

정신분열병 환자의 혈청에서

Brain-Derived Neurotrophic Factor 증가

김소연* · 민경준*[†] · 기백석* · 박두병* · 김주희*

Serum Brain-Derived Neurotrophic Factor in Schizophrenia

So Youn Kim, M.D.,* Kyung Joon Min, M.D., Ph.D.,*[†] Baik Seok Kee, M.D., Ph.D.,*
Doo Byung Park, M.D., Ph.D.,* Joo Hee Kim, M.D.***ABSTRACT**

Objectives : Abnormalities in neurotrophic factors that regulate neuronal development and synaptic plasticity are often implicated as some causes of schizophrenia. In previous studies, researchers reported that brain and serum BDNF levels underwent similar changes during maturation and aging processes in rats. They also found a positive correlation between serum and cortical BDNF levels. In this study, we investigated whether the serum levels of BDNF in Korean schizophrenic patients would be different from those of healthy controls.

Methods : Using an ELISA kit, serum BDNF levels were assessed in schizophrenic group(N=49) and control group(N=50).

Results : Serum BDNF levels in the schizophrenic group(36.29 ± 19.78 ng/ml) were significantly higher than those in control group(22.4 ± 14.4 ng/ml). The BDNF levels did not correlate with duration of treatment, age or daily dose of antipsychotics in patients with schizophrenia.

Conclusions : This result suggests that schizophrenia is characterized by high serum BDNF levels and supports the hypothesis of neurotrophic factor involvement in psychotic disorder. Serum BDNF level is likely to be one of the possible biological markers for schizophrenia.

KEY WORDS : BDNF · Schizophrenia · Neurotrophin.

서 론

1%

가

가

* Department of Psychiatry, College of Medicine, Chung-Ang University, Seoul, Korea
[†]교신저자 : , 100 - 727 2가 82 - 1
) (02) 2260 - 2282,) (02) 6263 - 1321 E - mail) mind61@chollian.net

1) 50% 가 가 , Karage , Toyooka 가 .
 2) 3) 4) neurotrophin 가 , BDNF
 5) 6) 가 .
 BDNF
 cyto- BDNF
 kine 가 , cytokine 가 BDNF BDNF
 가 BDNF 가

7) brain derived neurotrophic factor(BDNF) neurotrophic factor가
 9) BDNF ne- urotrophic factor nerve growth factor(NGF), glial cell derived neurotrophic factor(GDNF), ciliary neurotrophic factor(CNF) 가

8)9) Takahashi 10) BDNF neurotrophin - 3 cor- ticolimbic region 가 , BD- NF receptor(Trk B) . Durany 11) neurotrophin - 3 BDNF neurotrophin 가 .

rage 12) BDNF Ka- BDNF BDNF 가 가 BDNF 가 가 BDNF 가 가 BDNF 가 가 Toyooka 7)14) BDNF 가 BDNF BDNF

연구대상 및 방법

1. 연구대상

2002 4 2003 2 18 DSM - (American Psychiatric Association, 1994)

2. 연구방법

1) 임상 변인

chlorpromazine 100mg

2) BDNF 측정

(5cc) 가 가 1 가 가 4 1 (2000 x g x 10min at 4) -20 ELISA kit(BD-

NF Emax Immunoassay System, Promega, Madison, WI, USA) BDNF . BD-
 NF Emax immunoassay system BDNF ANCOVA(analysis of covariance)
 , 가 98 BDNF
 well plate 10 µl anti - BDNF mAb 9.99ml 가 ANCOVA
 carbonate coating .
 . coating BDNF Pearson 's correlation
 96 well 42.4ml deionized water 10.6ml . SPSS version 11.0
 block sample .

가 . **결 과**
 2

5 . anti - Human BDNF pAb 20 µl 1. 사회 인구학적 특성
 9.98ml , , , ,
 2 . anti - IgY HRP , ,
 conjugate 50 µl 9.95ml 28.61 ± 7.02 25.02 ±
 . 1 incubation 2.94 ($\chi^2=3.331$, df=
 5 . TMB One solution 97, p=0.01), 13.04 ± 1.96
 , well 100 µl 가 , 14.04 ± 1.74
 . 10 well ($\chi^2 = -2.687$, df=97, p=0.08) . ,
 100 µl 1N hydrochloric acid 가 ,
 . 30 A450 . (1).

3. 통계방법 2. 혈청 BDNF level
 BDNF level 36.19 ±
 , t - test 19.78ng/ml, 22.40 ± 14.40ng/ml
 , , , , (F=13.896, p=0.001, $\chi^2=$

Table 1. Demographic characteristics

		Schizophrenia(N=49)	Control(N=50)	p
Age(year)*	Mean ±SD	28.61 ± 7.02	25.02 ± 2.94	0.001
Duration of education(year)*	Mean ±SD	13.04 ± 1.96	14.04 ± 1.74	0.008
Sex(%) [†]	Male	20(40.8)	20(40.0)	0.934
	Female	29(59.2)	30(60)	
Religion(%) [†]	Yes	8(16.3)	7(14)	0.948
	No	41(83.7)	43(86)	
Marital state(%) [†]	Single	10(20.4)	9(18)	0.747
	Married	10(20.4)	11(22)	
	Others	29(59.2)	30(60)	
Economic state(%) [†]	Upper	8(16.3)	10(20)	0.892
	Middle	31(63.3)	30(60)	
	Low	10(20.4)	10(20)	

* : t-test, † : χ^2 -test

Table 2. Serum BDNF level in schizophrenia and normal control

	Schizophrenia		Normal		F	p	²
	N	BDNF level(ng/ml)	N	BDNF level(ng/ml)			
Total	49	36.29 ± 19.78	50	22.40 ± 14.40	13.896	0.001	0.128
Male	20	31.29 ± 19.78	20	24.80 ± 16.10	0.361	0.55	0.010
Female	29	39.51 ± 19.98	30	20.80 ± 13.20	24.554	0.001	0.309

ANCOVA, covariate : age, education

Table 3. Pearson's correlation between age, daily dose of antipsychotics, treatment duration and BDNF level in schizophrenia

	Correlation coefficient
Age(year)	0.036
Daily dose of antipsychotics*	0.227
Treatment duration(year)	0.201

* : mg of CPZ equivalent dose
no significance

0.128).
(F=0.972, p=0.30, ²=0.010) (F=1.065, p=0.305, ²=0.011) 가 (2).
(31.29 ± 19.78ng/ml)가
(24.80 ± 16.10ng/ml)
(F=0.361, p=0.55, ²=0.010),
(39.51 ± 19.98ng/ml)가 (20.80 ± 13.20
ng/ml) (F=24.554, p=0.001, ²=0.309)
(2).

3. 환자군에서 임상 변인과 BDNF level의 상관관계

BDNF
가 (3).

고 찰

BDNF 27kDa
, ,
,
,
9)
BDNF - gene knockout mice
(mutant mice)
BDNF

BDNF
BDNF
BDNF가 (marker)가
15)
16)17)
18)
19)
amyotrophic lateral sclerosis
alzheimer disease¹⁹⁻²¹⁾
BDNF가
BDNF
99%가 가
22)23)
BDNF
BDNF가 - 가 ,¹²⁾
BDNF 가 BDNF
BDNF BDNF
BDNF 가 가
BDNF 가 가
BDNF가
corticolimbic region 가
¹¹⁾
hippocampus BDNF 가
BDNF TrkB
corticolimbic area
¹⁰⁾
neurotrophic abnormality가
corticolimbic structure 가
8)

BDNF 가 immunoassay BDNF 가 , 가

가 60% , 가

가 (28.45 ± 5.79year) (28.85 ± 8.66 year)

Karage BDNF 가 , 가

¹¹⁾ Karage BDNF 가 , 가

가 BDNF 가 가 BDNF 가

BDNF 가 Tayooka 가 BDNF 가

BDNF BDNF

Toyooka ¹⁴⁾ BDNF 가 가 BDNF 가 BDNF

Toyooka BDNF 가 가 가 가 BDNF

가 가 가 가

가

Toyooka operidol BDNF 5 hal- , Karage

가 BDNF 가 ,

가 10 , 20 가 가 30 , 40

BDNF level

BDNF 가 가

chloropormazine 100mg , 가 20 30

957.14 ± 225.46mg 가

BDNF

Toyooka 가 ,

case ,

가

BDNF 가

결론

BDNF가 .
BDNF가
BDNF
BDNF가
가 , BDNF가
BDNF가
, BDNF
biologic marker
, biologic
marker 가 BD-
NF 가 ,

중심 단어 : BDNF .

참고문헌

- Gottesman II, Shields JA. Critical review of recent adoption twin, and family study of schizophrenia: Behavior genetics perspectives. *Schizophrenia Bulletin* 1976;2: 360-401.
- Mortensen PB, Pedersen CB, Westergaard T, Wohlfahrt J, Ewald H, Mors O, et al. Effects of family history and place and season of birth on the risk of schizophrenia. *New England J of Medicine* 1999;340:603-608.
- McNeil TF. Perinatal risk factors and schizophrenia: selective review and methodological concerns. *Epidemiology Review* 1995;17:107-112.
- O'Callaghan E, Sham P, Takei N, Glover G, Murray RM. Schizophrenia after prenatal exposure to 1957 A2 influenza epidemic. *Lancet* 1991;25:1248-1250.
- Susser E, Neugebauer R, Hoek HW, Brown AS, Lin S, Labovitz D. Schizophrenia after prenatal famine. *Arch Genetics Psychiatry* 1996;53:25-31.
- Pulver AE, Sawyer JW, Childs B. The association between season of birth and the risk for schizophrenia. *American Journal of Epidemiology* 1981;114:735-749.
- Lindsay RM, Wiegand SJ, Altar CA, Distefano S. Neurotrophic factors: from molecule to man. *Trends in Neurosciences* 1994;17:182-189.
- Bersani G. Low nerve growth factor plasma levels in schizophrenic patients. *Schizophrenia Research* 1999;37: 197-203.
- Radka SF, Holst PA. Presence of BDNF in brain and human and rat but not mouse serum detected by a sensitive and specific immunoassay. *Brain Research* 1996; 709:122-301.
- Takahashi M, Shirakawa O, Toyooka K, Kitamura N, Hashimoto T, Maeda K, et al. Abnormal expression of BDNF and its receptor in the corticolimbic system of schizophrenic patients. *Molecular Psychiatry* 2000;5: 293-300.
- Durany N, Michel T, Zochling R, Boissl KW, Cruz-Sanchez FF, Riederer P, et al. Brain-derived neurotrophic factor and neurotrophin-3 in schizophrenic psychoses. *Schizophrenia Research* 2001;9:79-86.
- Karege F, Schwald M, Cisse M. Postnatal developmental profile of brain-derived neurotrophic factor in rat brain and platelets. *Neuroscience Letter* 2002;328:261-264.
- Pan W, Banks WA, Fasold MB, Bluth J, Kastin AJ. Transport of brain-derived neurotrophic factor across the blood-brain barrier. *Neuropharmacology* 1998;37: 1553-1561.
- Toyooka K, Nawa H, Takahashi M. Decreased levels of brain-derived neurotrophic factor in serum of chronic schizophrenic patients. *Psychiatry Research* 2002;110: 249-257.
- MacQueen FM, Ramakrishnan K, Croll SD, Siuciak JA, Yu G, Young LT, et al. Performance of heterozygous brain-derived neurotrophic factor knockout mice on behavior analogues of anxiety, nociception, and depression. *Behavior Neuroscience* 2001;115:1145-1153.
- Chen B, Dowlatshahi D, MacQueen GM, Wang KF, Young L. Increased hippocampal BDNF immunoreactivity in subjects treated with antidepressant medication. *Biological Psychiatry* 2001;50:260-265.
- Nibuya M, Morinobu S, Duman RS. Regulation of BDNF and trkB mRNA in rat brain by chronic electroconvulsive seizure and antidepressant drug treatment. *Journal of Neuroscience* 1995;15:7539-7547.
- Nelson KB, Grether JK, Croen LA, Dambrosia M, Dickens BF, Jelliffe L, et al. Neuropeptides and neurotrophins in neonatal blood of children with autism or mental retardation. *Annals of Neurology* 2001;49:597-606.
- Connor B, Young D, Yan Q, Faull RLM, Synek B, Dragunow M. BDNF is reduced in Alzheimer's disease. *Molecular Brain Research* 1997;49:71-81.
- Durany N, Michel T, Zochling R, Cruz-Sanchez FF, Cervas-Navarro J, Riederer P. BDNF and neurotrophin-3 levels in Alzheimer's disease brains. *International Journal of Developmental Neuroscience* 2003;18:807-813.
- Yamamoto H, Gurney ME. Human platelet contain brain-derived neurotrophic factor. *Journal of Neuroscience* 1990;10:3469-3478.
- Serrano T, Lorigados LC, Armenteros S. Nerve growth factor levels in normal human sera. *Neuroreport* 1996;8: 179-181.
- Shibayama E, Koizumi H. Cellular location of the Trk neurotrophin receptor family in human non-neuronal tissues. *American Journal of Pathology* 1996;148:1807-1818.