Developing a Bespoke Neural Network Model for Diagnosing Alzheimer's Dementia: A Fit-for-Purpose Machine Learning Study

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BACKGROUND

- Artificial intelligence models have been around since the 1950s and have continually progressed, with the recent surge in machine learning (ML) taking place in early 2000s; further propelled by advanced computer techonology.[1]
- The goal of ML is to analyze existing data to identify patterns that can be applied to make predictions of other similar data.[1] These contribute to what is known as an Artificial Neural Network (ANN).[1]
- One type of ANN is a feedforward neural network (FNN), where data is transmitted in one direction, from input to output, without feedback loops, making this type of model suitable for tasks like pattern recognition and classification.[2]
- FNNs have been explored for many health research applications previously, but none have specifically assessed varying levels of data in difficult to diagnose diseases, such as Alzheimer's Dementia (AD).

OBJECTIVES

- Develop a feedforward neural network for diagnosing Alzheimer's dementia.
- Describe the impact of various data inputs for FNN diagnostic performance by evaluating multiple FNN data input scenarios.

METHODS

- The FNNs were made using a software called Modelist.
- Data was sourced from the Alzheimer's Disease Neuroimaging Initiative (ADNI) containing longitudinal clinical and diagnosis data from 8,904 total visits across 1,833 unique patients.
- ADNI contains imaging, lab, and biomarker data with a median follow-up length of 4.5 years [2.3 – 10 years] and mean age of 75 years old [55 – 95 years].
- When joining ADNI, patients have a wide variety of information and labs collected at baseline, then regularly scheduled follow-up visits.
- The model was trained, validated, and tested using unique patient data sets at each stage [Table 2 & Figure 3].
- FNN performance was measured as the model's ability to assign the same diagnosis as the physician [Table 4 and 5].
- FNN was run at five differing levels of data inputs to identify the impact on model performance [Table 1].
- Test accuracy results are used as the indicator for overall model performance, as this is the expected performance of the model for all new data.

OUTPUT VARIABLES

Physician diagnosis within ADNI is recorded at three levels:

1. Normal Limitations (NL)
2. Mild/moderate cognitive impairment (MCI)
3. Alzheimer's Dementia (AD)

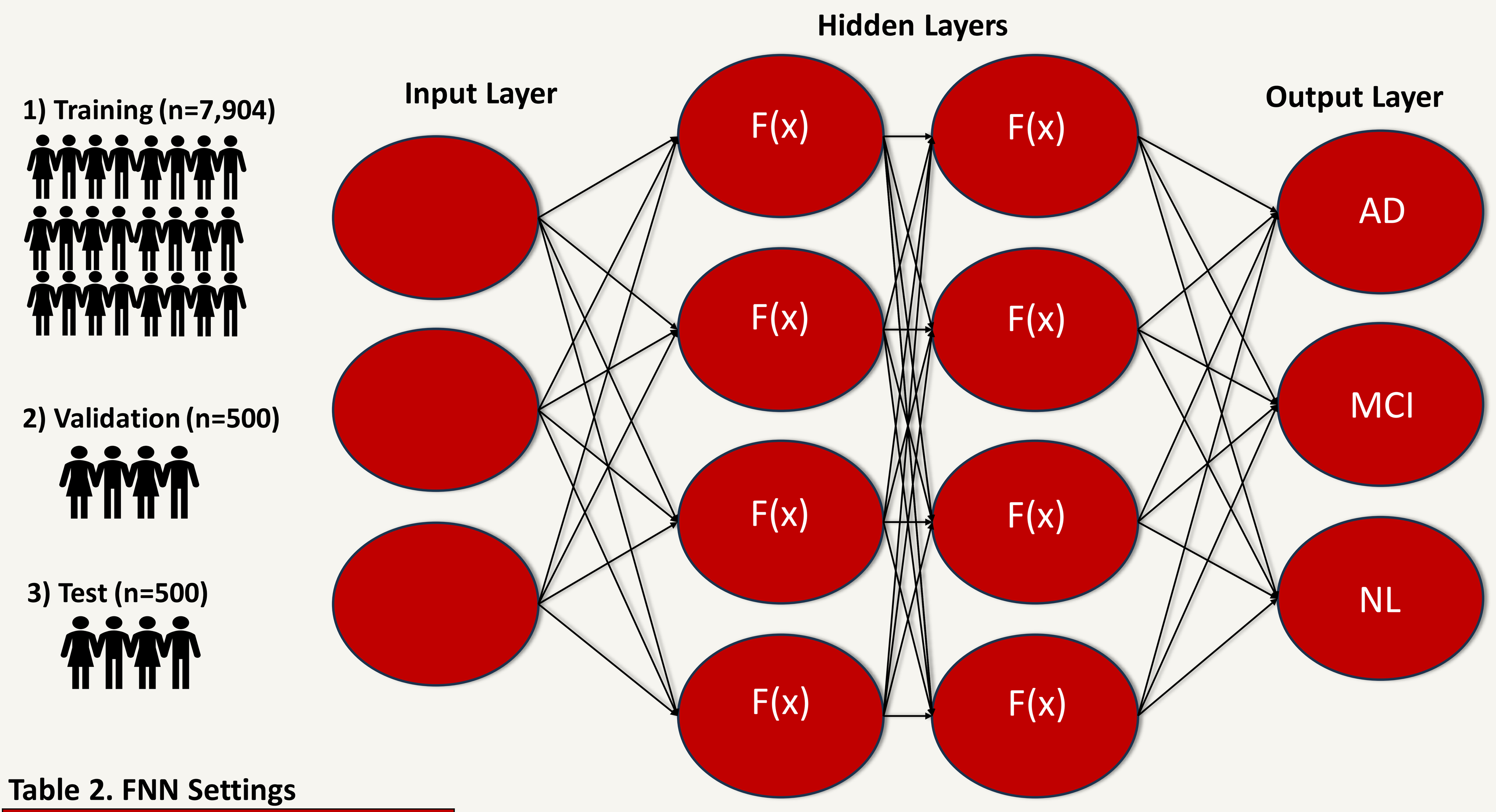

Table 2. FNN Settings

Neural Network Settings	
Number of Neurons	90
Number of Hidden Layers	3
Activation Function	Tanh
Regularization	L2 (Frobenius)
Initialization	Uniform Epsilon
Iterations	50
Optimization	Line search

Figure 3. Baseline Diagnoses of Data Sets

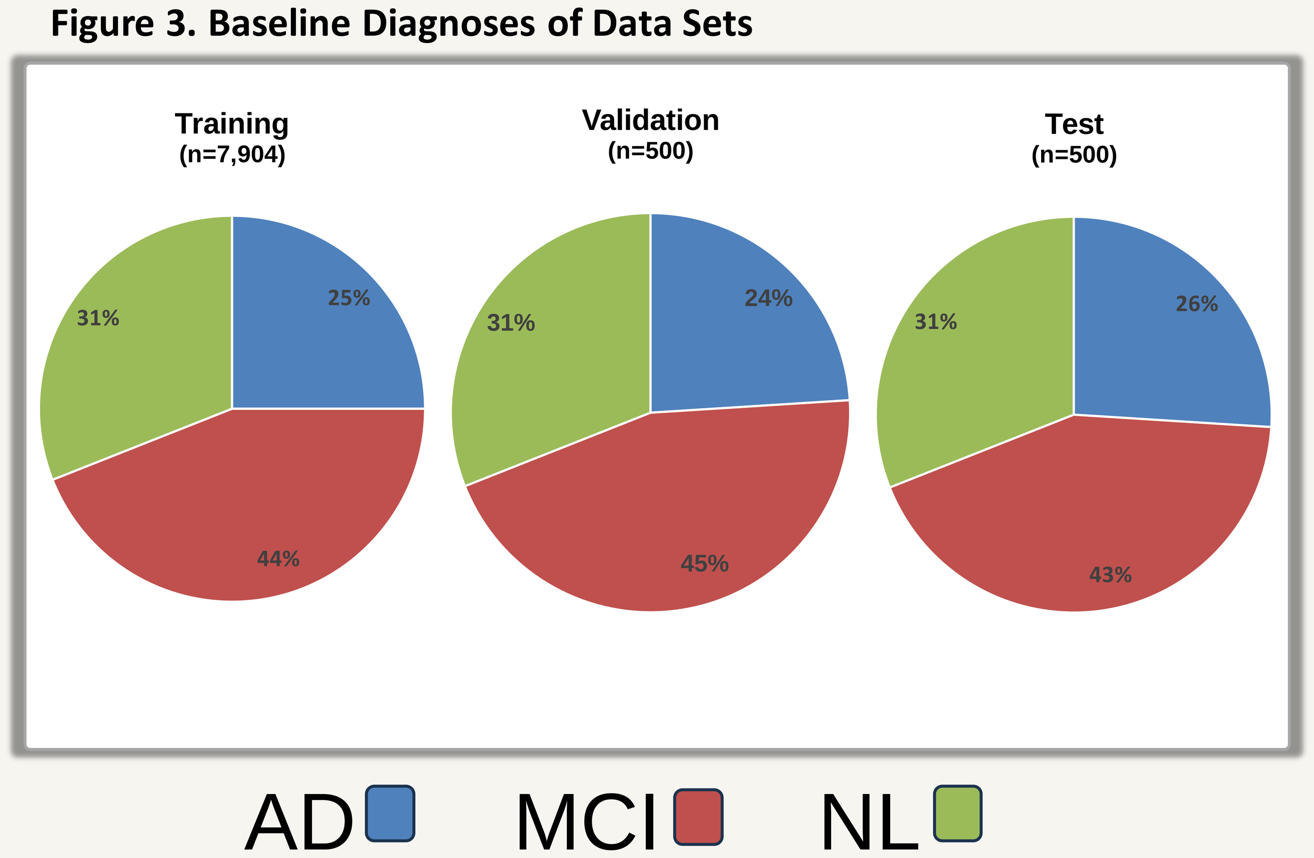

Table 4. Model Performance Results

Data Scenario	Training Accuracy (%)	Validation Accuracy (%)	Test Accuracy (%)	Log Loss	Avg. AUC	F1	MCC
1	45.7	44.0	**43.4**	1.0833	0.471	0.2870	0.0000
2	77.5	78.6	**76.4**	0.5082	0.9097	0.7647	0.6358
3	92.1	91.8	**92.0**	0.2444	0.9811	0.9202	0.8772
4	87.9	86.6	**86.2**	0.3869	0.9556	0.8619	0.7433
5	93.5	92.0	**91.8**	0.2387	0.9778	0.9181	0.8730

**Performance parameters specific to Test performance*

Table 1. Data Scenarios Tested

Data Scenario	Input Data Variables
1	**Baseline diagnosis SDOH CSF**
2	**Baseline diagnosis SDOH NCA (Baseline only)**
3	**Baseline diagnosis SDOH CSF NCA <u>x2</u> (Baseline & follow-up visit)**
4	**Baseline diagnosis SDOH CSF Imaging data <u>x2</u> (Baseline & follow-up visit)**
5	**Baseline diagnosis SDOH CSF NCA <u>x2</u> (Baseline and follow-up) Imaging data (Follow-up only)**

Table 5. Data Scenario 3 Test Performance Results (n=500)

	Presented as FNN assigned diagnosis : Physician assigned diagnosis	Patients (%)	
False Positive	**AD:MCI**	6	1.2%
False Negative	**MCI:AD**	15	3.0%
	NL:MCI	18	3.6%
	MCI:NL	1	0.2%
True Positive	**AD:AD**	113	22.6%
True Negative	**MCI:MCI**	238	47.6%
	NL:NL	109	21.8%

REFERENCES

1) Kaul, Vivek et al. "History of artificial intelligence in medicine." *Gastrointestinal endoscopy* vol. 92,4 (2020): 807-812
2) Zell, Andreas. *Simulation neuronaler netze*. Vol. 1. No. 5.3. Bonn: Addison-Wesley, 1994.

INPUT VARIABLES

Input Variables included:

1. Social determinants of health (SDOH)
   - Gender, age, education level, marriage status
2. Cerebral spinal fluid (CSF)
   - Reported as beta-tau protein levels
   - Common biomarker for AD detection
3. Neurocognitive assessment (NCA)
   - ADAS13, MMSE, RAVLT, MOCA
   - Each reported NCA was used as unique input
4. Imaging data
   - MRI, CT, or PET scans
   - Size of brain regions in mm and % of total brain volume (hippocampus, fusiform, temporal lobe, Entorhinal, ventricular system, whole brain)

- Missing data and blank cells were dummy coded to be included.
- Categorical variables (gender, marriage status, etc.) are treated as binary data.

RESULTS

- Data Scenario 3 resulted in the most accurate neural network model for identifying AD.
- The addition of imaging data provided no additional benefit to diagnostic accuracy when neurocognitive assessments were also used.

DISCUSSION AND LIMITATIONS

- The model is trained based on physician assigned diagnoses which may not always be accurate or consistent across clinicians.
- Although imaging data does not seem to provide benefit to FNN accuracy, it could introduce a pattern of early detection that is not able to be detected by clinicians.
- Further analyses could be conducted to assess the rate at which false positive AD patients receive AD diagnosis at later visits.
- Black box effect prevents interpretation of specific pattern identified.
- ML models are likely best suited for alerting clinicians of high-risk patients based on routinely collected data and assessments.

CONCLUSION

- The selection of input variables has considerable influence on the performance of a feedforward neural network model.
- This study serves as another example of a neural network's ability to identify diagnostic patterns in complex disease states, such as Alzheimer's Dementia.