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A Comparative Study of Cytoarchitectonics: Effects of Aging and Brain Weight Increase on Precentral Gyral and Insular Cortex of Human Brain†

Jeong Soo Suh, Byung Lan Lee* and Key June Seoung*

Department of Radiology, College of Medicine, Ewha University
**Department of Anatomy, College of Medicine, Seoul National University*

= Abstract =The cytoarchitectures of the Brodmann's cortical area 4 and 52 were compared along with the effects of aging and weight increase on both areas. Samples were taken from 209 brains for area 4 and 153 brains for area 52. Cortical thickness, relative total neuronal density (RTND), and relative total glial cell density (RTGD) were studied and statistically significant differences between each age-or brain weight-group were examined. The following results were obtained:

1. No difference between the cortical thickness of the two cortical areas was noticed in regard to age, side and sex.
2. There was no significant difference between RTND of most of the age-or brain weight-groups of the two areas of the same side brains.
3. Difference was shown between RTGD of 0-1 age group of area 4 and that of some age groups of area 52 of the same side brains and also between those of some brain weight-groups of the two cortical areas.
4. Mostly, sex or side didn't seem to cause different result in the above comparisons.

Key Words: ***Cytoarchitecture, Precentral gyral cortex, Insular cotex***

INTRODUCTION

All the regions of the cerebral cortex had been considered homogeneous until the white line on the visual cortex of cerebrum was noticed by Gennari (1882). Also, distinctive cellular morphology and lamination in regions of cerebral cortex was reported by Berlin (1858). However, the cytoarchitectonics of the cerebral cortex was started from the Meynert's(1968) systemic analysis of layered-pattern of the cerebral cortex. Vogt and Vogt (1919) tried cytoarchitectural research on the neurons, neurofibrils, neuroglial cells and cortical blood vessels in order to analyze the cerebral cortex in the functional aspects, and Brodmann (1908), Vogt and Vogt (1919) and von Economo (1929) prepared cortical maps which divided cerebral cortex into 80-200 distinctive areas. They differ from each other in total thickness, in the thickness and density of individual layers and in the arrangement of cells and fibers.

In 1946, Lashley and Clark severely criticized that those cortical divisions did not contribute to the functional analysis and insisted that various individual differences in each cerebral cortex should be considered to establish the correct observation criteria. Nevertheless, it is doubtless that those morphological studies became the basis of pursuit of functional anaysis of cerebral cortex.

Since 1963, many reports have been published by examining brains collected for 20 years in our department in order to study cytoarchitectonics of the cerebral cotex (Kang *et al.* 1968; Seoung 1983; Yang *et al.* 1983). Our present work intended to compare the cytoarchitectures of the summit of the precentral gyral (area 4 of Brodmann) and insular (area 52 of Brodmann) cortex and to investigate the differences between those two areas by means

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of quantitative assessment.

MATERIALS AND METHODS

Normal brains were used in this study. Precentral gyral cortices of 209 (115 male and 94 female) and precentral insular cortices of 153 (89 male and 64 female) brains were obtained after the fixation with 10% neutral formalin. The range of the age distribution was between 0-85 in male, and 0-61 in female. After cerebral hemispheres were divided longitudinally, samples were obtained from the junction area of the upper and the middle third of summit of the precentral gyral and precentral insular cortex at the right angle to the long axis of each gyrus. Specimens were further fixed with 10% neutral formalin followed by paraffin embedding procedure. Paraffin blocks were sectioned with a thickness of 20 μm and stained with aqueous cresyl violet and hematoxylin. The thickness of each section was measured under $\times 10$ ocular lens with an attached micrometer and $\times 10$ objective lens. The number of neurons or glial cells in a unit volume of cortex was computed from counts of nucleoli with the application of the Abercrombie (1946) correction. The counts were made using an eyepiece grid, that enabled the image of the section to be divided into a number of strips of known width (100 μ), length (100 μ) and thickness (20 μ) under $\times 10$ ocular and $\times 40$ objective lens, each strip being parallel to the pial surface. After the cell number in each strip with $20 \times 10^4 \mu^3$ was multiplied by 5, the relative total neuronal or glial cell density (number of neurons or glial cells/unit volume of cortex) could be computed. In the present study, the unit volume of cortex was taken as 0.001 mm^3 ($10^6 \mu^3$) (Sholl 1959).

Values, obtained by observation of precentral gyral and precentral insular cortex, were statistically processed for the biological significance (Snedecor 1956; Adler and Roessler 1960). Adult averages indicate the mean values of the relative total neuronal or glial cell densities obtained from 21-50 age groups, which is the stable period of the cytoarchitecture of the cerebral cortex.

RESULTS

1. Comparison of Cortical Thickness

a) Age-Cortical Thickness; Although area 4 of Brodmann showed mean value of the cortical thickness greater than that of area 52, statistically significant difference was not present between the two areas regardless of age, sex, or side ($p>0.05$).

b) Brain Weight-Cortical Thickness; No significant difference was noticed except between 500-600 gm group of area 4 and 1,300-1,399 gm group of area 52 of the left male brain ($p>0.042$). Sex or side didn't cause any difference in the result of the comparison.

2. Comparison of Neuronal Density

a) Age-Relative Total Neuronal Density; On both sides, there was statistically significant difference between the value of 0-1 age group of one cortical area and that of each of the age groups the other cortical area on the same side. However, in the comparison of the same age groups of the two areas, significant difference was not observed except between the 0-1 age groups of female brain on the left side ($p<0.77$). Above results were same in both sexes (Table 1, 2).

b) Brain Weight-Relative Total Neuronal Density; Although neuronal density of area of 4 was higher than that of area 52 on the same side in all of the brain weight groups (Table 3, 4), difference was statistically significant ($p<0.05$), on both sides, only between the groups of area 4 with the weight ranging 300-899 and each age group of area 52. Value of the same age groups of the two areas didn't show significant difference. Results were similar in both sexes and sides.

3. Comparison of Glial Cell Density

a) Age-Relative Total Glial Cell Density; In male, glial cell density of 0-1 age group of area 4 showed statistically significant difference from that of 2-50 age group and from that of 6-30 age group (2-20 in female) of area 52 on the right side and left side, respectively ($p<0.05$). Same results were obtained in both sexes.

b) Brain Weight-Relative Total Glial Cell Density; Statistically significant differences were seen between the groups shown in Table 5.

4. Comparison of Adult Averages

a) Cortical Thickness; Although area 4 showed greater adult averages than area 52, no significant difference was noticed between those of the two areas either in male or in female.

b) Relative Total Neuronal Density; There was no significant difference between the adult averages of the two areas. Only when the adult average of area 52 was compared to the mean value of 0-1 age group of area 4, significant difference ($p<0.01$) was shown. There was no side and sexual difference in the above results.

c) Relative Total Glial Cell Density; Between the adult average of area 52 and mean value of 0-1

Table 1. Statistical values (mean±S.D.) of corical thickness, neuronal and glial cell density of area 4 and area 52 of Brodmann in each age group (right side)

Item / Area / Sex / Postnatal age(year)		Cortical thickness (mm)				Relative total neuronal density(cells/$10^6\mu^3$)				Relative total glial density(cells/$10^6\mu^3$)			
		No.	Area 4	No.	Area 52	No.	Area 4	No.	Area 52	No.	Area 52	No.	Area 4
0–1	m	8	2.60±0.19	11	2.37±0.30	8	1032±119	11	772±114	8	687±72	11	697±78
	f	8	2.63±0.23	9	2.42±0.38	8	981±129	9	679± 84	8	664±80	9	594±74
2–5	m	10	2.96±0.30	14	2.86±0.36	10	440±104	14	378± 49	10	486±64	14	466±46
	f	15	3.01±0.29	13	2.85±0.38	15	460± 86	13	356± 49	15	489±61	13	426±52
6–10	m	9	3.11±0.41	8	2.92±0.41	9	398± 82	8	338± 49	9	454±59	8	473±42
	f	7	3.10±0.39	9	2.90±0.39	7	413± 71	9	358± 51	7	487±63	9	409±49
11–15	m	4	3.20±0.39	5	2.95±0.39	4	354± 67	5	327± 52	4	485±60	5	437±57
	f	5	3.20±0.43	7	2.89±0.37	5	362± 82	7	353± 49	5	488±61	7	442±57
16–20	m	10	3.20±0.39	8	2.89±0.36	10	356± 63	8	332± 47	10	482±74	8	442±60
	f	7	3.17±0.38	6	2.91±0.37	7	404± 60	6	355± 44	7	536±79	6	463±52
21–30	m	18	3.15±0.45	9	2.88±0.39	18	398± 62	9	362± 46	18	541±72	9	484±58
	f	15	3.23±0.44	10	2.92±0.36	15	409± 50	10	330± 46	15	520±63	10	485±65
31–40	m	19	3.11±0.45	9	2.90±0.38	19	381± 62	9	345± 48	19	599±68	9	506±56
	f	17	3.18±0.43	6	2.86±0.37	17	369± 43	6	372± 52	17	528±73	6	464±64
41–50	m	13	3.24±0.49	11	2.85±0.41	13	350± 61	11	339± 46	13	535±71	11	528±62
	f	10	3.21±0.55	3	2.79±0.41	10	339± 54	3	349± 36	10	513±64	3	482±62
51–60	m	16	3.10±0.57	5	2.76±0.27	16	345± 70	5	369± 60	16	582±80	5	563±74
	f	6	3.13±0.51	1	2.71——	6	325± 69	1	360—	6	520±65	1	615—
61—	m	8	3.02±0.32	9	2.68±0.43	8	324± 50	9	373± 49	8	545±63	9	579±77
	f	4	3.02±0.35	—	—	4	336± 51	—	—	4	507±56	—	—
Adult average (21–50)	m	50	3.16±0.44	29	2.88±0.40	50	358± 49	29	347± 51	50	518±76	29	510±63
	f	42	3.20±0.38	19	2.88±0.41	42	376± 58	19	346± 52	42	521±72	19	478±67

Table 2. Statistical values (mean±S.D.) of cortical thickness, neuronal and glial cell density of area 4 and area 52 of Brodmann in each age group (left side)

Item / Area / Sex / Postnatal age(year)		Cortical thickness (mm)				Relative total neuronal density(cells/$10^6\mu^3$)				Relative total glial density(cells/$10^6\mu^3$)			
		No.	Area 4	No.	Area 52	No.	Area 4	No.	Area 52	No.	Area 4	No.	Area 52
0–1	m	8	2.60±0.24	11	2.32±0.36	8	1076±129	11	795±109	8	579±78	11	658±82
	f	8	2.61±0.20	9	2.46±0.34	8	920±148	9	686± 89	8	603±66	9	557±67
2–5	m	10	3.02±0.25	14	2.84±0.38	10	441± 90	14	342± 45	10	498±67	14	478±43
	f	15	3.05±0.33	13	2.79±0.42	15	438±112	13	360± 45	15	502±75	13	414±60
6–10	m	9	3.13±0.38	8	2.96±0.39	9	390± 71	8	355± 51	9	452±61	8	440±52
	f	7	3.00±0.35	9	2.94±0.42	7	400± 77	9	327± 45	7	506±69	9	433±54
11–15	m	4	3.12±0.33	5	2.98±0.41	4	379± 60	5	311± 50	4	491±64	5	398±62
	f	5	3.06±0.42	7	2.94±0.34	5	397± 80	7	372± 46	5	557±60	7	451±55
16–20	m	10	3.25±0.41	8	2.99±0.42	10	352± 59	8	333± 48	10	502±81	8	423±59
	f	7	3.10±0.47	6	2.96±0.36	7	384± 67	6	315± 51	7	527±75	6	429±62
21–30	m	18	3.26±0.49	9	2.89±0.44	18	352± 54	9	354± 51	18	507±65	9	443±53
	f	15	3.17±0.46	10	2.89±0.41	15	402± 57	10	331± 44	15	489±71	10	499±59
31–40	m	19	3.22±0.50	9	2.88±0.35	19	357± 57	9	332± 47	19	522±59	9	491±51
	f	17	3.13±0.44	6	2.85±0.29	17	390± 48	6	370± 47	17	504±74	6	512±48
41–50	m	13	3.16±0.54	11	2.81±0.38	13	355± 51	11	318± 36	13	507±66	11	489±59
	f	10	3.25±0.54	3	2.88±0.38	10	354± 49	3	308± 48	10	491±63	3	497±59
51–60	m	16	3.17±0.60	5	2.81±0.36	16	384± 63	5	351± 50	16	574±74	5	548±72
	f	6	3.23±0.59	1	2.77——	6	340± 72	1	315—	6	530±65	1	595—
61—	m	8	3.09±0.30	9	2.60±0.36	8	350± 55	9	344± 48	8	516±60	9	601±82
	f	4	2.96±0.30	—	—	4	355± 53	—	—	4	489±54	—	—
Adult average (21–50)	m	50	3.22±0.47	29	2.86±0.46	50	358± 49	29	334± 49	50	518±76	29	475±59
	f	42	3.25±0.37	19	2.88±0.39	42	385± 51	19	339± 42	42	495±60	19	502±64

Table 3. Statistical values (mean±S.D.) of cortical thickness, neuronal and glial cell density of area 4 and area 52 of Brodmann in each age group (right side)

Item / Area / Sex / Brain wt. (gm)		Cortical thickness (mm)				Relative total neuronal density(cells/$10^6\mu^3$)				Relative total glial density(cells/$10^6\mu^3$)			
		No.	Area 4	No.	Area 52	No.	Area 4	No.	Area 52	No.	Area 52	No.	Area 4
300—499	m	3	2.48±0.24	4	2.20±0.28	3	1069±129	4	945±120	3	528±75	4	740±92
	f	6	2.46±0.22	6	2.28±0.41	6	970±136	6	832±118	6	523±64	6	605±92
500— 699	m	3	2.63±0.25	5	2.38±0.30	3	800± 90	5	705± 93	3	685±82	5	593±72
	f	5	3.71±0.33	1	2.44± ——	5	797±101	1	650——	5	668±89	1	530——
700— 899	m	9	3.88±0.39	2	2.98±0.53	9	962± 69	2	569± 68	9	578±76	2	526±66
	f	9	3.95±0.36	9	2.65±0.39	9	556± 73	9	439± 51	9	568±75	9	483±52
900—1099	m	14	3.90±0.33	13	2.79±0.37	14	523± 60	13	404± 62	14	483±61	13	474±41
	f	12	3.95±0.42	15	2.87±0.36	12	437± 73	15	355± 49	12	499±60	15	410±62
1100—1199	m	12	3.10±0.49	13	2.98±0.41	12	401± 59	13	332± 48	12	509±80	13	430±51
	f	16	3.06±0.47	15	2.89±0.42	16	414± 64	15	349± 56	16	505±73	15	465±59
1200—1299	m	26	3.15±0.49	17	2.90±0.39	26	482± 53	17	351± 42	26	558±64	17	509±62
	f	19	3.20±0.47	6	2.84±0.33	19	375± 53	6	346± 47	19	512±71	6	488±52
1300—1399	m	18	3.32±0.51	16	2.84±0.34	18	364± 57	16	345± 38	18	508±60	16	512±48
	f	14	3.23±0.43	7	2.91±0.29	14	381± 48	7	333± 49	14	511±72	7	499±56
1400—1499	m	19	3.44±0.54	11	2.87±0.42	19	380± 51	11	320± 42	19	507±66	11	434±72
	f	6	3.47±0.54	4	2.95±0.35	6	348± 49	4	214± 44	6	551±75	4	423±68
1500—1599	m	7	3.10±0.60	6	2.96±0.36	7	399± 63	6	280± 31	7	501±73	6	395±40
	f	7	3.32±0.59	1	2.98± ——	7	395± 70	1	315——	7	545±70	1	465——
1600—	m	4	3.00±0.30	2	2.94±0.40	4	377± 52	2	365± 56	4	506±60	2	489±49
	f	—	——	—	——	—	——	——		—	——	—	——

Table 4. Statistical values (mean±S.D.) of cortical thickness, neuronal and glial cell density of area 4 and area 52 of Brodmann in each age group (left side)

Item / Area / Sex / Brain wt. (gm)		Cortical thickness (mm)				Relative total neuronal density(cells/$10^6\mu^3$)				Relative total glial density(cells/$10^6\mu^3$)			
		No.	Area 4	No.	Area 52	No.	Area 4	No.	Area 52	No.	Area 4	No.	Area 52
300—499	m	3	2.31±0.20	4	2.23±0.31	3	1011±109	4	970±141	3	502±71	4	785±08
	f	6	2.40±0.24	6	2.33±0.36	6	948±119	6	821± 98	6	542±73	6	657±82
500— 699	m	3	2.59±0.31	5	2.46±0.29	3	849±104	5	723±101	3	653±75	5	611±80
	f	5	2.67±0.29	1	2.43——	5	740± 95	1	605——	5	626±80	1	500—
700— 899	m	9	2.84±0.42	2	2.59±0.26	9	607± 80	2	538± 62	9	542±69	2	543±51
	f	9	2.90±0.39	9	2.60±0.28	9	537± 69	9	427± 58	9	539±71	9	465±59
900—1099	m	14	3.01±0.39	13	2.77±0.39	14	439± 64	13	393± 52	14	474±59	13	412±49
	f	12	3.90±0.43	15	2.83±0.39	12	430± 81	15	349± 53	12	467±61	15	432±58
1100—1199	m	12	3.18±0.40	13	2.97±0.40	12	399± 62	13	331± 41	12	501±74	13	407±58
	f	16	3.02±0.38	15	2.93±0.36	16	410± 59	15	360± 51	16	527±77	15	465±48
1200—1299	m	26	3.07±0.45	17	2.85±0.31	26	383± 60	17	331± 46	26	538±71	17	499±64
	f	19	3.26±0.45	6	2.81±0.39	19	360± 49	6	316± 48	19	504±64	6	459±53
1300—1399	m	18	3.20±0.45	16	2.89±0.32	18	376± 60	16	345± 50	18	546±69	16	533±69
	f	14	3.28±0.46	7	2.90±0.37	14	344± 42	7	318± 45	14	541±73	7	485±60
1400—1499	m	19	3.32±0.50	11	2.91±0.41	19	390± 60	11	333± 38	19	528±70	11	464±69
	f	6	3.48±0.55	4	2.96±0.41	6	363± 51	4	350± 51	6	537±70	4	455±68
1500—1599	m	7	3.09±0.52	6	2.93±0.36	7	420± 69	6	396 ± 42	7	529±79	6	440±53
	f	7	3.26±0.54	1	2.95——	7	370± 68	1	340——	7	511±64	1	500——
1600—	m	4	3.15±0.32	2	2.89±0.43	4	388± 50	2	345± 51	4	589±69	2	531±71
	f	—	——	—	——	—	——	—	——	—	——	--	——

Table 5. Brain weight groups of area 4 and area 52 between which statistically significant different values of relative total glial cell density were shown

Male	Right	Area 4 (gm)	Area 52 (gm)
		between 500—699 and 900—1099	
		between 700—899 and 900—1099 or 1100—1199	
	Left	Area 4 (gm)	Area 52 (gm)
		between 500—699 and 900—1099, 1100—1199, 1200—1299 1300—1399, 1400—1499, or 1500—1599	
		between 700—899 and 1100—1199, or 1500—1599	
		between 1100—1199 and 1500—1599	
		between 1200—1299 and 1500—1599	
Female	Right	Area 4 (gm)	Area 52 (gm)
		between 500—699 and 700—899, 900—1099, 1100—1199, or 1200—1299	
	Left	Area 4 (gm)	Area 52 (gm)
		between 500—699 and 700—899, 900—1099, 1100—1199, or 1400—1499	
		between 700—899 and 900—1099	

age group on the right side, significant difference was observed ($p<0.019$ in female and $p<0.014$ in male).

DISCUSSION

Our investigation of the cerebral cytoarchitectures for 20 years has triggered the studies on comparative cytoarchitectonics of various cortical areas of cerebral hemispheres (Kim and Seoung 1984).

Insula(island of Reil), which was compared to precentral gyral cortex (motor area) in this study, is an area of cortex buried in the depth of the lateral fissure (fissure of Sylvius) and can be seen only when the temporal and frontal lobes are separated. During fetal development, insula appears to have been bound to the underlying corpus striatum and exposed to outside. However, growth of the surrounding cortex would then produce the deep lateral fissure and insula is concealed by the regions such as the frontal, parietal and temporal opercula. Therefore, due to the functions of the surrounding cortices-mastication, swallowing, taste sense, auditory sense, vestibular sense and olfactory sense, it has been called "visceral interpretative cortex" (Livingston 1959) and thought to have no specific function of that area proper in man (Minckler 1972).

On the contrary, Yakovlev (1948) included insular area into the expanded limbic system together with mesopallidal, orbitofrontal and anterior temporal cortical areas. The relationship of the insula as a component of limbic lobe with the subcortical centers, orbital cortex, pyriform cortex, hypothalamus, brainstem reticular formation and nucleus anterioriores and nucleus medialis thalami may suggest that insula is involved particularly in the vegetative function and emotional expression. The connection of the insula with the brainstem reticular formation is thought to be related to the somatomotor func-

tion of the insular cotex.

It is possible that the change and atrophy of the samples caused by the preparation procedures-fixation, hardening, embedding and staining- may result in the inconsistancy of the assessment. However, we tried to minimize the errors of measurement by means of the standard condition which had been recognized as the most reasonable way from the previous studies.

In the present study, it was noted that the cortical thickness of area 52 was almost similar to that of area 4 which had been thought to be the thickest cortical area since Smith (1907). However, in spite of no statistically significant difference between the cortical thickness of the two areas, that of area 4 reached adult average value in 11-15 age group while that of area 52 in 6-10 age group.

Relative total neuronal densities of area 4 was always higher than that of area 52 when compared to the group with the same weight range while it was not so in the comparison of age groups. In both sexes, neuronal densities of 0-1 age group in area 4 showed significant difference in statistical values compared to that of each of the age groupsin area 52 and vice versa. This was probably from high neuronal density of 0-1 age group due to incomplete parcellation. In the precentral insular cortex in man, lamination started in the 6th fetal month (Seoung 1978). Glial cell density decreased between 0-1 and 6-10 age groups and then increased in both areas.

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= 국문초록 =

人大腦 中心前回와 島中心前回 各皮質峯部間의 比較細胞構築學 및 兩皮質의 加齡影響에 關한 硏究

이화大學校 醫科大學 放射線科學敎室 및 서울大學校 醫科大學 解剖學敎室*

徐廷守 · 李秉蘭* · 成耆晙*

正常 人大腦 209例(男性 115例, 女性 94例)의 大腦半球 418側에서 얻은 中心前回 回峯部皮質(Brodmann 第4分野)과, 153例(男性 89例, 女性 64例)의 大腦半球 306側에서 얻은 島中心前回의 回峯部皮質(Brodmann 第52分野)間의 細胞構築相을 比較하고 加齡 및 腦重增加에 의한 影響을 追究하여 다음과 같은 결과를 얻었다.

1. 皮質厚徑에서는 第4分野値와 第52分野値間 全年齡群 全腦重群 比較에서 差異가 없었다.
2. 相對的 總神經細胞密度는 第四分野値가 높았으나 兩分野의 總計値間 有意한 分布差는 第4分野의 0—1歲群과 第52分野의 각 年齡群間 및 第4分野의 300—899 gm群과 第52分野의 각 腦重群値間에서만 보였다. 同等年齡間 및 同等腦重間에서는 有意한 分布差가 없었다.
3. 相對的 總膠質細胞密度는 第4分野의 0—1歲群値와 第52分野의 수개의 年齡群値間 및 兩分野의 수개의 腦重群値間에서 有意한 分布差가 있었다.
4. 男性,女性 및 左右側値間 差가 加齡에 미치는 影響은 없는 것으로 생각되었다.