



Role of Homocysteine in the Post-stroke Depression

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Background : The risk of depression after stroke is influenced by various factors such as age, severity of disability, the location of the brain lesion, etc. We examined whether plasma homocysteine and MTHFR genotypes are associated with depression after stroke. **Methods** : 173 patients with cerebral infarction whose Barthel 's index improved over 90 points were included. Beck Depression Inventory (BDI) was used to evaluate depression, and the patients were divided into two: depression (DG) and non-depression (NDG) groups according to their BDI score (cut off=21). We then analyzed factors, including plasma homocysteine and MTHFR genotype. **Results** : The DG was 49 patients (28.3%) and the NDG were 124 patients (71.7%). The genotype distribution consisted of 22.4%(CC), 57.2%(CT), 20.4%(TT) in DG and 27.4%(CC), 55.5%(CT), 16.1%(TT) in NDG, the frequency of which was not different from that in DG. Age, sex, lesion location (left/right/bilateral , anterior/posterior/lenticulo-striatal/ multiple), an interval from the stroke onset to the evaluation, the presence of diabetes mellitus, hypertension, hyperlipidemia, cardiac disease, and family history were not different between the two groups. The plasma homocysteine level was significantly higher in DG (14.70 $\mu\text{mol/L}$) than NDG (11.51 $\mu\text{mol/L}$) (OR 1.094;95% CI 1.013-1.180) after controlling of the factors described above. **Conclusions** : Our results suggest that homocysteine may play a role in the pathogenesis of post-stroke depression and support a vascular depression theory. Early identification of this risk factor may lead to effective therapeutic intervention.

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Key Words : Depression, Stroke, Homocysteine, MTHFR gene

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351 463-712

가 [1]
12 ~ 65% [2, 6],

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[1, 4].

2.

[7] 가

[8] 가

가 가 Beck Depression Inventory(BDI)[15] 21 (depression group : DG), (non-depression group : NDG)

가

140 mmHg

가

90 mmHg

[9]

가

240 mg/dℓ

200 mg/dℓ

[10].

24

[11].

(severe cardiac risk factor)

가

vascular depression theory

[12,13]

MTH

TT

[14]

가

magnetic resonance imaging(MRI), MRI (1.5T, Siemens) T2-weighted spin echo (TR/TE = 3700/90 ms), T1 weighted spin echo (TR/TE = 560/14 ms), Proton (TR/TE = 3700/22 ms), FLAIR (TR/TE = 9000/105 ms, inversion time 2500 ms)

MRI T2 FLAIR (fluid attenuated inversion recovery) (high signal)

T1 (low signal)

5 mm

가

1.

2001 9

2002 5

[16]

(lenticulostriate artery)

가

가 90

가

Barthel's index

B12

8

가

(trisodium) EDTA가

(vacutainer tube)

2,000 rpm 5

-20

()

Laboratories)

IMx Kit(Abbott

(FPIA:

Table 1. Depression according to the clinical profile

	DG (n=49)	NDG (n=124)	P value
Sex			0.078
Male:Female	26:23	82:42	
Mean age(y-o)	63.4	59.5	0.028
Time interval*	17.2	16.4	0.206
Family history of stroke	22.5%	15.3%	
Past history of stroke	8.2%	4.0%	
Stroke risk factor			
Hypertension	81.6%	75.8%	0.27
Diabetes mellitus	20.4%	22.6%	0.464
Hyperlipidemia	20.4%	11.3%	0.096
Heart disease	4.1%	3.2%	0.546

* time interval: time intervals between stroke onset to test(months)

fluorescence polarization immunoassay)

(folate) B12 ACS: 180 Barthel's index가 90
(Bayer) (competitive) 173 , 49
immunoassay) 28.3%
MTHFR DG 26:23, NDG 82:42 NDG
DNA DNA (extraction col- , BDI
umn, QIAmp blood kit, Qiagen) , DG, NDG가 63.4 , 59.5
DNA (primer set) 가 (p<0.05). , , ,
sense primer(5'-TGAAGGAGAAGGTGTC- DG 81.6%, 20.4%, 20.4%,
TGCGGGA-3') antisense primer(5' - 4.1% , NDG 75.8%, 22.6%, 11.3%,
AGGACGGTGCGGTGAGAGAGTC-3) 3.2% ,
GeneAmp PCR machine (Perkin Elmer 9600) 가
198bp 95 DG, NDG 8.2%,
60 62 90 4.0% , 가 22.5%,
(annealing) 72 60 15.3% , 가 DG
35
MTHFR 677C T BDI DG, NDG가
Hinfl(10unit/reaction mixture) 17.2 , 16.4
37 3~4 A(Ala) (Table 1).
(allele) 198 bp Hinfl MRI
V (Val) , , , 가 DG
Hinfl 175 bp 23 bp 7 (14.3%), 13 (26.5%), 29 (59.2%) ,
3.0% agarose gel NDG 31 (25.0%), 27 (21.8%), 66 (53.2%)
ethidium bromide , , ,
two-sample DG 6 (12.2%), 32 (65.3%), 6
t-test, chi-square test , 가 (12.2%), 5 (10.2%) , NDG 24
multiple logistic regression model stepwise mut (19.4%), 70 (56.5%), 17 (13.7%), 13
(10.5%)
0.05 ,
SAS 8.0 (Table 2).
B12,

Table 2. Depression according to the location of stroke

	DG n(%)	NDG n(%)	P value
Laterality			0.300
Left	7(14.3)	31(25.0)	
Right	13(26.5)	27(21.8)	
Bilateral	29(59.2)	66(53.2)	
A-P axis			0.671
Anterior	6(12.2)	24(19.4)	
Posterior	32(65.3)	70(56.5)	
Lenticulostriatal	6(12.2)	17(13.7)	
Multiple	5(10.2)	13(10.5)	

Table 3. Depression according to MTHFR type and serologic test

	DG n(%)	NDG n(%)	P value
MTHFR type			0.747
CC	11(22.4)	34(27.4)	
CT	28(57.1)	69(55.6)	
TT	10(20.4)	21(16.9)	
Serologic test			
Folic acid	13.22	10.43	0.073
Vitamin B12	619.26	598.66	0.143
Homocysteine	14.70	11.51	0.002

DG 13.22 ng/mL, 619.26 pg/mL, 14.70 μmol/L, NDG 10.43 ng/mL, 598.66 pg/mL, 11.51 μmol/L

가 [22],

DG MTHFR CC, CT, TT (p<0.05).
 , DG 11 (22.4%), 28 (57.2%), 10 (20.4%), NDG 34 (27.5%), 69 (55.6%), 21 (16.9%)

가 [2-6].

TT (Table 3).

12 ~ 65%

Barthel's index가 90

multiple logistic regression model

21

(p<0.05)(Table 4).

가

가

[9,16].

가 [17].

가 [3,21].

가 [7,18],

가 ,

가

가 [19].

[22].

Table 4. Factor analysis by multiple logistic regression model

Variables	Parameter estimate	Standard error	P value
Age	0.0411	0.0210	0.0505
Sex	0.2622	0.4606	0.5691
Time interval	0.00295	0.00889	0.7401
Laterality+	1.1414	0.6724	0.0896
A-P axis+	0.4411	1.1284	0.9926
DM	-0.6050	0.5301	0.2538
Heart disease	0.5633	0.9931	0.5706
Hyperlipidemia	0.9584	0.5633	0.0889
Hypertension	0.1843	0.5182	0.7221
Vit B12	0.000234	0.000445	0.5998
Folate	0.0169	0.0294	0.5649
Homocysteine*	0.0894	0.0389	0.0214
MTHFR type+	0.3242	0.4941	0.5117

+ : dummy variables

* : p<0.05

meta-analysis [23], [29], [30].

가

가 [3,16].

가 [24], [22,25].

가 [27], [23,31,32].

가 [16,33].

가 [26], [34,35], [36].

가 [3,27], [28].

가 63.4 59.5 hydroxy indoleacetic acid(5HIAA)가 [37], [38]

가 [23] 143 meta-analysis, Carso

vitamin B12
 adnosylmethionine(SAM) 가
 [39-41]. SAM
 monoamine
 , SAM
 [39,42].
 , SAM
 [43].
 MTFHR TT 가 [14].
 MTHFR TT MTHFR 가
 SAM
 (unipolar depression), bipolar disorder TT
 MTHFR TT
 20.4% , 16.9%
 가
 , SAM monoamine
 가
 SAM
 spectrum
 vascular depression theory

[44,46],
 MRI
 가
 가 , 가 ,
 [46,47].
 가 가 [48].
 가
 가
 spectrum
 가
 가
 SAM
 [43].

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