Exploring Neuro-structural Dynamics: Age-Related Changes and Alzheimer's Disease Patterns

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Abstract -

This research is to study the age-related changes and learn whether there is a possible correlation between Alzheimer's Disease (AD) and brain structure using T1-weighted MRI scans from the Open Access Series of Imaging Studies (OASIS) dataset. The study contains a wide range of datasets that comprise numerous elements required to determine whether or not an individual has Alzheimer's disease and also includes young, middle-aged, and older adults, in addition to those with extremely mild to moderate Alzheimer's disease diagnoses and non-demented counterparts. The main goal is to achieve insights about the relation between aging, Alzheimer's disease and structural variations in the human brain.

Introduction -

The human brain changes in complex ways during the course of a lifetime, and the effects of aging and neurodegenerative diseases like Alzheimer's disease can be seen in the anatomical features of the brain. With its high-resolution representation of brain architecture, T1-weighted MRI scans are a great tool for deciphering the intricate details of these changes. This study initiates a thorough investigation with the goal of clarifying age-related changes in brain architecture and identifying unique patterns linked to Alzheimer's disease.

Age-related Changes in Brain Structure:
The brain experiences a dynamic process of development, maturation, and, eventually, age-related alterations as people go from childhood to old age. Our main hypothesis asks if young, middle-aged, and elderly persons differ significantly in their brain structure. Using T1-weighted MRI images, we examine neuroanatomical differences in an effort to understand the complex relationship between aging and the structural integrity of the human brain.

Association between Alzheimer's Disease and Brain Structure:
The second hypothesis centers on the multifaceted relationship between brain anatomy and the development of Alzheimer's disease. We also include those with very mild to moderate dementia and their non-demented contemporaries in our emphasis. By carefully examining T1-weighted MRI scans, we aim to identify unique brain anatomical patterns that represent the transition from normalcy to the early stages of Alzheimer's disease. This investigation may have implications for early diagnostic markers in addition to furthering our knowledge of the disease's structural characteristics.
In order to identify minute patterns and statistically significant differences, our study uses advanced statistical techniques such as analysis of variance (ANOVA), multivariate analysis of variance (MANOVA), and post-hoc analyses.

This research project is well-positioned to further our understanding of the complex relationships between age, brain structure, and dementia in light of the aging population all over the globe and the increasing incidence of neurodegenerative diseases. We are driven to learn as much as we can about the illness and its early indicators by the possibility of revealing the underlying complexities.

Data - (*https://www.kaggle.com/datasets/jboysen/mri-and-alzheimers*)

The Open Access Series of Imaging Studies (OASIS) is a project aimed at making MRI data sets of the brain freely available to the scientific community. By compiling and freely distributing MRI data sets, we hope to facilitate future discoveries in basic and clinical neuroscience. OASIS is made available by the Washington University Alzheimer's Disease Research Center, Dr. Randy Buckner at the Howard Hughes Medical Institute (HHMI) (at Harvard University, the Neuroinformatics Research Group (NRG) at Washington University School of Medicine, and the Biomedical Informatics Research Network (BIRN).

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PROCESS & METHODOLOGY -

A thorough assessment is necessary to diagnose Alzheimer's disease, and this assessment usually consists of clinical evaluations, cognitive testing, and neuro-imaging. The Mini Mental State Examination (MMSE), the Clinical Dementia Rating (CDR), the Estimated Total Intracranial Volume (eTIV), and the Normalized Whole Brain Volume (nWBV) are among the variables listed that can help determine if someone has dementia or not.

1. Mini Mental State Examination (MMSE) -
   A cognitive screening tool that evaluates aspects such as memory, attention and language.
   Lower MMSE Score - Indicates cognitive impairment.
2. Clinical Dementia Rating (CDR) -
   Measures how severe dementia is.
   More advanced stages of dementia, are frequently correlated with higher CDR scores.
3. Estimated Total Intracranial Volume (eTIV) -
   Determines the entire volume inside the skull, inclusive of brain.
   Variations in brain volume could reveal information about neurodegenerative diseases, particularly when compared to expected values for the individual's age and demographic.
4. Normalized Whole Brain Volume (nWBV):
   Determines whole brain volume. It is a measurement that is adjusted for variables such as head size.
   Reductions in nWBV may be associated with brain atrophy, which is often observed in AD.
5. Atlas Scaling Factor (ASF)
   A scaling factor that is used to align brain structures with a standard atlas while processing terms of neuro-imaging data. The ASF aids in ensuring that individual brains are precisely aligned and equivalent in space, while the atlas acts as a reference template for brain regions.

To identify trends and significant differences, statistical techniques such as ANOVA, post-hoc tests and multivariate analysis of variance (MANOVA) will be used. Using T1-weighted MRI scans improves the accuracy of our structural evaluations.

Research - Statistics

Hypothesis Test - 1

Null Hypothesis: No significant relation between Alzheimer's Disease and Brain Structure when comparing the dataset's non-demented participants to those with extremely mild to moderate Alzheimer's disease.

Alternative Hypothesis: Significant relation between Alzheimer's Disease and Brain Structure when comparing the dataset's non-demented participants to those with extremely mild to moderate Alzheimer's disease.

```
> summary(cs)
      ID                M.F                Hand                Age              Educ            SES             MMSE            CDR              eTIV      
 Length:436         Length:436         Length:436         Min.   :18.00   Min.   :1.000   Min.   :1.000   Min.   :14.00   Min.   :0.0000   Min.   :1123  
 Class :character   Class :character   Class :character   1st Qu.:23.00   1st Qu.:2.000   1st Qu.:2.000   1st Qu.:26.00   1st Qu.:0.0000   1st Qu.:1368  
 Mode  :character   Mode  :character   Mode  :character   Median :54.00   Median :3.000   Median :2.000   Median :29.00   Median :0.0000   Median :1476  
                                                          Mean   :51.36   Mean   :3.179   Mean   :2.491   Mean   :27.06   Mean   :0.2851   Mean   :1482  
                                                          3rd Qu.:74.00   3rd Qu.:4.000   3rd Qu.:3.000   3rd Qu.:30.00   3rd Qu.:0.5000   3rd Qu.:1579  
                                                          Max.   :96.00   Max.   :5.000   Max.   :5.000   Max.   :30.00   Max.   :2.0000   Max.   :1992  
                                                                          NA's   :201     NA's   :220     NA's   :201     NA's   :201                    
      nWBV             ASF            Delay          
 Min.   :0.6440   Min.   :0.881   Length:436        
 1st Qu.:0.7428   1st Qu.:1.112   Class :character  
 Median :0.8090   Median :1.190   Mode  :character  
 Mean   :0.7917   Mean   :1.199                     
 3rd Qu.:0.8420   3rd Qu.:1.284                     
 Max.   :0.8930   Max.   :1.563                     
```

Analysis on the 'oasis_cross-sectional' dataset , concentrating on the brain structure variables ('eTIV, 'nWBV,' and 'ASF') in relation to various age groups. This is a synopsis of the procedure:

1. Data Loading and Exploration:
   The dataset has been loaded and divided people's ages into three categories: younger, middle-aged, and older, and created a new variable called "AgeGroup."
2. Calculating the Composite Score:
   ASF, nWBV, and eTIV are the brain structural variables that have been standardized (or "Z-scored"). Employing a custom normalization procedure, the standardized variables were normalized to a range of 0 to 1. The 'CompositeScore' was obtained by averaging the normalized variables for each participant.
3. Normality Test: -
   The "CompositeScore" was subjected to a Shapiro-Wilk normality test, which revealed that it wasn't distributed normally.
4. Group Comparison:
   Since the "CompositeScore" was not normally distributed, the Kruskal-Wallis non-parametric test was chosen. The Kruskal-Wallis test was used to see whether the "CompositeScore" among the age categories varied significantly.
5. Post-Hoc Tests: To find particular group differences, pairwise comparisons between age groups were conducted using the Dunn's test with Bonferroni correction.

The test results shed light on potential age-related changes in brain structure by assisting in determining whether there are notable differences in the composite brain structure scores among various age groups. Since the composite scores have a non-normal distribution, using non-parametric tests makes sense.

```
        Shapiro-Wilk normality test

data:  cross_sectional$CompositeScore
W = 0.95153, p-value = 9.18e-11
```

The Shapiro - Wilk normality test is used to test normality.
Strong evidence to reject the null hypothesis is suggested by the incredibly low p-value, which is almost zero. This suggests that there isn't a normal distribution for the 'CompositeScore' variable.

```
        Kruskal-Wallis rank sum test

data:  CompositeScore by AgeGroup
Kruskal-Wallis chi-squared = 320.58, df = 2, p-value < 2.2e-16
```

The Chi Square test statistic derived from your data is represented by this value. It shows how much the groups differ from one another. Greater values indicate more substantial variations.
The statistical significance of the p-value (< 2.2e-16) suggests a strong rejection of the null hypothesis. This indicates that there are significant differences between the groups, expressing it clearly.

```
Dunn (1964) Kruskal-Wallis multiple comparison
  p-values adjusted with the Bonferroni method.

          Comparison          Z      P.unadj        P.adj
1 Middle-Aged - Older   9.099211 9.099029e-20 2.729709e-19
2 Middle-Aged - Young  -4.848078 1.246633e-06 3.739899e-06
3       Older - Young -17.661973 8.231160e-70 2.469348e-69
```

After using the Bonferroni method to account for multiple comparisons, the results indicate that there are significant differences in "CompositeScore" between all pairs of age groups .

Conclusion (Hypothesis Test - 1)
Reject the Null Hypothesis.
We observe Significant relation between Alzheimer’s Disease and Brain Structure when comparing the dataset's non-demented participants to those with extremely mild to moderate Alzheimer's disease.

Research - Statistics

Hypothesis Test - 2

Null Hypothesis: No significant relation between Alzheimer's Disease and Brain Structure when comparing the dataset's non-demented participants to those with extremely mild to moderate Alzheimer's disease.

Alternative Hypothesis: Significant relation between Alzheimer's Disease and Brain Structure when comparing the dataset's non-demented participants to those with extremely mild to moderate Alzheimer's disease.

```
> summary(longitudinal_data)
  Subject.ID           MRI.ID             Group               Visit          MR.Delay          M.F                Hand
 Length:373         Length:373         Length:373         Min.   :1.000   Min.   :   0.0   Length:373         Length:373
 Class :character   Class :character   Class :character   1st Qu.:1.000   1st Qu.:   0.0   Class :character   Class :character
 Mode  :character   Mode  :character   Mode  :character   Median :2.000   Median : 552.0   Mode  :character   Mode  :character
                                                          Mean   :1.882   Mean   : 595.1
                                                          3rd Qu.:2.000   3rd Qu.: 873.0
                                                          Max.   :5.000   Max.   :2639.0

      Age             EDUC            SES             MMSE            CDR              eTIV            nWBV             ASF
 Min.   :60.00   Min.   : 6.0   Min.   :1.00   Min.   : 4.00   Min.   :0.0000   Min.   :1106   Min.   :0.6440   Min.   :0.876
 1st Qu.:71.00   1st Qu.:12.0   1st Qu.:2.00   1st Qu.:27.00   1st Qu.:0.0000   1st Qu.:1357   1st Qu.:0.7000   1st Qu.:1.099
 Median :77.00   Median :15.0   Median :2.00   Median :29.00   Median :0.0000   Median :1470   Median :0.7290   Median :1.194
 Mean   :77.01   Mean   :14.6   Mean   :2.46   Mean   :27.34   Mean   :0.2909   Mean   :1488   Mean   :0.7296   Mean   :1.195
 3rd Qu.:82.00   3rd Qu.:16.0   3rd Qu.:3.00   3rd Qu.:30.00   3rd Qu.:0.5000   3rd Qu.:1597   3rd Qu.:0.7560   3rd Qu.:1.293
 Max.   :98.00   Max.   :23.0   Max.   :5.00   Max.   :30.00   Max.   :2.0000   Max.   :2004   Max.   :0.8370   Max.   :1.587
                                NA's   :19     NA's   :2
```

Analysis on the 'oasis_longitudinal' dataset , concentrating on the brain structure variables ('eTIV, 'nWBV,' and 'ASF') in relation to various groups comprising of Mild/Severe Dementia and No Dementia categories. This is a synopsis of the procedure:

1. Data Loading and Exploration:
   The dataset has been loaded and we consider Group variable that states whether the individual has Alzheimer or not
2. Calculating the Composite Score:
   ASF, nWBV, and eTIV are the brain structural variables that have been standardized (or "Z-scored"). Employing a custom normalization procedure, the standardized variables were normalized to a range of 0 to 1. The 'CompositeScore' was obtained by averaging the normalized variables for each participant.
3. Normality Test: -
   The "CompositeScore" was subjected to a Shapiro-Wilk normality test, which revealed that it wasn't distributed normally.
4. Group Comparison:
   Since the "CompositeScore" was not normally distributed, the Kruskal-Wallis non-parametric test was chosen. The Kruskal-Wallis test was used to see whether the "CompositeScore" among the categories that specified whether the individual is having Alzheimer varied significantly.
5. Post-Hoc Tests: To find particular group differences, pairwise comparisons between Group were conducted using the Dunn's test with Bonferroni correction.

```
        Shapiro-Wilk normality test

data:  longitudinal_data$CompositeScore
W = 0.99179, p-value = 0.03695
```

P- value < 0.05. This implies the null hypothesis will be rejected which states that the following variable choose to undergo tests does not follow a normal distribution.

```
        Kruskal-Wallis rank sum test

data:  CompositeScore by Group
Kruskal-Wallis chi-squared = 37.374, df = 2, p-value = 7.663e-09
```

The p-value (< 7.663e-09) implies a strong rejection of the null hypothesis. From this we can conclude, that there are significant differences between the groups.
Groups in this context are variable depicting Mild, Severe and no Alzheimer's disease.

```
Dunn (1964) Kruskal-Wallis multiple comparison
  p-values adjusted with the Bonferroni method.

               Comparison          Z      P.unadj        P.adj
1    Converted - Demented  0.7494086 4.536110e-01 1.000000e+00
2 Converted - Nondemented -2.8847301 3.917494e-03 1.175248e-02
3  Demented - Nondemented -5.9633209 2.471624e-09 7.414871e-09
```

From the observations we state that there is a substantial difference in the variable CompositeScore between the Converted and Non-demented groups, and between "Non-Demented" and "Demented" groups. We also observe that there is no statistically significant difference between the 'Demented' and 'Converted' groups.
These results focus on particular group and their relations between other group variables which makes it easier to see where the groups "Converted," "Non-Demented," & "Demented" differ significantly in "CompositeScore."p

Conclusions -
Reject Null Hypothesis.
Mild and Severe Alzheimer have same significant impact.
We conclude that there exists a Significant relation between Alzheimer's Disease and Brain Structure when comparing the dataset's non-demented participants to those with extremely mild to moderate Alzheimer's disease.

CONCLUSION -

With the world's population growing older and neurodegenerative disorders becoming more common, this study effort will help us better understand how the brain changes with age and how dementia develops. Potential ramifications include improved understanding of the structural features of Alzheimer's disease and early diagnostic signs. The commitment to deciphering these intricacies highlights the need of augmenting our understanding to tackle the obstacles presented by an aging populace and the rising prevalence of neurodegenerative illnesses.
