Assessment of Cognitive Impairments and Dementia using AI/ML methods

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What is Cognitive Impairment and dementia?

Cognitive impairment is an umbrella term for various brain health issues associated with aging.
Mild cognitive impairment (MCI) causes a slight but noticeable and measurable decline in cognitive abilities, including memory and thinking skills.

Credit: Alzheimer's Association

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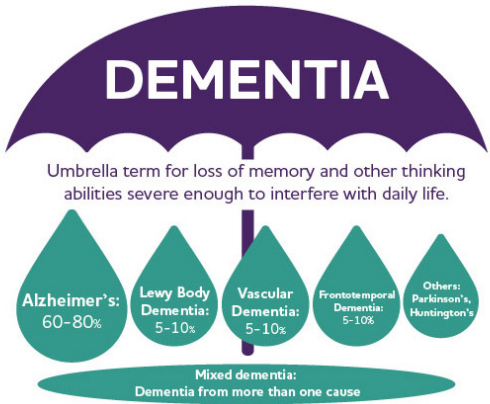Cognitive Disorders

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Types of Dementia

1. Frontotemporal Dementia (FTD)
   - Develops over time after the loss of nerve cells in the frontal and temporal lobes of the brain
   - Affects the areas of the brain linked to **personality, behavior and language**

2. Vascular Dementia
   - Used to describe brain damage resulting from a lack of blood flow to the brain
   - Interferes with thought processes such as **judgement, reasoning, planning and memory**.

3. Alzheimer's Disease (AD)
   - Most common form of dementia, progresses gradually and intensifies over time
   - confusion of time and space, **inability to understand and perform** daily life tasks and functions.

4. Lewy Bodies Dementia (LBD)
   - buildup of proteins (Lewy bodies) in nerve cells and regions of the brain associated with thinking, memory and movement.
   - Impairs **problem solving, complex reasoning and movement**

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Why is early diagnosis of dementia important?

1. Early Planning and Assistance
   - Helps the person with dementia and their family to **receive help in understanding and adjusting to diagnosis**

2. Checking concerns
   - Symptoms can be **caused by several different diseases, some of which are treatable and reversible** including infections, depression, medication side-effects or nutritional deficiencies.
   - Asking a doctor to check any symptoms and to identify the cause of symptoms can bring relief to people and their families.

3. Treatment
   - Evidence that the currently available medications for Alzheimer's disease may be **more beneficial if given early in the process**

4. Health Management
   - Help in the **management of other symptoms** which may accompany the early stage of dementia, such as depression or irritability

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How is diagnosis of dementia done currently?

1. Medical History
   - Doctor needs to establish whether the **change in function was sudden or gradual**
   - **Determining onset and progression of symptoms** can help to differentiate types of dementia

2. Medical Testing
   - Blood, Urine, Genetic Tests, Brain Scans - CT, MRI
   - Brain scans can be used to **detect brain tumors, strokes, hemorrhages, shrinkage, pressure of fluid** in brain

3. Psychological evaluation
   - Determine extent of memory or thinking problems
   - Used to **track progression over time**, identify type of dementia
   - Mini-Mental State Examination (MMSE), Brief Cognitive Rating Scale, Alzheimer's Disease Assessment Scale - Cognitive (ADAS-Cog)

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Problem Statements

The two problem statements majorly addressed in the current
literature related to Diagnosis and Assessment of Cognitive
Impairment and Dementia:

1. Disease Progression Prediction
   - Predict the conversion of MCI[1] to AD[2].

2. Identification of Clusters in Cognitive Disorder Subject Population

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[1]MCI = Mild Cognitive Impairment
[2]AD = Alzheimer's Disease

Predicting Disease Progression I

1. [PLOS Computational Biology, September, 2018]
   Modelling and prediction of clinical symptom trajectories in Alzheimer's Disease using Longitudinal Data (Bhagwat et al., 2018)
   - Multimodal and Longitudinal Data
   - Hierarchical Clustering for modelling
   - Longitudinal Siamese Network (LSN) for prediction

2. [2018] Learning the progression and clinical subtypes of Alzheimer's disease from longitudinal clinical data (Satone et al., 2018)
   - Gaussian Mixture Model (GMM) for subtyping
   - Random Forest to predict an individual's progression

3. [Alzheimer's & Dementia: Translational Research & Clinical Interventions, 2019]
   Forecasting the progression of Alzheimer's disease using neural networks and a novel preprocessing algorithm (Albright, 2019)
   - MLP, RNN for forecasting the progression

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Predicting Disease Progression II

- Novel Preprocessing Algorithm: The all-pairs technique to train the model

4. [NeuroImage: Clinical, 2019]
   Multi-study validation of data-driven disease progression models to characterize evolution of biomarkers in Alzheimer's disease (Archetti et al., 2019)

   - Train data-driven computational models for sequencing biological and clinical events along the course of Alzheimer's disease

5. [IPTA, 2020] Predicting Brain Degeneration with a Multimodal Siamese Neural Network (Ostertag et al., 2020)

   - a neural network architecture for
     - multimodal learning
     - to predict the evolution of a neurodegenerative disease

6. [Nature, 2019] Machine learning for comprehensive forecasting of Alzheimer's Disease progression (Fisher, 2019)

   - Unsupervised machine learning model called a Conditional Restricted Boltzmann Machine (CRBM) to simulate detailed patient trajectories

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Machine Learning Techniques for Diagnosis of Cognitive Disorders

1. The most widely used classification techniques for diagnosis of dementia are
   - support vector machine (SVM)
   - artificial neural network (ANN)
   - deep learning (DL) methods and ensemble methods
2. SVM based models have been widely used for Alzheimer's disease showing its robustness
3. Techniques like ANN suffers from the drawbacks of local minima, which is not the case with SVM
4. ANNs are more versatile and robust when it comes to incremental learning, modelling sequential data, and quantizing high dimensional spaces. Therefore, novel variants of ANN can be used for Alzheimer's in future.
5. The abundant usage of SVM also stems from the fact that it is easier to interpret as compared to deep neural networks which act as black box models

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Clusters in Cognitive Disorder Subjects Population I

1. [BioMedical Engineering OnLine, 2015] Homogeneous clusters of Alzheimer's disease patient population (Gamberger et al., 2016b)
   - Demonstrates that brain atrophy is the main driving force of dementia
2. [Brain Inform, 2016] Clusters of Male and Female AD patients (Gamberger et al., 2016a)
   - Existence of two male subpopulations with unexpected values of intracerebral and whole brain volumes
3. [Nature, 2017] Identification of clusters of rapid and slow decliners among subjects at risk for AD (Gamberger et al., 2017)

Clustering has been done using novel multi-layer clustering algorithms

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Clusters in Cognitive Disorder Subjects Population II

Why is cluster analysis important?

- In clinical populations, **substantial heterogeneity** exists in patient characteristics, illness severity and treatment responses.

- Better understanding of such heterogeneity may lead to more **effective and efficient treatment** by personalising care to better suit patient profiles

- Characterizing subgroups of at risk subjects, with diverse prognostic outcomes, may provide novel mechanistic insights and **facilitate clinical trials of drugs** to delay the onset of cognitive disorders

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Further work required in Diagnosis of Dementia using AI

- Identify themes of algorithmic bias and unfairness while developing mitigations to address these themes
- Reduce brittleness and improve generalisability to accommodate future datasets
- Develop methods for improved interpretability of machine learning predictions.

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- Less focus on clinical interpretability of ML models used in assessment
- Researchers have given more importance to the feature extraction phase, and not much to the classification phase
- More work is required in formulation of machine learning models which can integrate information from various modalities for early diagnosis of Cognitive Disorders.

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What am I planning to do?

- Build a **Boolean Expression Generator** for Cognitive Disorder Progression using Longitudinal and Cross-Sectional Data
- **Logical Explanation** of ML/AI based diagnosis of cognitive disorders to aid doctors in diagnosis
- Build an **Abductive Learning framework** for diagnosis of cognitive disorders and dementia
  - Abductive Learning helps bridge Machine Learning and Logical Reasoning
- Using data generated from **new computer based games** for detection of cognitive impairment

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