Atypical Dementias

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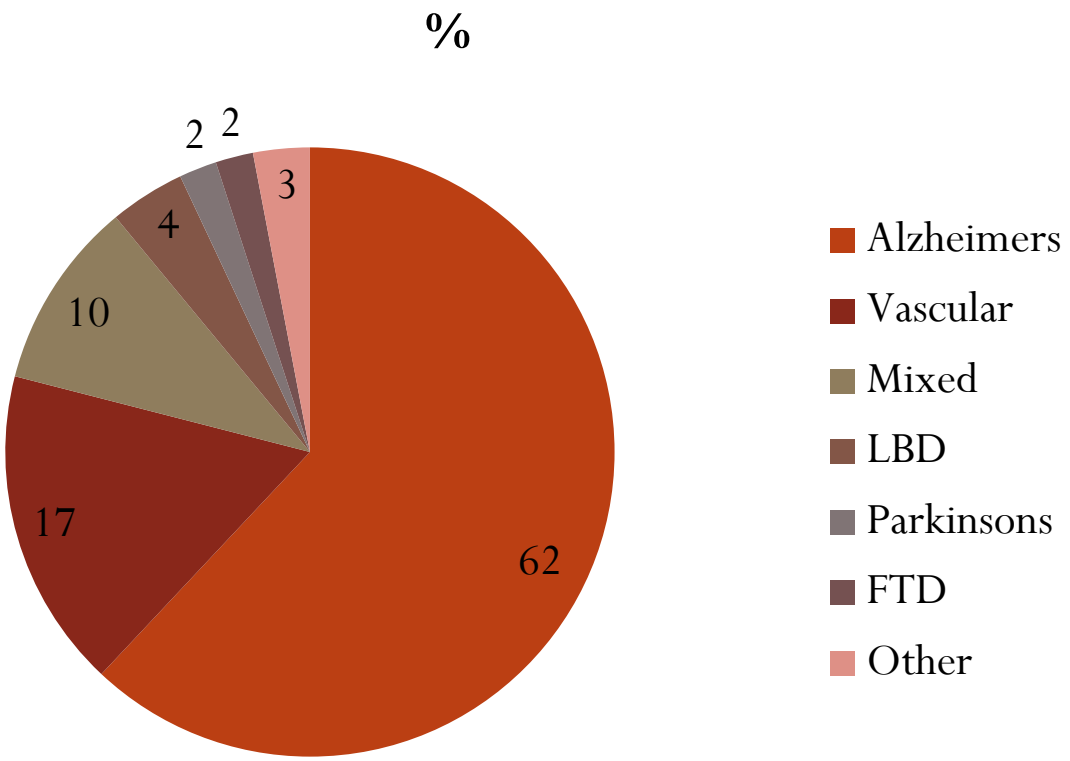
Proportion of people with each type of dementia



Adapted from figures at https://www.alzheimers.org.uk/about-us/policy-and-influencing/what-we-think/demography summarising the report Dementia UK: Second edition (2014).

Lewy Body Dementia

- Cause: Lewy bodies (alpha synuclein protein deposits) in brain cells; reduced acetylcholine and dopamine; reduced synaptic connections, brain cell death.[1]
- Features to look for:
  - Parkinsonian symptoms including non motor and autonomic symptoms (NB: not all patients will have motor symptoms)[1]
  - Visual hallucinations (often children or animals)[2] +/- associated delusions[1]
  - Variable attention[2]
  - Neuroleptic sensitivity (antipsychotics!)[1]

Lewy Body Dementia - Investigations

- Special tests: neuro exam for motor symptoms of Parkinson's, screen for non-motor symptoms (anosmia, REM sleep behaviour disorder, depression)
- Imaging: MRI/CT useful to exclude vascular Parkinsonism, often no specific structural changes, DAT/SPECT scan[3]

Dementia in Parkinson's Disease

- Similar to LBD but there is a pre-existing diagnosis of Parkinson's (ICD-10 doesn't distinguish between the two)[4]
- Significant numbers of patients with Parkinson's will end up with a diagnosis of dementia
- NB: depression is common in Parkinson's, remember to look for this as a possible differential dx (especially if attention/concentration deficits)

LBD/DPD Treatment

- Rivastigmine
  - Licenced for use in LBD[5]
  - Can help with cognition AND hallucinations[1]
  - Consider skin patch if swallowing difficulties[5]
- Memantine
  - Not licenced but could consider if contraindications to rivastigmine
- Antipsychotics
  - With caution! Avoid if possible.
  - Can help with distressing hallucinations
  - Quetiapine or clozapine best tolerated (very low doses)

Frontotemporal Dementia

- A group of disorders rather than one illness:
  - Behavioural variant (most common)
  - Semantic dementia
  - Progressive non-fluent aphasia
  - Logopenic variant
- Subtypes can be less distinct in advanced disease
- NB: relatively rare cause of dementia overall but second most common cause of young-onset dementias[6]

Behavioural Variant FTD

- Cause: nerve cell damage in the frontal and temporal cortex associated with either tau or TDP43
  - Genetic link in some cases (MAPT, GRN, C9ORF72)[7]
- Features to look out for:
  - Personality change[6], increased impulsivity[6], cravings for sweet or fatty foods[7]
  - Inflexibility in routine or compulsions[6]
  - Apathy[6]
  - Family history (10 – 15% of patients)[7]. Also ask about FHx of related disorders (MND)
  - Relatively young age[6]
  - Later: language problems.
  - See also: International Consensus Criteria for Behavioural Variant FTD[6]

Behavioural Variant FTD - Investigations

- Special tests: Frontal Assessment Battery, reflexes, neuropsychology, genetic testing (maybe)
  - NB: association with several neurological conditions including MND – so if you notice abnormal motor features consider referral to neurology
- Imaging: MRI/CT may show atrophy of frontal lobe, PET scan can show reduced metabolism in frontal lobe[3]
- Treatment: supportive care, genetic counselling for family if relevant. Cholinesterase inhibitors can worsen symptoms.[6]

Semantic Dementia

- Cause: most commonly TDP-based pathology[8]
  - Not usually familial[7]
- Features to look out for:
  - Fluent speech with loss of vocab[8], increased use of descriptions or umbrella words
  - Surface dyslexia (difficulty with irregular spellings)[8]
  - Impaired recognition of familiar people and objects[8]
  - Other cognitive function relatively preserved early in the illness
- Special tests: neuropsychology
- Imaging: atrophy in temporal lobes[3] often L > R[8]
- Treatment: supportive care

Progressive Non-Fluent Aphasia

- Cause: either tau (more common) or TDP (less common) pathology[8]
  - Not usually familial
- Features to look out for:
  - Slow hesitant speech, mispronunciations[8]
  - Omission of linking words/ prepositions ("telegraphic speech").[8]
  - Preserved understanding of individual words but struggle with complex sentences.[8]
  - Other cognitive functions relatively preserved early in the illness
- Special tests: neuropsychology
- Imaging: atrophy in temporal lobes (may be asymmetric affecting L side only)[3]
- Treatment: supportive care

Logopenic Variant

- Cause: similar to Alzheimers pathology[8]
- Features to look out for:
  - Slow speech with word-finding problems[8]
  - Grammar intact[8]
  - Single-word comprehension better than semantic dementia[8]
  - Impaired repetition[8]
- Special tests: neuropsychology
- Imaging: abnormalities in temporo-parietal region[8]

CJD

- Cause: accumulation of prions → large amounts insoluble proteins in neurones → cell damage and cell death → spongiform changes in brain tissue[9]
  - Subtypes: Sporadic (most common) – misfolding of normal brain protein forms prions[10]; vCJD: rare, linked to eating BSE-infected meat[10]; Inherited (rare); Iatrogenic (now very rare)[9]
- Features to look for:
  - Early features: minor memory problems, mood changes. Rapid progression: personality change, early onset of jerky movements, slurring then loss of speech, incontinence, severe dementia.[9,10]
  - Early features → severe impairment → death (around 90% die within 1 year)[10]
- Investigations: MRI, LP, EEG[10], genetic test (familial only)[10], post-mortem (precautions to avoid transmission)
- Treatment: supportive care

ARBD

- Causes: direct damage to brain from alcohol +/- thiamine deficiency +/- Wernicke's +/- head injuries +/- vascular damage[11]
- Features to look out for:
  - Alcohol history
  - Presentation can be variable. If drinking has stopped, there may be a lack of progression[11]
  - Features of Korsakoff's e.g. loss of short term memory with relatively preserved thinking skills, confabulation[12]
- Special tests: neuro exam for cerebellar features
- Treatment: Abstinence from alcohol (NB: may need medically supervised detox), thiamine supplementation[11]
  - Often a lack of services for this patient group (especially if younger)

Huntingtons

- Cause: genetic mutation (autosomal dominant) leads to defective huntingtin protein[13]
  - NB: trinucleotide repeat – can get anticipation effect (worsening in later generations)
- Features to look out for:
  - Abnormal movements (chorea)[13]
  - Obsessive behaviour[13]
  - Family history (but remember anticipation effect)
  - Relatively preserved orientation to place and person, impaired ability to plan and organise[13]
- Investigations: genetic testing (potentially before onset of symptoms if known family history)
- Treatment: supportive care, genetic counselling

HIV cognitive impairment

- Cause: several - viral and other infections, cancers. Much less common with antiretroviral treatment.[14]
- Features to look out for:
  - Vary according to part of brain affected
  - Known HIV or history suggesting high risk of HIV infection
  - Severity often MCI level rather than dementia[14]
- Investigations: HIV serology, CD4 count, screen for mood disorder
- Treatment: optimise antiretroviral treatment

Multiple Sclerosis

- Causes: autoimmune disease causes demyelination of neurones in the CNS[16]
- Features to look out for:
  - Known MS or history suggestive of this[15]
  - MCI-level cognitive impairment[15]
  - Can be variable depending on brain area affected and course of MS (relapsing-remitting vs progressive)
- Investigations: LP (if MS not confirmed), neuroimaging[17]
- Treatment: optimise MS treatment, social support

Other causes of cognitive impairment

- Corticobasal degeneration
  - Tau related, affects cortex and basal ganglia, abnormal movements, alien hand syndrome. Can overlap with FTD. Average survival 8 years.[18]
- Progressive supranuclear palsy
  - "Parkinson's plus", impaired eye movements, tau related, personality changes, slowing of thinking. Cognitive impairment may not be severe enough to classify as dementia.[19]
- Posterior cortical atrophy
  - Alzheimer's pathology, usually early onset (50 – 60), starts in occipital lobe and causes visual problems and impaired recognition, later spreads and presents with more typical Alzheimer's symptoms[20]

If you aren't sure what sort of dementia someone has...

- Full medical, psychiatric, prescription drug, substance use, personal and family history. Detailed collateral history if available.
- Neuro exam is helpful
  - Neuro exams can also crop up in CASC so it's worth staying practiced
- Detailed neuropsychology assessment may help identify pattern of cognitive impairment.
- Consider involving neurology esp if motor features

References 1

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19. https://www.alzheimers.org.uk/about-dementia/types-dementia/progressive-supranuclear-palsy#content-start
20. https://www.alzheimers.org.uk/about-dementia/types-dementia/Posterior-cortical-atrophy#content-start

Further Reading

- Radiology Assistant > Neuroradiology > Dementia: the role of MRI (www.radiologyassistant.nl)
  - for more information about imaging/ structural changes
- Alzheimer's Society > about dementia > types of dementia
  - Good information about various types of dementia in patient-friendly language (may be useful in thinking how you would explain these conditions in a jargon-free way in clinic or OSCEs)

Any Questions?