5) A 90 year old man with dementia is about to commence donepezil. Which one of the following is least likely to change with treatment?

A. Visuospatial function
B. Memory
C. Social engagement
D. Completion of activities of daily living
E. Rate of cognitive decline after 3 months

Answer:

Dementia
- Acquired, progressive deterioration in cognition that **impairs ADLs**
- Not just memory loss – *loss of executive function*
- Neuropsychiatric and social deficits +/- mood disturbances
- Many forms but Alzheimer's most common
    - Then vascular, Parkinson's related dementia (DLB) and alcohol

Alzheimer's Disease
- Usually subtle memory loss -> progress
- 20%: non-memory – word finding, organisational
- Evolves over **years**

- Pathology:
    - Diffuse atrophy of cortex
    - Secondary ventricular enlargement
    - **Plaques with Aβamyloid**
    - **Neurofibrillary tangles** (silver stain) in cytoplasm
    - Hyperphosphorylated *tau* protein
    - Aβamyloid in arteriolar walls -> amyloid angiopathy (may cause lobar bleeds)

- Imaging:
    - CTB: often normal early on -> diffuse atrophy
    - **MRI: hippocampal atrophy**
    - PET (functional): hypometabolism of posterior temporal parietal cortex
    - EEG: normal/ non-specific slowing

Pharmacological Treatment:

Cholinesterase inhibitors
Tacrine (rarely used due to hepatotoxicity), Donepezil, Rivastigmine, Galantamine
- Theory: ⇓ cerebral production of choline acetyl transferase -> ⇓ acetylcholine -> ⇓ cholinergic function
- Cholinesterase inhibitors ⇓ degradation of acetylcholine -> ⇑ levels

- **Does not modify disease**

- Generally: ⇑ carer ratings of patient's function, ⇓ rate of cognitive decline over 3 years

- AD 2OOO study (only one not funded by pharmaceutical companies)
    - Donepezil vs placebo: NO DIFFERENCE in endpoints: progression of disease and entry into institutionalised care

Australian Guidelines:
(Donepezil and rivastigmine PBS listed)
- Need to be diagnosed and prescribed by consultant geriatrician

- MMSE Score 10-24
- If MMSE > 25 + clinical features: need ADAS-Cog score
- Only 6 month prescription
    - To renew: ⇑ MMSE by ≥ 2 points (or) ⇓ ADAS Cog by ≥ 4

Others:

- Oestrogen: useless
- Anti-oxidants (selegiline/ vitamin E): small benefit to ⇓ institutionalisation and death
- Gingko biloba: little evidence
- Memantine (NMDA antagonist): small study showed ⇓ progression over 28 weeks
- NSAIDS: small study showing indomethacin slowed progression
- Statins: watch this space
- Vaccine against Aβ protein: great in mouse but bad in humans (meningioencephalitis)

Other possible dementia-related questions:

1. Which of the following is not a risk factor for developing dementia?
    A. A positive family history
    B. Increasing age
    C. Low level of education
    D. Chronic alcohol abuse
    E. Parkinson's disease

Answer: C. The strongest risk factor is age, followed by family history. Another risk factor is vascular disease.

2. Which of the following genes have not been found to be associated with Alzheimer's disease?
    A. Presenilin-1 (PS-1) gene
    B. Presenilin-2 (PS-2) gene
    C. APP gene
    D. Apo E gene
    E. APC gene

Answer: E – APC gene germline mutation (chromosome 5) is autosomal dominant and associated with familial adenopolyposis coli (FAP)/ colorectal cancer.

PS-1, PS-2 and APP are all autosomal dominant and associated with familial, early onset dementia.

APO E on chromosome 19 – strongly implicated in familial late-onset and sporadic forms of Alzheimer's. May be associated with poor clearance of amyloid. APO E4 worst, APO E2 possibly protective. Testing not indicated even though available.