

# Neurodegenerative Diseases

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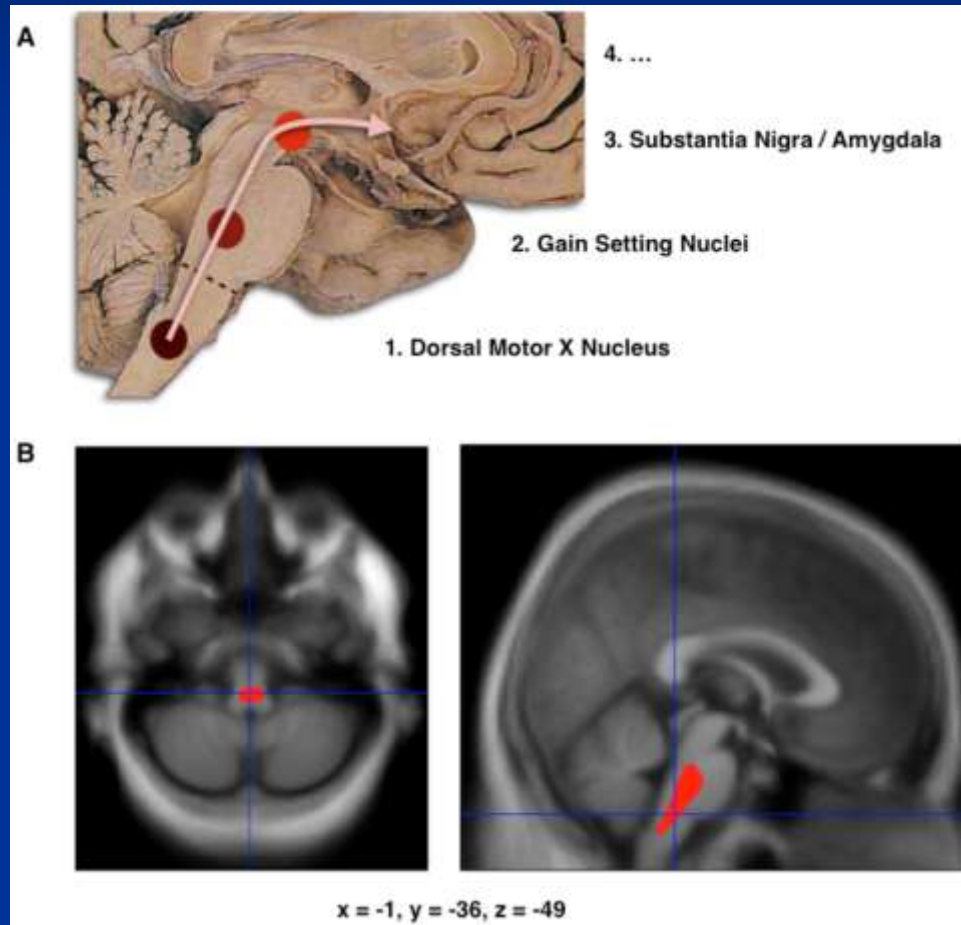
# Introduction

- Common neurodegenerative diseases
  - Alzheimer disease
  - Parkinson disease
- Their incidence increases with age
- They are major causes of disability and dependency in old age

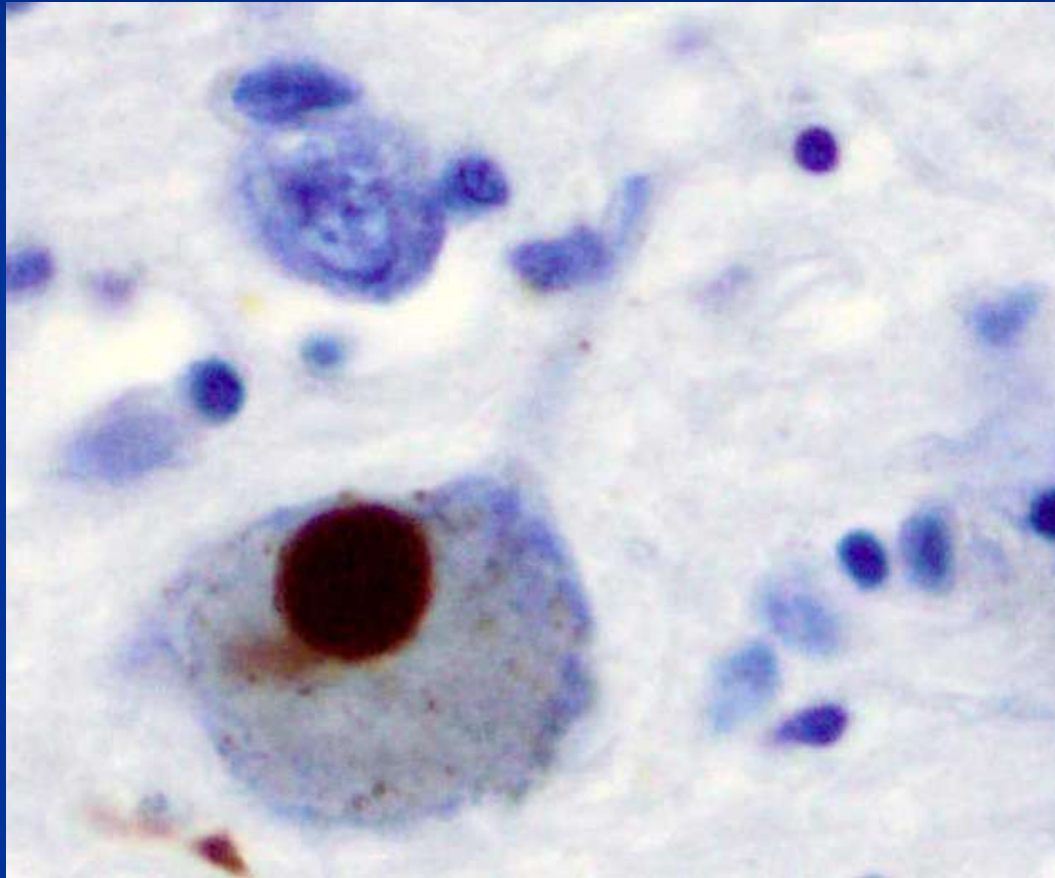
# Parkinson disease

- Second commonest neurodegenerative disease
- Degeneration (Reduced dopamine release) in basal ganglia
  - motor, oculo-motor, associative, limbic and orbitofrontal circuits

# Atrophy of basal ganglia



# Lewy body (alpha-synuclein) in a neurone in substantia nigra



# Clinical features

- Insidious onset in 6<sup>th</sup> -7<sup>th</sup> decade of life
- Genetic and environmental (pesticide, manganese, amphetamine, repeated head injury)
- Motor symptoms
  - Rigidity
  - Resting Tremor in limbs (asymmetrical)
  - Slow movement
  - Fall



# Non-motor symptoms

- Sleep disturbance
- Unstable bladder
- Constipation
- Cognitive impairment
- Anxiety and depression

# Treatment

- Drugs
  - L dopa and an inhibitor of conversion which cannot cross blood brain barrier
  - Dopamine agonist
  - Monoamine oxidase type B inhibitor
- Deep brain electrical stimulation
- ? Stem cell therapy



# Limitations of current treatment

- Symptomatic only
- Gradual deterioration over ten years
- Side effects – dyskinesia, confusion, hyperactivity (sex, shopping, gambling)
- On-off effect of L Dopa
- Not effective for non-motor symptoms or fall
- Dementia after ten years on average
- Atypical forms of Parkinsonism do not respond to treatment

# Dementia (Alzheimer disease)

# Symptoms of Dementia

- Forgetfulness
- Getting lost in familiar settings
- Lose interest in family
- Deterioration of work performance
- Disorientation (time and place)
- Behavioral changes
- Slower walking/ falls

# Diagnosis of Dementia

- Cognitive impairment affecting daily living – short term memory, orientation, ADL function, mood
- Corroborated by caregivers
- Objective evidence of cognitive impairment

# Early Stage

- Loss of advanced ADL
- Insight
- Anxiety, Depression
- Social relationship problems
- Drug/ lifestyle non-adherence
- Nutritional problems
- Financial management
- Home safety

# Moderate Stage

- Loss of Basic ADL
- Home safety
- Caregiver support
- Behavioral problems
- Depression
- Psychosis
- Loss of insight

# Late Stage

- Instability
- Physical dependency
- Somnolence
- Feeding problems
- Psychiatric problems
- End of life issues

# Behavioural Problems

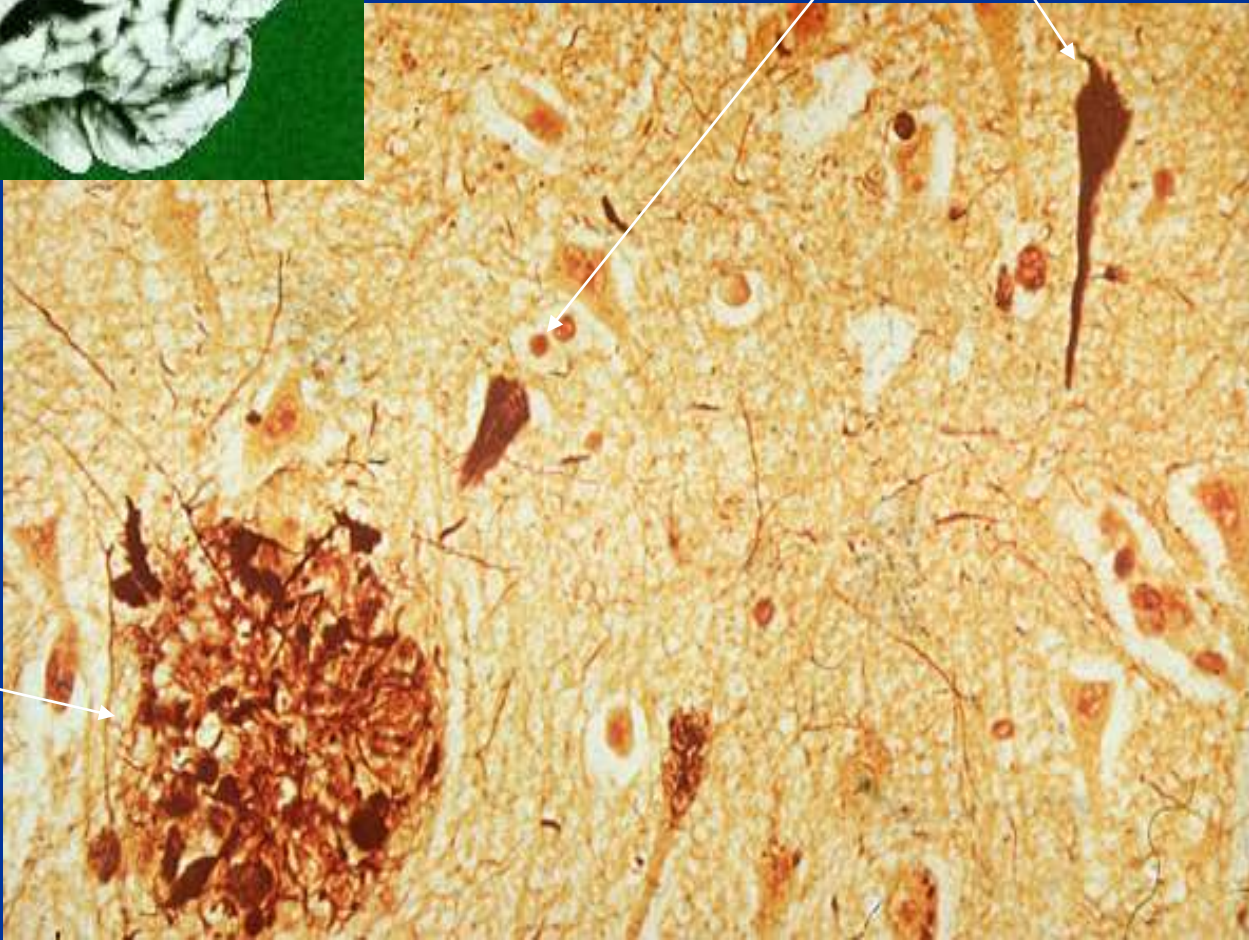
- Emotional outburst
- Accusation of theft/ infidelity
- Wandering
- Refusal to bath
- Urinate outside toilet
- Sexual harassment
- Delusion/Hallucination
- Day night reversal



# Alzheimer's Disease



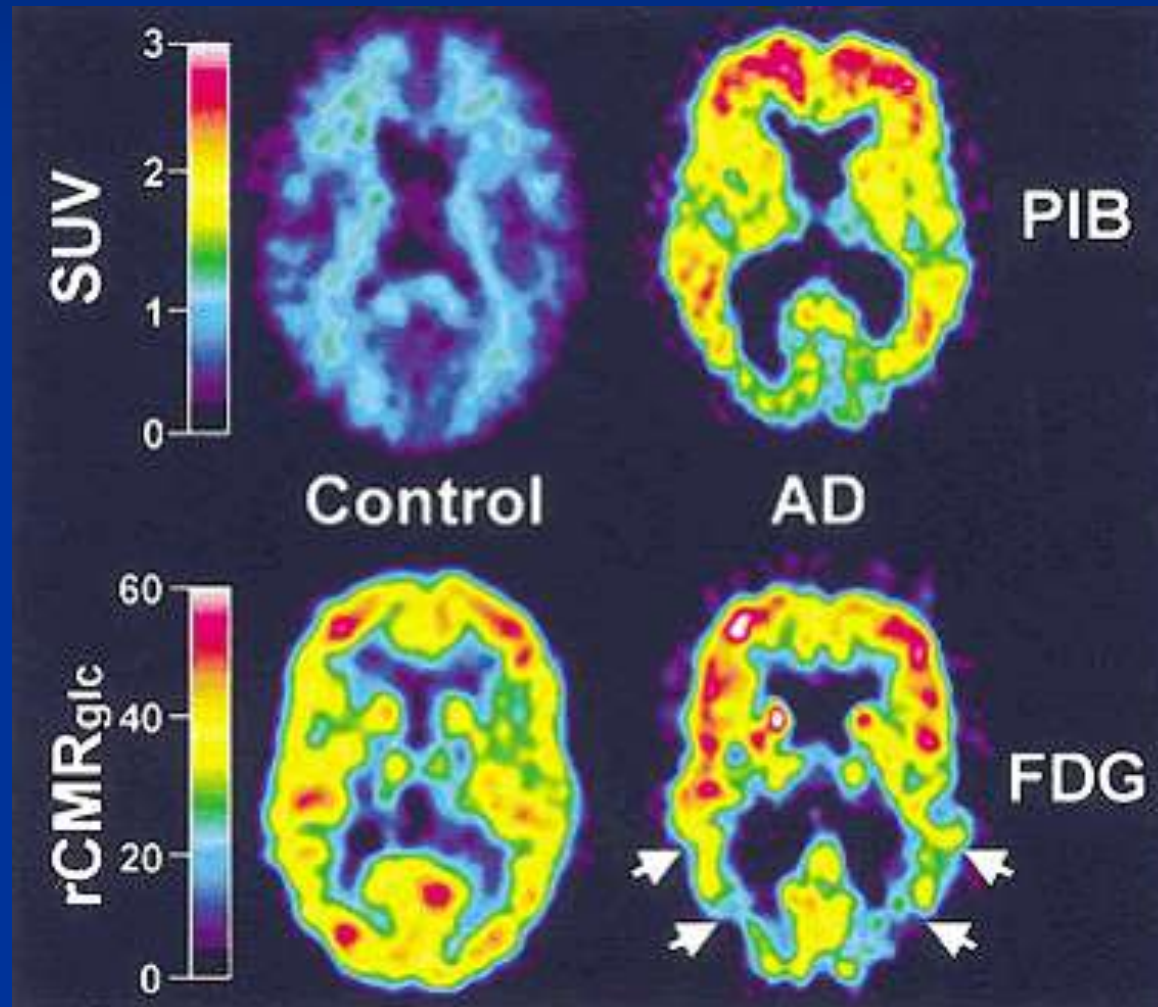
Atrophy



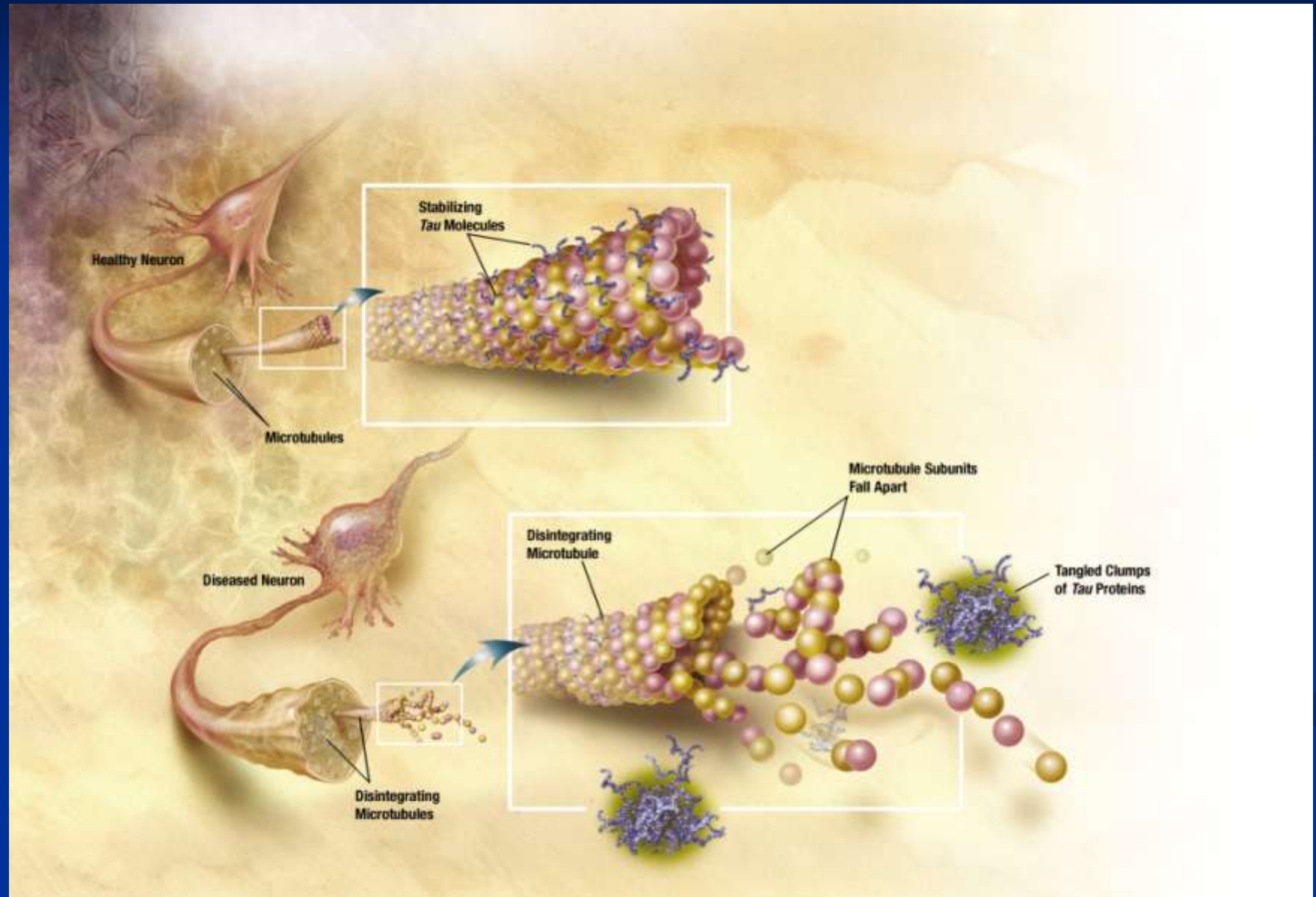
Tangles

Plaque

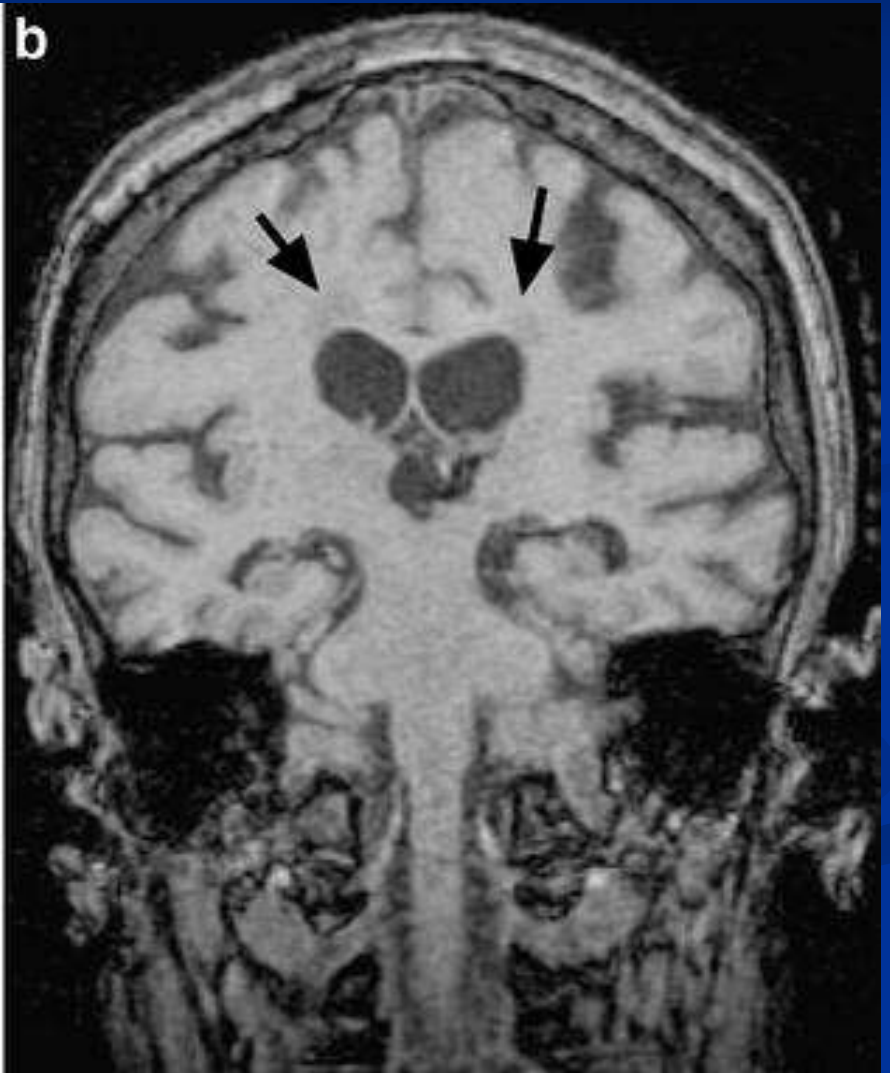
# Discrepancy between amyloid deposit and brain hypoactivity



# Functional and dysfunctional Tau protein

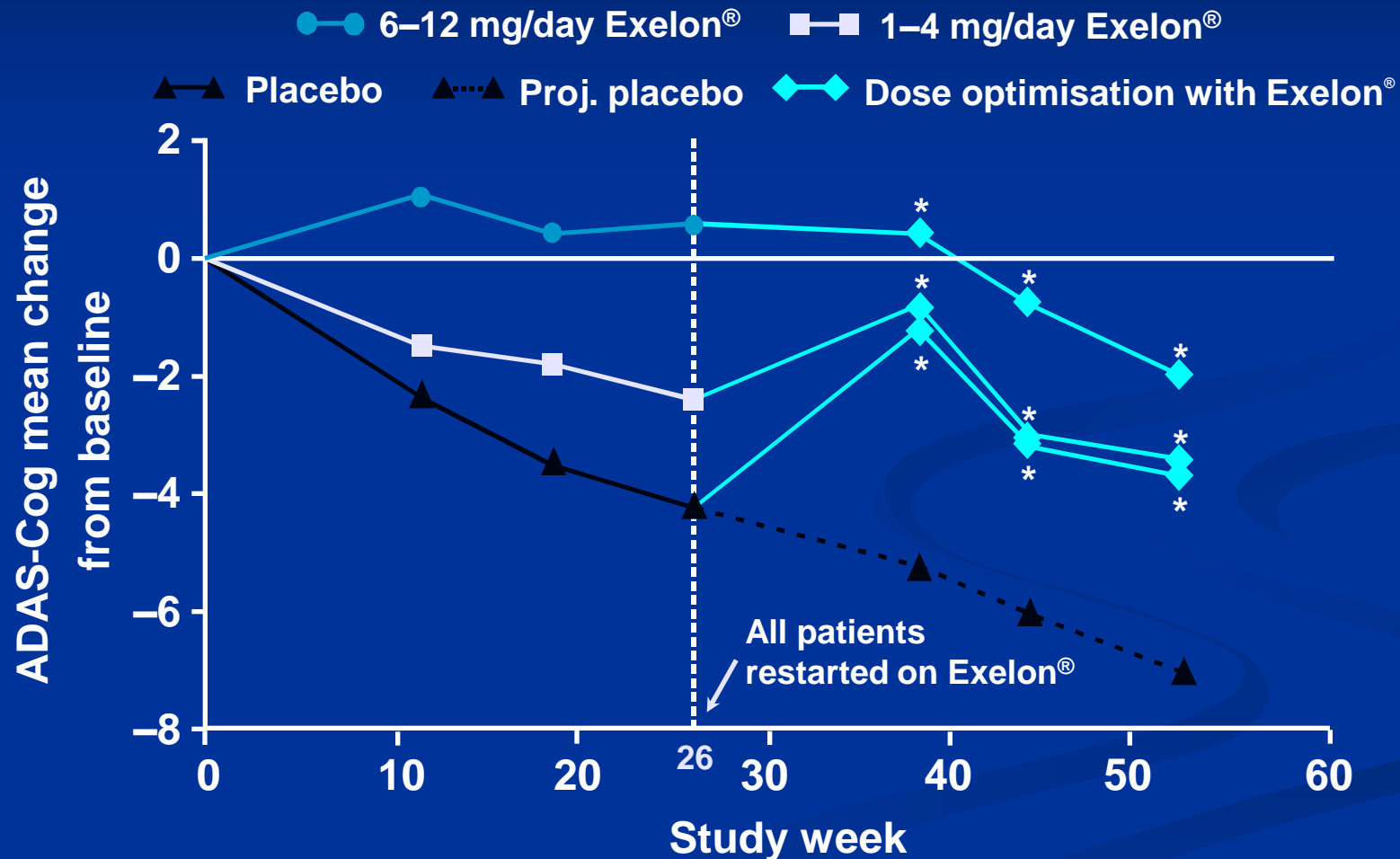


# Alzheimer disease and cerebrovascular disease



# Drug therapy for AD

# Exelon<sup>®</sup> on cognition: greater benefits with earlier therapy



B352 patients in Study B353 (OC) at week 52

\* $p < 0.05$  vs projected placebo

Messina et al., 2000

# Adverse effects of cholinesterase inhibitors

- Nausea (11%)
- Anorexia (10%)
- Vomiting (5%)
- Insomnia (9%)
- Dizziness (8%)
- Muscle cramps (5%)
- Nightmares (up to 10%)

# Adverse effects of Cholinesterase inhibitors

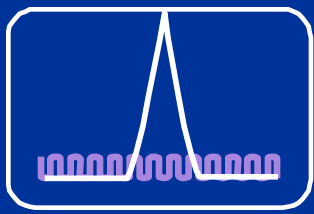
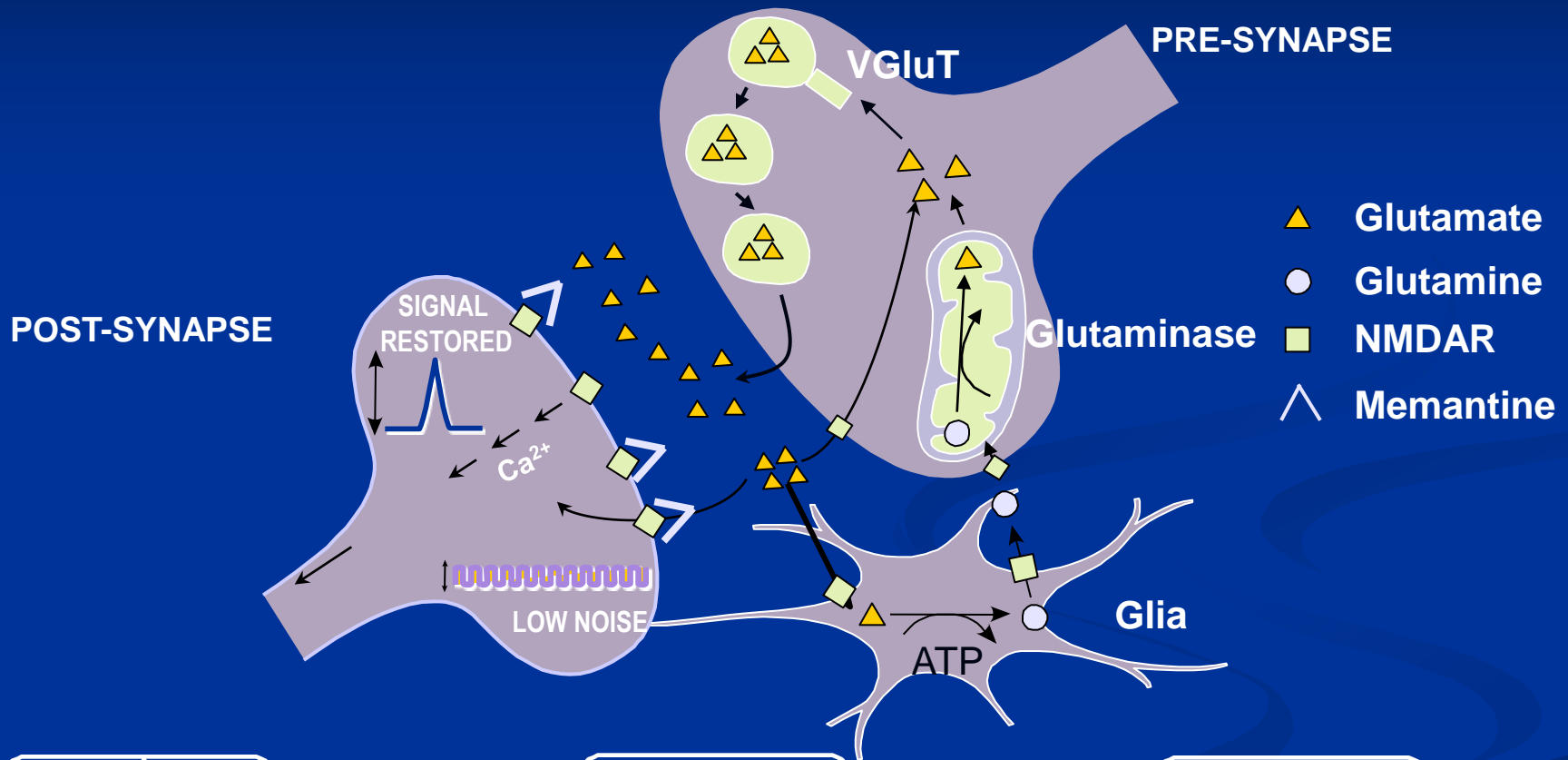
- Most patients do not have adverse effects
- Side effects are dose dependent
- less frequent if dose is titrated up
- Usually remit over time or if dose reduced
- Exelon patch may have less GI upset



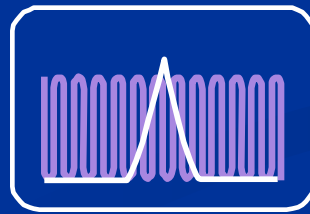
# Ebixa (memantine)

- An uncompetitive NMDA antagonist
- Effective for AD and VaD
- Well tolerated
- Proven efficacy and safety by FDA & EMEA ( moderate/severe AD)
- Available in tablets (10mg b.d.)

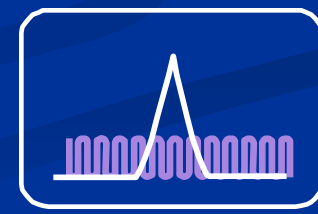
# Glutamate-glutamine cycle in AD



Normal



AD



AD + Memantine

# Major tranquillizer (dopamine antagonist)

- Commonly used to “control” behavioral problems in AD
- They reduce agitation and aggression, but most other behavioral problems do not respond
- There is evidence that they lead to dependency and increased mortality
- Side effects include Parkinsonism, sedation, falls

# Other drugs to stabilize mood

- Memantine
- Anti-depressants
  - SSRI
  - Trazodone
- Anti-convulsants
  - Sodium valproate
  - Carbamazepine



手工藝小組



書法小組



烹飪小組



園藝小組

# Day Care

- Group & Individualized activities



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Funded by Kao's walkathon 2010,  
Knowledge transfer grant (CUHK)

短片：「小小花」  
讓我們了解多一點腦退化症患者的世界

## Short Film: “The Little Flower”

“Understanding dementia: A different reality”



**SK Yee Grant**



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# Conclusions

- Neurodegenerative disease is a major challenge to health and quality of life in old age
- Current treatments have limited effectiveness
- Psychosocial interventions are important in the management of these incurable diseases
- Alternative medicine may have a significant role to play in symptom relief or prevention