

우울증의 신경생물학

Neurobiology of Depression

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Yong Ku Kim, M.D.

Department of Psychiatry

Korea University College of Medicine, Ansan Hospital

E - mail : yongku@korea.ac.kr

Abstract

Depression is a heterogeneous group of syndromes comprised of numerous diseases of distinct causes and pathophysiologies. Recently, several promising hypotheses of depression and antidepressant action have been formulated. These hypotheses are largely based on dysregulation of neural plasticity, CREB, BDNF, corticotropin - releasing factor, glucocorticoid, hypothalamic-pituitary-adrenal axis and cytokines. Recent work has revealed that several brain regions such as hippocampus, prefrontal cortex, amygdala, nucleus accumbens, and other hypothalamic nuclei are involved in the neural circuit of depression. The brain regions are critical in regulating memory, mood, motivation, sleep, eating, circadian rhythm and responses to rewarding and adverse stimuli, which are all abnormal in depressed patients. The neurobiological understanding of depression will fundamentally improve the treatment and prevention of that illness.

Keywords : Depression; Neurobiology; Monoamine; Cytokine; CRF; CRH

: ; ; 가 ; ;

(melan-
cholia) (black bile)

400

가

가

20

가

가

가

가

가

(external stress)

(internal stress)

psychosocial

biological

(neurogenesis)

corticotropin releasing factor(CRF)

CRF

(structural plasticity)

(neuronal adaptation)

rine ; NE) .

가 5 - HT NE

,

5 - HT NE

, 5 - HT

NE

가 5 - HT

가 , NE

가 5 - HT

가 NE

5 -

HT NE

,

가

가 3 4

가

가 (monoamine receptor sensitivity hypothesis)(2)

, 가 가

가

reserpine 1950 가

15% , 가

(down - regulation)

reserpine 가 , (up - regulation)

가

가 가 (monoamine depletion hypothesis)(1) . 가

(se- HT2A

rotonin ; 5 - HT) (norepineph- 가

가 AR

5 -

가

가 AR

5 - HT2A	CREB and BDNF
가	가 (molecular and cellular
AR 5 - HT2A	theory)(7)
AR	가
가 ,	가
AR 가	가
AR	,
가	.
가	.
가 5 - HT2A	,
가	.
5 - HT1A 가 Blier	.
deMontigny(3) 가	.
somatodendritic 5 - HT1A 가	가 neurotrophic factor
가 ,	가 가
presynaptic 5 - HT1A	
. SSRIs 5 - HT	
presynaptic 5 - HT1A (adap-	cyclic adeno-
tive desensitization) 5 - HT	sine monophosphate(cAMP) neu-
가 가	rotrophic factor 가 .
dorsal raphe 5 - HT1A	[
, 5 - HT 가	cyclic adenosine monophosphate response element-
(4). 5 - HT1A	binding protein(CREB)]. CREB
pindolol SSRIs	, BDNF(brain - derived neu-
(5)가	rotrophic factor) TrkB(transmembrane receptor
(6) pindolol	protein tyrosine kinase B) (target
.	gene)
pindolol	(target neuron)
.	가 가 .

가, NE 5-HT 가, GABA/benzodiazepine (10). CRF CRF 가, - - CRF (paraventricular nucleus) CRF CRF mRNA 가, 가 CRF (adrenocorticotropin hormone, ACTH) 가

가 (8). CRF

Corticotropin Releasing Factor(CRF)

CRF CRF PVN (parvocellular division) (brain stem) CRF bed nucleus stria terminalis(BNST) CRF 가 [(locus coeruleus), (parabrachial nucleus), (raphe nucleus)] CRF (immunoreactivity) (phenotype) (9). 가 (early maternal separation) (maternal deprivation) (11). CRF가 CRF receptor 1(CRF - R1) CRF receptor 2(CRF - R2)가

CRF - R1 (free cortisol)
, CRF - R2 (dexamethasone test)
가
(12).
CRF 가
(13), CRF - R1 , ,
, (explicit process) 3 (MRI) (16).
, CRF - R2
(implicit process), , 가 ,
(11). CRF - R1
CRF ACTH 가 가
CRF - R1
(antagonist) 가 , 가 (corticosteroid
CRF - R2 receptor hypothesis)(17) 가
(14) .
(Glucocorticoid) mifepristone(RU486)
(18).
(Cytokine)
가
가
(nega-
tive feedback)
(15).
CA3
gyrus)
cytokines
(dentate
(19~23).
proinflammatory

generation) quinolinate (neuro-
protection) ky-nurenate
HPA
TNF - 가 IL - 1, IL - 2, IL - 6, (24).
(27).
(28). cytokines 가
inflammatory
cytokines receptor antagonist, anti -
cytokine antibody, anti - inflammatory cytokines
IL - 1 receptor antagonist(IL - 1ra) mRNA가
(25). IL - 1 가 , IL - 1ra inescapable
NE (turnover) shock (learned helplessness)
가, 5 - HT 가,
DA 가 IL - 1 가
in vitro IL - 1가 5 - HT
5 - HT CRF receptor
transporter 가 (26). antagonist
, IL - 1
가 CRF IL - 1
IL - 1, IFN - 가 CRF
5 - HT 가
indoleamine - 2,3 - dioxygenease(IDO) 가
가 5 - HT
(Neural Circuitry)
cytokines 가가 IDO 가 tryptophan
degradation pathway가 (neurode-

(anhedonia) , 가 (anergy) (31). (meso-
limbic dopamine system) (ventral teg-
(caudate nucleus), (putamen), mental area) (nucleus accumbens)
(motivation)
(limbic - cortical - striatal - pallidal - thalamic tract)가 (reward) ,
(29). 가 .
가 . 가 .
가 가 .
가 가 .
(consolidation) , (explicit memory)
가 .
(working memory),
(32).
(ventral tegmental area), (dorsal raphe nucleus), (locus coeruleus)
BDNF
NE 5-HT
cAMP - CREB BDNF
가 .
cAMP - CREB BDNF
3~4
(30). 가 .

neurotrophic factor MAP

kinase ribosome S6 kinase(Rsk) . phosphatidyl inositol

CREB . - AR HT1A lithium 가

G MAP kinase

. NE

HT 가 .

CREB , MAP kinase Rsk

, 가

가 . MAP kinase

 가 가

, , CRF , substance P ,

가 , cAMP (34).

5 - HT NE BDNF

가 . cAMP Ca^{2+} -

activated AR 5 - HT_{4,6,7}

가 . , 가

cAMP

. cAMP Ca^{2+} - activated kin-ase 가

CREB .

. cAMP cAMP phos-

phodiesterase(PDE4) rolipram . 가 5 - HT

가 NE

. rolipram , 가 CRF

PDE4 isoenzyme ,

가 PDE 4A 4B isoform 가 가 CRF

(33)

가 . 가 -

-

가 .

,

가 IL - 1 가 가
가
TNF IL - 1
NA
5 - HT
가
가
가

가



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