Regional Brain Volume and Luteinizing Hormone in Girls with Idiopathic Central Precocious Puberty

Eun Young Kim, MD[1], Shin Eui Park[2]
[1]Department of Pediatrics, Chosun University College of Medicine, Gwangju, Republic of Korea
[2]Interdisciplinary Program of Biomedical Engineering, Chonnam National University, Gwangju, Republic of Korea

Abstract

Background: During puberty, gray matter volume decreases and white matter volume increases in brain. It has been suggested that pubertal hormones may induce some neuroanatomical changes during puberty. Central precocious puberty (CPP) is caused by premature activation of the hypothalamus-pituitary-gonadal axis in inappropriately early age. However, little is known about the differences of brain structure (especially brain volume) in idiopathic CPP. Also the relation between luteinizing hormone (LH) and brain morphology in CPP remains unclear.

Objective and hypotheses: This study aimed to evaluate the difference of brain structure in idiopathic CPP, age-matched healthy control, and the normal puberty girls, and the association between LH and brain structure.

Method: The study enrolled fifteen girls with idiopathic CPP, 15 age-matched healthy girls and 15 normal puberty girls as controls. The subjects underwent on a 1.5 Tesla Avanto MR Scanner. Anatomical T1-weighted images were acquired with a T1 spin echo sequence. MR image data were processed by using SPM8 with DARTEL algorithm.

Results: The mean age of CPP, age-matched group and puberty group were 8.0±0.9 year, 7.8±0.9 year and 11.9±0.9 year. Compared with controls, CPP showed a significant increase in gray matter (GM) volume of the left cerebellar cortex, and in white matter (WM) volume; the left superior temporal lobule (STL), right middle temporal pole (MTP) and left lingual gyrus (LiG) (p<0.001). Especially, the WM volume of the STL (r=0.56), MTP (r=0.56) and LiG (r=0.57) was positively correlated with LH concentrations (p<0.05).

Conclusion: Regional GM and WM volumes were increased in girls with idiopathic CPP compared with age-matched and pubertal controls. The growth of white matter might be directly or indirectly mediated by LH production in idiopathic CPP. These data suggest that the presence of early sexual maturation-related variations in structure of developing brain of girls with idiopathic CPP.

Purpose

Puberty is the important period during development in which major physical, psychological and complex social skills occur. It has been suggested that pubertal hormones may induce some neuroanatomical changes during adolescence.

Central precocious puberty (CPP) is caused by premature activation of the hypothalamo-pituitary-gonadal axis in inappropriately early age (before 8 ages in girls and 9 ages in boys). In adolescents with early pubertal timing, there is a tendency of severe emotional problems and antisocial behavior. Psychosocial changes may be related to cerebral development, including widespread changes in brain morphology.

However, little is known about brain structure (especially brain volume) in idiopathic CPP. Therefore, this study aimed to evaluate the difference of brain structure in idiopathic CPP, age-matched healthy control, and the normal puberty girls, and the association between LH and brain structure.

Subjects and Methods

The study enrolled fifteen girls with idiopathic CPP, 15 age-matched healthy girls and 15 normal puberty girls as controls.

The subjects underwent on a 1.5 Tesla Avanto MR Scanner (Siemens Medical Solutions, Erlangen, Germany). Anatomical T1-weighted images were acquired with a T1 spin echo sequence.

MR image data were processed by using SPM8 software (Statistical Parametric Mapping 8, The Welcome Department of Cognitive Neurology, University College London, U.K.) with Diffeomorphic Anatomical Registration through Exponentiated Lie Algebra (DARTEL) algorithm. Regional measures of gray matter and white matter concentration (density) were evaluated using voxel-based morphology.

Results

The mean age of CPP, age-matched group and puberty group were 8.0±0.9 year, 7.8±0.9 year and 11.9±0.9 year.

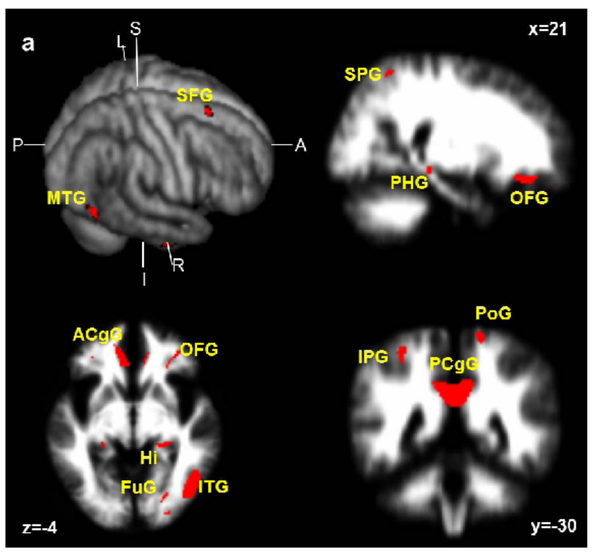

Fig. 1. Brain areas with an significant increase in gray matter (a) and white matter (b) volumes in female patients with precocious puberty as contrast to normal puberty controls (uncorrected; p<0.001, excluded 100 voxels). Hi, hippocampus; PHG, parahippocampal gyrus PCgG, posterior cingulate gyrus; ACgG anterior cingulate gyrus; PoG, Postcentral gyrus; PCC, posterior corpus callosum; OFG, orbitofrontal gyrus; ITG inferior temporal gyrus; FuG, fusiform gyrus; IPG, inferior parietal gyrus; MTG, middle temporal gyrus; SFG, superior frontal gyrus.

Table 1. Brain regions with an significant increased in gray matter volumes in female patients with precocious puberty over normal puberty controls (uncorrected; p<0.001, excluded 100 voxels)

Brain area	Anatomical area	Abbr.	Side	MNI coordinate x	y	z	t-value	Cluster size (voxels)
Frontal lobe	Orbitofrontal gyrus	OFG	L	23	29	-12	6.91	550
	Superior frontal gyrus	SFG	R	15	15	51	5.09	145
Temporal lobe	Middle temporal gyrus	MTG	R	51	-31	-12	5.69	1109
	Inferior temporal gyrus	ITG	R	42	-60	-5	5.75	1145
	Inferior temporal gyrus	ITG	L	-51	-18	-23	6.04	688
	Fusiform gyrus	FuG	R	26	-73	-6	5.04	179
Parietal lobe	Superior parietal gyrus	SPG	L	-29	-42	49	5.56	167
	Inferior parietal gyrus	IPG	R	24	-52	48	6.37	186
	Inferior parietal gyrus	IPG	L	-45	-24	36	5.27	316
	Supramarginal gyrus	SMG	L	51	-25	34	3.95	149
	Postcentral gyrus	PoG	R	42	-24	40	4.34	149
Limbic lobe	Hippocampus	Hi	R	24	-30	-5	4.27	236
	Parahippocampal gyrus	PHG	L	-21	-31	-11	4.09	761
	Anterior cingulate gyrus	ACgG	L	-12	36	-5	5.77	514
	Posterior cingulate gyrus	PCgG	L	-9	-43	25	6.87	1929

Table 2. Brain regions with an significant differential in white matter volumes between female patients with precocious puberty and normal puberty controls (uncorrected; p<0.001, excluded 100 voxels)

Brain area	Anatomical area	Abbr.	Side	MNI coordinate x	y	z	t-value	Cluster size (voxels)
precocious puberty								
Diencephalon	Posterior corpus callosum	PCC	R	15	-30	19	4.20	160
	Posterior corpus callosum	PCC	L	-15	-34	18	4.65	194
Puberty								
Limbic lobe	Posterior cingulate gyrus	PCgG	L	-3	-43	21	4.60	172

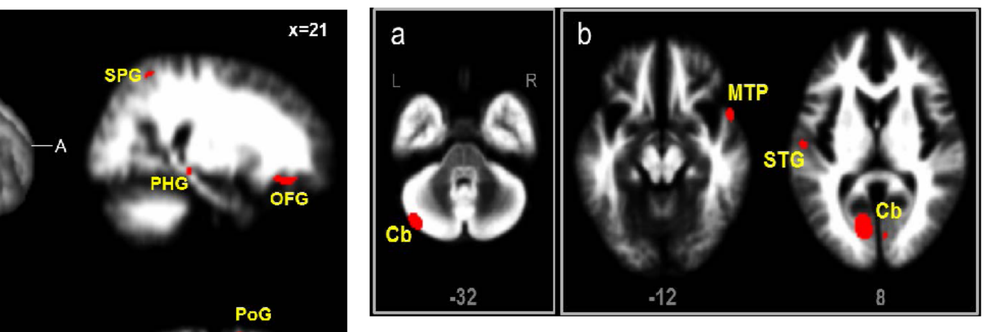

Fig. 2. Brain areas with an significant increase in gray matter (a) and white matter (b) volumes in female patients with precocious puberty as contrast to age matched and normal puberty controls (uncorrected; p<0.001, excluded 100 voxels). Statistical tests between groups were performed using ANOVA analysis; covariated for age. MTP, middle temporal pole; STG, superior temporal gyrus; Cb, cerebellar cortex.

Table 3. Brain regions with an significant increased in gray matter in gray matter (a) and white matter (b) volumes in female patients with precocious puberty as contrast to age matched and normal puberty controls (ANOVA analysis; covariated for age, uncorrected; p<0.001, excluded 100 voxels)

Anatomical area	Abbr.	Side	MNI coordinate x	y	z	t-value	Cluster size (voxels)
gray matter							
Cerebellar cortex	Cb	L	-36	-72	-30	4.57	2382
white matter							
superior temporal gyrus	STG	L	-54	-10	3	5.14	836
middle temporal pole	MTP	R	54	9	-18	3.81	125
Cerebellar cortex	Cb	L	-9	-70	6	5.78	905

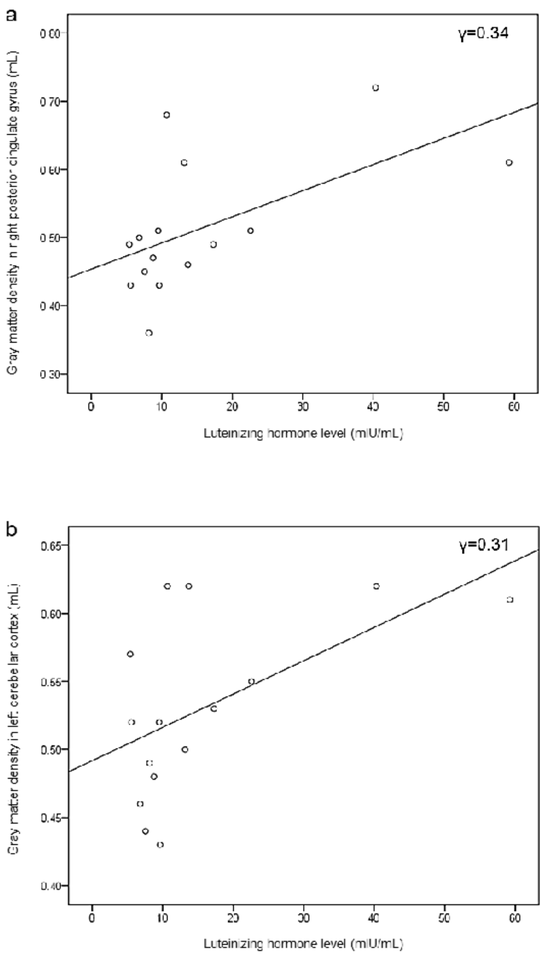

Fig. 3. Scatterplot of correlation between peak LH level and increased gray matter; posterior cingulate gyrus (MNI x,y and z coordinates 3,-48 and 21) (a) and cerebellar cortex (-23,-69,-47) (b) in female patients with precocious puberty. The each correlation coefficients (pearson's correlation) are 0.57 (p<0.03) and 0.53 (p<0.04) in post cingulate gyrus and cerebellar cortex.

Summary

Compared with controls, CPP showed a significant increase in gray matter (GM) volume of the left cerebellar cortex, and in white matter (WM) volume; the left superior temporal lobule (STL), right middle temporal pole (MTP) and left lingual gyrus (LiG) (p<0.001).

Especially, the WM volume of the STL (r=0.56), MTP (r=0.56) and LiG (r=0.57) was positively correlated with LH concentrations (p<0.05).

Conclusion

Regional GM and WM volumes were increased in girls with idiopathic CPP compared with age-matched and pubertal controls.

The growth of white matter might be directly or indirectly mediated by LH production in idiopathic CPP.

These data suggest that the presence of early sexual maturation-related variations in structure of developing brain of girls with idiopathic CPP.

ESPE 2015
531--P2
Puberty and Neuroendocrinology
Eun Young Kim
DOI: 10.3252/pso.eu.54espe.2015
Poster presented at: 54th Annual Meeting 1-3 October ESPE 2015 BARCELONA European Society for Paediatric Endocrinology