

세로토닌 수송체와 기분장애*

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5-HT Transporter and Mood Disorder*

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ABSTRACT

As numbers of serotonin's function are so many, studies of serotonin are numerous nowadays. In the beginning, concentration of metabolites such as 5 - HIAA was a key issue, but recent studies have been challenged for serotonin receptor genes and their relation to mood disorder. Serotonin transporter(5 - HTT) gene is a strong candidate gene of mood disorder for following reason. Serotonin transporter is a key protein in the serotonin pathway as it regulate the concentration of serotonin in the synaptic cleft and essential pathophysiology of depression is dysregulation of 5 - HTT so that all antidepressants have effect of 5 - HTT antagonist.

The decrease of 5 - HTT in the platelet and in brain of the depressive patients is much consistent results in the studies of the pathophysiology of mood disorder till now. By this, we will be able to develop simple and easy marker for diagnosis, type, and treatment monitoring of depression.

Many psychiatrists have sought the independent genes in relation to depression or schizophrenia. Obviously, the hereditary vulnerability contributes to etiology of mood disorders, but it is difficult to discriminate the independent genes because of many environmental factors. Moreover, in the hereditarily complex diseases such as mood disorder, the only vulnerability of gene can not sufficiently explain the etiology.

In the future, to exclude the role of the gene - environmental interaction, the methods such as gene transfer can be considered. In the opposite direction, by using the gene destruction method, the role of target genes can be examined. As yet the concept of the gene expression, neural plasticity, neurogenesis and etc, is the elementary stage. The development of this field will help to establish the treatment strategy of chronic and refractory mood disorders.

KEY WORDS : Serotonin transporter · Mood disorder.

서 론

19

(tonic)

(serotonin, 5 - HT)

, 1946

(enterochromaffin cell)

“ enteramine ”

. 1948

LSD

2001

“ Postgenomic Era in Biological Psychiatry ”

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가 , 가 (synaptic cleft) (Stahl 1998). 가 (monoamine oxidase) 5 - hydroxyindoleacetic acid(5 - HIAA) 가 (vesicular monoamine transporter) (secretory vesicle) 5 - HTT (homeostasis) (selective serotonin reuptake inhibitor)가 (clozapine) (risperidone) (Stahl 1998). (" ") (Lesch 2001). 5 - Hydroxyindoleacetic acid (5 - HIAA) 가 (serotonin transporter, 5 - HTT)가 5 - HTT 가 가 5 - HTT (Owen Nemeroff 1998).

세로토닌 수송체의 구조와 기능

5 - HTT Mayser (1991) , Lesch (1993) (Polymerase chain reaction, PCR) 5 - HTT (encoding) cDNA (cloning) 5 - HTT (1). 5 - HTT 630 12 hydrophobic membrane spanning region 가 (Barker and Blakely 1995). 5 - HTT (norepinephrine), (dopamine), (glycine), GABA 가 (Sodium - dependent monoamine transporter) (Ogilvie Harmar 1997). 5 - HTT

가 가 (synaptic cleft) (Stahl 1998). 가 (monoamine oxidase) 5 - hydroxyindoleacetic acid(5 - HIAA) 가 (vesicular monoamine transporter) (secretory vesicle) 5 - HTT (homeostasis) (selective serotonin reuptake inhibitor)가 (clozapine) (risperidone) (Stahl 1998). (" ") (Lesch 2001). 5 - HTT 가 (fenfluramine) (Lesch 2001).

세로토닌 수송체 유전자의 구조

17q11 - 12 , 14 (exon) 30kb (promoter) TATA like motif AP1, AP2, SP1, CRE (transcription factors) 가 5 ' - flanking region (2)(Lesch 2001). 가 (intron) 17 가 9, 10 12 VNTR(variable number tandem repeat) 가 (promotor) (upstream) GC - rich sequence (528

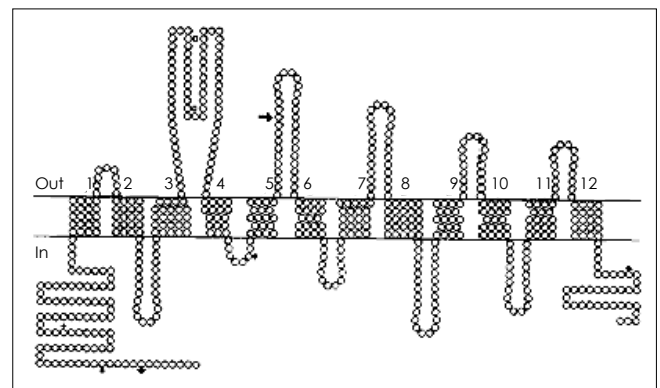


Fig. 1. Structural model of the human platelet serotonin transporter. Circles represent individual amino acids. The bold arrow indicates the position of an infrequent polymorphism or rare variant (Gly308). Open squares reflect putative glycosylation sites. Potential phosphorylation sites for AMP-dependent protein kinase and protein kinase C are indicated by crosses and triangles, respectively (Lesch et al 1995).

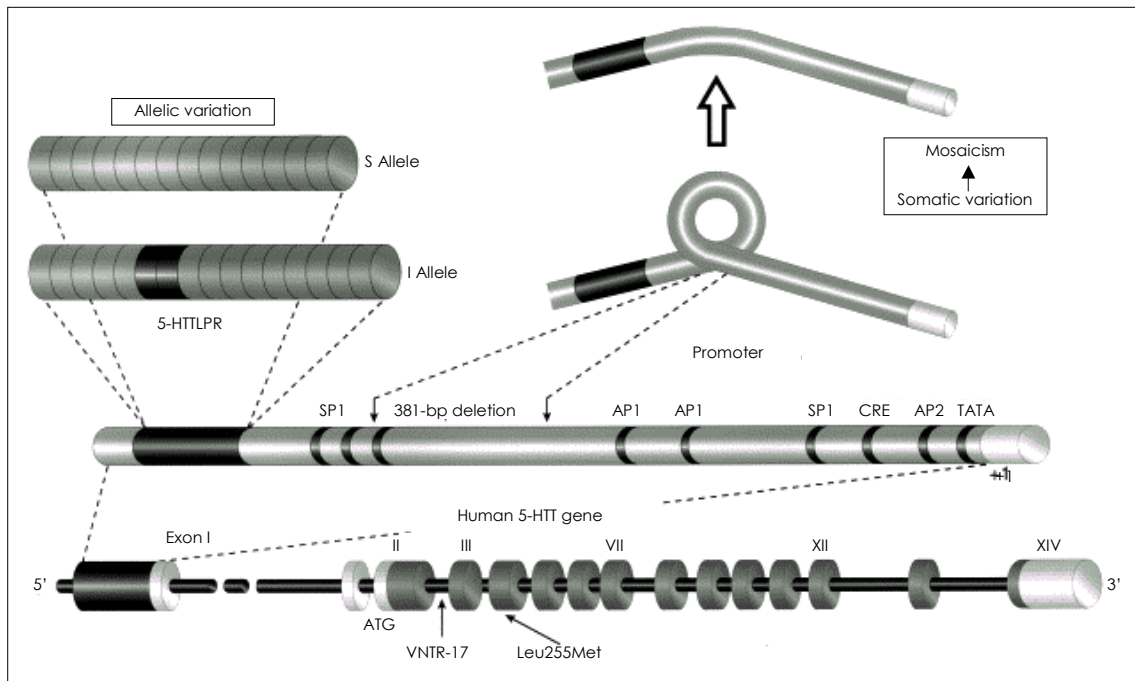


Fig. 2. Structure of the human 5-HT transporter gene and its 5'-flanking transcriptional control region. The 5-HT transporter gene promoter is defined by a TATA-like motif and several potential binding sites for transcription factors including AP1, AP2, SP1, and a CRE-like motif are present in the 5'-flanking region. The positions of the 5-HTT gene-linked polymorphic region (5-HTTLPR) and a 381 bp somatic deletion [del (17) (q11.2)] resulting in tissue-specific mosaicism of the 5-HT transporter gene promoter are also indicated. The localization of the deletion breakpoints adjacent to identical putative signal sequences (CAGCC) suggests a recombinase-like rearrangement event. The locations of a 17 bp variable tandem repeat (VNTR-17) located in intron 2 with two common (with 10 or 12 repeats) and one rare allele (with nine repeats), and a rare structural variant of the 5-HTT protein (Leu255Met) are also indicated (Lesch 2001).

bp “long” 484bp “short”)가

세로토닌 수송단백질과 우울증

1976 Asberg 68 5 -
HIAA 40% 가
가
가
가
1987). 5 -HTT (Melzer
가
5 -HTT (Owen
Nemeroff 1994). mRNA가
5 -HTT tine
가
(Malone Mann 1993),
5 -HTT가
(Perry 1983 ; Malison 1998) 5 -HTT
가

1. 항우울제와 5-HTT mRNA 발현(Expression)

5 - HTT

(presynaptic serotonin transporter gene)

가
가
2
,
5 - HTT 가
Lopez (1994), 가
3
5 - HTT mRNA
Lesch (1993a)
fluoxetine 5 - HTT
Pineyro (1994) paroxe-
5 - HTT
Hrdina and Vu(1993) fluoxetine
가
DNA

2. 혈소판의 세로토닌 수송체

5 - HTT

paroxetine Zanardi 가
 (2000) l/l l/s s/s
 (Be-
 nedetti 1998). (2000) 6
 (long variant ho-
 mozygote, l/l) s/s
 5-HTTLPR
 가

세로토닌 수송체와 양극성 장애

5-HTT 가
 5-HTT
 VNTR 12 가
 (Collier 1996 ; Kirov 1999).

결론

5-HTT
 가
 Gene
 transfer
 gene expression, neural plasticity, neu-
 rogenesis

중심 단어 :

참고 문헌

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