

## 우울증의 실험적 모델\*

정 영 인\*\*†

## Experimental Models of Depression\*

Young In Chung, M.D., Ph.D.\*\*†

## ABSTRACT

There are a number of approaches in developing experimental models for depression, but there is no such thing as a best model for depressive syndrome. Animal models are subject to the obvious limitations inherent in the assumption that human psychopathology can be represented accurately in lower animals. Recently, the concern increasingly is to develop a variety of experimental paradigms in animals to study selected aspects of human psychopathology, and animal models should be understood as basically experimental preparations that are developed to carry out these objects. Therefore, a battery of a variety of animal models should be applied to permit detailed pathophysiological studies and to develop new antidepressant treatments.

Animal models of depression basically consider behavioral isomorphism with the human depression a plus, but not a requirement, and the model behavior should be defined operationally in order to be reproduced reliably by other researchers and be responsive to those agents possessing demonstrated clinical efficacy in human depression.

In conclusion, animal models of depression have played a significant role in elucidating pathophysiology of depression and developing current treatments for depression, but there is no single comprehensive model for depression until now. Each of the proposed animal model has its advantages and limitations. In other words, certain paradigms are suitable for studying certain phenomena, whereas others are more suitable for studying other aspects. The best model for depression depends upon what the question is.

**KEY WORDS** : Depression · Animal models · Validity.

## 서 론

우울증의 실험적 모델\*

정 영 인

가

가

가가

가

1998 10 22

Department of Psychiatry, College of Medicine, Pusan National University, Pusan, Korea

† : , 602 - 739 1가 10  
) (051) 240 - 7305, ) (051) 248 - 3648

## 동물모델의 타당성을 평가하는 기준

McKinney Bunney(1969)

4가 가

, Willner(1984)

가

가

가  
validity),  
identity)

(face validity),

가

(predictive va -  
(construct val -

가,

가(potency)

가

가

가

가,

가,

가

가

(homologous) 가,

가

(biological marker)가

가

(experimental paradigm)

## 우울증의 실험적 모델

model)

(homologous model)

가

가

(assay

가

(screening)

가

가

( 1).

가

### 1. 검사모델

#### 1) Muricide 모델

가,

(TCA) 가

(muricide)  
(MAOI)

Horovitz (1965)

가

(psychostimulant),

(anticholinergics),

(antihistamines)

가

(Barnet 1969 ; Horovitz 1965 ; Horovitz 1966 ;

Sofia 1969).

**Table 1.** Overall assessment of homologous models Willner(1984)

Model	Validity		
	Predictive	Face	Construct
Swim test immobility	++	+	
Chronic mild stress	++	++	+
Separation	+	++	+
Exhaustion stress	+	+	
Circadian rhythm readjustment	++	+	
Olfactory bulbectomy	+	+	
Uncontrollable shock	++	+	+

2) Yohimbine potentiation 모델  
 yohimbine(Alpha 2 - ) corticosteroids 가 ,  
 (sublethal doses) yo - (Cairncross 1978 ; Janscar Leonard  
 himbine TCAs MAOIs yohim - 1980). corticosteroids  
 bine 가 가

(Quinton 1963). Yohimbine potentiation  
 (bupropion, mianserin, nomifensine, iprindole) (Cairncross 1977 ;  
 (Malick 1981). (electroconvulsive Rigter 1977 ; van Riezen 1977).  
 shock)

(Lapin 1980 ; (SSRIs) 1  
 Malick 1981) 가 . (Earley Leonard 1985). Amphetamine tranlycyp -  
 romine (Nor -

### 3. Kindling 모델

Kindling (subthreshold) Kindling 가 가 (sensitization) 가 (Lloyd 1982 ; Watanabe  
 1979) muricide .  
 (Goddard Muricide olfactory bulbec -  
 1969). kindling TCAs (Babin - tomy (Nelson  
 gton 1975) .

(neocortex) (amygdala) kindling Charney 1981), corticosteroids가 (Ca -  
 rroll 1976) . Olfactory bulbectomy

kindling kindling corti costeroids가 (Tyrer 1979) MAOIs  
 dling TCAs 가 가 ,  
 (Babington Wedeking 1973). MAOIs

(iprindole, mianserin) (Babing - corticosteroids  
 ton 1981), 가 (van Riezen Leonard 1991),  
 가 SSRIs가

### 4) Circadian rhythm readjustment 모델

(light -  
 dark cycle) 10

2 TCAs MAOIs

(Baltzer Weiskrantz 1975).

(circad -  
 ian rhythm) 가 (Aki -  
 skal 1980 ; Goodwin 1982 ; Kupfer 1976 ; Wehr Wirz -  
 Justice 1982). 2

### 6) Isolation-induced hyperactivity 모델

TCAs, MAOIs, (iprindole, mianserin, trazo -  
 done) ,  
 (Garzon  
 1979 ; Garzon Del Rio 1981). olfactory bul -  
 bectomy

(Va -  
 Izelli Bernasconi 1971)

### 5) Olfactory bulbectomy 모델

(olfactory bulb) (Nelson

Charney 1981) 가 , imipramine 4 REM

2. 상동모델 가 가 (Vogel 1990b).

1) Reserpine reversal 모델 Reserpine reserpine tetrabenazine 가 , clomipramine 가 . Reserpine (presynaptic nerve terminal) 가 . Reserpine 가 TCAs MAOIs (Costa 1960 ; Maxwell Palmer 1961). (behavioral despair) (Porsolt 1977 ; Porsolt 1978). reserpine 가 TCAs, MAOIs, REM (Browne 1979 ; Ferris 1982 ; Hawkins 1980 ; Porsolt 1977 ; Porsolt 1978). , , , pentobarbital, opiate (Browne 1979 ; Kastin 1978 ; Schechter Ch - ance 1979 ; Wallach Hedley 1979) , 가 가 Reserpine reversal 가 (mianserin, trazodone) 가 (Colpaert 1975 ; Day Rand 1963 ; Sigg 1965 ; Silvestrini 1982 ; van Riezen 1972) reserpine 5% (Goodwin 1972) , reserpine (Abel 1991 ; De Pablo 1989), 가 가 (Colpaert 1975 ; Will ner Clark 1978) , (Armario 1988 ; Kitada 1981). , 가 , 1 (Kitada 1981 ; Porsolt 1981) 가 가 가 가 가 가 (learned help -

lessness) 3 가

가 가 , . Imipramine (Hatotani  
(Borsini Meli 1988) 1982). 가  
, stress 가  
stress 가

4) Clonidine withdrawal 모델 clonidine 2 가 (Hoffman Weiss 1986).  
ramine 2 . Desip- 가 , 2 3  
mine 가 . Desipra- decibels (electric shock), 가 95  
corticosteroids가 가  
(Katz 1982 ; Katz 1981 ; Roth Katz 1981).  
cor-  
ticosteroids 가 TCAs, MAOIs, (iprin-  
dole, mianserin, bupropion), ,  
(Katz 1981 ; Katz Bal-  
drighi 1982 ; Katz Hersh 1981 ; Katz Sibel 1982a,b).  
corticosteroids가 가 , stress

5) Tail suspension 모델 가 , TCAs,  
MAOIs, , ,  
(Steru 1985). , ,  
, 가 ( )

6) Dorsomedial amygdala lesion 모델 (dorsomedial amygdala) 가 , , , stress  
(Fonberg 1972). stress가 , stress가  
가 . lateral hypothalamic syndrome ,  
(Fonberg 1972). lateral hypothalamic sy- stress 가  
ndrome , 가 stress

7) Exhaustion stress 모델 가

8) Chronic mild stress 모델 가 , 2 3  
(electric shock), , 가 95  
decibels  
corticosteroids가 가  
(Katz 1982 ; Katz 1981 ; Roth Katz 1981).  
cor-  
ticosteroids 가 TCAs, MAOIs, (iprin-  
dole, mianserin, bupropion), ,  
(Katz 1981 ; Katz Bal-  
drighi 1982 ; Katz Hersh 1981 ; Katz Sibel 1982a,b).  
corticosteroids가 가 , stress

9) Uncontrollable shock모델 , ,

(Overmier Seligman 1967 ; Seligman Maier 1967 ; Weiss 1968 ; Weiss 1991).

(Hinde 1978 ; Kaufman Rosenblum 1967 ; Mckinney Bunney 1969 ; Suomi 1976).

cortisol (Higley 1982).  
가

imipramine desipramine

가

(Hrdina 1979 ; Suomi 1978).  
가 가

(Lewis Mckinney 1976).

(learned helplessness) (Overmier

Seligman 1967 ; Seligman Maier 1967)

(anacletic depression)

가

TCA, MAOIs, SSRIs,

가

(Bow-

(Leshner 1979 ; Martin 1990 ; lby 1976),

Petty Sherman 1980 ; Sherman 1982).

5%

가

가 가

### 결론

(passiveness)

(Gersh Fowles 1979)

가

(Blaney 1977)

가

가

(Anisman Big-

nami 1978 ; Weiss 1980)

가

### 10) Separation모델

(operationally)

(protest stage) 1 2

가 (despair stage)

가  
가 가 가

참고문헌

Abel EL (1991) : Alarm substance emitted by rats in the forced swim test is a low volatile pheromone. *Physiol Behav* 50 : 723-727

Akiskal HS (1980) : External validating criteria for psychiatric diagnosis : Their application in affective disorders. *J Clin Psychiatry* 41 : 6-15

Anisman H, Bignami G (1978) : A comparative neurochemical, pharmacological, and functional analysis of aversively motivated behaviors : caveats and general consideration, In : *Psychopharmacology of Aversively Motivated Behavior*, Ed by Anisman H, Bignami G, New York, Plenum, pp487-512

Armario A, Gavaldà A, Martí O (1988) : Forced swimming test in rats : effect of desipramine administration and the period of exposure to the test on struggling behavior, swimming, immobility and defecation rate. *Eur J Pharmacol* 158 : 207-212

Babington RG (1975) : Antidepressives and the kindling effect, In : *Antidepressants*, Ed by Fielding S, Lal H, New York, Futura Publishing, pp113-124

Babington RG (1981) : Neurophysiologic techniques and antidepressive activity, In : *Antidepressants : Neurochemical, Behavioral, and Clinical Perspectives*, Ed by Enna SJ, Malick JB, Richelson E, New York, Raven Press, pp157-173

Babington RG, Wedeking PW (1973) : The pharmacology of seizures induced by sensitization with low intensity brain stimulation. *Pharmacol Biochem Behav* 1 : 461-467

Baltzer V, Weiskrantz L (1975) : Antidepressant agents and reversal of diurnal activity cycles in the rat. *Biol Psychiatry* 10 : 199-209

Blaney PH (1977) : Contemporary theories of depression : critique and comparison. *J Abnorm Psychol* 86 : 203-223

Borsini F, Meli A (1988) : Is the forced swimming test a suitable model for revealing antidepressant activity? *Psychopharmacology (Berl)* 94 : 147-160

Bowlby J (1976) : Human personality development in an ethological light, In : *Animal Models in Human Psychobiology*, Ed by Serban G, Kling A, New York, Plenum Press, pp27-36

Browne RG (1979) : Effects of antidepressants and anticholinergics in a mouse "behavioral despair" test. *Eur J Pharmacol* 58 : 331-334

Cairncross KD, Cox B, Forster C, Wren AF (1978) : A new model for the detection of antidepressant drugs : Olfactory bulbectomy in the rat compared with existing models. *J Pharm Methods* 1 : 131-143

Carroll BJ, Curtis GC, Mendels J (1976) : Cerebrospinal fluid and plasma free cortisol levels in depression. *Psychol Med* 6 : 235-244

Colpaert FC, Lanaerts FM, Niemegeers CJE, Janssen PAJ (1975) : A critical study on RO-4-1284 antagonism in mice. *Arch Int Ph-*

*armacodyn Ther* 215 : 40-90

Costa E, Garattini S, Valzelli L (1960) : Interactions between reserpine, chlorpromazine, and imipramine. *Experientia* 16 : 461-463

Day MD, Rand MJ (1963) : Awakening from reserpine sedation by alphanethyl dopa. *J Pharm Pharmacol* 15 : 631-632

De Pablo JM, Parra A, Segovia S, Guillaumon A (1989) : Learned immobility explains the behavior of rats in the forced swimming test. *Physiol Behav* 46 : 229-237

Earley B, Leonard BE (1985) : Effects of two specific-serotonin reuptake inhibitors on the behaviour of olfactory bulbectomized rat in the "open field" apparatus, In : *Clinical and Pharmacological Studies in Psychiatric Disorders*, Ed by Burroes GD, Norman TR, Dennerstein L, London, John Libby, pp234-240

Ferris RM, Maxwell RA, Cooper BR, Soroko FE (1982) : Neurochemical and neuropharmacological investigations into the mechanisms of action of bupropion-Hcl-a new atypical antidepressant agent, In : *Typical and Atypical Antidepressants : Molecular Mechanisms*, Ed by Costa E, Racagni G, New York, Raven Press, pp 277-286

Fonberg E (1972) : Control of emotional behaviour through the hypothalamus and amygdaloid complex. *Ciba Found Symp* 8 : 131-161

Garzon J, Del Rio J (1981) : Hyperactivity induced in rats by long-term isolation : further studies on a new model for the detection of antidepressants. *Eur J Pharmacol* 74 : 287-294

Garzon J, Fuentes JA, Del Rio J (1979) : Antidepressants selectively antagonize the hyperactivity induced in rats by long-term isolation. *Eur J Pharmacol* 59 : 293-296

Gersh FS, Fowles DC (1979) : Neurotic depression : The concept of anxious depression, In : *The Psychobiology of the Depressive Disorders : Implications for the Effect of Stress*, Ed by Depue RA, New York, Academic Press, pp81-104

Goddard GV, McIntyre DC, Leech CK (1969) : A permanent change in brain function resulting from daily electrical stimulation. *Exp Neurol* 25 : 295-330

Goodwin FK, Ebert MH, Bunney WE (1972) : Mental effects of reserpine in man : A review, In : *Psychiatric Complications of Medical Drugs*, Ed by Shader RI, New York, Raven Press, pp73-101

Goodwin FK, Wirz-Justice A, Wehr TA (1982) : Evidence that pathophysiology of depression and the mechanism of action of antidepressant drugs both involve alterations in circadian rhythms, In : *Typical and Atypical Antidepressants : Clinical Practice*, Ed by Costa E, Racagni G, New York, Raven Press, pp1-11

Hatotani N, Nomura J, Kitayama I (1982) : Changes of brain monoamines in the animal model for depression, In : *New Vistas in Depression*, Ed by Langer SZ, Takahashi R, Segawa T, Briley M, New York, Pergamon Press, pp65-72

Hawkins J, Phillips N, Moore JD, Gilliland MA, Dunbar S, Hicks RA (1980) : Emotionality and REMD : a rat swimming model. *Physiol Behav* 25 : 167-171

Higley JD, Suomi SJ, Scanlon JM, McKinney WT (1982) : Plasma cortisol as a predictor of individual depressive behaviour in rhesus monkeys (*Macaca mulatta*). *Soc Neurosci Abstr* 8 : 461

Hinde RA, Leighton-Shapiro ME, McGinnis L (1978) : Effects of various types of separation experience on rhesus monkeys 5 months later. *J Child Psychol Psychiatr* 19 : 199-211

Hoffman LJ, Weiss JM (1986) : Behavioral depression following

- clonidine withdrawal : a new animal model of long-lasting depression? *Psychopharmacol Bull* 22 : 943-949
- Horovitz ZP, Piala JJ, High JP, Burke JC, Leaf RC(1966)** : Effects of drugs on the mouse-killing (muricide) test and its relationship to amygdaloid function. *Int J Neuropharmacol* 5 : 405-411
- Horovitz ZP, Ragozzino PW, Leaf RC(1965)** : Selective block of rat mouse-killing by antidepressants. *Life Sci* 4 : 1909-1912
- Hrdina PD, Von Kulmiz P, Stretch R(1979)** : Pharmacological modification of experimental depression in infant macaques. *Psychopharmacology* 64 : 89-93
- Janscar S, Leonard BE(1980)** : The effects of olfactory bulbectomy on the behaviour of rats in the open field. *Isr J Md Sci* 149 : 80-81
- Kastin AJ, Scollan EL, Ehrensing RH, Schally AV, Coy DH(1978)** : Enkephalin and other peptides reduce passiveness. *Pharmacol Biochem Behav* 9 : 515-519
- Katz RJ(1981)** : Animal model of depression : effects of electroconvulsive shock therapy. *Neurosci Biobehav Rev* 5 : 273-277
- Katz RJ(1982)** : Animal model of depression : pharmacological sensitivity of a hedonic deficit. *Pharmacol Biochem Behav* 16 : 969-972
- Katz RJ, Baldrighi G(1982)** : A further parametric study of imipramine in an animal model of depression. *Pharmacol Biochem Behav* 16 : 969-972
- Katz RJ, Hersh S(1981)** : Amitriptyline and scopolamine in an animal model of depression. *Neurosci Biobehav Rev* 5 : 265-271
- Katz RJ, Roth KA, Schmaltz K(1981)** : Amphetamine and tranlycypromine in an animal model of depression : pharmacological specificity of the reversal effect. *Neurosci Biobehav Rev* 5 : 259-264
- Katz RJ, Sibel M(1982a)** : Animal model of depression : tests of three structurally and pharmacologically novel antidepressant compounds. *Pharmacol Biochem Behav* 16 : 973-977
- Katz RJ, Sibel M(1982b)** : Further analysis of the specificity of a novel animal model of depression : Effects of an antihistaminic, antipsychotic and anxiolytic compound. *Pharmacol Biochem Behav* 16 : 979-982
- Kaufman IC, Rosenblum LA(1967)** : The reaction to separation in infant monkeys : Anaclitic depression and conservation-withdrawal. *Psychosom Med* 29 : 648-675
- Kitada Y, Miyauchi T, Satoh A, Satoh S(1981)** : Effects of antidepressants in the rat forced swimming test. *Eur J Pharmacol* 72 : 145-152
- Kupfer DJ(1976)** : REM latency : A psychobiological marker for primary depressive disease. *Biol Psychiatry* 11 : 159-174
- Lapin IP(1980)** : Adrenergic nonspecific potentiation of yohimbine toxicity in mice by antidepressants and related drugs and antiyohimbine action of antiadrenergic and serotonergic drugs. *Psychopharmacology* 70 : 179-185
- Leshner AI, Remler H, Biegen A, Samuel D(1979)** : Effects of desmethylimipramine (DMI) on learned helplessness. *Psychopharmacology* 66 : 207-213
- Lewis JK, McKinney WT(1976)** : Effects of electroconvulsive shock on the behaviour of normal and abnormal rhesus monkeys. *Behav Psychiatr* 37 : 687-693
- Lloyd KG, Garrigou D, Broekkamp CLE(1982)** : The action of monoaminergic, cholinergic and gabaergic compounds in the olfactory bulbectomized rat model of depression, In : *New Vistas in Depression*, Ed by Langer SZ, Takahashi R, Segawa T, Briley M, New York, Pergamon Press, pp179-186
- Malick JB(1981)** : Yohimbine potentiation as a predictor of antidepressant action, In : *Antidepressants : Neurochemical, Behavioral, and Clinical Perspectives*, Ed by Enna SJ, Malick JB, Richelson E, New York, Raven Press, pp141-155
- Martin P, Soubrie P, Puech AJ(1990)** : Reversal of helpless behavior by serotonin uptake blockers in rats. *Psychopharmacology (Berl)* 101 : 403-407
- Maxwell DR, Palmer HT(1961)** : Demonstration of antidepressant or stimulant properties of imipramine in experimental animals. *Nature* 191 : 84-85
- McKinney WT, Bunney WE(1969)** : Animal model of depression. *Arch Gen Psychiatry* 21 : 240-248
- Neill D, Vogel D, Hagler M, Kors D, Hennessey A(1990)** : Diminished sexual activity in a new animal model of endogenous depression. *Neurosci Biobehav Rev* 14 : 73-76
- Nelson JC, Charney DS(1981)** : The symptoms of major depressive illness. *Am J Psychiatry* 138 : 1-13
- Noreika L, Pastor G, Liebman J(1981)** : Delayed emergence of antidepressant efficacy following withdrawal in olfactory bulbectomized rats. *Pharmacol Biochem Behav* 15 : 393-398
- Overmier JB, Seligman MEP(1967)** : Effects of inescapable shock upon subsequent escape and avoidance learning. *J Comp Physiol Psychol* 63 : 28-33
- Petty F, Sherman AD(1980)** : Reversal of learned helplessness by imipramine. *Commun Psychopharmacol* 3 : 371-373
- Porsolt RD(1981)** : Behavioral despair, In : *Antidepressants : Neurochemical, Behavioral, and Clinical Perspectives*, Ed by Enna SJ, Malick JB, Richardson E, New York, Raven Press, pp121-139
- Porsolt RD, Anton G, Blavet N, Jalfre M(1978)** : Behavioral despair in rats, a new model sensitive to antidepressant treatments. *Eur J Pharmacol* 47 : 379-391
- Porsolt RD, Bertin A, Jalfre M(1977)** : Behavioral despair in mice : A primary screening test for antidepressants. *Arch Int Pharmacodyn* 229 : 327-336
- Rigter H, van Riezen H, Wren A(1977)** : Pharmacological validation of a new test for the detection of antidepressant activity of drugs. *Br J Pharmacol* 59 : 451-452
- Roth KA, Katz RJ(1981)** : Further studies on a novel animal model of depression : therapeutic effects of a tricyclic antidepressant. *Neurosci Biobehav Rev* 5 : 253-258
- Schechter MD, Chance WT(1979)** : Non-specificity of "behavioral despair" as an animal model of depression. *Eur J Pharmacol* 60 : 139-142
- Seligman MEP, Maier SF(1967)** : Failure to escape traumatic shock. *J Exp Psychol* 74 : 1-9
- Sherman AD, Sacquitne JL, Petty F(1982)** : Specificity of the learned helplessness model of depression. *Pharmacol Biochem Behav* 16 : 449-454
- Shopsin B, Cassano GB, Conti L(1981)** : An overview of new "second generation" antidepressant compounds : Research and treatment implications, In : *Antidepressants : Neurochemical, Behavioral, and Clinical Perspectives*, Ed by Enna SJ, Malick JB, Richelson E, New York, Raven Press, pp219-251
- Sigg EB, Gyermek L, Hill RT(1965)** : Antagonism to reserpine

- induced depression by imipramine, related psychoactive drugs and some autonomic agents. *Psychopharmacology* 7 : 144-149
- Silvestrini B(1982)** : Trazodone-A new type of antidepressant : A discussion of pharmacological data and their clinical implications, In : *Typical and Atypical Antidepressants : Molecular Mechanisms*, Ed by Costa E, Racagni G, New York, Raven Press, pp327-340
- Sofia RD(1969)** : Effects of centrally active drugs on four models of experimentally-induced aggression in rodents. *Life Sci* 8 : 705-716
- Steru L, Chermat R, Thierry B, Simon P(1985)** : The tail suspension test : a new method for screening antidepressants in mice. *Psychopharmacology (Berl)* 85 : 367-370
- Suomi SJ, Collins ML, Harlow HF(1976)** : Effect of maternal and peer separation on young monkeys. *J Child Psychol Psychiatr* 17 : 101-112
- Suomi SJ, Seaman SF, Lewis JK, DeLizio RB, McKinney WT (1978)** : Effects of imipramine treatment on separation-induced social disorders in rhesus monkeys. *Arch Gen Psychiatry* 34 : 321-325
- Tyrer P(1979)** : Clinical use of monoamine oxidase inhibitors, In : *Psychopharmacology of Affective Disorders*, Ed by Paykel ES, Coppen A, Oxford, Oxford University Press, pp159-178
- Valzelli L, Bernasconi S(1971)** : Psychoactive drug effects on behavioural changes induced by prolonged socio-environmental deprivation in rats. *Psychol Med* 6 : 271-276
- van Riezen H(1972)** : Different central effects of the 5-HT antagonists mianserin and cyproheptadine. *Arch Int Pharmacodyn Ther* 198 : 256-269
- van Riezen H, Leonard BE(1991)** : Effects of psychotropic drugs on the behavior and neurochemistry of olfactory bulbectomized rats, In : *Psychopharmacology of Anxiolytics and Antidepressants*, Ed by File SE, New York, Pergamon, pp231-250
- van Riezen H, Schnieden H, Wren AF(1977)** : Olfactory bulb ablation in the rat : behavioural changes and their reversal by antidepressant drugs. *Br J Pharmacol* 60 : 521-528
- Vogel G, Hartley P, Neill D, Hagler M, Kors D(1988)** : Animal depression model by neonatal clomipramine : reduction of shock induced aggression. *Pharmacol Biochem Behav* 31 : 103-106
- Vogel G, Neill D, Hagler M, Kors D(1990b)** : A new animal model of endogenous depression : a summary of present findings. *Neurosci Biobehav Rev* 14 : 85-91
- Vogel G, Neill D, Kors D, Hagler M(1990a)** : REM sleep abnormalities in a new animal model of endogenous depression. *Neurosci Biobehav Rev* 14 : 77-83
- Wallach MD, Hedley LR(1979)** : The effects of antihistamines in a modified behavioral despair test. *Commun Psychopharmacol* 3 : 35-39
- Watanabe S, Inoue M, Ueki(1979)** : Effects of psychotropic drugs injected into the limbic structures on mouse-killing behaviour in the rat with olfactory bulb ablation. *Jpn J Pharmacol* 29 : 493-496
- Weiss JM(1968)** : Effects of coping responses on stress. *J Comp Physiol Psychol* 65 : 251-260
- Weiss JM(1980)** : Coping behavior : explaining behavioral depression following uncontrollable stressful events. *Behav Res Ther* 18 : 485-504
- Weiss JM(1991)** : Stress-induced depression : critical neurochemical and electrophysiological changes, In : *Neurobiology of Learning, Emotion and Affect*, Ed by Madden J IV, New York, Raven Press pp123-154
- Willner P(1984)** : The validity of animal models of depression. *Psychopharmacology (Berl)* 83 : 1-16
- Willner P, Clark D(1978)** : A reappraisal of the interaction between tricyclic antidepressants and reserpine-like drugs. *Psychopharmacology* 58 : 55-62