**Background**

This report summarizes a longitudinal cohort study following healthy, community dwelling, and cognitively intact elders. Participants were enrolled and followed up with annually for cognitive assessment to examine memory changes. There were 187 participants that completed at least three animal category for fluency tests and were included in the analysis. Investigators collected additional information such as, gender, age, Hollingshead scale for SES, and Clinical Dementia Rating scale to determine MCI diagnosis. Short-term this study aimed to define noticeable rates of decline using memory tests and compare to the normal aging process. Long-term the goals are to develop biomarkers for the rate of memory decline.

The primary hypotheses for this report were that rate of memory decline will be different for participants with a MCI diagnosis compared to aging controls. And the rate of decline accelerates four years prior to MCI diagnosis. The statistical hypotheses are as follows: 1) The animal category fluency scores will decline significantly different for participants diagnosed with an MCI compared to those with the normal aging process. 2) Four years prior to the MCI diagnosis the rate of decline splines and significantly changes for those with MCI.

**Methods**

There was minimal data management for this report. Univariate descriptive statistics were used to examine variables for outliers, extreme values, and missing-ness. Visit number and animal total were counted to determine average visits. Participants that had less than three animal scores were removed from the analysis. Bivariate descriptive statistics were performed to determine demographic differences between MCI groups at first visit and five years using chi-squared (gender) and independent t-tests (age, SES, average years in study). Spaghetti plots were created to examine the rate of animal test decline per participant as they age by MCI group.

The primary explanatory variables in the analysis were MCI status (demind) and age. Participants’ ages were subtracted by 67 (the minimum age in the study) to assist with intercept and interaction interpretability. A change point was created to assess if the rate of memory decline accelerated four years prior to diagnosis for the MCI group. The equation to create a change variable was *max(0, age- (age onset – 4)).* The *max* will select when the age is greater than zero, and allow for the rates to spline when participants’ ages are at four years before their diagnosis. Until participants reach a time point greater than zero the rate of memory scores do not change. Covariates were decided apriori based on investigator clinical knowledge and prior use. The final model included gender, SES status, and an interaction term for age and case status. The age and case status interaction variable was created by running a separate data step to create *demind\_age = age\*demind.*

Mixed linear regression analysis was used to differentiate the rates of memory decline by MCI status. “Proc Mixed” was used to account for the multiple observations for each participant. This mixed model was designed with a *random* *statement* to allow for the variation among subjects while not using up degrees of freedom. Examination of spaghetti plots for the animals’ outcome suggested that there were unique intercepts and slopes for each participant. By adding random intercept or slope is to do something on population but acknowledge that each subject has their own line or slope, therefore by using random effects we accounted for variation of subjects but not using up degrees of freedom by not adding each individual to the model. Restricted maximum likelihood estimates (REML) were used to account for estimated fixed effects. Three models were tested to determine if random intercept, random slope, or both and likelihood ratio tests were performed to determine which random effects components were the best fit. Although REML was used for log likelihood estimates, all three models were nested, had the same fixed effects, and the same data was used allowing for a valid likelihood ratio test. An alpha of <0.05 was considered significant. SAS University Edition Software was used for this analysis.

**Results**

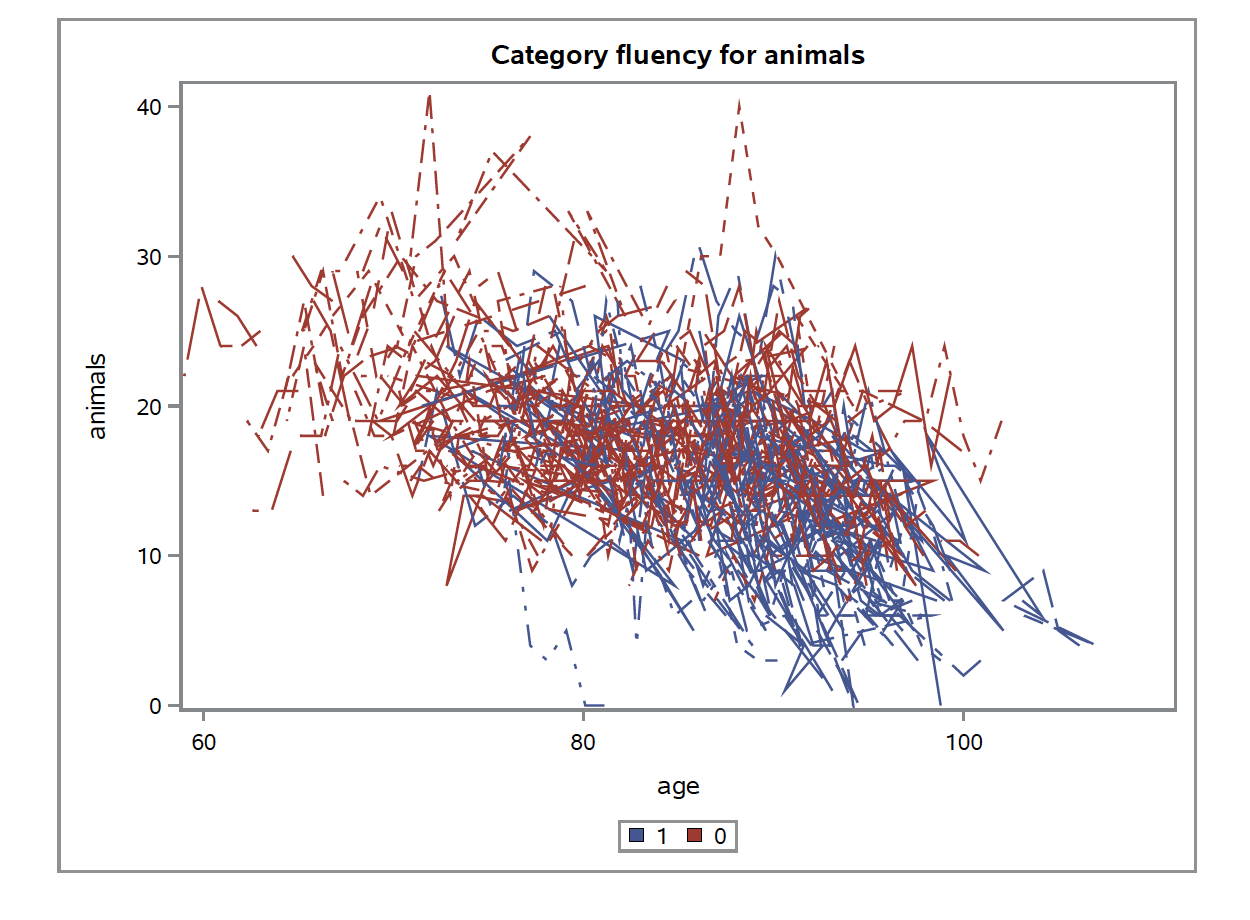
Table 1 has demographic differences between MCI group at first visit and five years into the study. There were 68 participants categorized as having an MCI by two consecutive CDRs greater than 0.05 that completed at least three animal fluency tests. Those who developed a MCI diagnosis entered the study at an average older age (94 [6.21]) compared to those who did not (84[9.62]). There were more females (68%) than males in the MCI group compared to the controls (50%). There were no demographic changes by year five. Graph 1 shows the spaghetti plot of each individual’s animal memory score as they age. The graph identifies a downward trend with age, but the MCI group (1-blue) has average lower scores compared to no MCI (0-red).

**Appendix**

**Table 1:** MCI group Demographics at first visit and five years

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **No MCI n=119** | | **MCI/Dementia n=68** | |  |
|  | **First visit** | | | |  |
| Variable | Mean | Std Dev/% | Mean | Std Dev/% | Pr > |t| |
| Age | 84.84 | 9.62 | 93.56 | 6.21 | <.0001 |
| SES | 49.66 | 10.86 | 48.74 | 13.07 |  |
| Gender- Male | 59.00 | 49.58% | 23.00 | 33.82% | 0.0367 |
| Age MCI Onset | N/A | N/A | 90.54 | 4.87 |  |
| Average Visits | 10.74 | 7.18 | 10.96 | 6.76 | 0.4071 |
|  | n=56 | | n=20 | |  |
| Animal Score | 15.89 | 5.47 | 8.55 | 5 |  |
|  | **Five years** | | | |  |
| Age | 78.61 | 8.84 | 86.45 | 5.9 | <.0001 |
| SES | 49.65 | 10.86 | 48.73 | 13.06 | 0.6057 |
| Gender- Male | 59 | 49.58% | 23 | 33.82% | 0.0367 |

**Graph 1:** Spaghetti Plot of Animal Memory Scores with Age and MCI status

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