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## Psychiatric Side Effects of Psychotropic Drugs

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### Abstract

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The history of the discovery and development of the major psychotropic drugs provides an ideal way of introducing a chapter on side effects. Phenothiazines, tricyclic antidepressants, monoamine oxidase inhibitors, and lithium were all initially investigated for purposes entirely unrelated to their current usage. It was the recognition of a useful 'psychiatric (behavioral) side effects' by an astute observer that led to their ultimate utilization as psychotropic drugs. Unfortunately, while many books have been written about 'physical side effects' (e.g., extrapyramidal side effects, et al), psychiatric side effects have received little attention. But, the clinical significances of psychiatric side effects relate correct diagnosis and therapy, drug compliance, predictor of outcome in drug therapy, quality of life, etiopathology of mental disorders, new indications for older psychotropic drugs, and research for new psychotropic drugs with fewer side effects. Therefore, author will try to serve as the basis for the studying of

psychiatric side effects of psychotropic drugs. This brief review would be invaluable for evaluating the psychiatric side effects in psychotropic drugs-medicated patients as well as strategies targeted as ameliorating these side effects

KEY WORDS: Psychotropic drugs. Side effects. Psychiatric side effects.  
Clinical significance

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(psychotropic drug)' (1)  
(nonpsychotropic drugs) (psychiatric side effect)' (2) 가 (3)  
(Bernstein 1995; Boshes Davis 1986) ( 1). 가  
가  
( 1994; 1995).  
Lithium 1817 가 1855 . 19  
. 1940  
John Cade 가 lithium 가

가 lithium lithium lithium Cade lithium lithium 1-2

1949 9 Medical Journal of

Australia lithium 가 1950

Mogens Schou lithium 가 (Moriarty 1984).

1950 chlorpromazine

가 Henri Laborit chlorpromazine 가

가 1937 가 , 1947 phenothiazine Rhone-Poulenc 1951 chlorpromazine Laborit

Val-de-Grace Hospital , 1952 chlorpromazine (Moriarty 1984) barbiturate Jean Delay

chlorpromazine Pierre Deniker 가 St Anne (Frankenburg 1994).

Roche iproniazid 1952 가

가 (monoamine oxidase inhibitor, MAOI) 1 (tricyclic antidepressant, TCA) imipramine

MAO 1972 Roche moclobemide

sulpiride 가

MAO 가 20 MAOI MAOI 3 MAOI moclobemide MAOI

(Prada 1994).  
 Ciba Geigy 가 imipramine chlorprazine  
 Thomas Kuhn  
 가 1958 가  
 TCA 가 (Boshes Davis 1986; Moriarty 1984).

(1)  
 (neuroleptic-induced akathisia), (neuroleptic  
 dysphoria), (supersensitivity psychosis)  
 (cholinergic rebound), ,  
 (rapid cycling bipolar disorder) , (2)  
 , , ( )  
 , ,  
 , (3) , (behavioral disinhibition), (4)  
 lithium (?) ( )  
 1995) ( 2).

(neuroleptic-induced akathisia)

· ( ) , , ,  
 , , ( 2).

· , 가  
 1 ( ) 2 ( ) 가  
 (Stahl 1985) ( 3). 가

(tardive dyskinesia,  
 TD) TD .  
 , 가 , TD 가  
 (Adler 1992).

(neuroleptic dysphoria)

가

(Van Putten May 1978).

(extrapyramidal side effects, EPSs)

(Van Putten 1981).

EPS,

( 2) (Crine Polinsky 1979).

mesolimbic

pathway

(Emerich Sanberg 1991).

(1)

):

(2)

(postpsychotic depression):

(3)

(akinetiC depression):

(4)

(revealed depression):

가

가

(5)

(prodromal depression to a psychotic relapse):

(6)

:

(Barnes 1989). ( :

)

(supersensitivity psychosis)

TD

(supersensitivity)

Chouinard

( 4)

6

가

(

)

prolactin

가

TD

(Steiner 1990).

(1989) TD

가 .

(cholinergic rebound)

가

( 2).

1-3

가

(Gardos 1981). TCA

150-300 mg 3

2

(Janicak 1993).

Benzodiazepine

( 2) (Janicak 1993).

(anticholinergic syndrome)

( 2).

thioridazine, clozapine

가

(Berstein 1995).

(serotonin syndrome)

1960

가

L-tryptophan

MAOI

1980

(selective serotonin reuptake inhibitor,

SSRI)가

MAOI

(

). Lejoyeux (1992) clomipramine

TCA

TCA amitriptyline imipramine

가 (

).

(1994) clomipramine

SSRI fluoxetine

. Sternbach (1991)

1982

38

(myoclonus), (hyperreflexia), (incoordination), 가 10 ( 5).  
3 2 가

(neuroleptic malignant syndrome)

( 6). 가 , CPK  
가 (Bernstein 1995).

( )

(Goodwin Jamison 1990). 가  
( ) (1) , (2)  
, (3)

3-4

25%

가 ( )  
(Bowden 1995). 1 (

) 2 ( ) . 1  
, 2

21 , 35 가  
- ( ) 가 ( )-  
( ) (Goodwin Jamison 1990).

가  
(Stoll 1994). (%)

imipramine (> 10), bupropion (> 10), sertraline (> 10), phenelzine (> 10),  
tranylcypromine (> 10), fluoxetine (> 10), moclobemide (> 2), paroxetine (> 2),  
isocarboxazid (> 2), nortriptyline (> 2), amoxapine (> 2), maprotiline (> 2),  
desipramine (> 2), doxepin (< 2), amitriptyline (< 2), clomipramine (< 2),  
trazodone ( - ) (Benzchlibnyk-Butler Jeffries 1995). MAOI MAO-B

MAO-A moclobemide 가 MAO-A  
MAO-B phenelzine, tranylcypromine

. ECT (Goodwin  
Jamison 1990) ( ). ECT 가 ( )  
1989). ( )

가 (Altshuler 1995).

(rapid cycling bipolar disorder)

DSM-IV 4 ( ) (APA 1994) 13-20 %

2 (82%) 1 (18%) 4.5 lithium 72-82 % lithium 23%, 77%

(Calabrese Woysville 1995). (1)

, (2) , (3) , (4) , (5) , (6) , (7) , (8) 2 , (9) , (10) , (11) (41-60%)

TCA , lithium, ECT

(Akiskal 1995; APA 1994; Calabrese Woysville 1995;

McElroy Keck 1993). ECT 가 (Goodwin Jamison 1990).

( 1991), 1988; 1984; 1994), ( 1989) 가 .

Azorin(1995)

가 , . ( : ) (1) :

가 . (2)

(post-psychotic depression): TCA 가 TCA 가

TCA

TCA MAOI, SSRI, bupropion 가 .

. (3) TCA , :



Table 1. Psychiatric side effects, discovery of major psychotropic drugs,  
and biological psychiatry.

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Drugs developed or marketed for other purpose (nonpsychotropic drugs) ---->  
Recognition of a useful `psychiatric (behavioral) side effect'  
by thoughtful observer with fertile minds ---->  
New breed of `psychotropic drugs' ----->  
Additional useful psychiatric effects ----->  
New indication of older psychotropic drugs ----->  
(1) Research for new psychotropic drugs with fewer side effects  
(2) Link between this clinical and biochemical observation ----->  
Milestone in `biological psychiatry'

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(Bernstein 1995; Boshes Davis 1986)

Table 2. Psychiatric side effects of psychotropic drugs

Side effects	Related drugs
1. Neuroleptic-induced akathisia Sense of inner restlessness, most often referable to legs, compulsion to move one's legs, dysphoria, anxiety, worsening of psychosis, aggressive behavior, violence, suicidal attempt	APs
2. Neuroleptic dysphoria Mood swing, crying, sadness, depression, dysphoria, lack of motivation, agitation, anxiety attack, panic attack, work avoidance, school phobia, separation anxiety	APs
3. Withdrawal symptoms	
Supersensitivity psychosis	APs
Positive symptoms of schizophrenia	
Cholinergic rebound	APs, ADs
Insomnia, anxiety, agitation	
BZD type	BZD
Anxiety, restlessness, depersonalization, depression, insomnia, psychosis, delirium, catatonic features, panic attack, agoraphobia	
4. Anticholinergic syndrome	APs, ADs
Agitation, somnolence, bizarre behavior, delusion, paranoia, hallucination (visual and tactile), delirium, memory loss, worsening of existing psychotic symptoms	
5. Serotonin syndrome	ADs
Confusion, disorientation, hypomanic symptoms, dysphoria	
6. Inducing mania (or hypomania) in depression	ADs
7. Rapid cycling bipolar disorder	APs, ADs, Li(?)
8. Precipitation of psychotic symptoms in schizophrenia	ADs
9. Behavioral disinhibition/paradoxical excitement	AAs

APs, antipsychotics. ADs, antidepressants. AAs, antianxiety drugs.

Li, lithium. BZD, benzodiazepine.

( 1995; Adler 1992; Caine Polinsky 1979; Janicak 1993; McElroy  
Keck 1993; Steiner 1990)

Table 3. Akathisia variants

Variant	Description
Hysterical akathisia	Haskovec's syndrome
Bing's akathisia	Muscular impatience and motor restless in Parkinson's disease and basal ganglia disorders
Spontaneous akathisia	Restless legs syndrome; Ekbom's syndrome
Neuroleptic-induced acute akathisia	Acute response to start of neuroleptic dosing; motor and subjective restlessness
Neuroleptic-induced pseudoakathisia	Response to chronic neuroleptic dosing in schizophrenic patient with negative symptoms; overt motor restlessness without subjective restlessness
Neuroleptic-induced chronic akathisia type 1	Acute persistent akathisia; onset since last increase in neuroleptic dose; motor and subjective restlessness
Neuroleptic-induced chronic akathisia type 2	Tardive akathisia; withdrawal akathisia

(Stahl 1985)

Table 4. Chouinard's criteria for supersensitivity psychosis

History of receiving antipsychotics for at least 6 months

Patient has had a decrease or discontinuation of medication with appearance  
of psychosis

or

Patient has had no decrease or discontinuation of medication during  
treatment but has more relapses or increased tolerance to antipsychotic  
effects

Exclusion criteria:

Patients in the acute phase of the illness

Patients with continued psychotic illness that did not respond to  
neuroleptic treatment

(Steiner Chouinard 1990, an abbreviated form)

Table 5. Sternbach's diagnostic criteria for serotonin syndrome

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A. Coincident with the addition of or increase in a known serotonergic agent to an established medication regimen, at least three of the following clinical features are present:

- 1) Mental status changes (confusion, hypomania)
- 2) Agitation
- 3) Myoclonus
- 4) Hyperreflexia
- 5) Diaphoresis
- 6) Shivering
- 7) Tremor
- 8) Diarrhea
- 9) Incoordination
- 10) Fever

B. Other etiologies (e.g., infection, metabolic, substance abuse or withdrawal) have been ruled out.

C. A neuroleptic had not been started or increased in dosage prior to the onset of the signs and symptoms listed above.

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(Sternbach 1991)

Table 6. Comparison of neuroleptic malignant and serotonin syndrome

	Neuroleptic malignant syndrome	Serotonin syndrome
Mental status	Dazed mutism	Confusion, disorientation, mania
Hyperthermia	Mild to marked	Mild
Autonomic dysfunction		
Tachycardia	+	+
Labile BP	+	+
Diaphoresis	+	+
Tremor	+	+
Incontinence	+	0
Sialorrhea	+	0
Dyspnea	+	0
Shivering	0	+
Restlessness	0	+
Extrapyramidal effects	+	0
Leukocytosis	+	0
CPK elevation	+	0
Muscular rigidity	+	0
Myoclonus	0	+
Hyperreflexia	0	+
Ataxia	0	+

(Bernstein 1995)

Fig . Drug effects on manic-depressive illness

(Goodwin Jamison 1990)

serotonin : Clomipramine fluoxetine 37  
 . , 1994, p247

27:765-769 3 . 1988;

: Rapid cycling bipolar disorder. 1984; 8:164-171

28:523-526 1 . 1989;

3:55-61 . 1994;

가  
 1989; 28:705-710

1989; 28:245-257

1994; 1:7-16

1995; 38:1196-1202

: Serotonin 2 . ( )

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