a series of responses
- Different part of prefrontal cortex may mediate different types of working memory
 - Some evidence from functional brain imaging studies

- Cerebellum and striatum

- Cerebellum
 - Stores memories of sensorimotor skills
- Striatum
 - Habit formation

Why would the brain develop separate stores

- Protection

- To prevent devastating effects of damage to one particular area.
 - some memory items will be damaged but others preserved.
- Link to other brain facets, such as amygdala being important for emotion.
 - Memories are stored in brain structures that were involved in their formation and processing.