ORIGINAL ARTICLE

# Drift Diffusion Model of Animacy Categorization Task Can Detect Patients with Mild Cognitive Impairment and Mild Alzheimer's Disease

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## Abstract

**Purpose:** The process of neurodegeneration in Alzheimer's Disease (AD) is irreversible using current therapeutics. An earlier diagnosis of the disease can lead to earlier interventions, which will help patients sustain their cognitive abilities for longer. Individuals within the early stages of AD, shown to have trouble making confident and sounds decisions. Here we proposed a computational approach to quantify the decision-making ability in patients with mild cognitive impairment and mild AD.

**Materials and Methods:** To study the quantified decision-making abilities at the early stages of the disease, we took advantage of a 2-Alternative Forced-Choice (2AFC) task. We applied the Drift Diffusion Model to determine whether the information accumulation process in a categorization task is altered in patients with mild cognitive impairment and mild AD. We implemented a classification model to detect cognitive impairment based on the Drift Diffusion Model's estimated parameters.

**Results:** The results show a significant correlation of the classification score with the standard pen-and-paper tests, suggesting that the quantified decision-making parameters are undergoing significant change in patients with cognitive impairment.

**Conclusion:** We confirmed that the decision-making ability deteriorates at the early stages of AD. We introduced a computational approach for measuring the decline in decision-making and used that measurement to distinguish patients from healthy individuals.

**Keywords:** Alzheimer's Disease; Mild Cognitive Impairment; Drift Diffusion Model; Machine Learning; Decision Making.


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## 1. Introduction

Alzheimer's Disease (AD) is the major cause of dementia in elderly individuals [1]. The process of neurodegeneration in AD is irreversible by the time of the diagnosis of severe symptoms [2-5]. Although the disease cannot be reversed or stopped using current therapeutics, an early diagnosis can result in some interventions to help individuals sustain their cognitive abilities for longer [6, 7].

Mild Cognitive Impairment (MCI) is a condition in which an individual has mild but measurable changes in cognitive abilities. These changes are noticeable to the person affected and to family members and friends, but the individual is still able to carry out everyday activities [8]. A systematic review of 32 cohort studies shows an average of 32% conversion from MCI to AD within a five-year follow-up [9]. Although numerous factors can cause MCI, this conversion rate suggests MCI as an initial point to AD.

Memory deficits are known to be one of the major symptoms of AD [10-12]. However, several studies have addressed other higher-order cognitive abilities such as decision-making undergoing significant changes during the disease [13-15]. MCI patients are shown to have trouble in the ability to make a sound decision or to anticipate the steps needed to complete a complex task [16]. They have difficulties in their daily activities, such as medical decision or complex reasoning [17-19].

Despite these reports, no accurate measurement of the decision-making ability has been made in cognitively impaired individuals. Here, to study the quantified measures of decision-making abilities at the early stages of the disease, we took advantage of the Integrated Cognitive Assessment (ICA) [21] as a 2-Alternative Forced-Choice (2AFC) task. ICA has previously shown to be sensitive to a decrease in speed and accuracy of categorization in patients with cognitive impairment [22, 23]. We applied the Drift Diffusion Model (DDM) [24] in line with the ICA task to determine whether the information accumulation process in a categorization task is altered in patients with MCI and mild AD.

We took advantage of recent machine learning techniques to determine whether the quantified decision-making parameters are affected in patients with cognitive impairment. We observed that the DDM parameters which are related to the accumulation speed of information while doing a 2AFC task can detect patients with cognitive impairment significantly above chance (accuracy=0.73, P-value=0.0001). This result suggests that decision-making is among the first high-level cognitive abilities affected in early stages of Alzheimer's Disease.

participants with MCI and mild AD were diagnosed by a neurologist (ZV) following the international diagnostic criteria described by the working group of the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) and the Alzheimer's Disease and Related Disorders Association (ADRDA) (referred to as the NINCDS-ADRDA criteria; [25]) in addition to the National Institute on Aging and Alzheimer's Association (NIA-AA) diagnostic guidelines [26]. All subjects are in the age range of 55 to 85 years old. Each individual was asked to do two cognitive paper tests: Montreal Cognitive Assessment (MoCA) [27] and Addenbrooke's Cognitive Examination (ACE-R) [28] alongside the Integrated Cognitive Assessment (ICA) task (Figure 1).

## 2. Materials and Methods

### 2.1. Subject Recruitment and Data Acquisition

We recruited 33 participants diagnosed with MCI or mild AD and 34 Healthy Controls (HC) (Table 1). All Additionally, caregivers report low confidence in making daily decisions in individuals with early-stage to moderate AD/dementia [20].

**Table 1.** Demographic information of participants. The P-values are computed by applying a two-tailed two-sampled t-test with unequal variance

| Characteristic | HC(n=33) | MCI(n=34) | P-value |
|---|---|---|---|
| **Age-mean year$\pm SD$** | $63.44 \pm 6.18$ | $66.96 \pm 6.4$ | 0.1 |
| **Education in years-mean$\pm SD$** | $14.32 \pm 4.63$ | $13.22 \pm 5.27$ | 0.35 |
| **Gender(%Female)** | 15(45%) | 19(55%) | 0.77 |

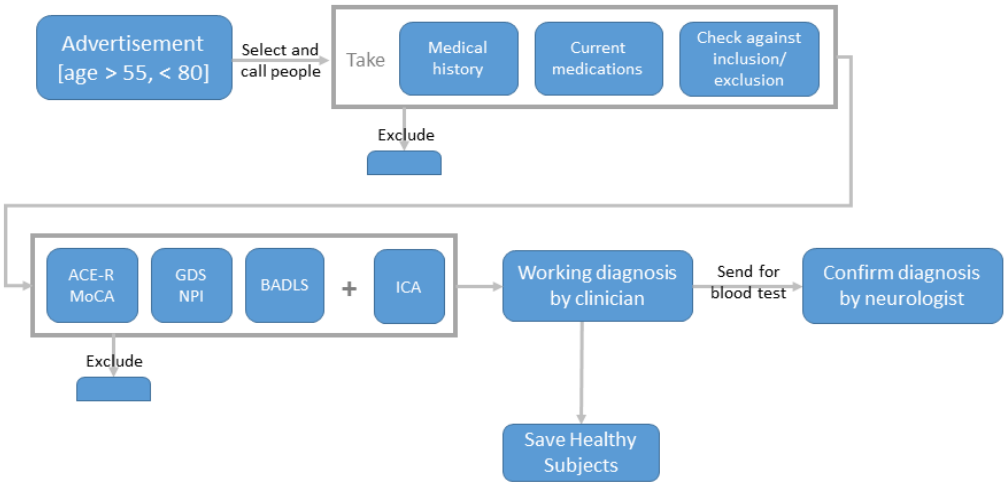


**Figure 1.** Subject recruitment procedure. We recruited individuals between 55 and 80 years old. After a visit with the General Practitioner (GP) we excluded those who did not match the criteria. Also, individuals with GDS score more than 20 are considered as severely depressed and are excluded from the study. The subjects completed two cognitive paper tests: MoCA and ACE. The patients' companions also completed two paper tests (i.e., Bristol Activities of Daily Living Scale (BADLS) and Neuropsychiatric Inventory (NPI)) to assess the patients' ability to carry out daily activity and to assess dementia-related behavioral symptoms. All the subjects performed the ICA test alongside with other cognitive tests. After a working diagnosis by the clinician the subjects are sent for blood test to ensure that the observed cognitive impairment is not because of a vitamin B deficiency or Hyperthyroidism/ Hypothyroidism

### 2.1.1. Inclusion Criteria for the Control Group

Males and females aged between 55-85 years with ACE-R score above 84 who are not currently on medication that may interfere with the study results and are in good general health.

### 2.1.2. Main Exclusion Criteria for the Control Group

• Presence of significant cerebrovascular disease (i.e., history of Cerebrovascular Accident (CVA))

• Major medical comorbidities (e.g., congestive cardiac failure, diabetes mellitus with renal impairment)

• Major psychiatric disorder (e.g., psychosis, depressive), generalized anxiety disorder.

• The use of cognitive enhancing drugs (e.g., cholinesterase inhibitors)

• A concurrent diagnosis of epilepsy

Subjects completed one run of the ICA task, and the reaction time and accuracy of categorization are recorded for the analysis phase.

According to the selection criteria, all the participants are asked to take the Geriatric Depression Scale (GDS) test [29].

• A history of alcohol misuse

• A history of illicit drug use

• A history of severe visual impairment (e.g., macular degeneration, diabetic retinopathy, as determined by the clinical team)

• A history of repeated head trauma

### 2.1.3. Inclusion Criteria for MCI Group

Males and Females aged between 55-85 years with a clinical diagnosis of MCI according to validated criteria who are willing and able to provide informed consent.

### 2.1.4. Exclusion Criteria for MCI Group

• Presence of significant cerebrovascular disease (i.e., history of CVA)

• Major medical comorbidities (e.g., congestive cardiac failure, diabetes mellitus with renal impairment)

• Major psychiatric disorder (e.g., psychosis, depressive disorder, generalized anxiety disorder)

• Any use of cognitive-enhancing drugs (e.g., cholinesterase inhibitors)

• Concurrent diagnosis of epilepsy

• History of alcoholic dependency

### 2.1.5. Inclusion Criteria for the Mild AD Group

• A clinical diagnosis of mild AD according to Implantable Cardioverter Defibrillator (ICD)-10 criteria, diagnosed by an Old Age Psychiatrist.

• Mini Mental State Examination (MMSE) <24 and >19.

• Males and females aged 55-85 years.

• Capable of indicating informed consent for participation.

### 2.1.6. Exclusion Criteria for the Mild AD Group

• Patients who fulfill the criteria for a diagnosis of moderate AD or other mild dementias

• Major medical comorbidities (e.g., congestive cardiac failure, diabetes mellitus with renal impairment)

• Major psychiatric disorder (e.g., chronic psychosis, recurrent depressive disorder, generalized anxiety disorder)

• A concurrent diagnosis of epilepsy

• A history of alcohol misuse

• A history of illicit drug use

• A history of severe visual impairment (e.g., macular degeneration, diabetic retinopathy, as determined by the clinical team)

• A history of repeated head trauma

• MMSE scores less than 24

• Presence of sleep apnea

## 2.2. ICA Task

ICA [21] is a rapid visual categorization task. One hundred natural images (50 animals and 50 non-animals) with different levels of difficulty were presented to the subjects, each of them for a duration of 100ms. Participants were asked to detect whether the image contained an animal as quickly and accurately as possible. The Reaction Time (RT) and the accuracy of the responses were recorded for initiating the Drift Diffusion Model.

## 2.3. Drift Diffusion Model (DDM)

The DDM is a mathematical model that accounts for the information accumulation procedure, underlying a 2-Alternative Forced-Choice (2AFC) task [24, 30]. The model estimates several parameters: Average slope of the information accumulation process as drift rate (v), Average duration of all non-decisional processes (encoding and response execution) as Response Time Constant ($t_0$), Amount of information that is considered for a decision as Threshold Separation (a), etc. It is hypothesized in the DDM that an individual decides when the brain's integrated information reaches a certain threshold. The mentioned parameters are estimated using both the reaction time and accuracy. The parameters of the DDM was estimated using fast-dm [31].

## 2.4. Paper Test

Paper tests (e.g., MoCA and ACE) are conventional tools for diagnosing clinical symptoms of patients with cognitive impairment. We considered the scores of ACE and MoCA as a reliable measurement of cognitive impairment.

## 2.5. Discrimination Model

We have normalized all the features by removing the mean and scaling to unit variance.

We trained a logistic regression model to classify HC vs. Impaired subjects. The hyperparameters of the model have been optimized using a leave-one-out grid search algorithm. The preprocessing and the implementation of the model were developed using Scikit-learn [32].

The logistic regression model estimates the weight of features to fit a logistic sigmoid function for a two-class classification of samples. A sigmoid function is defined by Equation 1:

$$\sigma(x) = \frac{1}{1+e^{-x}} \quad (1)$$

The probability of a sample with a feature vector ∅ being classified as the first class is (Equation 2):

$$p\,(C1/\emptyset) = \sigma\,(WT.\emptyset) \quad (2)$$

And the second class is (Equation 3):

$$p\,(C2/\emptyset) = 1\text{-}\sigma\,(WT.\emptyset) \quad (3)$$

## 2.6. Statistical Significance

### 2.6.1. Permutation Test

The permutation test consists of randomly relabeling the samples from two populations to form a

null distribution and computing a P-value by testing a target statistic against the null hypothesis. Here the formulation of our permutation test is (Equation 4):

$$pvalue = \frac{number\ of\ classification\ accuracies\ greater\ than\ the\ main\ accuracy+1}{number\ of\ permutations\ (10000)+1} \quad (4)$$

### 2.6.2. Correlation Significance

We calculated the probability density function (pdf) of the sample correlation coefficient r as follows, Where n is the number of samples, and β is the beta function [33] (Equation 5):

$$pdf(r) = \frac{(1-r^2)^{\frac{n}{2}-2}}{\beta(\frac{1}{2},\frac{n}{2}-1)} \quad (5)$$

The Cumulative Distribution Function (CDF) of the above pdf is a distribution on the interval of [-1, 1] (Equation 6):

$$cdf(r) = \int_{-1}^{r} pdf(t) \times dt \quad (6)$$

Given r' as the correlation of two random samples x' and y' drawn from two populations with zeros correlation, the correlation P-value of the target distributions x and y is the probability of | r' | being greater than or equal to | r | (i.e., the absolute value of r) [34] (Equation 7):

$$p - value = 2 \times cdf(-|r|) \quad (7)$$

## 3. Results

To study early-stage AD's effect on decision-making ability, we asked whether we could discriminate healthy individuals from patients with cognitive impairment using a quantified measurement of decision-making ability. We have implemented a leave-one-out cross validation logistic regression using the DDM parameters estimated by fast-dm (threshold separation, drift rate, response time constant, and the inter-trial-variability of non-decision components).

We found that a simple classification model (i.e., logistic regression) can effectively detect patients with cognitive impairment using DDM (Table 2).

Furthermore, we measured the logistic regression classification score's effectiveness by comparing the model with the paper tests. Determining the stage of the AD in a patient is a complicated task and can only be accurately measured by invasive imaging techniques (e.g., PET scan). To overcome this complication, we hypothesized the standard paper tests as the ground truth and assumed their scores to be a demonstration of the disease stage in a patient.

We computed the correlation of classification scores with the paper test scores (Table 3). We found out that each group's classification score has a significant negative correlation with MoCA and ACE scores (as

**Table 2.** Measurement of accuracy and confidence of the discrimination model. We applied permutation test by randomly permuting the labels of subjects for 10000 time and then training a new classification model to classify subjects with label 'Impaired'. The P-value is computed according to the mentioned formulation

| Model | Feature Set | Sensitivity | Specificity | Accuracy (%) | p-value |
|---|---|---|---|---|---|
| Logistic Regression | DDM Parameters | 0.75 | 0.7 | 73 | 0.0001 |

**Table 3.** Pearson correlation coefficients of classification model with the paper tests scores. The P-values are computed using a two-tailed t-test for two independent samples with equal variances

| Group | Paper Test | Correlation with Logistic Regression Score | P-value |
|---|---|---|---|
| HC | MoCA | -0.42 | 0.001 ** |
| | ACE | -0.55 | 0.0000147 *** |
| MCI | MoCA | -0.62 | 0.02 * |
| | ACE | -0.67 | 0.0000466 *** |

* P-value < 0.05, ** P-value < 0.01, *** P-value < 0.001

the test scores get higher, the classification score should get lower; therefore, the correlation is negative). Although the amounts of correlations are not very high, the statistical measures for effective correlation (i.e., P-values) confirms the existence of a significant correlation, implying that the classification probability has a meaningful and significant relationship with the standard paper tests. The classification score is the probability of an individual to be patient (i.e., the probability of being classified as the second class by the logistic regressions model). Table 3 illustrates these negative correlations. The P-values of the estimated coefficients are all significant, showing that these coefficients are significantly non-zero.

## 4. Discussion

The purpose of this study is not only to show a good detection of MCI and mild AD patients but to shed light on the high-level cognitive abilities that are changing at the early stages of the disease. We showed that decision-making ability is one of these high-level abilities.

### 4.1. Early-Stage Diagnosis and Effective Treatments

Detecting the cognitive functions that are affected earlier in the disease's progression is the key solution to reducing the prevalence of the disease. Such detection is critical to the interventions that help slowing the progression of the disease. Early-stage diagnosis can lead to early interventions, which have shown to be effective in improving cognitive abilities [6, 7].

### 4.2. Confidence in Making a Decision in Patients with MCI and Mild AD

Previous studies have reported a decline in the confidence and robustness of making a decision in patients with dementia and cognitive impairment [17-20].

Here, by quantifying this ability using the parameters of DDM, we found that the brain of patients with cognitive impairment needs more information to reach a decision. Additionally, we found that this information accumulates slower in the brain of patients with MCI and mild AD.

### 4.3. Future Studies

Staging studies have shown that particular brain areas (e.g., temporal lobe) are affected earliest in the process of AD [35]. Detecting subtle changes in the early stages of AD is possible when we stimulate these brain areas. Therefore, we need to engage the human cognitive abilities that are associated with such brain areas. Future studies should focus on designing tasks that engage the early affected brain areas. Additionally, as the abnormalities in memory function are known to be the major symptoms of the disease, future studies should also investigate whether the deficits in the decision-making ability are prior to the memory function problems or not.

## 5. Conclusion

In addition to previous behavioral measures, including performance and speed of information processing, addressed by ICA, we found that cognitive impairment is likely to affect decision-making in an animacy categorization task. We observed that a simple classification model could use DDM parameters as a quantified measurement of decision-making ability to detect patients with cognitive impairment. We also showed that the classification scores significantly correlate with the conventional paper tests (i.e., MoCA and ACE) that are among the major assessments of mental well-being.

We showed that a self-administrated animacy task could detect the subtle changes in the decision-making ability. As all the standard pen-and-paper tests need an examiner to administrate and are all language and education dependent, this task can be used as an alternative to assess an individuals' cognitive health.

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