

# 정신분열병의 병태생리 및 치료영역에서의 serotonin의 역할

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## Role of Serotonin in Pathophysiology and Treatment of Schizophrenia

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### ABSTRACT

There is no doubt that dopamine plays a critical role in the etiopathogenesis of schizophrenia. However, there appeared some limitations in explaining the complex phenomena of schizophrenia. Recent research data suggest that dysfunction in serotonergic system may be involved. Before the dopamine hypothesis of schizophrenia became established, the interest in serotonin(5-hydroxytryptamine, 5-HT) as an etiological substrate of this illness occurred. Recently the importance and extent of 5-HT's involvement in the pathophysiology and mechanism of action of antipsychotic drug is actively investigated. In recent years, therapeutic success of clozapine and risperidones has increased attention on the interaction between the 5-HT and dopamine systems in schizophrenia. This led to the concept of serotonin-dopamine antagonist for antipsychotics. The authors review the evidence for the role of 5-HT in schizophrenia and serotonin-dopamine interaction.

**KEY WORDS** : Serotonin · Schizophrenia · Serotonin-dopamine antagonist.

서 론

5 - HT

Serotonin(5 - hydroxytryptamine, 5 - HT) DA 가 5 - HT . 1950 , LSD(lysergic acid diethylamide) 가 5 - HT

5 - HT (SSRI) fl - 5 - HT

fluoxetine(Prozac) . LSD가 5 - HT 'serotonin deficiency hypothesis'가 (Breier 1995).

가 5 - HT

risperidone, clozapine 5 - HT LSD 5 - HT

5 - HT DA , DA

가 , DA 가 DA

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5-HT

가

5-HT

가

### Serotonin과 정신분열병의 병태생리학

1. 5-HT 기능의 뇌척수액과 말초혈액에서의 지표  
5-hydroxyindoleacetic acid(5-HIAA) 5-HT  
5-HT

1986).  
가

(Crow 1979 ; Korpi  
(prefrontal cortex) 5-HT2

(Arora 1991 ; Laruelle 1992 ; Mita 1986).  
, 5-HT -

5-HT

DA

5-HIAA

가

가

5-HT2, 5-HT1A

Tuckwell Koziol(1996)

가(Hashimoto 1991 ; Joyce 1993),  
5-HT1A 가, 5-HT2

5-HIAA

(Hashimoto 1993).

가

5-HT (transporter) [<sup>3</sup>H]par -

serotonergic turnover

oxetine

5-HT

(dorsal raphe nucleus) 5-HT1A

가

, 5-HT

(Stockmeier 1996),

(hippocampus) 5-HT

5 -

5-HT

HIAA (Potkin 1983 ; Loso -  
nczy 1986 ; Nyback 1983),

ylor 1996).

가

(Na -

5-HT

(Breier 1995).

5-HT

가

가

(Bleich 1988). , 5-HT 가

가

, DA

가

### 3. 유전적 연관성 연구(Linkage study)

5-HT

5-HT  
phate

adenosine diphos -  
dense granule sec -

Warren (1993)

retion(DGS)

haloperidol

5-HT2A

exon 102

T가 C

가

5-HT2A (polymorphism)

DGS

가

102T/C

(Ishigaki 1996 ; Wi -

5-HT

가

(Yao

lliams 1996).

1996).

### 2. 사후뇌조직 연구

### Serotonin과 정신분열병의 치료

5-HT

가

serotonin 가

LSD

5-HT, clozapine, Clozapine 5-HT2/D2 serotonin-dopamine antagonist(SDA) (Meltzer 1989). SDA

Risperidone(4~8mg) haloperidol (Chouinard 1993 ; Marder Meibach 1994). Risperidone, 5-HT2A D2 D2 5-HT2A clozapine D3, D4, noradrenergic, histaminergic (Leyson 1994).

### Serotonin-Dopamine 상호작용

SDA clozapine risperidone 5-HT DA

#### 1. Clozapine

clozapine 가 Clozapine 5-HT2A, D2, D4 (Van Tol 1991). histaminergic, cholinergic, noradrenergic receptor (McMillen Shore 1978 ; Peroutka 1980).

DA 5-HT 가 5-HT clozapine Meltzer Arora(1994) clozapine 5-HT2

clozapine 5-HT2 가 Farde(1992) Crouzel (1992) PET(Positron Emission Tomography) clozapine D2 20~67% 5-HT2 80% 5-HT2 가 clozapine D2 5-HT2

5-HT (agonist) m-chlorophenyl-piperazine(mCPP) mCPP

prolactin, cortisol, growth hormone 가 (Krystal 1993). clozapine mCPP prolactin 가 (Owen 1993). mCPP

가 clozapine (Kahn 1994). clozapine 5-HT, 5-HT clozapine

#### 2. Risperidone

Risperidone SDA

Serotonergic system DA DA neuron, 5-HT (agonist), serotonergic, SSRI DA 5-HT DA 가 clozapine risperidone 5-HT 가 5-HT 가 DA 가 5-HT DA 가 5-HT DA

#### 1. 추체외로 증상

clozapine D2 (Fa-rde 1992). 5-HT DA (raphe nucleus), 5-HT2 5-HT, 5-HT, SSRI (Bersani 1990 ; Miller 1990 ; Hicks 1990 ; Wadenberg 1992 ; Bethany 1993). Clozapine

Meltzer(1989) clozapine clozapine 5-HT2A clozapine 5-HT 5-HT DA 가 D2 75~80%

20~67% (Nordstrom 1995). serotonin - dopamine 가 D2

Risperidone clozapine . Risperidone 4~8mg/day

haloperidol 가 (Marder Meibach 1994 ; Chouinard 1993 ; Claus 1992). PET risperidone haloperidol D2 가 D2 가 risperidone haloperidol (Kapur 1995 ; Nyberg 1995). serotonin - dopamine . Risperidone 6mg/day , 5 - HT2 80% D2 74~83%

risperidone 5 - HT2 Gary 1996). D2 5 - HT risperidone 6mg/day 가 serotonin - dopamine (Shitij Gary 1996). DA D2 antagonism serotonin 5 - HT2A antagonism

## 2. 음성증상

clozapine 가 가 가 가

DA 가 (Weinberger Berman 1988 ; Davis 1991 ; Weinberger Lipska 1995). levodopa, amphetamine, bromocriptine DA (Rao Moller 1994 ; Owens 1994). 5 - HT 가 가 ( = . 5 - HT 가

## 결론

5 - HT 가  
5 - HT 가

antagonists)가 , SDA(serotonin - dopamine , SDA

중심 단어 : Serotonin - Serotonin - dopamine an -  
tagonist.

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