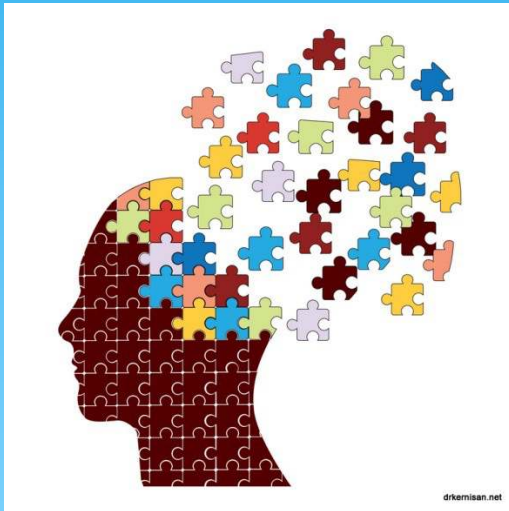


# Dementia, Medications and Non-Pharmacological Approaches.



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GY&W Care Group

# What is dementia?

- \* Dementia is an umbrella term for a range of progressive conditions that affect the brain. (Dementia UK, 2022).
- \* Dementia is used to describe a collection of symptoms including memory loss, problems with reasoning, perception and communication skills. It also leads to a reduction in a person's abilities and skills in carrying out routine activities such as washing, dressing and cooking. (RCN March 2019).
- \* Other symptoms; Disturbed behaviour, mood and or personality changes, psychosis.



# Types of Dementia

- \* Alzheimers Disease - most common
  - \* Vascular Disease – also known as multi-infarct
  - \* Lewy Body Dementia – motor symptoms affected
  - \* Fronto-Temporal Dementia – (Pick's)
  - \* Others;
  - \* Mixed Type – AD/Vas
  - \* Parkinsons and dementia
  - \* Huntingdon's Chorea
  - \* Creutzfeldt-Jakob Disease (CJD)
  - \* HIV related
- to name a few....



# Draw a One Penny Coin Circa 1971-2008:

## 10 Points – Face side

Queen  
Facing right  
Elizabeth II  
D.C Reg .F.D/date  
Dots



**Rear side**  
One Penny  
No.1  
Portcullis  
Chains  
Dots

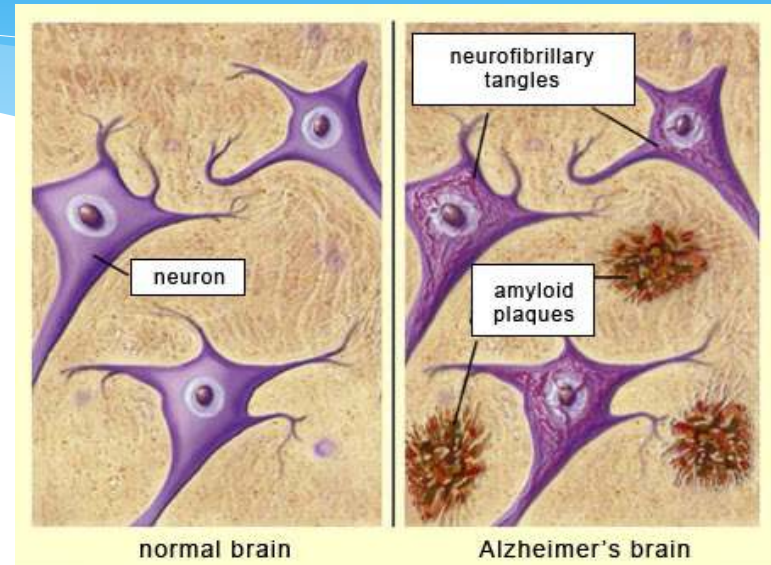
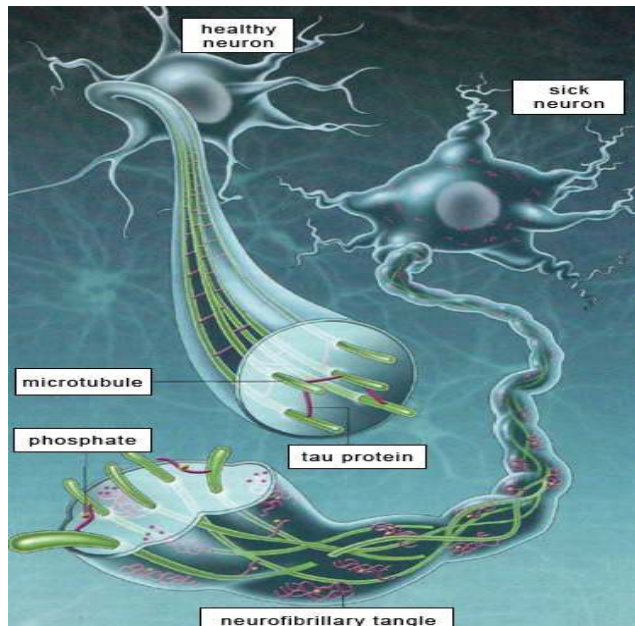
# Assessment (not in 10 mins)

- |   |   |
|---|---|
| <ul style="list-style-type: none"><li>• History of patient</li><li>• Cognitive assessment – ACEIII/MMSE</li><li>• Neuropsychiatric symptoms</li><li>• Depression</li><li>• Activities of daily living</li><li>• PMH</li><li>• Family history</li><li>• Medication</li><li>• Head injury</li></ul> | <ul style="list-style-type: none"><li>• General examination</li><li>• Other investigations –<ul style="list-style-type: none"><li>• FBC</li><li>• ESR/CRP</li><li>• Clinical chemistry profile (U&amp;E, calcium, glucose)</li><li>• Thyroid function</li><li>• B12 and folate</li><li>• Neuroimaging</li></ul></li></ul> |
|---|---|

# What is happening in Alzheimers:

## \* Amyloid Plaques

- \* Beta-Amyloid protein molecules are chemically adhesive and bind together to form plaques in the brain. Beta-amyloid is a larger protein molecule present in the membrane of nerve cells.



## Neurofibrillary Tangles

Tau Protein provides structural support to the microtubules in a Neuron. Tau protein molecules disaggregate into filaments that form tangles and the microtubules structure is lost. The nerve endings are first to degenerate and therefore communication between cells is lost.



# AD Symptoms overview

Activities of Daily Living	Behaviour	Cognition	Communication
showering/bath	agitation/ aggression	memory/ confusion	following conversation
being left alone	personality changes	concentration/ attention	comprehension of language
incontinence	irritability	orientation	irritability
finding belongings	wandering/ restlessness	recognising people	speaking
moving in general	depression		writing/reading
sleeping			

(Georges et al, 2008)

# Vascular Dementia (or mixed):

- \* Due to a lack of oxygenated blood to parts of the brain.
- \* Symptoms include STM loss, getting lost in familiar environments, laughing or crying at inappropriate times. Difficulty concentrating, following instructions, planning or completing tasks; like managing money. Loss of bowel or bladder control. Hallucinations and delusions.



# Lewy Body Dementia:

- \* Abnormal deposits of the protein Alpha-Synuclein (aSyn) in the brain in inclusions known as Lewy bodies.
- \* Second largest neurodegenerative dementia.
- \* Tends to have a poorer prognosis, higher healthcare cost and greater impact on quality of life (Rodriguez-Porcel et al, 2022).
- \* Symptoms: Parkinsonian presentation which deteriorates rapidly in the first 12/12. Falls, visual hallucinations in 80% of Pts. Fluctuating cognition, REM sleep disorder. These form the core criteria for diagnosis.

# Fronto-Temporal Dementia:

- \* Degeneration of the fronto and temporal lobes of the brain. Previously known as Picks Disease.
- \* Area responsible for language, behaviour and personality.
- \* Personality changes: either impulsive, disinhibited, apathetic or listless. Shows a lack of empathy or sympathy. Blunted emotions.
- \* Expressive or receptive dysphasia, or both.
- \* Research suggests 1/3 of FTD are familial with autosomal dominant mutation in 3 genes. (Wang et al , 2022).

Any Questions?

break..

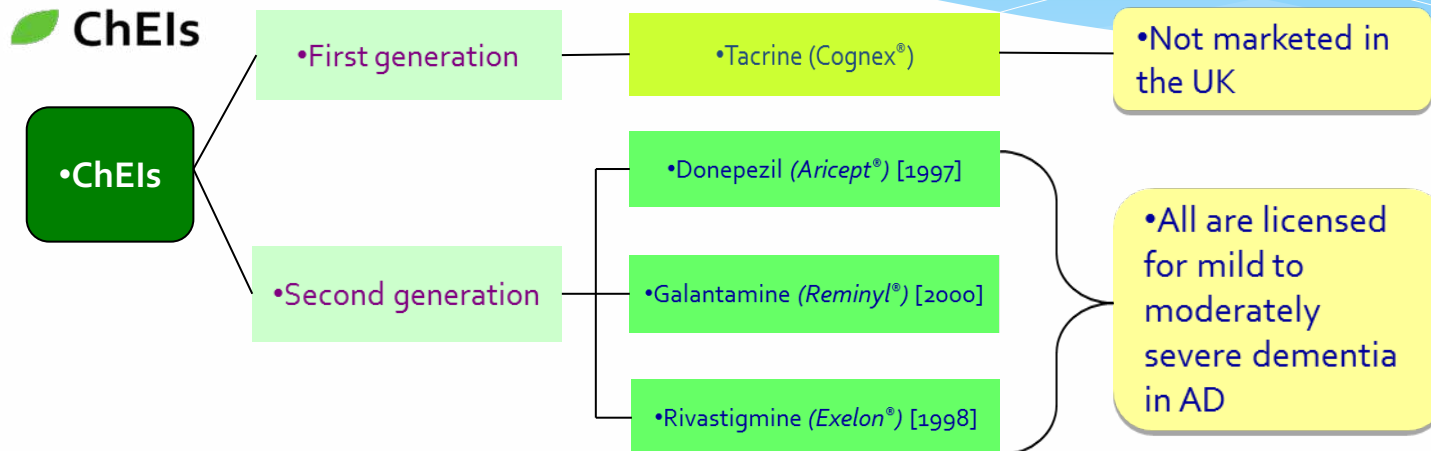
# Dementia Treatment

# Treatment in AD, Role of medications:

- Do not change / modify the course of the disease deterioration
- Not a cure
- May slow down disease progression
- May improve memory and functioning in the short-term (?long-term)
- May have benefits with quality of life and behavioural disturbances
- ? May delay or reduce the need for nursing home placement or institutionalisation
- ? May reduce mortality



# An overview of drugs used for AD



## **NMDA receptor antagonist** Blocking the NMDA receptor

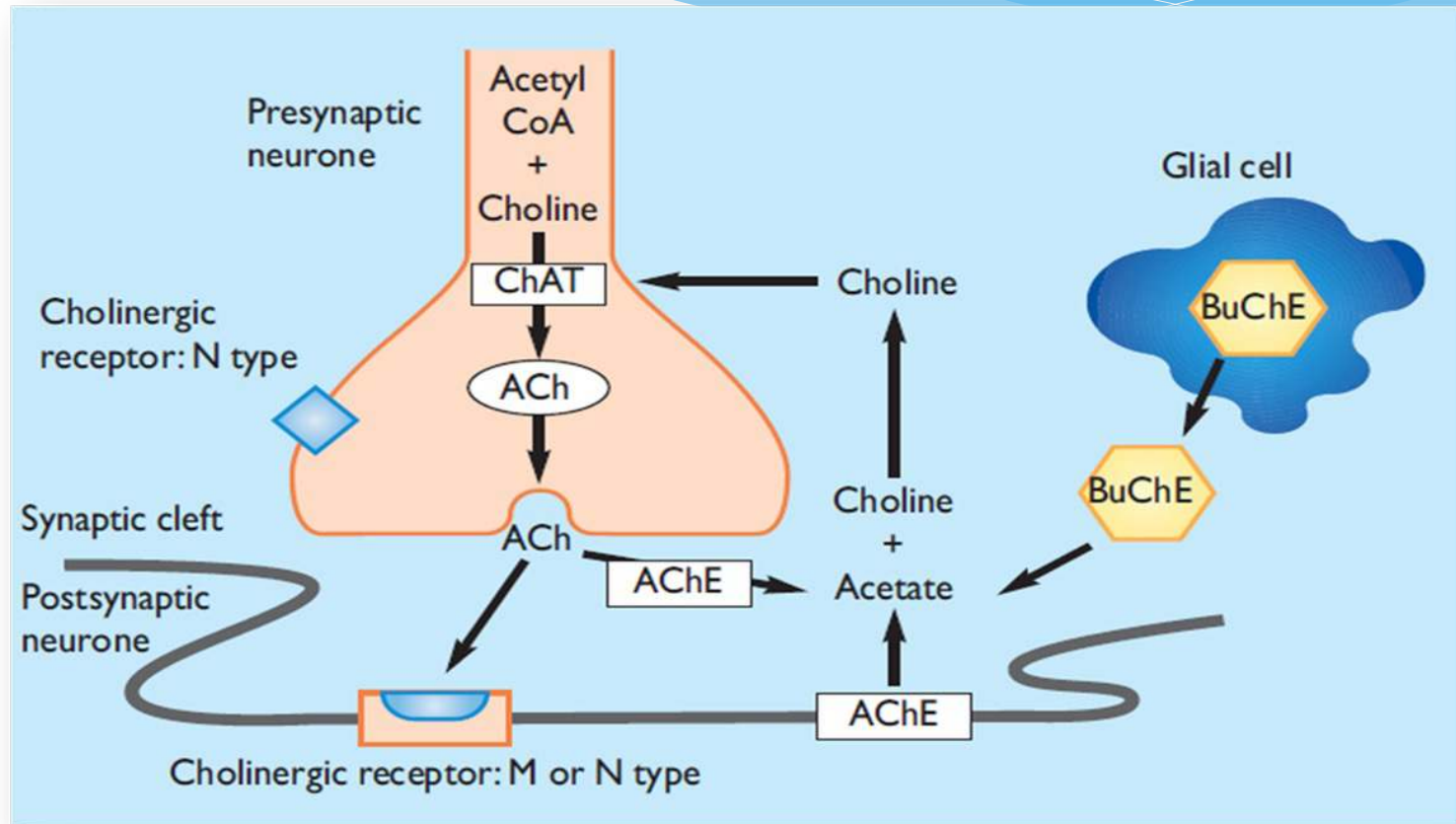
- Memantine (*Ebixa*®) [2002] – Licensed for moderately severe to severe AD

# How does it work?

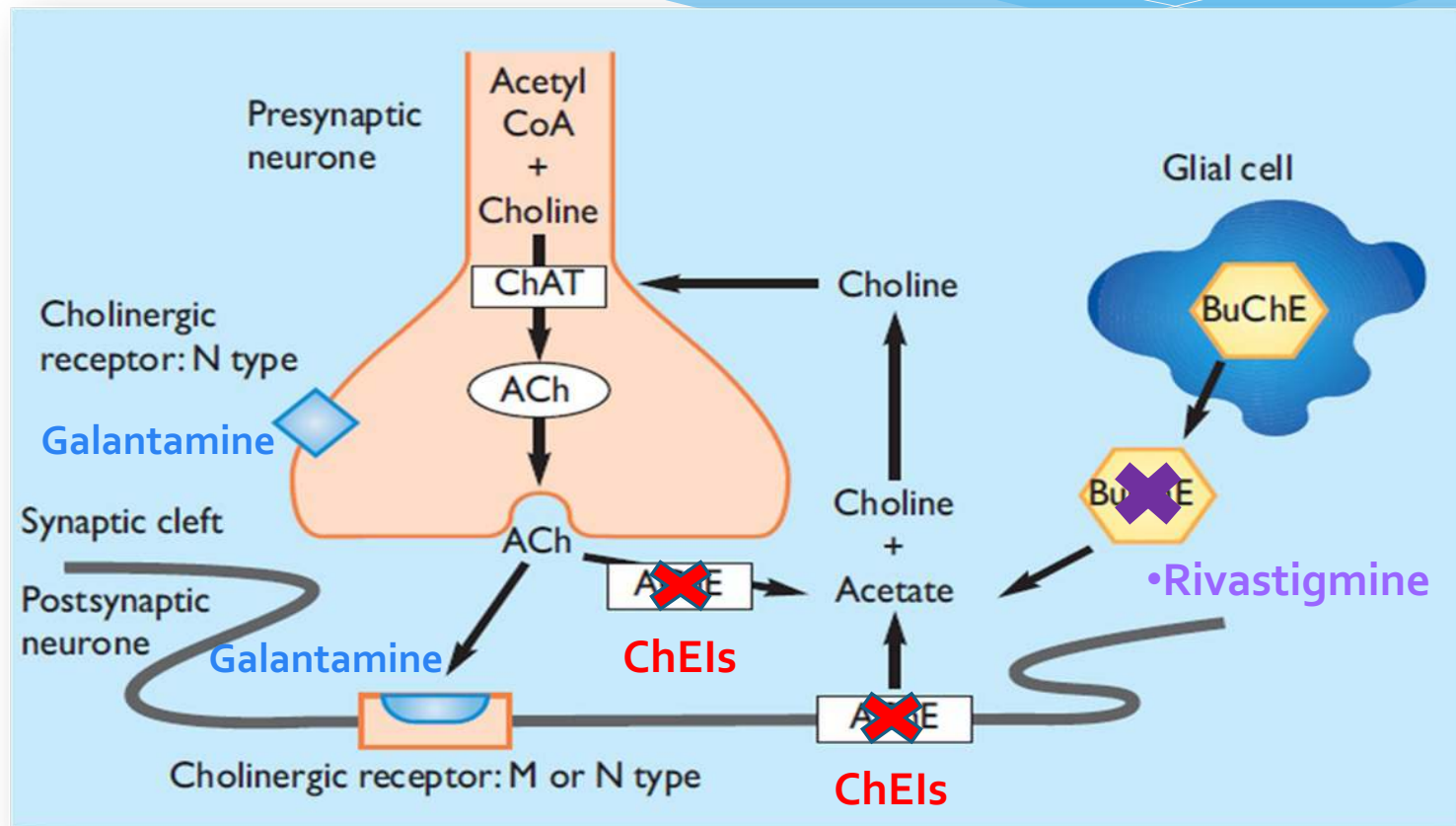
- \* All ChEIs primarily work by enhancing the action of ACh (Acetylcholine).
  - by inhibiting the enzyme Acetylcholinesterase (AChE) from breaking down ACh
- \* Relies on some intact cholinergic neurones to synthesise ACh. Hence, they are more beneficial in early stages of the disease.
- \* Rivastigmine also a BuChE inhibitor (BuChEI)
- \* Galantamine also an allosteric modulator at nicotinic (N) cholinergic receptor



# ACh synthesis and metabolism



# ACh synthesis and metabolism



# Memantine

## Mode of action -

- Memantine blocks the NMDA receptor
- This reduces neuronal damage caused by excessive glutamate
  - Excess glutamate causes over stimulation of NMDA receptors, which allows the free flow of calcium ( $\text{Ca}^{2+}$ ) into the cell
  - A rise in intracellular  $\text{Ca}^{2+}$  ions is believed to trigger the events that lead to neuronal cell death
- \* Memantine is thought to bind to NMDA receptor sites, thereby reducing the amount of calcium that gets into nerve cells.

# Dementia Medications:

## Donepezil:

Long duration of action ( $t_{1/2}$  = 70h)

- Once daily dosing, preferably in the morning
- Initial dose: 5mg/day
- After 4 weeks, may increase dose to 10mg/day if tolerated
- Maximum recommended daily dose is 10mg
- Dose >10mg/day have not been approved in the UK

Patients with renal impairment - no dosage adjustment (as clearance is not affected)

Patients with mild to moderate hepatic impairment - dose escalation should be performed according to individual tolerability

## Rivastigmine:

Capsules and solution:

- BD dosing ( $t_{1/2}$ =2h)
- Starting dose 1.5mg BD
- May increase to 3mg BD after at least 2 weeks, if tolerated
- Maintenance dose 3 to 6mg BD (max: 6mg BD)

Moderate renal and mild to moderate hepatic impairment - dose escalation should be considered according to individual tolerability

Patches:

- Starting dose 4.6mg/24h
- May increase to 9.5mg/24h, after at least a minimum of 4 weeks, if tolerated
- Recommended effective dose is 9.5mg/24h
- May increase to 13.3mg/24h, after a minimum of 6 months, if tolerated

## Galantamine:

Tablets and oral solution:

- BD dosing ( $t_{1/2}$  = 7-8h)
- Starting dose 4mg BD
- May increase to 8mg BD after at least 4 weeks, if tolerated
- A further increase to 12mg BD may be considered

XL capsules:

- Once daily dosing ( $t_{1/2}$  = 8-10h)
- Starting dose 8mg/day for 4 weeks
- May increase to 16mg/day and maintain for at least 4 weeks
- A further increase to 24mg/day may be considered

Renal impairment - no dosage adjustment if creatinine clearance is >9ml/min.

Avoid if creatinine clearance <9ml/min

Moderate hepatic impairment – start with 4mg/daily in the morning for at least 1 week, then increase to 8mg/day for at least 4 weeks. Maximum daily dose 16mg/day. Avoid in severe hepatic impairment.

## Memantine:

Once daily dosing interval ( $t_{1/2}$  = 60-100h) for tablets and oral pump solution, with or without food

Recommended dose titration regimen:

- Week 1: 5mg/day; week 2: 10mg/day; week 3: 15mg/day and week 4: 20mg/day

Recommended maintenance dose is 20mg/day

Maximum daily dose is 20mg/day

Dosage adjustment is required for patients with moderate to severe renal impairment

No dosage adjustment for mild to moderate hepatic impairment.

Avoid in severe hepatic impairment

Oral pump solution device

Risk of medication errors and accidental overdose [*Drug Safety Update Nov.2010;4(4):A2*]

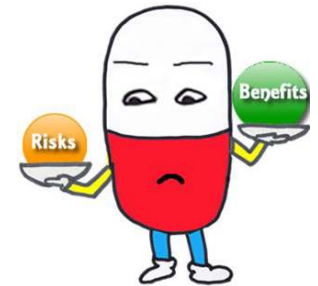
One actuation of the pump device delivers 0.5ml of solution, corresponding to 5mg memantine.

The max. daily dose is 20mg (four actuations)

Be vigilant regarding dose delivery for Memantine

# Antipsychotic prescribing for BPSD

- Antipsychotic prescribing for BPSD is a 'hot topic'
- Over-prescribing of antipsychotic in BPSD is considered a huge problem
  - ⇒ inappropriate prescription for management of behaviours
  - ⇒ continued too long
  - ⇒ risks not fully appreciated
- All antipsychotics are unlicensed in the UK for dementia-related behavioural disturbances except Risperidone and Haloperidol



10yrs ago it was estimated that 180,000 people with dementia were Px antipsychotics – but only 36,000 derived some benefit!

# New Dementia Medication in 2020

## **Idalopirdine**

- a potent and selective 5-HT<sub>6</sub> receptor antagonist
- Lundbeck
- as an augmentation therapy for the treatment of cognitive deficits associated with Alzheimer's disease and schizophrenia

## **LMTM** (Leuco-methylthioninium bis(hydromethanesulfonate))

- Stabilised form of methylene blue which is a first-in-class tau aggregation inhibitor
- TauRx Pharmaceuticals Ltd
- developed for the treatment of mild to moderate Alzheimer's disease and behavioural variant frontotemporal dementia

# Dementia??? Clinical Example:


## Patient Details:

- ❖ Alice is 81yrs old – not pregnant. Referred for a memory assessment - ?Dementia?
- ❖ PMH – Anxiety, Depression, Osteoarthritis, ID Anaemia, Parkinsons and Hiatus Hernia.
- ❖ CT Head 2014 - small vessel disease (SVD).
- ❖ Alice was born in Norfolk and left school at 14yrs, working in her parents chip shop. She is married and ran a grocery shop with her husband. She has two girls, both live near her and provide support.
- ❖ Currently experiencing depression following friends sudden death, anxiety, poor STM/confusion, auditory hallucinations, sleeping during the day, reduced ADL's and mobility.
- ❖ Non-smoker, no alcohol.

Calgary –Cambridge (1996)

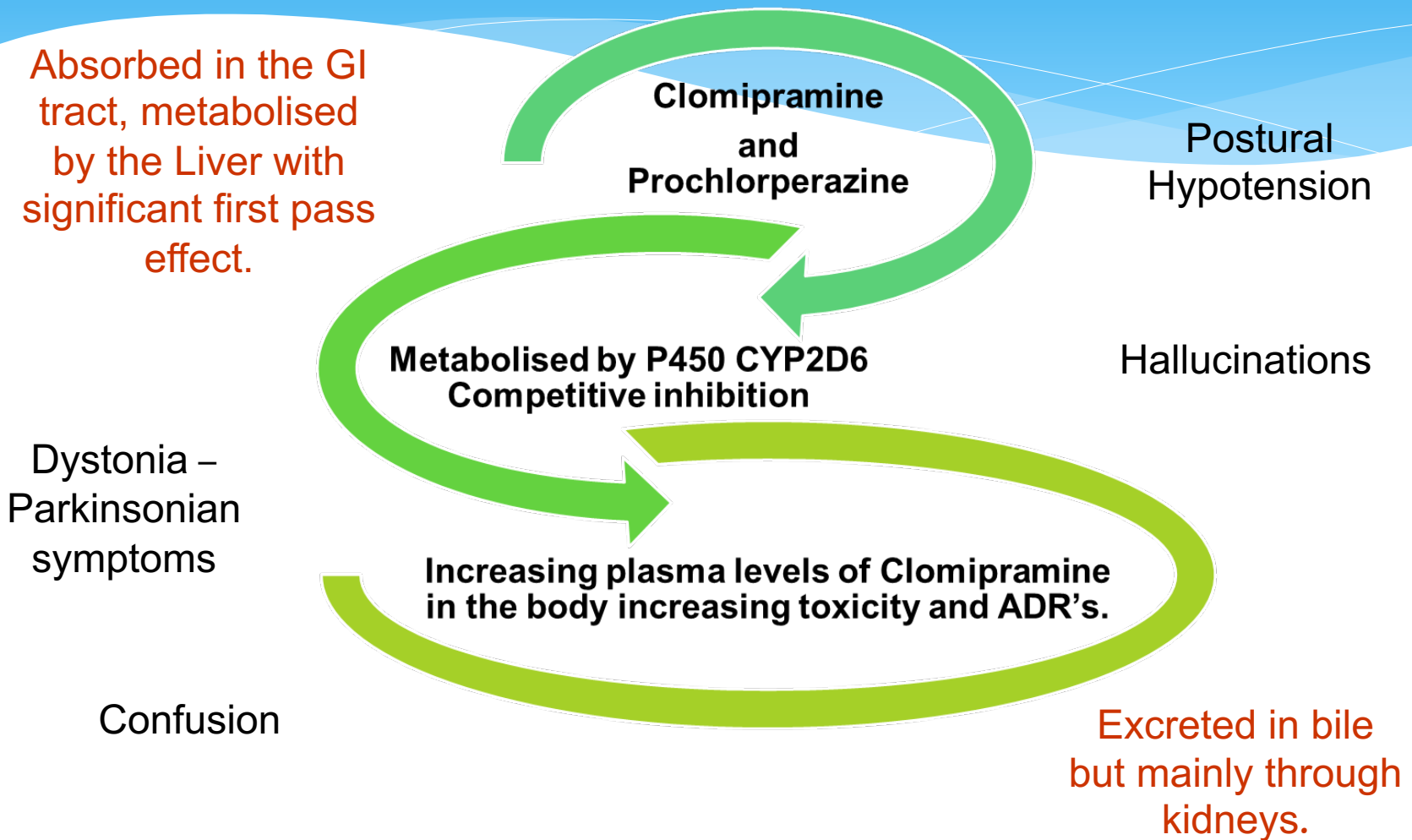


# Medications/Presentation

Medication	Indication	Comments
Clomipramine 35mg at night and 25mg in morning	Depression	Increased at Christmas by GP
Prochlorperazine 5mg twice daily (reduced from 5mg three times a day)	Nausea	Parkinson's team recommended reduction in 2014
Sinemet 12.5/50mg 2 tabs three times a day	Parkinson's	Started 2014
Lorazepam 1mg three times a day	Anxiety	
Lansoprazole 30mg daily	Hiatus hernia	
CosmoCol™ 6.9g sachet daily	Constipation	

Nil OTC medications

# Pharmacokinetics, Metabolism...



# Actions:

- ❖ Further bloods to rule out physiological reasons for confusion - Folate, VitB12.
- ❖ **Stop Prochlorperazine prescription, due to contraindication with Parkinsons and interaction with Clomipramine. (Alice did not want to – as did not want to vomit due to HH, however did eventually agree).**
- ❖ Reduce with view to stop Lorazepam – reducing titration over 6/52 – reduce over sedation.
- ❖ Request ECG to review cardiac rhythm (Assessed prior to memory medications being prescribed).
- ❖ Request MRI brain, Diagnostic tool: Vas/Alz dementia?
- ❖ If diagnosed with a dementia, possibly prescribe Memantine (due to SVD).
- ❖ **Informed GP, Follow up – 6/52.**

# Outcome:

- \* Alice reduced and stopped the Prochlorperazine over the 6 weeks.
- \* She managed to reduce the Lorazepam to 0.5mg three times a day, halving the dose.
- \* Presentation: more alert, no evidence of hallucinations, spontaneous in speech, stated mood had improved although she was still upset about losing her friend. Alice was also able to walk more – short distances.
- \* Review in 3 months (following MRI) and repeat the ACEIII.

# ANY QUESTIONS?

The Patient Experience. . .



HikingArtist.com

V

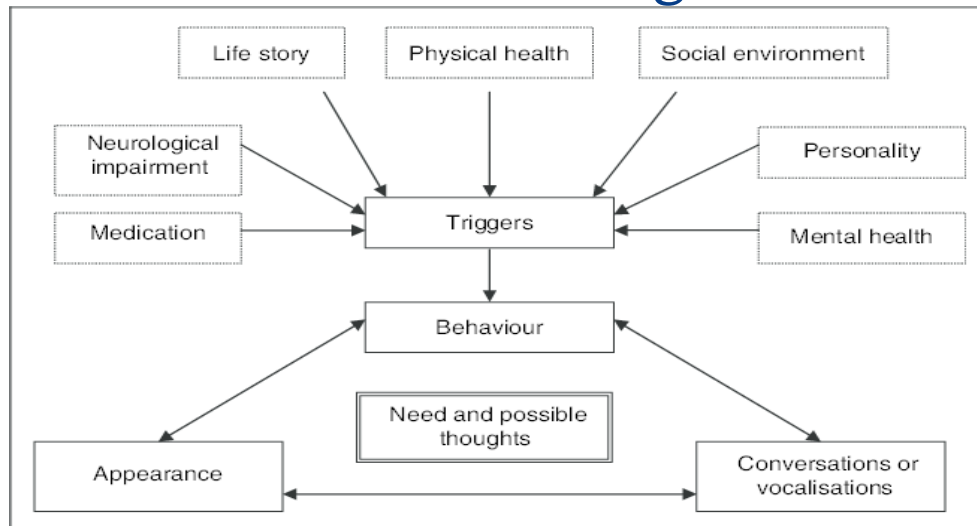


Quick break.....

# Dementia – Nonpharmacological Approaches

# Person-Centre Approach

- \* Kitwood (1997) Dementia Reconsidered. Person-centred Care:  $D = NI + B(L) + H + P + SP$ .
- \* Newcastle Formulation Model: 'behaviour that challenges'





# Cognitive Stimulation Therapy (CST)

- \* Using orientation sensitively and implicitly
  - \* Concentrating on peoples opinions rather than facts
  - \* Providing triggers to aid concentration and recall
  - \* Mental stimulation and stimulating language
  - \* Respect and choice
  - \* Inclusion and maximising potential
  - \* Continuity, consistency and building relationships
- 
- \* 18 Key principles of CST which with understanding and practice can increase the likelihood of people being able to live well with dementia.

## Music Mirror:

Try this simple exercise: go to your music library, pick a song, and play the first 3 s of it. Give yourself 1 point if you can manage to sing or hum at least the next 5 s of that song. Do this for 20 songs. How many points did you score? WHY?

Memory of events or information is stored in the hippocampus, neocortex and amygdala. Motor memories in the basal ganglia and cerebellum.

So why is the brains ability to recall music is not affected by degeneration of the above areas.

The link between music and emotions is believed to why it is able to be recalled and re-enable recall of events and feelings.

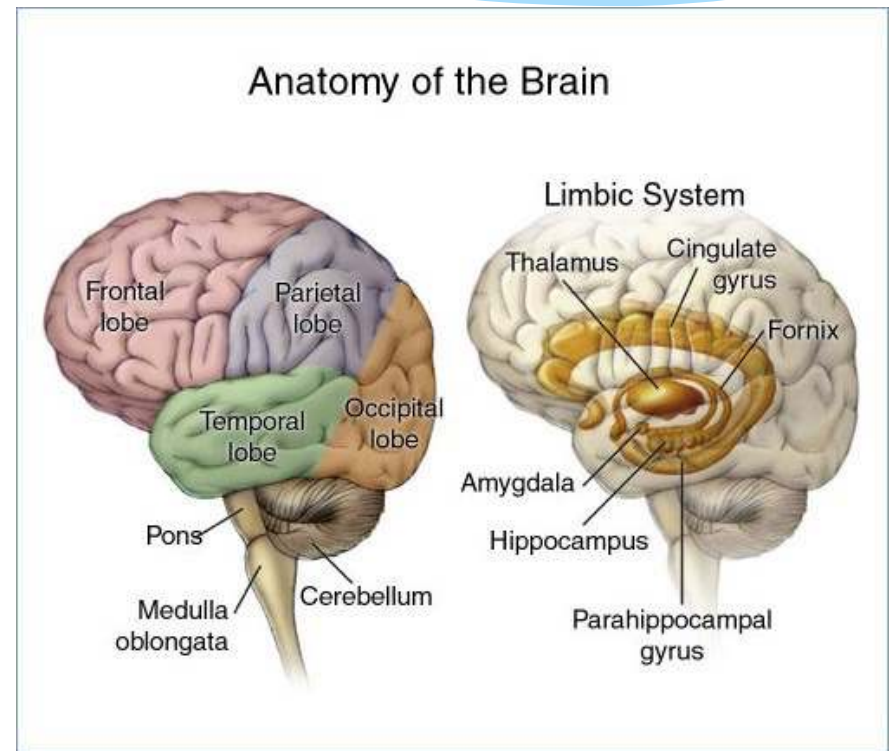
Research studies show the Ventral Pre-supplementary motor area and caudal anterior cingulate gyrus are stimulated when well-known music is heard. These areas are more likely to stay intact.

(Foo & Johnson, 2017)

Naomi Feil and Gladys Wilson:

<https://www.youtube.com/watch?v=CrZXz10FcVM>

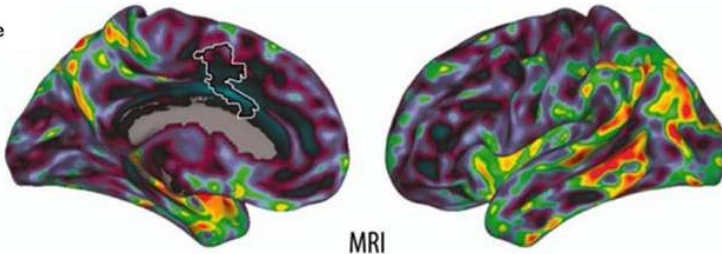
[Power Of Music On The Brain | Dementia & Parkinson's - YouTube](#)



Location of the  
Musical Memory  
Area (MMA)

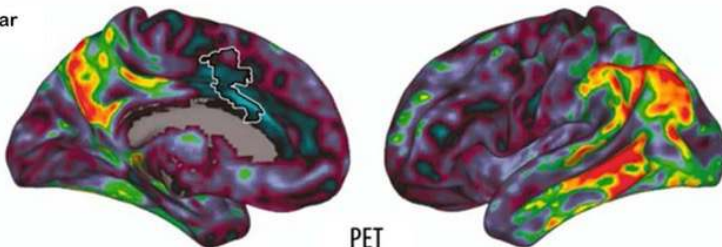


Brain shrinkage



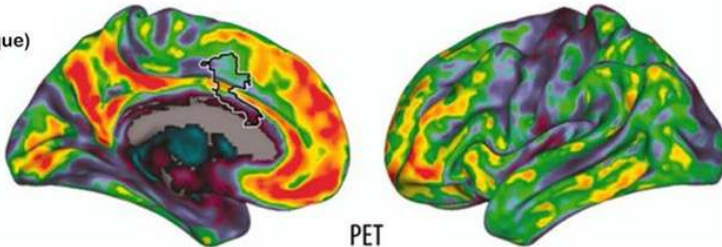
MRI

Decreased sugar  
uptake



PET

Sticky buildup  
( $\beta$ -amyloid plaque)



PET



Foo & Johnson, (2017) suggest the red area highlighted is where music memory is stored. The images show this area appears to be least affected by AD.

Music consists of pitch and rhythm, which are processed and stored independently (why we can still remember a melody if the rhythmic elements are omitted), (Schellenburg et al. 2014).



# Music Mirrors

Music has memories...



- ❖ It is a language beyond words: we understand and enjoy it without conscious thought. It can change our mood, the atmosphere, allow expression of feelings and make physical movement and speech easier.
- ❖ Dementia does not necessarily lessen music's power to open doors to feelings.
- ❖ Music Mirror is a toolkit that links the person's own life story with sounds and music associated with key positive memories. It is not 'just listening to music'.
- ❖ It is an aid to conversation, interaction, reminiscence and ultimately comfort.
- ❖ It allows a deeper understanding of 'the Person' and can be a form of advanced care planning.

## References:

- \* Georges J. et al (2008) Alzheimer's Disease in real Life – the Dementia Carer's survey. *International Journal of Psychiatry*. Vol 23 (5) Pg. 546-551
- \* Foo F. & Johnson E. (2017) Music: The Last thing we forget. *Frontiers Neuroscience and Psychology*. 5:5. doi: 10.3389/fnry.2017.00005
- \* RCN (2019) Dementia. Available at: <https://www.rcn.org.uk/clinical-topics/Dementia>
- \* Rodriquez-Porcel F. et al (2022) Clinical outcome measures in dementia with Lewy bodies trials: Critique and recommendations. *Translational Neurodegeneration*. Vol 11.(1) Pg. 1-18.
- \* Schellenberg, E. G., Stalinski, S. M., and Marks, B. M. (2014). Memory for surface features of unfamiliar melodies: independent effects of changes in pitch and tempo. *Psychological Research*. 78, 84–95. doi: 10.1007/s00426-013-0483-y
- \* Wang J. et al (2022) The Advance of Frontotemporal Dementia's Neuropathology and Molecular Genetics. *Mediators of Inflammation*. Available at: 5003902. doi:10.1155/2022/5003902.

# ANY QUESTIONS?

Thank you for listening.