The contribution of informants reports of functional activity level at baseline in prediction of stable MCI versus conversion to AD.

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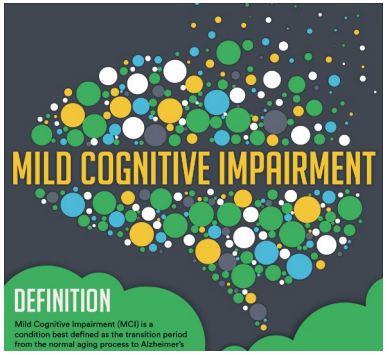
Introduction: Stable MCI versus converting AD

Cognitive aging is a process characterized by individual differences in both pace and characteristics. Whereas some adults show preserved cognitive function into old age, unfortunately, old age is also one of the highest risk factors for developing Alzheimer's disease (AD) and other neurodegenerative diseases. The intermediate stage between normal cognitive aging and dementia is referred to as mild cognitive impairment (MCI). It has been shown that about 10 -15 % of the MCI patients will progress to dementia each year. Thus, identifying and predicting already at baseline those characterized as stable MCI versus those more likely converting to AD at an earlier stage is highly warranted.



Method: The data set

In the current study we define two subgroups:

i) Stable MCI (sMCI): MCI diagnosed maintained across all visits.

ii) Converted Alzheimer's Disease (cAD): adults progressing from MCI to AD at one time point during the examination period

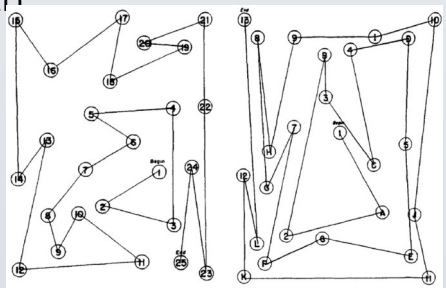
	sMCI (360) Train (285)/Test (75)	cAD (320) Train (255)/Test (65)
Demographics		
Sex (F:M)	114:171/32:43	99:156/25:40
Age at inclusion [years]: mean (SD)	73.9 (7.4)/72.7(7.3)	73.9 (7.7)/73.9 (6.9)
Age at inclusion [years]: range	55-91/57.8-87.8	55.2-88.3/55-88.4
Education [years]: mean (SD)	15.8 (2.9)/16.2(2.9)	15.8 (2.9)/16.2(2.9)
Number of Visits Cog/Func: mean (SD)	8.4 (3.7)/8.4(3.3)	9.3 (3.8)/10.2(4.2)
Number of Visits MRI: mean (SD)	5.3 (1.6)/5.4(1.4)	5.8 (1.6)/6.0(1.7)

Table 1: Subject Demographics. Subsample from the ADNI cohort.

Predicting diagnose progression from multimodal neurocognitive baseline data:

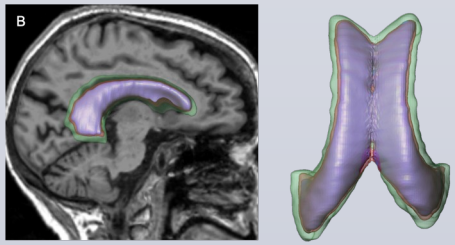
Neuropsychological Tests:

- Rey auditory verbal test (RAVLT)
- Trail making test (TMT)
- Category fluency test (CFT)



Notes: Part A (left) involves connecting 25 numbered dots in increasing order. Part B (right) involves connecting 25 dots labelled with numbers and letters, in the alternating sequence "1-A-2-B-3-C…".

- Functinal activity level: FAQ
- sMRI: global and local measures derived From FreeSurfer (long stream ver. 7.1)



Reprinted from Mofrad et al., (2021). Illustrates expansion of lateral ventricle volume (LVV) for one subject at one scan diagnosed as healthy control (HC), MCI and Alzheimer's disease (AD).

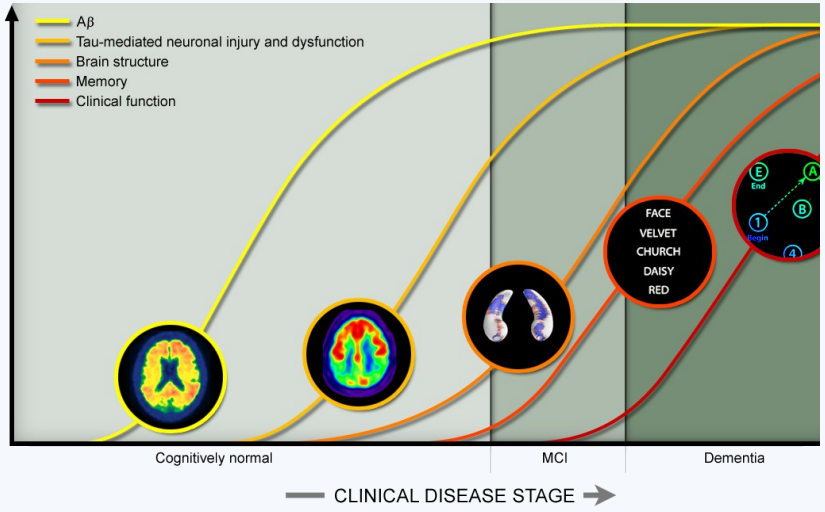
Machine Learning classification

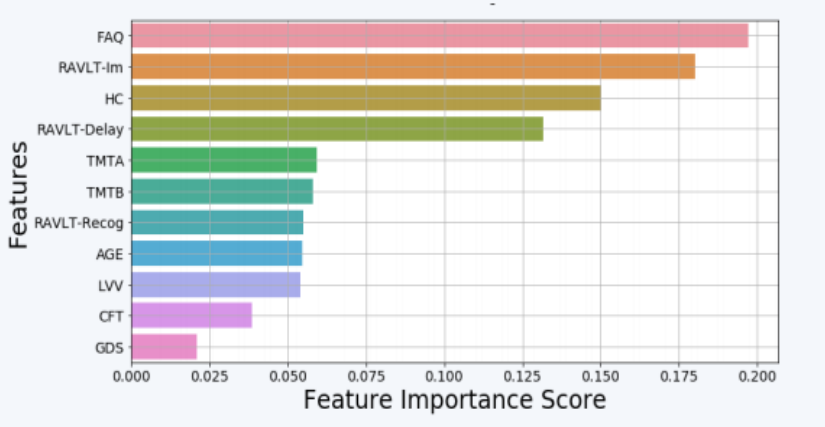
Binary classifier:
Random Forest

Stable MCI
(sMCI, N=360)
MCI to MCI

Converted AD
(cAD, N= 320)
MCI to AD

When these eleven neurocognitive measures were used as input in a Random Forest (RF) binary classifier (sMCI vs. cAD) we obtained an accuracy, recall, precision and F1 scores of 73%/ 69%/72% and 70% on the hold-out test set.





Functional Activities Questionnaire

Administration

Ask informant to rate patient's ability using the following scoring system:

- Dependent = 3
- Requires assistance = 2
- Has difficulty but does by self = 1
- Normal = 0
- Never did [the activity] but could do now = 0
- Never did and would have difficulty now = 1

Writing checks, paying bills, balancing checkbook	
Assembling tax records, business affairs, or papers	
Shopping alone for clothes, household necessities, or groceries	
Playing a game of skill, working on a hobby	
Heating water, making a cup of coffee, turning off stove after use	
Preparing a balanced meal	
Keeping track of current events	
Paying attention to, understanding, discussing TV, book, magazine	
Remembering appointments, family occasions, holidays, medications	
Traveling out of neighborhood, driving, arranging to take buses	
TOTAL SCORE:	

Evaluation

Sum scores (range 0-30). Cutpoint of 9 (dependent in 3 or more activities) is recommended to indicate impaired function and possible cognitive impairment.

Pfeffer RI et al. Measurement of functional activities in older adults in the community. J Gerontol 1982; 37(3):323-329. Reprinted with permission of The Gerontological Society of America, 1030 15th Street NW, Suite 250, Washington, DC 20005 via Copyright Clearance Center, Inc.