

Mild Cognitive Impairment – What is  
it and does it matter?

Antipsychotics in Dementia

Recent Research and Future  
Developments

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# MILD COGNITIVE IMPAIRMENT – WHAT IS IT AND DOES IT MATTER?

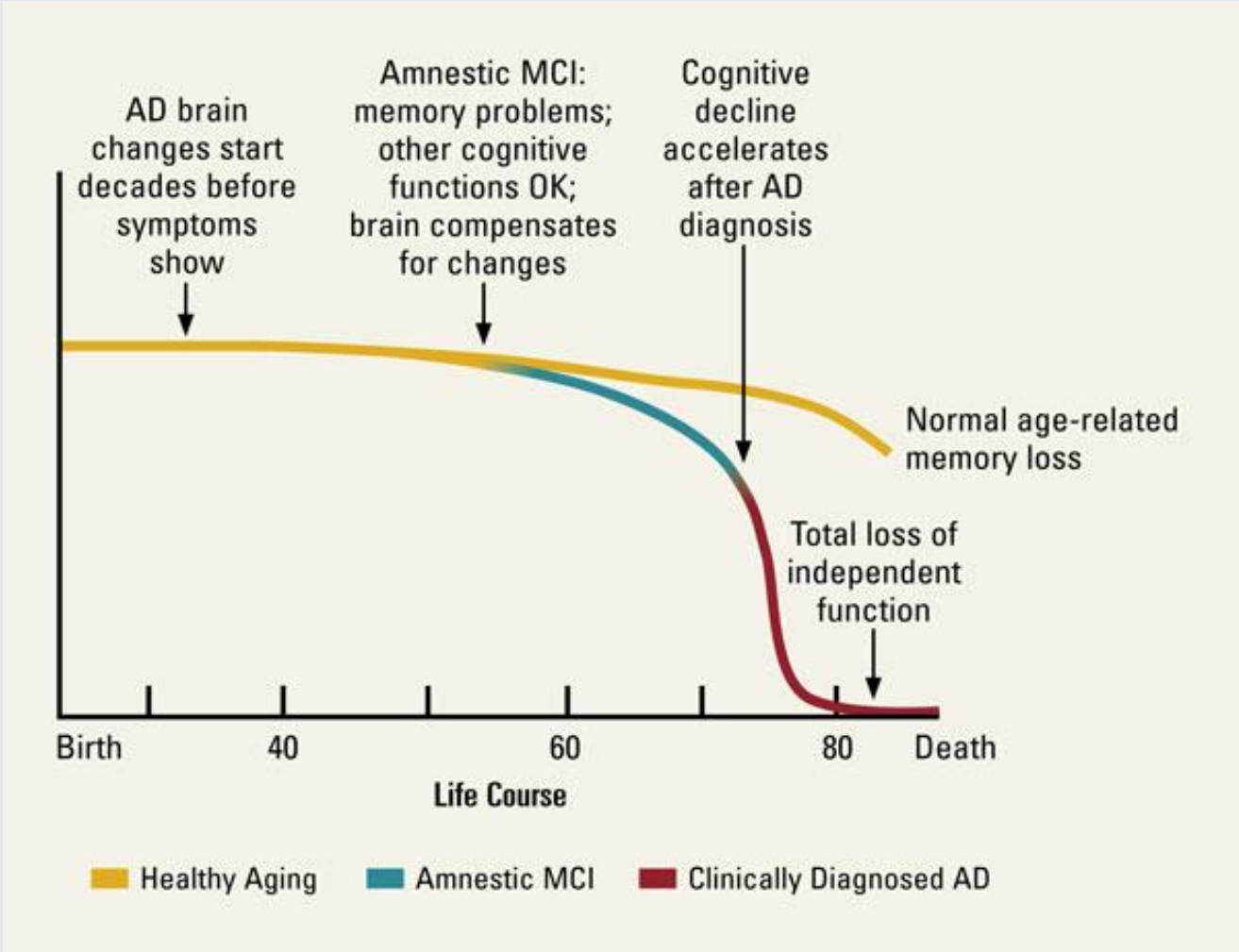
# Mild Cognitive Impairment

- What is mild cognitive impairment?
- What happens to people with MCI?
- Which people with MCI will develop dementia?
- Treatment of MCI
- Why diagnose MCI

# What is mild cognitive impairment?

- Concern regarding a change in cognition
- Impairment in one or more cognitive domains
- Preservation of independence in functional abilities
- Not demented

# Progression of Dementia



# What happens to people with MCI?

- 10-15% per year go on to have diagnosis of dementia (memory clinic patients)
- About 50% in total go onto have dementia
- So at increased risk of getting dementia – about 3-5 times normal population
- Important – some people don't deteriorate, some people improve when retested.

# Which people with MCI will develop dementia?

- We don't really know – but it would make a big difference if we could predict accurately
- Current research focus
- Cognitive tests – amnestic MCI
- Biomarkers – amyloid PET, CSF, Other blood markers, sequential brain scans
- Locally – developing system for risk stratification

# How do we treat people with MCI?

- No current pharmacological treatments
- No evidence for acetylcholinesterase inhibitors helping or preventing progression to dementia
- No evidence of clinical improvement with vitamin B
- Follow up arrangements on individual basis



# What you should get from a memory clinic

- Clear diagnosis of mild cognitive impairment
- Advice about what plans are for follow up (re-review in 12 months / discharge with follow up if deterioration).
- What the patient has been told
- Advice about non-pharmacological interventions and lifestyle (and DVLA!)
- Risk stratification for conversion is an ambition

# ANTIPSYCHOTICS AND DEMENTIA

# Antipsychotics and dementia

- History
- What is BPSD?
- What are the problems with antipsychotics?
- Why is use called “inappropriate”?
- What should I do?
- Antipsychotic guidelines

# History

- Antipsychotics introduced in the 1950's
- The older "Typical" Antipsychotics – Haloperidol, Thioridazine, Promazine commonly used to treat BPSD
- When atypicals introduced, people gradually switched – now most commonly prescribed drugs
- Most countries used largely unlicensed or "off-label"
- 2002 – Risperidone manufacturer notified concerns about higher rate of CVA's
- 2004 – MHRA in UK said Risperidone and Olanzapine should not be used for BPSD because of stroke risk
- 2009 – "Time for Action" Recommendations from DoH

# What is BPSD

- Behavioural and Psychological Symptoms of Dementia
- 90% of patients with dementia
- Aggression, agitation, loss of inhibitions, psychosis (delusions and hallucinations)

# What are the problems with antipsychotics?

- Increased risk of stroke
- Increased mortality
- Risk of venous thromboembolic events
- Worsens cognitive function
- Sedation, Parkinsonism, Dehydration, Falls
- 2009 report said that of the 180,000 antipsychotic prescriptions for people with dementia. 140,000 were inappropriate

# Why is use called “inappropriate”?

- High risk of side-effects
- Inappropriately targeted symptoms
- The BPSD which is being treated could be the result of unmet need requiring different solutions
- Antipsychotics have modest benefits (and only for specific symptoms and for short time period)

# What should I do?

- Identify BPSD
- Look for “PAID” – P = Physical problems (infection / pain)A= Activity-related e.g. dressing, washing. I = Intrinsic to dementia e.g. wandering. D = Depression and Delusions
- Mild to moderate symptoms – watchful waiting
- Consider non-pharmacological approaches
- Only use pharmacological symptoms if psychosis, depression or behaviour where there is extreme risk or distress
- Identify dominant target symptom group (e.g. psychosis, depression, apathy, aggression, agitation, sleep disturbance)
- Be aware and wary of Lewy Body Dementia!



# Risperidone Licensed Treatment

- Based on 3 RCT's in 2008
- Licensed for treatment of dementia-related behavioural disturbance
- Specifically short term use (6 weeks)
- For treatment of persistent aggression in moderate to severe Alzheimer's dementia unresponsive to non-pharmacological approaches
- Risk of harm to patient or others

# Antipsychotic Recommendations

- Full discussion with patient / carer about risks and benefits
- Start atypical antipsychotic at low doses and increase every 2-4 days if no response
- Patients who respond should have drug cautiously withdrawn after 6- 12 weeks
- Half dose for 2 weeks and if symptoms do not re-emerge stop drug after further 2 weeks
- Review again after 1 week
- If symptoms re-emerge reintroduce drug at starting dose
- BPSD can persist and treatment with atypical antipsychotics maybe needed in long term (but should be reviewed 3 monthly).

Neuroleptic drug	Starting dose	Optimum dose
Risperidone	250 microgram b.d.	500 microgram b.d.
Olanzapine	2.5mg o.d.	5-10mg o.d.
Quetiapine	25mg o.d.	25-150mg daily
Aripiprazole	5mg o.d.	10mg o.d.

Key Symptom	First Line	Evidence Type	Second Line	Evidence Type
Depression	Citalopram	3 + £		
Apathy	Citalopram	3 + £	Donepezil Rivastigmine Galantamine	2
Psychosis	Risperidone	1	Olanzapine Aripiprazole Memantine	2 + 3
Aggression	Risperidone	1	Olanzapine Aripiprazole Memantine	2 + 3
Moderate Agitation / Anxiety	Citalopram	3	Trazodone Mirtazapine Memantine	4
Severe Agitation / Anxiety	Risperidone Olanzapine	1	Aripiprazole Memantine	2 + 4
Poor sleep	Temazepam Zopiclone	3 + £	Zolpidem	3

# RECENT RESEARCH AND FUTURE DEVELOPMENTS

# Research In Dementia

- Questions patients might ask
- Recent developments in dementia research
- Local research - MARC

# Research

- The Daily Mail, as you know, is engaged in a philosophical project of mythic proportions: for many years now it has diligently been sifting through all the inanimate objects in the world, soberly dividing them into the ones which either cause – or cure – cancer.
- Ben Goldacre

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Cheap drug slows memory loss

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**DEMENTIA RISK FROM SLEEPING TABLETS**  
Pensioners on pills taken by 1.5m are 50% more likely to be hit, warns Harvard study

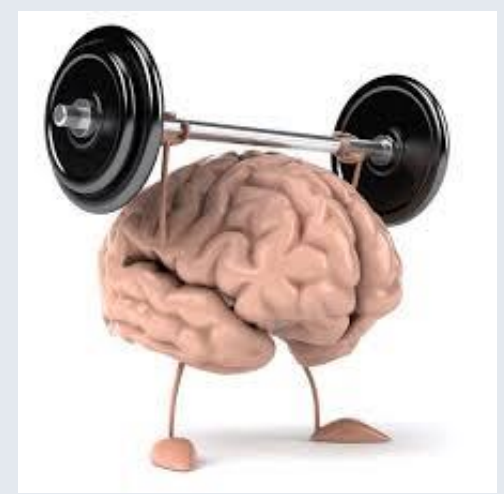
**Tears of runaway teacher's mother**



UK NEWS

CAKE 'CURE' FOR DEMENTIA





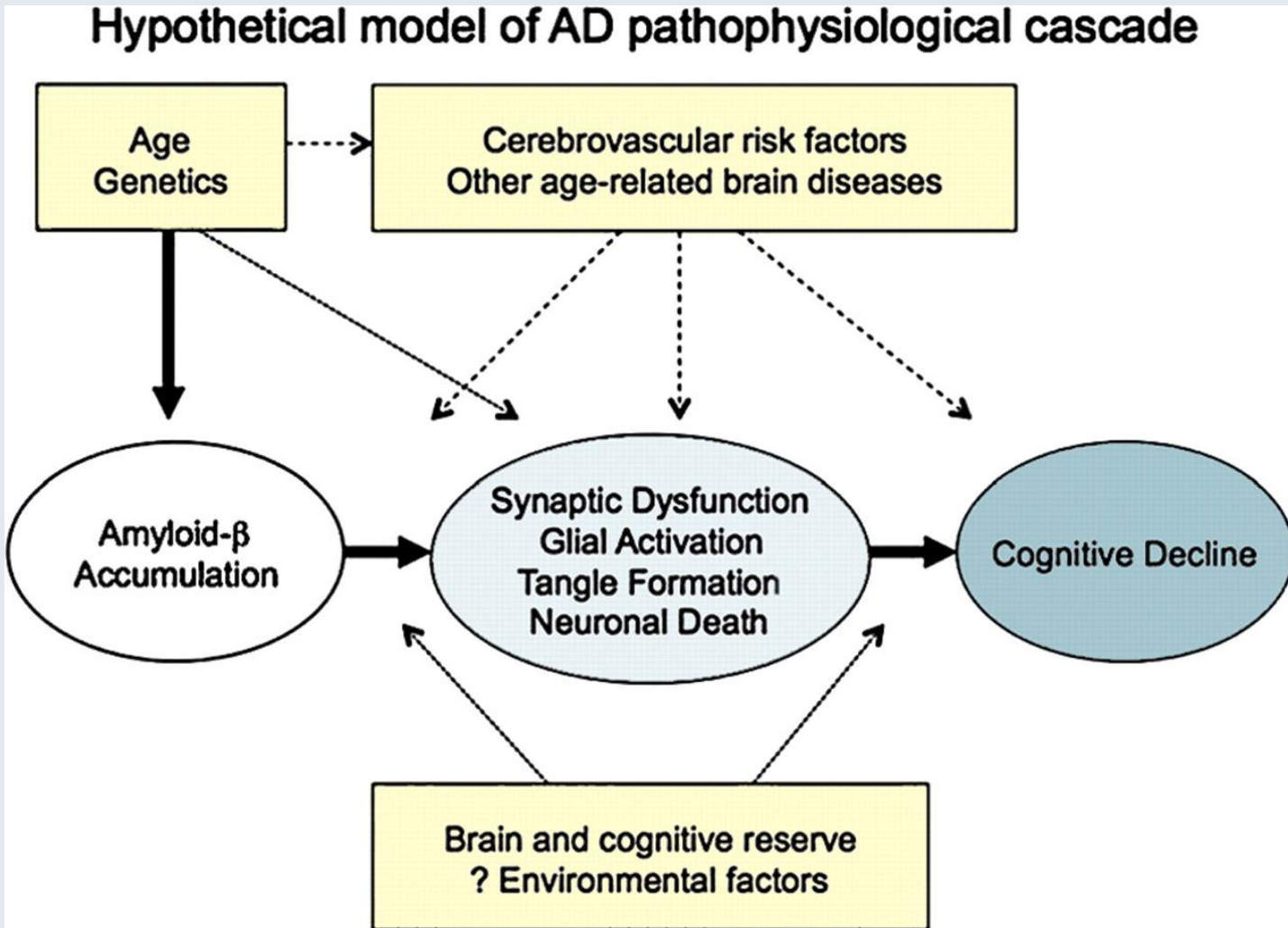
# Does ..... Prevent Dementia?

- Chocolate – people without dementia, improved cognition
- Mediterranean Diet – systematic review
- Brain Training – some evidence
- Curry – turmeric , in vitro studies
- Wine – tricky – some evidence for small intake.
- Exercise – some evidence in mid / later life
- Vit D – association - ?causal
- Vit B – brain shrinkage improvements, no clinical effects
- Losartan – current trials
- Coconut Oil – no evidence, flawed basic science
- Cake – cinnamon, in vitro studies, toxic levels?

# Current dementia research

- Improving quality of life for people with dementia / carers
- Trying to diagnose dementia earlier / identify those at risk of dementia
- Basic science – understanding pathology behind dementia process
- Novel drug treatments
- Adopting existing medication to treat dementia
- Disease modifying / treating symptoms

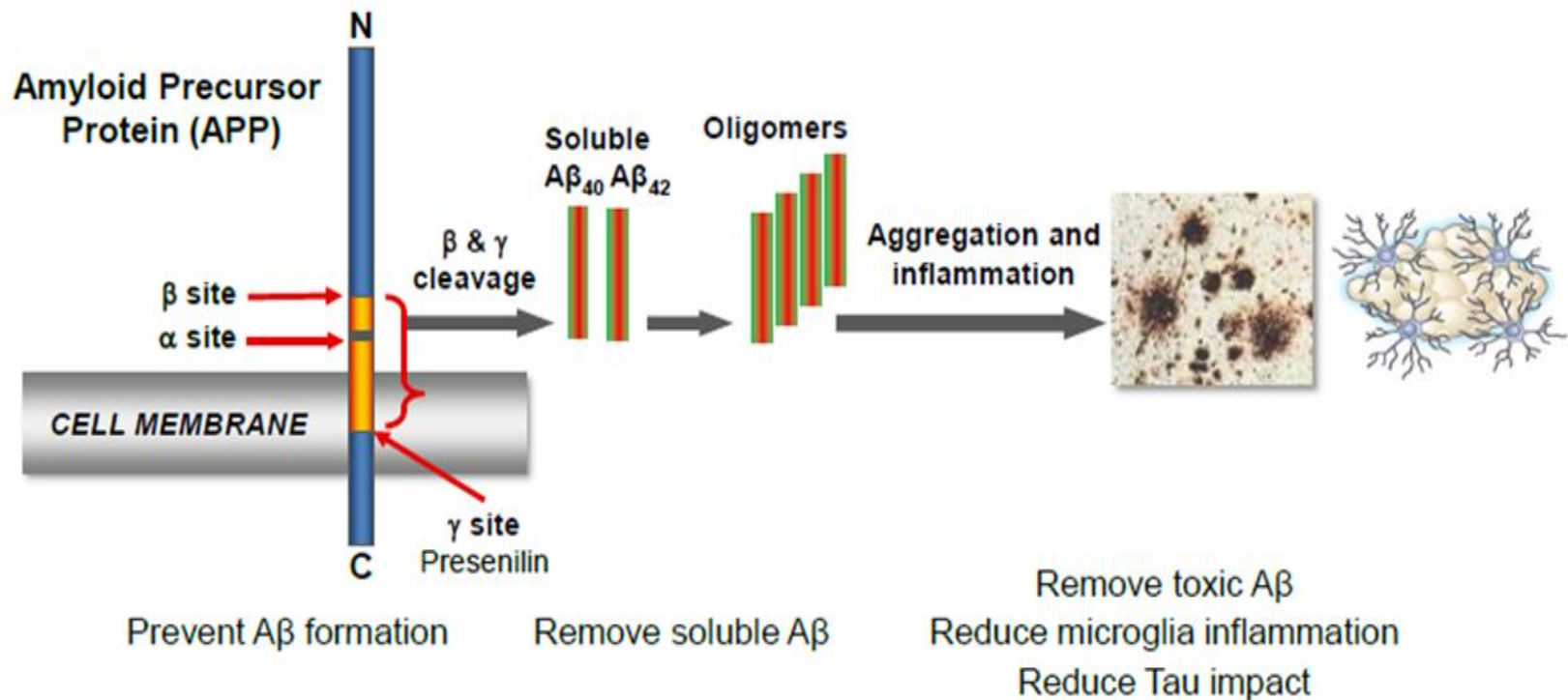
# Hypothetical model of Alzheimer's disease (AD) pathophysiological cascade sequence (from Sperling et al).5.



Budson A E , and Solomon P R Pract Neurol 2012;12:88-96

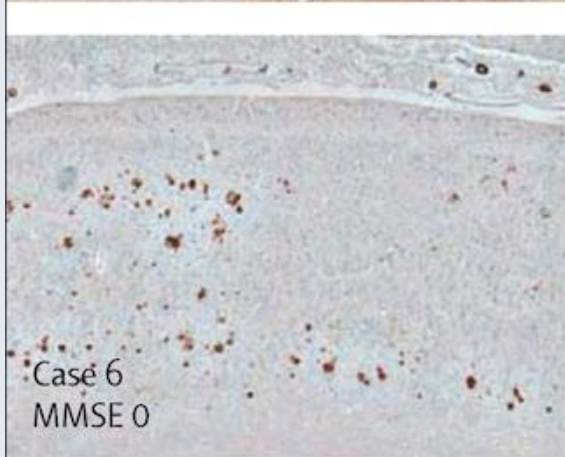
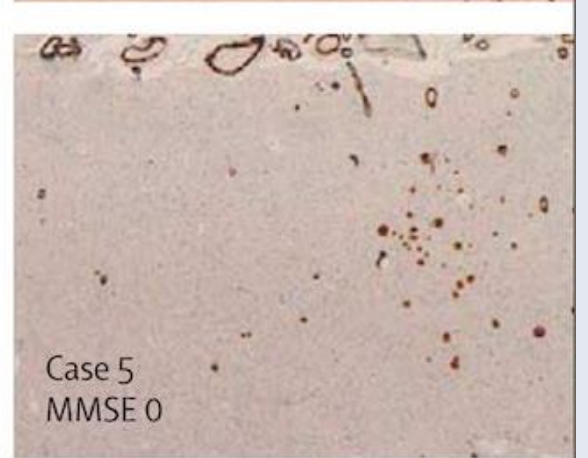
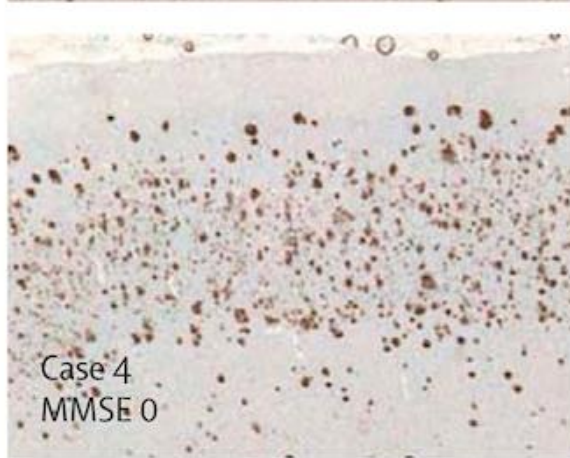
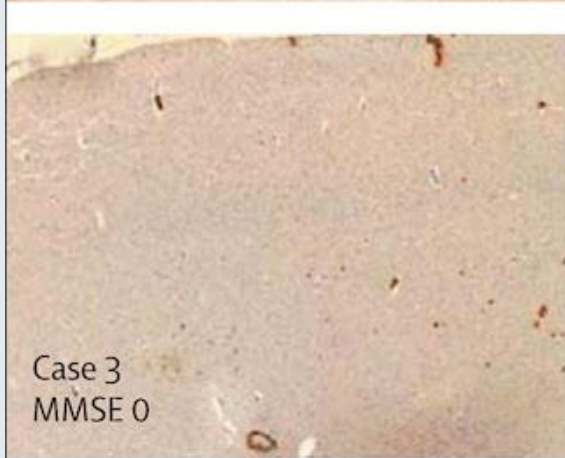
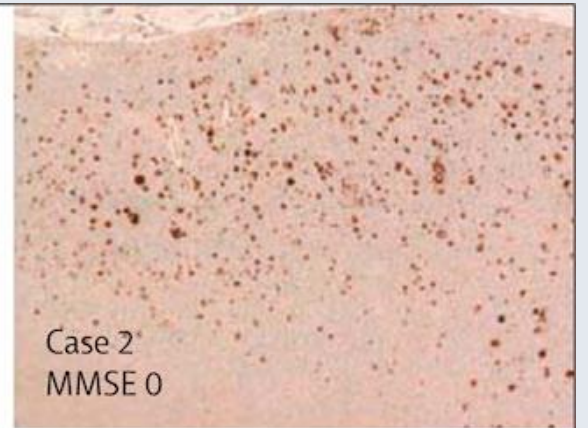
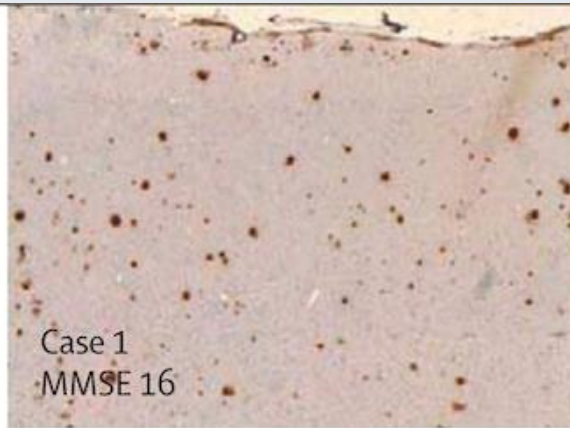
# Amyloid model: abnormal processing

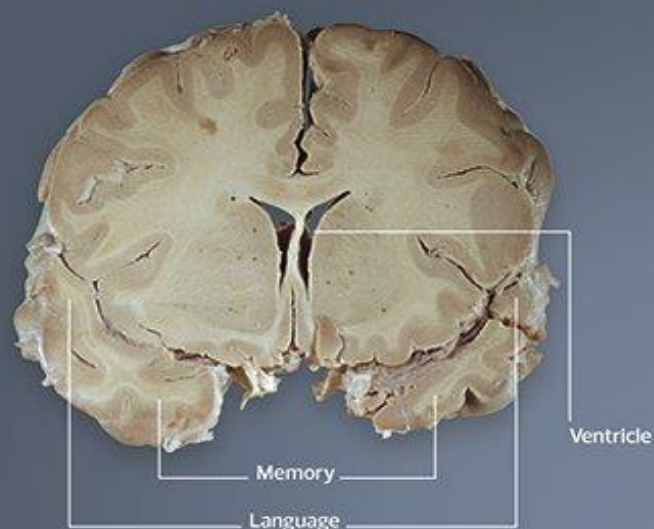
## *Areas for intervention*



# Recent targets for dementia research

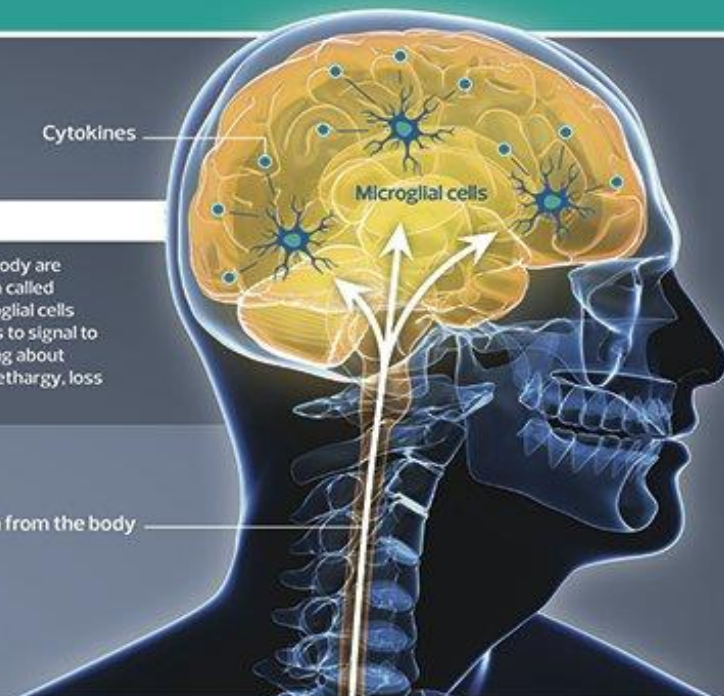
- Amyloid vaccines
- Monoclonal antibodies targeting amyloid
- Tau
- BACE inhibitors
- Infection / Inflammation



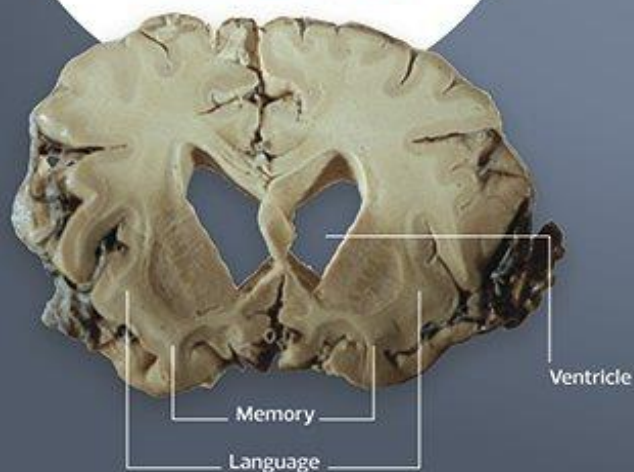


## HEALTHY BRAIN

Signals of inflammation from the body are relayed to immune cells in the brain called microglial cells. In turn, these microglial cells secrete molecules called cytokines to signal to different areas of the brain and bring about specific sickness behaviours (eg, lethargy, loss of appetite, depression, etc)



The brain below is that of a person who had Alzheimer's. It has shrunk and lost definition because nerve cells in the brain are killed during the course of the disease. Much like memory in a computer, fewer brain cells mean reduced processing power and storage. This is how Alzheimer's disease robs people of memory and language ability

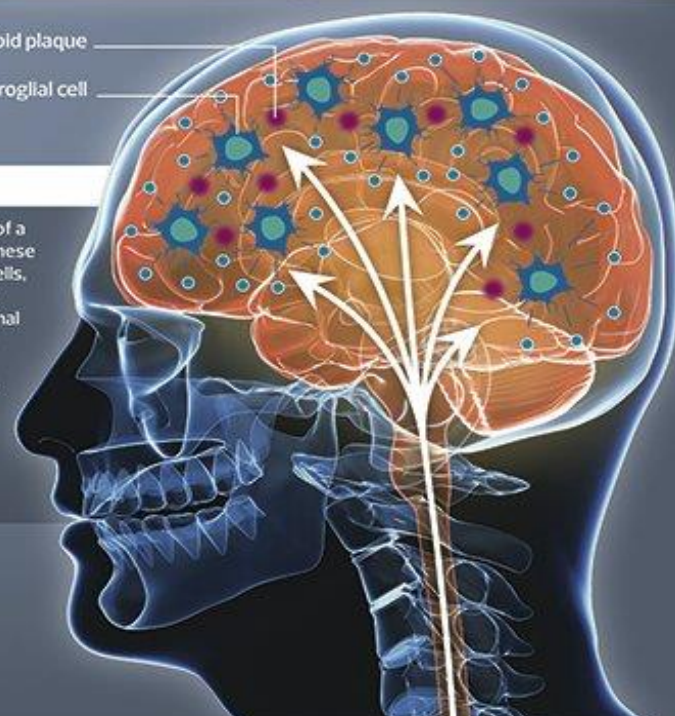


## DISEASED BRAIN

One hallmark of Alzheimer's is deposits of a protein called amyloid. The presence of these deposits excites or "primes" microglial cells, causing them to increase in number and respond more aggressively to an additional inflammation. According to the research of Holmes and his colleagues, when the secondary inflammation comes in to the diseased brain, the microglial cells secrete cytokines as they usually would, but secrete them at such high concentrations that it leads to the death of nerve cells in the brain

Amyloid plaque

Primed microglial cell





# MARC – Memory Assessment and Research Centre

- International reputation
- Recent 25 year anniversary
- Based at Moorgreen Hospital, Southampton
- Grant funded trials
- Pharmaceutical company RPCT's
- Non-drug trials
- Happy to accept all referrals!!

# MARC

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- Tel No. : 02380 475206
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