

# 향정신성약물의 행동학적 독성\*

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## Behavioral Toxicity of Psychotropic Drugs\*

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### ABSTRACT

Any compound which disrupts the integrity of psychological aspects of performance, in particular, cognitive ability and psychomotor function analogous to the psychological behaviors of routine life, is known to be behaviorally toxic. A significant level of behavioral toxicity will interfere with patient safety and quality of life, and also may be counter-therapeutic by exacerbating the condition that the drug was prescribed for. Now, behavioral toxicity of psychotropic drugs has become one of the main growth areas of psychopharmacological research. Evaluation of the potential of drug-induced behavioral toxicity is important not only to the experimental researcher involved in human psychopharmacology, but also to the clinical practitioner treating psychiatric patients. This article attempts to describe behavioral toxicity of the three classes of psychotropic drugs - benzodiazepines, antidepressants and neuroleptics. After a brief discussion of some methodological issues arising in the investigation of behavioral toxicity, each of these drug classes is reviewed in the context of practical importance rather than purely scientific concern. The last session summarizes some suggestions for future studies on drug-induced behavioral toxicity.

**KEY WORDS** : Behavioral toxicity · Psychotropic drugs.

머리말 (human psychopharmacology)  
(behavioral toxicity)  
(risk/benefit ratio)가 (Hindmarch 1990).  
가 가  
가

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2. 객관적 평가(인지 및 정신운동성 검사)

가 (quantitative) (qualitat-  
 가 ive) 가 가  
 가 가  
 benzodiazepine , , metric) 가 (psycho-  
 가

향정신성 약물의 행동학적 효과의 평가

1. 연구방법

가  
 (Parrott 1991a, 1991b, 1991c)  
 (test battery)  
 (component) (validity)  
 가 (reliability)  
 (pharmacosenitivity)가  
 가  
 (behavioral activity)  
 1  
 (do - (an information -  
 uble - blind, placebo - controlled trial) processing model) (Hindmarch 1980).  
 (within (performance)  
 subject design), (positive control) 가  
 (pre - drug baseline) , Latin sq - 가  
 uare ( ) , ( ) , ( ) , ( )

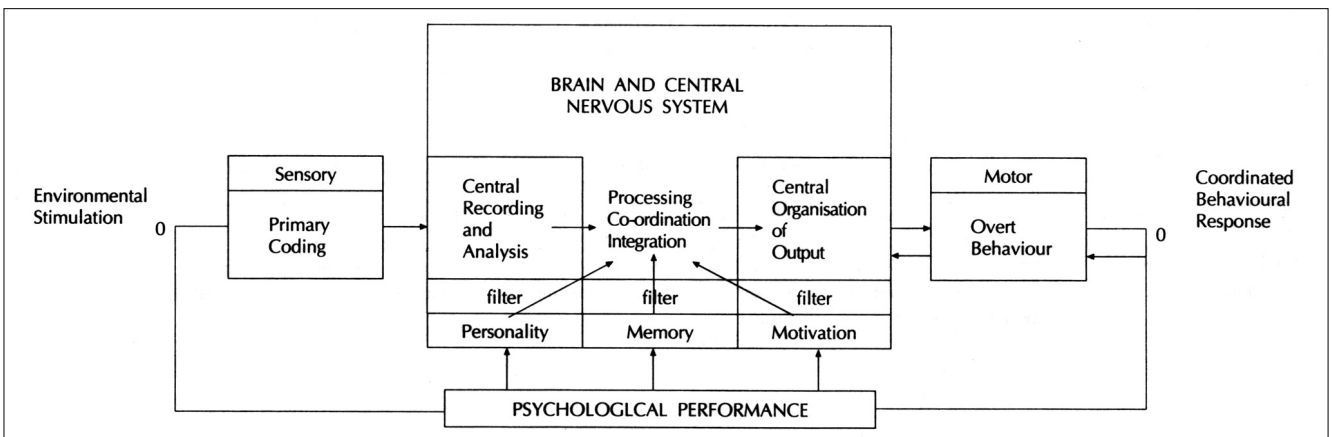


Fig. 1. Psychomotor performance results from the co-ordination of sensory and motor systems through the integrative and organizational processes of the CNS. The processing of sensory information is influenced by personality, memory and individual motivation, while the overall function of the integrative mechanism is governed by the state of arousal of the CNS. Complex feed back and adoptive systems complete the process by which environmental stimuli produce appropriate, co-ordinated behavioural responses(From I. Hindmarch, Br. J. Clin. Pharmacol. 10, 189, 1980).

### 3. 주관적 평가

가 (task) 가 ( ) (therapeutic, beneficial or desirable effects) (toxic, unwanted or side effects) 가 (value judgement) (Hindmarch 1980). (analogues of the real-life skill) 가 가 가 가 가 (rating scale) (simulator) 가 가 가 (Klonoff 1974). 가 (Dunbar 1992 ; Beaumont 1992 ; Stoker 1970). 가 (Cronbach 1992) (Naber 1994 ; Naber 1995) 가 가

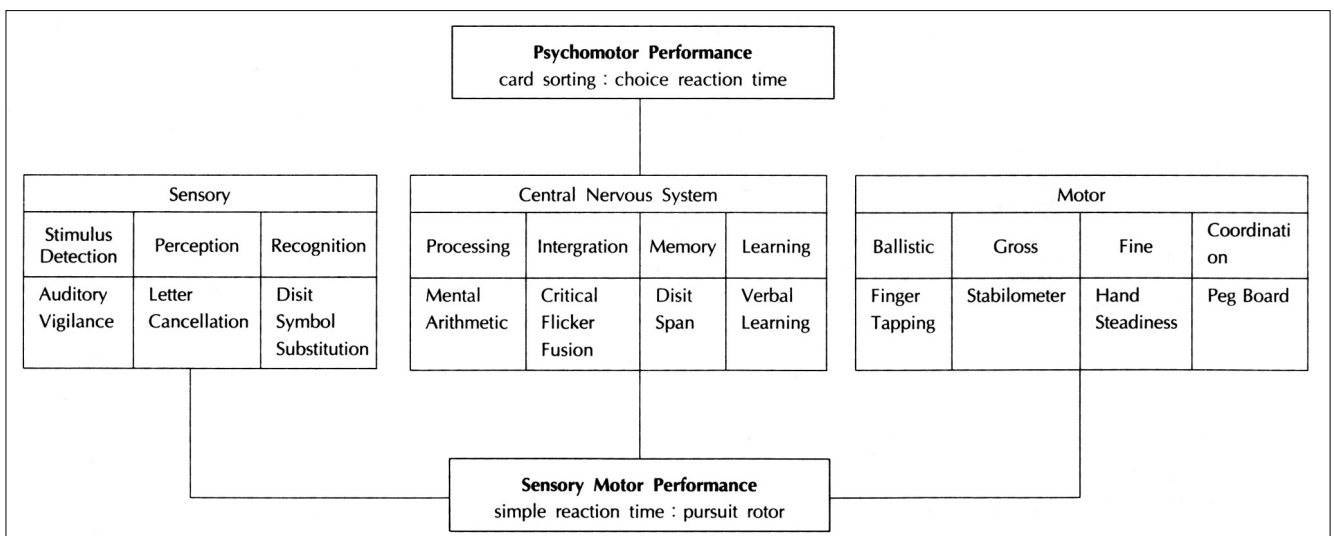


Fig. 2. A summary of tests of psychomotor function which have been shown to be sensitive to a wide range of psychoactive drugs(From I, Hindmarch, Br. J. Clin. Pharmacol. 10, 189, 1980).

# 항정신성 약물의 행동학적 독성의 사례

## 1. Benzodiazepines(BZs)

BZs

(social drug) 가 BZs

BZs  
? BZs  
(Christ -  
ensen 1990 ; Honkanen 1980 ; Jick 1981 ; Merlin  
1990 ; Oster 1990). 1970  
11%( 2%) dia -  
zepam  
(impaired driver) 37%  
4% BZs 79% (Hin -  
dmarch 1985). BZs minor tranquilizer

5 (Skegg 1979). Merlin (1990)  
363

enobarbitone 39

가 BZs  
“ no smoking ” “ no benzodiazepine ”  
. BZs

1 BZs

(Hindmarch 1985). 가

가  
가

**Table 1.** The effects of benzodiazepine anti-anxiety agents on aspects of car driving(From I. Hindmarch, Psychiatry in the 80's, 3(3), 2, 1985)

	'On-the- road' car driving	Car driving simulators	Psychomotor performance	Memory and/or information processing
Alprazolam	2	2	2	2
Bromazepam	2	3	3	5
Clobazam	0	0	1	0
Diazepam	5	5	5	4
Lorazepam	5	5	5	5

Scale 0=no detrimental effect with respect to placebo controls  
5=maximum detrimental effect

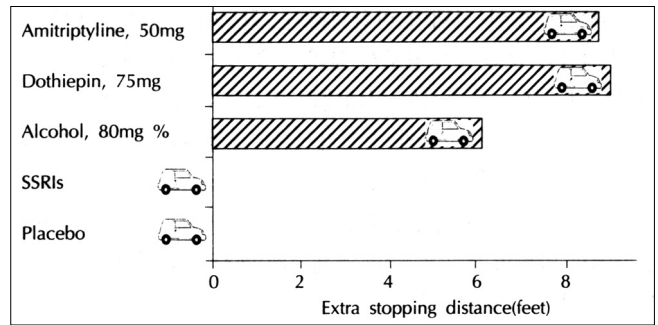
BZs  
가  
(hangover)  
가  
(Boatwright  
1987)  
가  
(actigram)  
가  
REM  
(polysomnogram)  
가가  
가  
LSEQ(Leeds Sleep Evaluation Qu -  
estionnaire : Parrott Hindmarch 1980) (ease of ge -  
tting to sleep), (quality of sleep),  
(ease of waking the mornig after sleep),  
(integrity of behavior of follo -  
wing wakefulness : BFW) 가 . LSEQ BZs  
가  
(Hindmarch 1984). 가

## 2. 항우울제

**Table 2.** Effects of antidepressants on aspects of car driving (From I. Hindmarch, *Psychiatry in the 80's*, 3(3), 3, 1985)

	'On-the-road' car driving	Car driving simulators	Psychomotor performance	Memory and/or information processing
Amitriptyline	5	5	5	5
Bupropion	0	0	0	0
Mianserin	5	5	4	5
Nomifensine	0	0*	0+	0*
Paroxetine	ND	0	0+	0
Sertaline	ND	0	0	0
Trazodone	5	5	4	5

Scale 0=no detrimental effect with respect to placebo controls  
 5=maximum detrimental effect  
 \*=an augmentation of performance better than placebo controls  
 +=Significant improvements with respect to placebo controls have been found with critical flicker fusion thresholds  
 ND=no data



**Fig. 3.** Effect of antidepressant and alcohol on stopping distance at 112km (70 miles) per hour (1 foot=0.3m). SSRIs, selective serotonin reuptake inhibitors (From I. Hindmarch, *Primary Care Psychiatry*, 3(suppl 1), 19, 1997).

Hindmarch (1988) 가 : ,  
 가 . , 가  
 가 (Ray , )  
 (1987) (hip - fracture)  
 가 (Beck 1963, 1964 ; Wright 1988)  
 가 가? 가  
 가 (Hindmarch 1985).  
 가 가? 가  
 가 (Siegfried 1989 ; Hindmarch 1992). , 3  
 CFF(critical flicker fusion) CRT(cho-  
 ice reaction time)  
 (Hindmarch 1992).  
**3. 항정신병 약물**  
 가 (He-  
 rrrera 1988, Van Puten 1990).  
 가 (Baldessarini 1985).  
 가 (Ger-  
 hard Hobi 1984).  
 가 (postpsychotic  
 depression) (Carpenter 1985 ; Emerich  
 Sanberg 1991).

**Table 3.** Ranked magnitudes of drug effects on critical flicker fusion(CFF) and choice reaction time(CRT). The top and bottom groups of drugs have been found to be significantly better and worse respectively as compared to placebo at  $p < 0.05$  or better. The drugs grouped with placebo have not been found to be significantly different from placebo on this measure at the doses indicated(From I. Hindmarch, et al. J. Pharmacol. 6, 199, 1992)

Drug(dose)	d CFF	Drug(dose)	d CRT
Zimeldine(200)	2,698	Nomifensin(100)	1,740
Sertraline(100)	1,769	Bupropion(100)	1,143
Paroxetine(30)	1,153	Desipramine(50)	1,028
Fluoxetine(40)	0,895	Lofepramine(140)	0,937
Nomifensin(100)	0,685	Sertraline(100)	0,802
Lofepramine(140)	0,347	Midalcipran(100)	0,541
Jouveinal(400)	0,141	Paroxetine(30)	0,276
Placebo	0,000	Placebo	0,000
Fluvoxamine(50)	0,017	Jouveinal(400)	0,189
Bupropion(100)	0,204	Moclobemide(400)	0,258
Moclobemide(200)	0,251	Zimeldine(400)	0,331
Midalcipran(100)	0,439	Fluvoxamine(50)	0,386
		Fluoxetine(40)	0,432
Desipramine(50)	0,834	Trazodone(50)	1,029
Dothiepin(50)	1,279		
Trazodone(50)	1,305	Mianserin(10)	1,242
Amitriptyline(25)	1,769	Dothiepin(50)	1,601
Mianserin(10)	3,496	Amitriptyline(25)	2,086

pharmacogenic depression(Helmchen Hippius 1969), post - remissive exhaustion(Heinrich 1967) dyscognitive syndrome(Heinrich Tegeler 1983), neuroleptic dysphoria(Emerich Sanberg 1991, Weiden 1989), akinetic depression(Rifkin 1975 ; Van Putten May 1978), subjective aspects of akathisia(Van Putten May 1975), neuroleptic anhedonia(Wise 1991)

(cortical and/or limbic equivalent of tardive dyskinesia) supersensitivity psychosis(Chouniard 1978 ; Chouniard Jones 1982), tardive dysmentia(Wilson 1983), tardive psychosis tardive schizophrenia(Berger Davis 1986)

neuroleptics induced deficit syndrome(NIDS) (Lader 1993) 가 NIDS (Lewander 1994 ; Schooler 1994), (deficit syndrome) (Marsden 1976 ; Lidsky 1981) (neuroleptic resistant) (Crow 1980) (Meitzer 1986 ; Kane Mayerhoff 1989 ; Boyer 1995) NIDS (neuroleptic induced behavioral toxicity : NIBT) NIDS , NIBT CNS , NIDS NIBT 4 (Casey 1994) : (drowsiness, somnolence) (psychomotor inhibition, psychic indifference) D<sub>2</sub> (mental equivalent) 가 (mannerism) 가 가 a<sub>1</sub> CNS 가







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