Topological Data Analysis of Human Brain Data

Internship report

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Ufuk Cem Birbiri

Academic tutor: Mathieu Desroches

Inria Center at UCA

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1 The Final Dataset

The link of the dataset is in the following link (just copy paste all the URL written in bold) :

https ://wiki.humanconnectome.org/display/PublicData/HCP-YA+Data+Dictionary+Updated+for+the+1200+Subject+Release#
HCPYADataDictionaryUpdatedforthe1200SubjectRelease-Category :Cognition

The final dataset(998,51) consists of following features :

1. Cognition columns(14)

2. Motor columns(4)

3. Emotion columns(8)

4. Age and Gender columns(2)

5. **Anterior Cingulate Cortex(8) :**

- Left caudal-anterior-cingulate Surface Area,

- Left rostral-anterior-cingulate Surface Area,

- Right caudal-anterior-cingulate Surface Area,

- Right rostral-anterior-cingulate Surface Area,

- Left caudal-anterior-cingulate Average Thickness,

- Left rostral-anterior-cingulate Average Thickness,

- Right caudal-anterior-cingulate Average Thickness,

- Right rostral-anterior-cingulate Average Thickness,

6. **Orbitofrontal Cortex(8) :**

- Left lateral-orbitofrontal Surface Area,

- Left medial-orbitofrontal Surface Area,

- Right lateral-orbitofrontal Surface Area,

- Right medial-orbitofrontal Surface Area,

- Left lateral-orbitofrontal Average Thickness,

- Left medial-orbitofrontal Average Thickness,

- Right lateral-orbitofrontal Average Thickness,

- Right medial-orbitofrontal Average Thickness

7. Total cortical gray matter volume(1)

8. Total subcortical gray matter volume(1)

9. Total gray matter volume(1)

10. Supratentorial volume(1)

11. Total cortical white matter volume(1)

12. Topological features(2) extracted from connectivity matrices of patients.

2 RESULTS

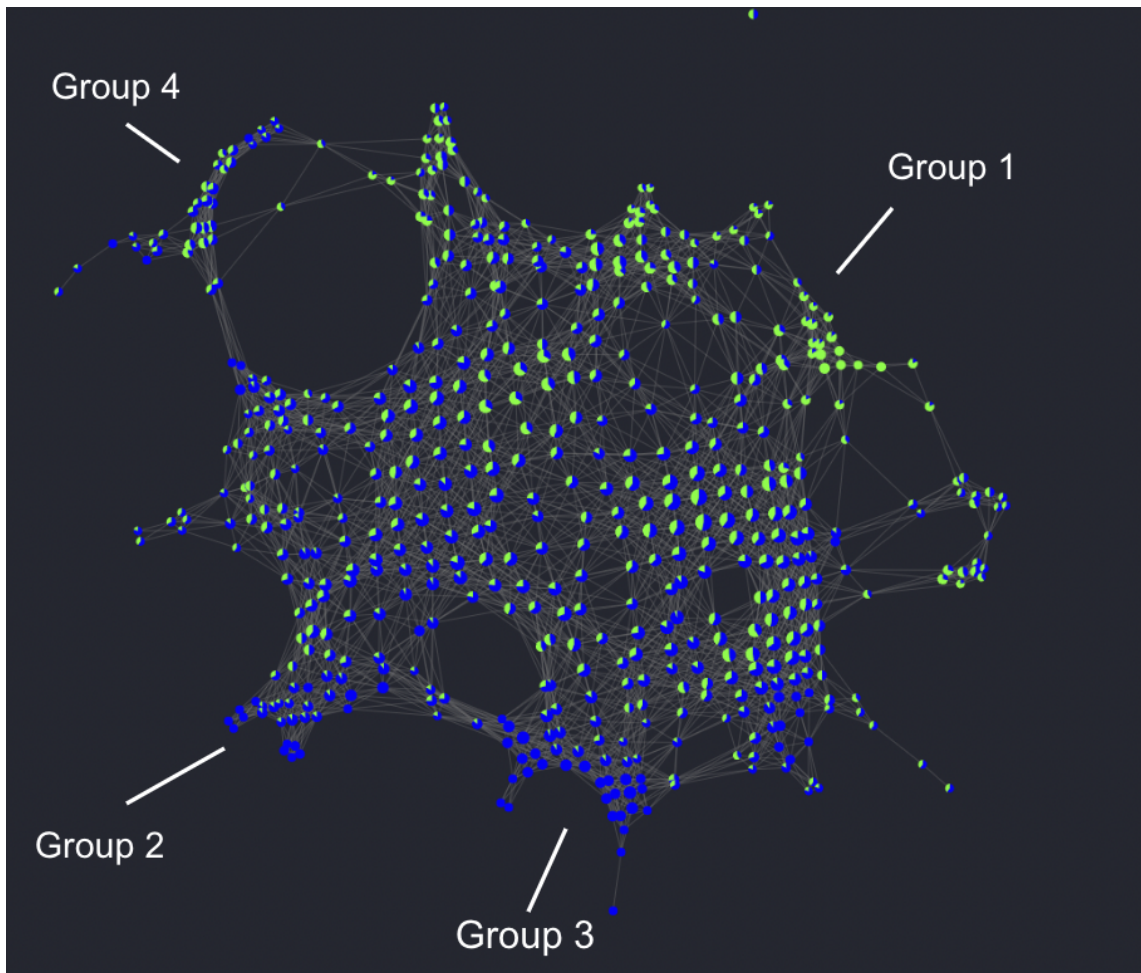The Mapper result and the 4 different groups can be seen in Fig.1.

FIGURE 1 – *Green color is 31+. Blue color is age 22-30*

2.1 Significant characteristics and clinical features specific to subgroups :

$\boxed{\text{G}_1}$ We found 25 clinical variables significantly specific to $\text{G}_1[31+]$ (n=197). Among these clinical variables, there is only one clinical feature that is unique to $\text{G}_1[31+]$, which is *Negative Affect (Sadness)*. The clinical variables of this group can be found in Table.1

$\boxed{\text{G}_2}$ There are 24 clinical variables significantly specific to $\text{G}_2[22\text{-}30]$ (n=263). There is no feature that is only unique to this group. The clinical variables of this group can be found in Table.2

$\boxed{\text{G}_3}$ 24 clinical variables were found to be significantly specific to $\text{G}_3[22\text{-}30]$ (n=335). There are two variables that are unique to this group such as *Left rostral-anterior-cingulate Avg Thickness* and *Sustained Attention.* The clinical variables of this group can be found in Table.3

$\boxed{\text{G}_4}$ This group(n=282) consists of patients with mixed age i.e. both [22-30] and [31+]. There are 23 clinical features specific to this group with only one variable that is unique : *Executive Function/ Cognitive Flexibility.* The clinical variables of this group can be found in Table.4

Clinical features	G_1[31+]	G_2[22-30]	G_3[22-30]	G_4[mix]
Total Gray Matter Volume	✓	✓	✓	✓
Total Cortical Gray Matter Volume	✓	✓	✓	✓
Supratentorial volume	✓	✓	✓	✓
Total subcortical gray matter volume	✓	✓		✓
Right lateral-orbito-frontal SA	✓	✓		✓
Left lateral-orbito-frontal SA	✓	✓	✓	✓
Left rostral-anterior-cingulate SA	✓	✓	✓	✓
Total cortical white matter volume	✓	✓	✓	✓
Right medial-orbito-frontal SA	✓	✓		✓
Gender	✓	✓	✓	✓
Age	✓	✓	✓	
Right caudal-anterior-cingulate SA	✓	✓	✓	✓
Right rostral-anterior-cingulate SA	✓	✓	✓	✓
Left medial-orbito-frontal SA	✓	✓	✓	✓
Left caudal-anterior-cingulate SA	✓	✓	✓	✓
Language/Vocabulary Comprehension(COG)	✓		✓	✓
Left lateral-orbito-frontal Avg Thickness	✓	✓	✓	✓
Strength(Grip Strength Dynamometry)(Motor)	✓	✓		✓
Self-regulation/Impulsivity(Cognitive)	✓	✓	✓	
Endurance (2 minute walk test)(Motor)	✓	✓		✓
Spatial Orientation(Cognitive)	✓			✓
Language/Reading Decoding(Cognitive)	✓		✓	✓
Right lateral-orbito-frontal Avg Thickness	✓	✓	✓	
Negative Affect(Sadness)(Emotion)	✓			
Working Memory (List Sorting)(Cognitive)	✓		✓	✓

TABLE 1 – **(A) Significant characteristics and clinical features specific to G1 :[31+] (n=197)**.

Clinical features	G_1[31+]	G_2[22-30]	G_3[22-30]	G_4[mix]
Total Gray Matter Volume	✓	✓	✓	✓
Total Cortical Gray Matter Volume	✓	✓	✓	✓
Supratentorial volume	✓	✓	✓	✓
Total cortical white matter volume	✓	✓	✓	✓
Total subcortical gray matter volume	✓	✓		✓
Left lateral-orbito-frontal SA	✓	✓	✓	✓
Right lateral-orbito-frontal SA	✓	✓		✓
Right medial-orbito-frontal SA	✓	✓		✓
Left rostral-anterior-cingulate SA	✓	✓	✓	✓
Gender	✓	✓	✓	✓
Strength(Grip Strength Dynamometry)(Motor)	✓	✓		✓
Right caudal-anterior-cingulate SA	✓	✓	✓	✓
Left lateral-orbito-frontal Avg Thickness	✓	✓	✓	✓
Left medial-orbito-frontal SA	✓	✓	✓	✓
Right rostral-anterior-cingulate SA	✓	✓	✓	✓
Right lateral-orbito-frontal Avg Thickness	✓	✓	✓	
Left caudal-anterior-cingulate SA	✓	✓	✓	✓
Left caudal-anterior-cingulate SA	✓	✓	✓	✓
Fluid Intelligence(COG)		✓	✓	
Endurance (2 minute walk test)(Motor)	✓	✓		✓
Age	✓	✓	✓	
Right medial-orbito-frontal Avg Thickness		✓	✓	
Right rostral-anterior-cingulate Avg Thickness		✓	✓	✓
Left medial-orbito-frontal Avg Thickness		✓	✓	
Self-regulation/Impulsivity(Cognitive)	✓	✓	✓	

TABLE 2 – **(A) Significant characteristics and clinical features specific to G2 :[22-30] (n=263)**.

Clinical features	G_1[31+]	G_2[22-30]	G_3[22-30]	G_4[mix]
Total Cortical Gray Matter Volume	✓	✓	✓	✓
Total Gray Matter Volume	✓	✓	✓	✓
Total cortical white matter volume	✓	✓	✓	✓
Supratentorial volume	✓	✓	✓	✓
Age	✓	✓	✓	
Left lateral-orbito-frontal Avg Thickness	✓	✓	✓	✓
Fluid Intelligence(COG)		✓	✓	
Left lateral-orbito-frontal SA	✓	✓	✓	✓
Right lateral-orbito-frontal Avg Thickness	✓	✓	✓	
Left rostral-anterior-cingulate SA	✓	✓	✓	✓
Language/Vocabulary Comprehension(COG)	✓		✓	✓
Right caudal-anterior-cingulate SA	✓	✓	✓	✓
Right medial-orbito-frontal Avg Thickness		✓	✓	
Left medial-orbito-frontal SA	✓	✓	✓	✓
Working Memory (List Sorting)(Cognitive)	✓		✓	✓
Right rostral-anterior-cingulate SA	✓	✓	✓	✓
Right rostral-anterior-cingulate Avg Thickness		✓	✓	✓
Left medial-orbito-frontal Avg Thickness		✓	✓	
Language/Reading Decoding(Cognitive)	✓		✓	✓
Self-regulation/Impulsivity(Cognitive)	✓	✓	✓	
Gender	✓	✓	✓	✓
Left caudal-anterior-cingulate SA	✓	✓	✓	✓
Left rostral-anterior-cingulate Avg Thickness			✓	
Sustained Attention			✓	

TABLE 3 – **(A) Significant characteristics and clinical features specific to G3 :[22-30] (n=335)**.

Clinical features	G_1[31+]	G_2[22-30]	G_3[22-30]	G_4[mix]
Total Cortical Gray Matter Volume	✓	✓	✓	✓
Total Gray Matter Volume	✓	✓	✓	✓
Supratentorial volume	✓	✓	✓	✓
Total cortical white matter volume	✓	✓	✓	✓
Total subcortical gray matter volume	✓	✓		✓
Right lateral-orbito-frontal SA	✓	✓		✓
Left lateral-orbito-frontal SA	✓	✓	✓	✓
Left medial-orbito-frontal SA	✓	✓	✓	✓
Right medial-orbito-frontal SA	✓	✓		✓
Strength (Grip Strength Dynamometry)(Motor)	✓	✓		✓
Gender	✓	✓	✓	✓
Left rostral-anterior-cingulate SA	✓	✓	✓	✓
Right rostral-anterior-cingulate SA	✓	✓	✓	✓
Right caudal-anterior-cingulate SA	✓	✓	✓	✓
Left caudal-anterior-cingulate SA	✓	✓	✓	✓
Endurance(2 minute walk test)	✓	✓		✓
Spatial Orientation	✓			✓
Working Memory (List Sorting)(Cognitive)	✓		✓	✓
Executive Function/ Cognitive Flexibility			✓	
Right rostral-anterior-cingulate Avg Thickness		✓	✓	✓
Language/Reading Decoding(Cognitive)	✓		✓	✓
Left lateral-orbito-frontal Avg Thickness	✓	✓	✓	✓
Language/Vocabulary Comprehension(COG)	✓		✓	✓

TABLE 4 – **(A) Significant characteristics and clinical features specific to G4 :[22-30, 31+] (n=282)**.

2.2 Our results vs Literature

In this section, we will compare the clinical features appeared in each group with the literature results.

Gray Matter Volume   This feature appeared in every group as a significant clinical feature. [1] shows smaller bilateral gray matter(GM) volume in the older group(avg age=71) relative to the middle-age group(avg age=41 years), in several cerebral and right cerebellar regions involved in language and executive functions. Importantly, their results also revealed smaller GM volume in the right cerebellum in older group relative to middle-age group, supporting the idea of a complex cognitive role for this structure.

In addition, [2] found a significant, nonlinear decline in GM density with age, which was most rapid between 7 and about 60 years, over dorsal frontal and parietal association cortices on both the lateral and interhemispheric surfaces.

In our dataset we have three features for GM volume : *Total Gray Matter Volume, Total Cortical Gray Matter Volume*, and *Total subcortical gray matter volume.* In the Table. 5, the mean values of the clinical variables of each group are shown. If there is a check mark, that clinical variable is significantly specific to that group.

Clinical Variables	G1[31+]	G2[22-30]	G3[22-30]	G4[mixed]
Total GMV	592655.32 (✓)	771533.94 (✓)	714666.40 (✓)	752002.16 (✓)
Total Cortical GMV	435261.56 (✓)	578701.44 (✓)	534875.82 (✓)	562891.96 (✓)
Total Subcortical GMV	55629.67 (✓)	65507.86 (✓)	60928.54	66823.75 (✓)

TABLE 5 – The mean values of clinical variables of each group are shown in the table. The check marks represents the appearance of the variable in the group.

As we can see in the Table.5, the *Total GMV, Total Cortical GMV*, and *Total subcortical GMV* mean values in G1[31+] are less than G2[22-30] and G3[22-30], separately. We can conclude that the *Total GMV, Total Cortical GMV*, and *Total subcortical GMV* are decreasing when age increase. These findings are parallel with the papers [1, 2].

Cognitive Scores The average cognitive test scores of each different age groups can be seen in Table.6. Only the clinical features that are appeared as a significant characteristics of a group is shown i.e. among 14 clinical cognitive features in the dataset, only 8 of them appeared as significant. [1] suggests that the degree of cognitive decline is not identical for all cognitive processes, i.e., some functions undergo more severe change than others. For example, while executive functions are typically the first to show impairment during normal aging, language abilities remain relatively intact [3]. According to our dataset, language ability features are *Language/Vocabulary Comprehension* and *Language/Reading Decoding* where average scores of these features are lower in older group than younger groups. The other the average cognitive scores(except *Sustained Attention* are also lower in older group than younger groups.

Clinical Variables	G1[31+]	G2[22-30]	G3[22-30]	G4[mixed]
Language/Vocabulary Comprehension	100.13 (✔)	114.50	115.41 (✔)	114.78 (✔)
Self-regulation /Impulsivity (Delay Discounting)	0.18 (✔)	0.32 (✔)	0.35 (✔)	0.29
Spatial Orientation	13.14 (✔)	15.92	16.03	16.86(✔)
Language/Reading Decoding	101.09 (✔)	111.92	113.08 (✔)	111.98(✔)
Working Memory(List Sorting)	100.72 (✔)	103.62	108.19 (✔)	107.69(✔)
Fluid Intelligence	15.75	19.21 (✔)	19.15 (✔)	17.97
Sustained Attention	0.96	0.96	0.95 (✔)	0.96
Executive Function/Cognitive Flexibility	101.18	103.68	103.45	105.51 (✔)

TABLE 6 – The mean values of clinical variables of each group are shown in the table. The check marks represents the appearance of the variable in the group.

On the other hand, *Sustained Attention* seems to have similar average scores in both older and younger groups in the Table.6. According to [4], sustained attention shows improvements with maturation in early adulthood but then does not change with aging in older adults, which is paralel to our results(0.96, 0.96, 0.95 in G1[31+], G2[22-30], and G3[22-30], respectively).

It is interesting to see that the clinical feature of Executive Function/Cognitive Flexibility appeared as a significant feature only in the mixed aged group.

In addition, [5] reports an age-related decline in performance on fluid intelligence tasks. Our results also support this result where fluid intelligence score in G1[31+] group is less than both younger groups(G2[22-30] G3[22-30]).

Surface Area in Orbito-frontal Cortices [6] claims that with aging, there is a smaller surface area in orbito-frontal cortices. We have 4 orbito-frontal surface area features in the dataset : *Right lateral-orbito-frontal surface area(SA), Left lateral-orbito-frontal SA, Right medial-orbito-frontal SA,* and *Left medial-orbito-frontal SA.* In Table 7, the check marks represents the appearance of the variables in each group.

Clinical Variables	G1[31+]	G2[22-30]	G3[22-30]	G4[mixed]
Right lateral-orbito-frontal SA	2241.25 (✓)	2832.70 (✓)	2646.64	2874.59 (✓)
Left lateral-orbito-frontal SA	2312.82 (✓)	2922.33 (✓)	2718.40 (✓)	2943.30 (✓)
Right medial-orbito-frontal SA	1657.86 (✓)	2038.35 (✓)	1853.58	2053.96 (✓)
Left medial-orbito-frontal SA	1742.49 (✓)	2161.33 (✓)	1916.35 (✓)	2228.36 (✓)

TABLE 7 – The mean values of orbito-frontal surface areas(SA) each group are shown in the table. The check marks represents the appearance of the variable in the group.

We can see that there is a smaller orbito-frontal surface area when people get old, which supports the [6]'s results.

Lateral-frontal Cortical Thickness [7] claims that with aging, there is a smaller lateral-frontal cortical thickness in older age(64–68 years old) than middle aged(44–48 years old). Smaller frontal cortical thickness was also associated with better episodic memory ($p < 0.01$) and Symbol-Digit Modalities Test ($p < 0.01$) performance in older age. However, in middle age greater cortical thickness was associated with better episodic memory($p <$

0.01) and reaction time (RT)(p < 0.01).

We have 4 orbito-frontal surface area features in the dataset : *Left lateral-orbitofrontal Average Thickness, Right lateral-orbitofrontal Average Thickness, Left medial-orbitofrontal Average Thickness,* and *Right medial-orbitofrontal Average Thickness.* In Table 8, the average thicknesses of orbito frontal regoins are shown and the check marks represents the appearance of the variables in each group.

Clinical Variables	G1[31+]	G2[22-30]	G3[22-30]	G4[mixed]
Left lateral-orbitofrontal Avg Thickness	2.76 (✓)	2.89 (✓)	2.88 (✓)	2.79 (✓)
Right lateral-orbitofrontal Avg Thickness	2.80 (✓)	2.89 (✓)	2.88 (✓)	2.81
Left medial-orbitofrontal Average Thickness	2.56	2.62 (✓)	2.62 (✓)	2.54
Right medial-orbitofrontal Average Thickness	2.71	2.78 (✓)	2.79 (✓)	2.70

TABLE 8 – The mean values of orbito-frontal thickness each group are shown in the table. The check marks represents the appearance of the variable in the group.

We can see that there is a smaller orbito-frontal average thickness when people get old, which supports the [7]'s results. According to [7] result, smaller lateral frontal cortical thickness was associated with better episodic memory. We also have a clinical feature for episodic memory in our dataset such as *Episodic Memory (Picture Sequence Memory)*, however it didn't appeared as a significant feature for any groups.

Total Cortical White Matter Volume [8] demonstrated significant loss of white matter with normal aging. We have a clinical feature for *Total cortical white matter volume* in the dataset. When we look at Table 9, we can see that total cortical white matter volume decreases when people get old, which is parallel to [8]'s result.

Clinical Variables	G1[31+]	G2[22-30]	G3[22-30]	G4[mixed]
Total cortical white matter vo-lume	399841.67 (✓)	481352.40 (✓)	424107.74 (✓)	529137.17 (✓)

TABLE 9 – The mean values of Total cortical white matter volume in each group are shown in the table. The check marks represents the appearance of the variable in the group.

2.3 Our Novel Findings

1. Supratentorial volume   According to our results, Supratentorial volume decreases over age that can seen in Table10

Clinical Variables	G1[31+]	G2[22-30]	G3[22-30]	G4[mixed]
Supratentorial volume	905980.23 (✓)	1144966.52 (✓)	1037582.75 (✓)	1179358.45 (✓)

TABLE 10 – The mean values of Supratentorial volume

2. Rostral-anterior-cingulate Avg Thickness   According to our results, Right and Left rostral-anterior-cingulate thickness decreases over age that can seen in Table11

Clinical Variables	G1[31+]	G2[22-30]	G3[22-30]	G4[mixed]
Right Rostral anterior-cingulate Avg Thickness	3.02	3.07 (✓)	3.08 (✓)	2.96 (✓)
Left Rostral anterior-cingulate Avg Thickness	3.03	3.07	3.06 (✓)	3.01

TABLE 11 – The mean values of Rostral-anterior-cingulate Avg Thickness

Discussion

Our research is based on comparison between age and other clinical variables.
We have demonstrated and proved the following comparisons by citing other papers in the literature :
1. Age vs Total gray matter volume(GMV), Total cortical GMV and Total subcortical GMV
2. Age vs cognitive performance
3. Age vs Surface Area in Orbito-frontal Cortices
4. Age vs Lateral-frontal Cortical Thickness
5. Age vs Total Cortical White Matter Volume

Our novel findings are :
1. Age vs Supratentorial volume
2. Age vs Rostral-anterior-cingulate Avg Thickness

To Do
1. Male/Female percantage in each group.
2. We can color the Mapper result by clinical variables (ex : Gender, GMV, White matter volume etc.) to visualize and analyse better.

Bibliographie

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Appendix

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GROUP- 1
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Clinical features	Cat.	G1	G2	G3	G4
Total gray matter volume	GMV	X_592655.32	X_771533.94	X_714666.40	X_752002.16
Total cortical gray matter volume	GMV	X_435261.56	X_578701.44	X_534875.82	X_562891.96
Supratentorial volume	FSS	X_905980.23	X_1144966.52	X_1037582.75	X_1179358.45
Total subcortical gray matter volume	GMV	X_55629.67	X_65507.86	._60928.54	X_66823.75
Right lateral-orbito-frontal SA	SA_	X_2241.25	X_2832.70	._2646.64	X_2874.59
Left lateral-orbito-frontal SA	SA_	X_2312.82	X_2922.33	X_2718.40	X_2943.30
Left rostral-anterior-cingulate SA	SA_	X_717.11	X_1005.62	X_916.79	X_1001.03
Total cortical white matter volume	WMV	X_399841.67	X_481352.40	X_424107.74	X_529137.17
Right medial-orbito-frontal SA	SA_	X_1657.86	X_2038.35	._1853.58	X_2053.96
Gender	OTH	X_1.95	X_1.16	X_1.38	X_1.14
Age	OTH	X_1.75	X_1.16	X_1.08	._1.38
Right caudal-anterior-cingulate SA	SA_	X_674.07	X_935.22	X_874.46	X_926.20
Right rostral-anterior-cingulate SA	SA_	X_558.58	X_758.89	X_693.57	X_771.91

FIGURE 2 – *PART-1 : The average mean values of each significant clinical feature appeared for G1[31+]. "X" is used for check-mark*

Left medial-orbito-frontal SA	SA_	X_1742.49	X_2161.33	X_1916.35	X_2228.36
Left caudal-anterior-cingulate SA	SA_	X_589.96	X_763.54	X_714.10	X_761.83
Language/Vocabulary Comprehension	COG	X_100.13	._114.50	X_115.41	X_114.78
Left lateral-orbito-frontal Avg Thickness	Thc	X_2.76	X_2.89	X_2.88	X_2.79
Strength (Grip Strength Dynamometry)	MOT	X_94.36	X_116.13	._108.38	X_118.37
Self-regulation/Impulsivity (Delay Discounting)	COG	X_0.18	X_0.32	X_0.35	._0.29
Endurance (2 minute walk test)	MOT	X_102.29	X_114.84	._110.50	X_112.83
Spatial Orientation	COG	X_13.14	._15.92	._16.03	X_16.86
Language/Reading Decoding	COG	X_101.09	._111.92	X_113.08	X_111.98
Right lateral-orbito-frontal Avg Thickness	Thc	X_2.80	X_2.89	X_2.88	._2.81
Negative Affect (Sadness)	EMO	X_43.36	._46.97	._46.11	._46.19
Working Memory (List Sorting)	COG	X_100.72	._103.62	X_108.19	X_107.69

FIGURE 3 – *PART-2 : The average mean values of each significant clinical feature appeared for G1[31+]. "X" is used for check-mark*

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-------------------------------------------------------------
GROUP- 2
    Clinical   | Cat. |     G1      |      G2      |     G3      |      G4
    features   |      |            |             |            |
==============+======+============+=============+============+=============
  Total gray  | GMV  | X_592655.32 | X_771533.94 | X_714666.40 | X_752002.16
matter volume |      |            |             |            |
Total cortical | GMV | X_435261.56 | X_578701.44 | X_534875.82 | X_562891.96
  gray matter |      |            |             |            |
    volume     |      |            |             |            |
Supratentorial | FSS | X_905980.23 | X_1144966.52| X_1037582.75| X_1179358.45
    volume     |      |            |             |            |
Total cortical | WMV | X_399841.67 | X_481352.40 | X_424107.74 | X_529137.17
 white matter |      |            |             |            |
    volume     |      |            |             |            |
    Total      | GMV  | X_55629.67  | X_65507.86  | ._60928.54  | X_66823.75
 subcortical  |      |            |             |            |
 gray matter  |      |            |             |            |
    volume     |      |            |             |            |
Left lateral- | SA_  | X_2312.82   | X_2922.33   | X_2718.40   | X_2943.30
orbito-frontal |      |            |             |            |
    SA         |      |            |             |            |
Right lateral- | SA_ | X_2241.25   | X_2832.70   | ._2646.64   | X_2874.59
orbito-frontal |      |            |             |            |
    SA         |      |            |             |            |
Right medial- | SA_  | X_1657.86   | X_2038.35   | ._1853.58   | X_2053.96
orbito-frontal |      |            |             |            |
    SA         |      |            |             |            |
Left rostral- | SA_  | X_717.11    | X_1005.62   | X_916.79    | X_1001.03
  anterior-   |      |            |             |            |
 cingulate SA |      |            |             |            |
    Gender     | OTH  | X_1.95      | X_1.16      | X_1.38      | X_1.14
Strength (Grip | MOT | X_94.36     | X_116.13    | ._108.38    | X_118.37
   Strength   |      |            |             |            |
 Dynamometry) |      |            |             |            |
Right caudal- | SA_  | X_674.07    | X_935.22    | X_874.46    | X_926.20
  anterior-   |      |            |             |            |
 cingulate SA |      |            |             |            |
```

FIGURE 4 – *PART-1 : The average mean values of each significant clinical feature appeared for G2[22-30]. "X" is used for check-mark*

```
Left lateral-    | Thc  |   X_2.76    |   X_2.89    |   X_2.88    |   X_2.79
orbito-frontal   |      |             |             |             |
Avg Thickness    |      |             |             |             |
 Left medial-    | SA_  |  X_1742.49  |  X_2161.33  |  X_1916.35  |  X_2228.36
orbito-frontal   |      |             |             |             |
      SA         |      |             |             |             |
Right rostral-   | SA_  |  X_558.58   |  X_758.89   |  X_693.57   |  X_771.91
   anterior-     |      |             |             |             |
 cingulate SA    |      |             |             |             |
Right lateral-   | Thc  |   X_2.80    |   X_2.89    |   X_2.88    |   ._2.81
orbito-frontal   |      |             |             |             |
Avg Thickness    |      |             |             |             |
 Left caudal-    | SA_  |  X_589.96   |  X_763.54   |  X_714.10   |  X_761.83
   anterior-     |      |             |             |             |
 cingulate SA    |      |             |             |             |
    Fluid        | COG  |  ._15.75    |  X_19.21    |  X_19.15    |  ._17.97
 Intelligence    |      |             |             |             |
Endurance (2     | MOT  |  X_102.29   |  X_114.84   |  ._110.50   |  X_112.83
minute walk      |      |             |             |             |
   test)         |      |             |             |             |
     Age         | OTH  |   X_1.75    |   X_1.16    |   X_1.08    |   ._1.38
Right medial-    | Thc  |   ._2.71    |   X_2.78    |   X_2.79    |   ._2.70
orbito-frontal   |      |             |             |             |
Avg Thickness    |      |             |             |             |
Right rostral-   | Thc  |   ._3.02    |   X_3.07    |   X_3.08    |   X_2.96
   anterior-     |      |             |             |             |
cingulate Avg    |      |             |             |             |
  Thickness      |      |             |             |             |
 Left medial-    | Thc  |   ._2.56    |   X_2.62    |   X_2.62    |   ._2.54
orbito-frontal   |      |             |             |             |
Avg Thickness    |      |             |             |             |
Self-regulatio   | COG  |   X_0.18    |   X_0.32    |   X_0.35    |   ._0.29
n/Impulsivity    |      |             |             |             |
   (Delay        |      |             |             |             |
Discounting)     |      |             |             |             |
-------------------------------------------------------------------
```

FIGURE 5 – *PART-2 : The average mean values of each significant clinical feature appeared for G2[22-30]. "X" is used for check-mark*

```
GROUP- 3
    Clinical    | Cat. |      G1       |      G2       |      G3       |      G4
    features    |      |              |              |              |
===============+======+==============+==============+==============+==============
Total cortical | GMV  | X_435261.56  | X_578701.44  | X_534875.82  | X_562891.96
  gray matter  |      |              |              |              |
     volume     |      |              |              |              |
  Total gray    | GMV  | X_592655.32  | X_771533.94  | X_714666.40  | X_752002.16
matter volume  |      |              |              |              |
Total cortical | WMV  | X_399841.67  | X_481352.40  | X_424107.74  | X_529137.17
 white matter  |      |              |              |              |
     volume     |      |              |              |              |
Supratentorial | FSS  | X_905980.23  | X_1144966.52 | X_1037582.75 | X_1179358.45
     volume     |      |              |              |              |
     Age        | OTH  |   X_1.75     |   X_1.16     |   X_1.08     |   ._1.38
Left lateral-  | Thc  |   X_2.76     |   X_2.89     |   X_2.88     |   X_2.79
orbito-frontal |      |              |              |              |
Avg Thickness  |      |              |              |              |
    Fluid       | COG  |   ._15.75    |   X_19.21    |   X_19.15    |   ._17.97
 Intelligence  |      |              |              |              |
Left lateral-  | SA_  |  X_2312.82   |  X_2922.33   |  X_2718.40   |  X_2943.30
orbito-frontal |      |              |              |              |
      SA        |      |              |              |              |
Right lateral- | Thc  |   X_2.80     |   X_2.89     |   X_2.88     |   ._2.81
orbito-frontal |      |              |              |              |
Avg Thickness  |      |              |              |              |
Left rostral-  | SA_  |  X_717.11    |  X_1005.62   |  X_916.79    |  X_1001.03
   anterior-   |      |              |              |              |
 cingulate SA  |      |              |              |              |
Language/Vocab | COG  |  X_100.13    |  ._114.50    |  X_115.41    |  X_114.78
    ulary       |      |              |              |              |
Comprehension  |      |              |              |              |
Right caudal-  | SA_  |  X_674.07    |  X_935.22    |  X_874.46    |  X_926.20
   anterior-   |      |              |              |              |
 cingulate SA  |      |              |              |              |
Right medial-  | Thc  |   ._2.71     |   X_2.78     |   X_2.79     |   ._2.70
orbito-frontal |      |              |              |              |
Avg Thickness  |      |              |              |              |
```

FIGURE 6 – *PART-1 : The average mean values of each significant clinical feature appeared for G3[22-30]. "X" is used for check-mark*

```
   Left medial-   | SA_  | X_1742.49  | X_2161.33  | X_1916.35  | X_2228.36
  orbito-frontal  |      |            |            |            |
       SA         |      |            |            |            |
 Working Memory   | COG  | X_100.72   | ._103.62   | X_108.19   | X_107.69
 (List Sorting)   |      |            |            |            |
  Right rostral-  | SA_  | X_558.58   | X_758.89   | X_693.57   | X_771.91
     anterior-    |      |            |            |            |
   cingulate SA   |      |            |            |            |
  Right rostral-  | Thc  | ._3.02     | X_3.07     | X_3.08     | X_2.96
     anterior-    |      |            |            |            |
  cingulate Avg   |      |            |            |            |
    Thickness     |      |            |            |            |
   Left medial-   | Thc  | ._2.56     | X_2.62     | X_2.62     | ._2.54
  orbito-frontal  |      |            |            |            |
  Avg Thickness   |      |            |            |            |
 Language/Readi   | COG  | X_101.09   | ._111.92   | X_113.08   | X_111.98
   ng Decoding    |      |            |            |            |
 Self-regulatio   | COG  | X_0.18     | X_0.32     | X_0.35     | ._0.29
 n/Impulsivity    |      |            |            |            |
     (Delay       |      |            |            |            |
  Discounting)    |      |            |            |            |
     Gender       | OTH  | X_1.95     | X_1.16     | X_1.38     | X_1.14
  Left caudal-    | SA_  | X_589.96   | X_763.54   | X_714.10   | X_761.83
     anterior-    |      |            |            |            |
   cingulate SA   |      |            |            |            |
  Left rostral-   | Thc  | ._3.03     | ._3.07     | X_3.06     | ._3.01
     anterior-    |      |            |            |            |
  cingulate Avg   |      |            |            |            |
    Thickness     |      |            |            |            |
    Sustained     | COG  | ._0.96     | ._0.96     | X_0.95     | ._0.96
    Attention     |      |            |            |            |
  -------------------------------------------------------------
```

FIGURE 7 – *PART-2 : The average mean values of each significant clinical feature appeared for G3[22-30]. "X" is used for check-mark*

```
----------------------------------------------------------------
GROUP- 4
```

Clinical features	Cat.	G1	G2	G3	G4
Total cortical gray matter volume	GMV	X_435261.56	X_578701.44	X_534875.82	X_562891.96
Total gray matter volume	GMV	X_592655.32	X_771533.94	X_714666.40	X_752002.16
Supratentorial volume	FSS	X_905980.23	X_1144966.52	X_1037582.75	X_1179358.45
Total cortical white matter volume	WMV	X_399841.67	X_481352.40	X_424107.74	X_529137.17
Total subcortical gray matter volume	GMV	X_55629.67	X_65507.86	._60928.54	X_66823.75
Right lateral-orbito-frontal SA	SA_	X_2241.25	X_2832.70	._2646.64	X_2874.59
Left lateral-orbito-frontal SA	SA_	X_2312.82	X_2922.33	X_2718.40	X_2943.30
Left medial-orbito-frontal SA	SA_	X_1742.49	X_2161.33	X_1916.35	X_2228.36
Right medial-orbito-frontal SA	SA_	X_1657.86	X_2038.35	._1853.58	X_2053.96
Strength (Grip Strength Dynamometry)	MOT	X_94.36	X_116.13	._108.38	X_118.37
Gender	OTH	X_1.95	X_1.16	X_1.38	X_1.14
Left rostral-anterior-cingulate SA	SA_	X_717.11	X_1005.62	X_916.79	X_1001.03

FIGURE 8 – *PART-1 : The average mean values of each significant clinical feature appeared for G4[mixed]. "X" is used for check-mark*

```
Right rostral-  | SA_ | X_558.58  | X_758.89  | X_693.57  | X_771.91
   anterior-    |     |           |           |           |
 cingulate SA   |     |           |           |           |
Right caudal-   | SA_ | X_674.07  | X_935.22  | X_874.46  | X_926.20
   anterior-    |     |           |           |           |
 cingulate SA   |     |           |           |           |
 Left caudal-   | SA_ | X_589.96  | X_763.54  | X_714.10  | X_761.83
   anterior-    |     |           |           |           |
 cingulate SA   |     |           |           |           |
Endurance (2    | MOT | X_102.29  | X_114.84  | ._110.50  | X_112.83
minute walk     |     |           |           |           |
   test)        |     |           |           |           |
  Spatial       | COG | X_13.14   | ._15.92   | ._16.03   | X_16.86
Orientation     |     |           |           |           |
Working Memory  | COG | X_100.72  | ._103.62  | X_108.19  | X_107.69
(List Sorting)  |     |           |           |           |
  Executive     | COG | ._101.18  | ._103.68  | ._103.45  | X_105.51
  Function/      |     |           |           |           |
  Cognitive     |     |           |           |           |
 Flexibility    |     |           |           |           |
Right rostral-  | Thc | ._3.02    | X_3.07    | X_3.08    | X_2.96
   anterior-    |     |           |           |           |
cingulate Avg   |     |           |           |           |
  Thickness     |     |           |           |           |
Language/Readi  | COG | X_101.09  | ._111.92  | X_113.08  | X_111.98
ng Decoding     |     |           |           |           |
Left lateral-   | Thc | X_2.76    | X_2.89    | X_2.88    | X_2.79
orbito-frontal  |     |           |           |           |
Avg Thickness   |     |           |           |           |
Language/Vocab  | COG | X_100.13  | ._114.50  | X_115.41  | X_114.78
   ulary        |     |           |           |           |
Comprehension   |     |           |           |           |
-------------------------------------------------------------
```

FIGURE 9 – *PART-2 : The average mean values of each significant clinical feature appeared for G4[mixed]. "X" is used for check-mark*