

자살 행동과 연관된 생물학적, 유전적 예측인자*

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Biological and Genetic Prediction Factors Associated with Suicidal Behavior*

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ABSTRACT

Most suicides (about 90%) occur in the context of psychiatric disorders. Prediction of suicide risk in patients with mental illness is very important in preventing suicide attempts. However, current approaches to predict suicidality are based on clinical history and have low specificity and biological markers are not yet included. Many studies have explored the association between different biological parameters and suicidality. Studies of cerebro - spinal fluid (CSF) demonstrated that 5 - HIAA and HVA levels were lower in patients with a history of suicide. Platelet serotonin transporter and the 5 - HT₂ serotonin receptor have also been studied in relation to violence and suicide. Depressive patients with greater suicidal tendency had significantly lower cholesterol concentrations but some researchers failed to find the correlation. DST non - suppression is reported to predict suicidality in major depression. Several studies demonstrated a relationship between intron 7 polymorphism of tryptophan hydroxylase and suicidal behavior. Since suicide is not occurred in a single disease, the systematic and comprehensive study in large samples with various diagnoses is necessary to find the biological and genetic predictors of suicidal behavior.

KEY WORDS : Suicide · Biological marker · Genetic marker · Prediction · Serotonin · Neurotransmitter.

서 론

(suicide) 90% , 1-3)
60% ,
20% ,
15% .

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14-24) Kreiger cortisol 17 - hydroxycorticosterone , cortisol
 가 , 33) ,
 23) prefrontal lobe corticotropin releasing factor
 25-27) 가 가 가
 28) 가 가 가 34) CRF 35)
 가 150mg/ml 가 가
 가 , CRH mRNA CRH - R1 R2
 가 (pitui-
 tary) CRH - R1/CRH - R2 36)
 가
 , HPA noradrenergic system
 Dexamethasone Suppression Test(DST) 37)38)
 가 가 가 DST 39)
 (lipid micro-
 viscosity) Neuropeptide Y(NPY) ,
 29) , presynaptic (caudate nucleus)
 sites 5 - HT 가 post- NPY 가 40) Westrin
 synaptic sites 5 - HT DST cortisol
 , 30)
 가 n - 6 n - 3 NPY cortisol
 , n - 3 41)
 (synaptic membrane) , Hurd opioid neuropep-
 (neurotransmit- tide system 가
 ter) (signal transduction), prodynorphin mRNA
 , 2 , in situ hybridization histochemistry
 MAO(monoamine oxidase) prodynorphin, proenkephalin D1, D2
 31) mRNA 가 ,
 가 prodynorphin mRNA 가
 42) opioid neuropeptide sys-
 tem 가

3. 자살과 신경펩타이드

- - (HPA)
 Fawcett
 17 - hydro-
 32)
 xycorticosterone 가

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, 21 TPH
 U
 1%
 가
 가
 , Catechol - O - methyltransferase , Brain -
 derived neurotrophic factor(BDNF) , Neuro-
 trophic tyrosine kinase receptor, type 2(NTRK2)
 corticotropin re-
 leasing hormone, neuropeptide Y, prodynorphin, so-
 matostatin
 가 ,⁴³⁾ ⁴⁴⁾
⁴⁵⁾ trait
 marker
 45%가 가
⁴⁶⁾ 55% 가
⁴⁶⁾ 가
 가
 (complete suicide) 가
 가
 가
 (candidate gene)
 가
 가
 5 - HIAA ¹²⁾
 가
 tryptophan hy- 5 - HIAA
 droxylase(TPH)
 TPH intron 7
 TPH U 가 가
 가 ⁴⁷⁾ U
 5 - HIAA fenfluramine
 가 ⁶⁾
 가

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유전자적 예측인자**

Table 1. Candidate genes and polymorphisms associated with suicidal behavior

Candidate gene and polymorphism	Methods	Findings	Ref.
Tryptophan hydroxylase gene			
TH gene : A-218C A-6526G 5HT2A gene : A-1438G	a) 28 postmortem brains of suicide victims b) TPH immunoreactivity as a pre-synaptic marker & 5-HT2A receptor density as post-synaptic marker c) TPH(A218C & A-6526G) & 5-HT2A(A-1438G)	a) AA genotype of A218C polymorphism of TPH gene showed higher TPH immunoreactivity & lower 5HT2A receptor density than any other genotypes b) A218C polymorphism of TPH gene is a candidate gene for neurobiological studies of suicide	53)
A-218 polymorphism	Meta-analysis 898 patients	Weak increase in frequency of A218 allele & an over-representation if A-carriers in suicide attempters/victims	54)
Serotonin transporter gene			
5-HTTLPR gene	24 depressed suicide victims	Higher frequency of 5-HT transporter gene long(L) allele in depressed suicides	55)
5-HTTLPR gene	Moderate of 5-HTT gene in relation to stressful life events on depression and suicidality	Two copies of the short allele of 5-HTT promoter polymorphism exhibited more depressive symptoms, diagnosable depression & suicidality than homozygous for long allele	56)
5-HTTLPR gene	a) 180 suicide attempter b) Classify to S type with low expression(s/s, s/l) & L type with high expression(l/l)	a) S type were overrepresented in female attempters compared to male attempters b) S females were overrepresented among non-lethal female attempters	57)
5-HTTLPR gene	a) 47 volunteers b) Questionnaires about family history of suicide	Allelic homozygosity (short variant) was associated with family history of suicidality	58)
Serotonin 2A receptor gene			
102T/C polymorphism	159 patients with major depression	a) Association between 5HT(2A)-C allele and suicidality in MDD b) Increased risk for suicidality conferred by 5-HT(2A)-C allele is primarily associated with suicidal behavior and not with the diagnosis of MDD itself	5)
102T/C polymorphism	142 homogenous population of UPAD with suicidal attempt	No association of the HTR2A polymorphism was found	59)
1438A/G polymorphism	127 bipolar disorder 65 unipolar disorder	a) Higher frequency of A4 allele in affected patients b) Patients with no personal &/or familial history of suicide attempts mainly accounted for the excess of A allele in affected patients	60)
Serotonin 1A receptor gene			
C(-1019)G promoter polymorphism	In previous cohort study in depressed patients, homozygous G(-1019) allele was enriched two(-)fold versus controls and in completed suicide cases the G(-1019) allele was enriched fourfold	A transcriptional model in which the G(-1019) allele derepresses 5-HT1A autoreceptor expression to reduce serotonergic neurotransmission, predisposing to depression and suicide	61)
Pro16Leu & Gly272Asp polymorphism	Examined the association between suicide victims who completed suicide	No significant difference in genotype distribution or allele frequencies between suicide victims and controls	62)

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