

강박장애의 병태생리와 치료에 있어 세로토닌의 역할*

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Role of Serotonin in Pathophysiology and Treatment of OCD*

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ABSTRACT

The clinical efficacy of serotonin reuptake inhibitors such as clomipramine in the treatment of obsessive compulsive disorder(OCD) has fueled interest in the neurobiological basis of this illness. OCD is responsive exclusively to potent serotonin reuptake inhibitors clomipramine, fluoxetine, fluvoxamine, sertraline, and paroxetine and this point forms the important evidence supporting a central role for serotonin in the pathogenesis of the disorder. Other serotonergic medications such as lithium, buspirone, trazodone, or fenfluramine may be useful as adjuvant treatments in treatment-refractory OCD and adjuvant antipsychotics are useful in tic disorders, personality disorders, and psychotic disorders. This paper reviews results of treatment studies, investigations of biological markers, and neuroendocrine challenges and implications for the role of serotonin in pathophysiology and treatment of OCD.

KEY WORDS : Serotonin · Obsessive-compulsive disorder.

서 론

강박장애 (obsessive-compulsive disorder : OCD)는 강박관념 (obsession)과 강박행위 (compulsion)을 특징으로 하는 만성적인 정신질환이다. 강박장애의 병태생리에 있어 세로토닌의 역할에 대한 관심이 증가되고 있다. 세로토닌 재흡수 억제제인 클로미프라민, 플루옥세틴, 플루보キサ민, 세트라린, 파록세틴은 강박장애에 효과적이며, 이는 세로토닌이 강박장애의 병태생리에 중요한 역할을 한다는 증거를 제공한다. 리튬, 부스피론, 트라조돈, 또는 펜플라민은 치료-refractory 강박장애에 보조요법으로 사용될 수 있으며, 항정신병약은 틱장애, 성격장애, 및 정신병장애에 사용된다. 본 논문은 치료 연구의 결과, 생물학적 표지자 연구, 그리고 신경내분비학적 도전과제와 세로토닌의 병태생리 및 치료에서의 역할을 검토한다.

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강박장애의 병태생리

가

(5 - hydroxytryptamine ; 5 - HT) 가 가

(peripheral marker) , (pharm - 1982 ; Flament 1987 ; Thoren 1980b) SRI 5 - HT

acological challenge test) 가 가 가 SRI 5 - HT

가 가 .

1. 세로토닌 가설

1) 세로토닌 가설의 근거

(1) 가 가

(3) (pharmacological challenge test) 가

clomipramine serotonergic raphe system

가 (Fernandez Lop - prolactin, growth hormone, ACTH

eizbor 1967) , 5 - HT

clomipramine 가

(serotonin reuptake inhibitor : SRI) fluoxetine, fluvox - amine, paroxetine, sertraline 가

(Goodman 1992 ; Greist 1995 ; Jenike 1992).

(, mCPP(meta - chloro - phenyl - piperazine) 5 - HT_{2C}, 5 - HT₃ , 5 - HT_{1A}, 5 - HT_{1D} (Barr 1992), dopamine, acetylcholine, 1 adrenergic, -adrenergic (Hamik Peroutka 1989). Zohar (1987) mCPP 12

가 (Ananth 1981 ; Thoren 1980a ; Zo - olactin cortisol , 가

har Insel 1987).

가 SRI 20 kg 0.5mg pr -

가 가 , 30% . Clomipramine (Clomipramine Collaborative Study Group 1991), SRI 가 . Hollander mCPP

(2) (peripheral marker) 가 Flament 가 prolactin (blunted)가 Charney (1988)

(1987) . mCPP 가 가

clomipramine 가 mCPP (Hollander 1992 ; Zohar 1987) mCPP

mCPP (Pigott (1992a), mCPP, MK-212, 5-HT_{1A}, 5-HT_{1D}, 5-HT_{2C}, 5-HT_{1A}, 5-HT_{2C}, MK-212, 5-HT_{1D}, sumatriptan, prolactin, cortisol, erg (1996). (Dolb-
 가, mCPP, 가, 5-HT_{1D}, 가, (4)
 mCPP, sumatriptan, prolactin, cortisol, 가 (Dolb-
 metergoline, mCPP, erg (1996).
 (Pigott 1991 ; Pigott 1993). mCPP, 가, 가
 가, (neural circuits) 가, (4)
 가, mCPP, 가, 가, positron emission tomography(PET)
 가, mCPP, 가, 가, (orbito-frontal region)
 , prolactin, cortisol, 가, (Baxter 1992 ; Nordahl
 가, (Hollander 1991 ; Zohar 1988). 1989).
 SRI, 가, (Baxter 1992)
 (adaptive down regulation)
 Ipsapirone, 5-HT_{1A}, Lesch (1991a)
 12 kg 0.3mg ipsapirone, tor, 'mo-
 가, 5-HT_{1A}, flu-, memory', 'Motor'
 oxetine, ipsapirone, 가, (Rolls
 ACTH, cortisol, Williams 1987 ; Stahl 1988). 'memory'
 (Lesch 1991b) SRI, (Stahl
 1988).
 MK-212, 5-HT_{1A}, 5-HT_{2C}, (Zo-
 har 1992). Bastini (1990) MK-212, 2. 도파민 가설
 cortisol, prolactin, 가, 40% SRI
 (1994) MK-212
 가, prolactin, cortisol, 가, 가
 212, Fluoxetine, MK-
 가, prolactine, 가, 가
 SRI
 (1995). 가, amphetam-
 ine, bromocriptone, apomorphine, L-DOPA
 가

(Pitman 1989),

약물 치료

amphetamine (psychostimulant)
cocaine Tourette's syndrome(TS)

1. 세로토닌 재흡수 억제 약물 : 단독치료(monopharmacotherapy)

clomipramine, fluoxetine, fluvoxamine, paroxetine, sertraline

(Von Economo's encephalitis, TS, Sydenham's chorea)

Clomipramine FDA

가 . 가
TS . TS 45 90%
(Swedo 1989 ;
Swedo 1993).
가 . 가 TS
(Leonard 1992),

fluoxetine 20mg, 40mg, 60mg
가 . Wheadon (1993)
348
paroxetine
paroxetine 40mg, 60mg
가 20mg 가
sertraline 가
(Jenike 1990 ; Greist 1995). SRI
clomipramine(1990),
fluoxetine(1995 ; 1994) 가

가
가 . TS "tics of the body"
"tics of the mind" , OCD

fluoxetine 20mg, 40mg, 60mg
가 . Wheadon (1993)
348

SRI 가
SRI
(McDougle 1990).

paroxetine
paroxetine 40mg, 60mg
가 20mg 가
sertraline 가
(Jenike 1990 ; Greist 1995). SRI
clomipramine(1990),
fluoxetine(1995 ; 1994) 가

가 가 가
(McDougle 1990 ; Mcdougle 1991).

SRI buspi-
rone trazodone . Buspi-
rone 가
(Jenike Baer 1988 ; Pato 1991), trazodone
가

3. 세로토닌-도파민 상호작용 가설

(TS
가
가
(preclinical study)

(Pigott 1992b).
가 5-HT NE
venlafaxine 가
(Rauch 1996), duloxetine

tonic inhib-
itory influence 가
, TS
가

mirtazepine .
clomi-
pramine, fluoxetine, fluvoxamine, paroxetine, sertraline 5

가 . 가
가 . Jenike (1990) Greist (1995)
meta - analyses

Table 1. 강박장애의 약물치료 전략

Clomipramine	250mg/day	10
Fluvoxamine	300mg/day	10
Fluoxetine	80mg/day	10
Sertraline	200mg/day	10
Paroxetine	60mg/day	10
SRI		
lithium		
bupirone		
clonazepam		
fenfluramine		
trazodone		
SRI		
SRI	SRI	

(Goodman 1993 ; Jenike Rauch 1994)

ird 1996).

1) 세로토닌 활성도의 강화
30%

SRI , 가
SRI
lithium, bu -
spirone, clonazepam, fenfluramine, trazodone
(Table 1).

SRI 5 - HT
5 - HT , 5 - HT
가
5 - HT SRI

가 가
Jenike (1990) clomipramine
, clomipramine
가

가
, SRI
L - tryp -
tophan 가 (Ra -
smussen 1984).

clomipramine
가
, 가

impilse
가 ,
5 - HT 5 - HT 가
Bupirone 5 - HT_{1a}
neronal impulse flow
SRI bupirone
가 SRI가

2. 병합강화치료(polypharmacotherapeutic augmentation)

가 ,
가
가
가

(Jenike 1991 ; Markovitz
1990) fluoxetine bupirone 가
가 (Pigott 1992c ;
McDougle 1993) 가
bupirone
, 가
SRI
fenfluramine
5 - HT 가
fenfluramine 5 - HT 가 가 SRI가
가 . Hollander
(1990) 7 7 6 fe -

nfluramine SRI , 5HT 가 SRI , Clonazepam SRI
 가 , ,
 SRI , clonazepam
 , 5-HT₂ 가 가 5-HT
 가 가
 5-HT₂ 가 down - regulation
 trazodone nefa -
 zodone serotonin - 2 antagonist/reuptake inhibitor (SA -
 RI) SARI (Joffe 1996)
 5-HT₂ 5-HT₂
 가 SRI SARI
 가 가
 trazodone SRI
 가 (Lydiard 1986)
 가 (Pigott 1992b)가 SRI
 SRI 5-HT₂
 , SRI SARI
 가 가
 SRI trazodone 가 SRI
 , nefazodone, venlafaxine, rispe -
 ridone 가

3) SRI와 다른 SRI의 병합

3. 새로운 약물

2) 세로토닌 이외의 신경전달물질체계에 작용하는 약물의 병합강화

결론

SRI
 SRI
 SRI 가
 2가 가
 , TS가
 가 SRI 가
 McDougle (1990) fluoxetine 가
 17 가
 9 가 Jacob - SRI
 sen(1995) risperidone 가
 5 3 가
 가 TS
 중심 단어 :
 , schizophreniform - type
 , schizopreniform - type
 , clonazepam benzodiazepine 가
 김찬형 · 송동호 · 이홍식 · 최낙경(1995) : 강박장애 환자에서
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