

여성 강박장애의 임상적 특성과 치료 전략

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Clinical Characteristics and Treatment Strategies in Female Patients with Obsessive-Compulsive Disorder

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This article reviews clinical characteristics, neurobiological aspects and treatment strategies in female patient with obsessive-compulsive disorder (OCD) compared to male. Female with OCD had a later age of onset and different patterns of OCD symptomatology and comorbidity. Female with OCD showed more favorable course and also reported more frequently stressful event in preceding OCD onset. The onset or worsening of OCD was related to female reproductive cycle events, especially at menarche and postpartum. There is a paucity of investigation regarding gender difference in treatment response in OCD. It has been suggested that gender may contribute to the clinical and biological heterogeneity of OCD and also sexually dimorphic pattern of genetic susceptibility to OCD may be present. (J Korean Neuropsychiatr Assoc 2006;45 (2) :93-99)

KEY WORDS : Female · Obsessive-compulsive disorder · Clinical characteristics · Treatment response.

서론

강박장애(OCD)는 전 세계적으로 1.5%~3.3%의 유병률을 보이는 흔한 정신질환이다. 그러나 아직까지도 그 병인, 임상적 특성, 치료 전략에 대한 연구는 부족한 실정이다. 특히 여성 환자에 대한 연구는 더욱 부족한 편이다. 본 연구는 여성 환자와 남성 환자를 비교하여 OCD의 임상적 특성과 치료 전략을 살펴보았다. 연구 결과, 여성 환자는 남성 환자에 비해 발병 연령이 늦고, 증상 발현 전의 스트레스 사건이 더 빈번하게 보고되었다. 또한, 여성 환자는 남성 환자에 비해 치료 반응이 더 좋았다. 이러한 결과는 성별이 OCD의 임상적 특성과 치료 반응에 영향을 미칠 수 있음을 시사한다. 또한, 성별에 따른 유전적 취약성의 차이를 시사하는 성적 이형성 패턴이 존재할 수 있다.

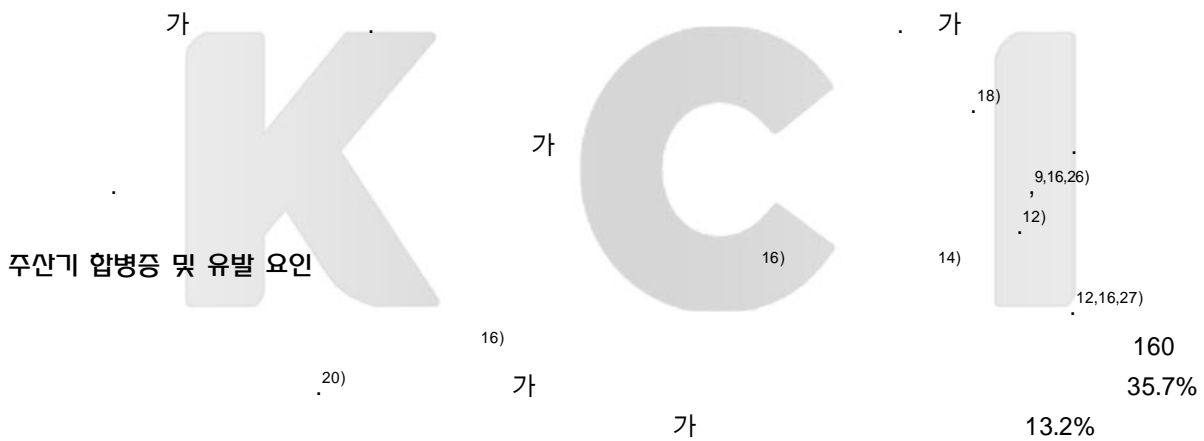
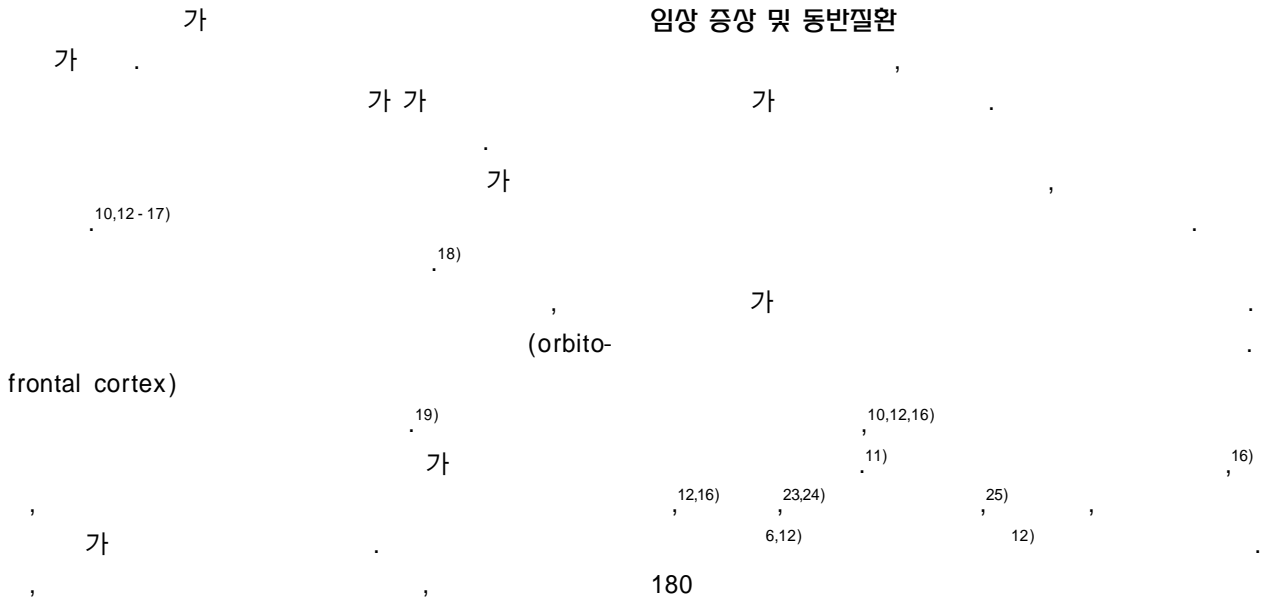
본론

역학 및 발병 연령

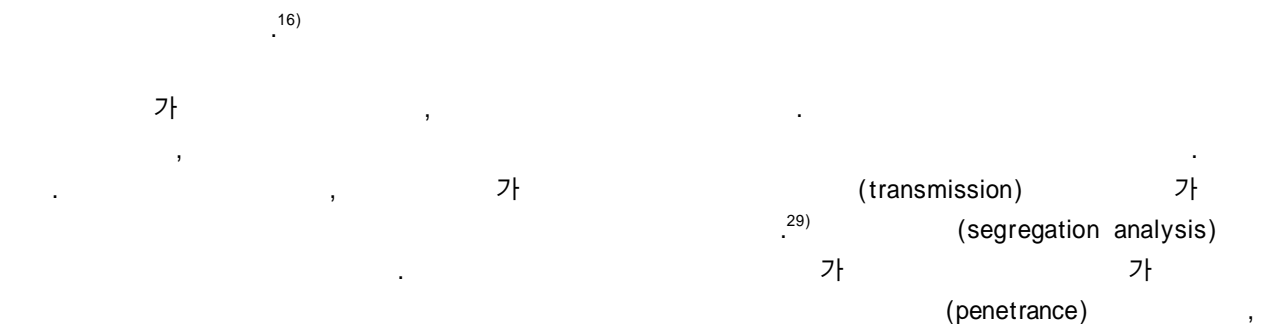
본 연구는 2006년 2월 15일부터 2006년 3월 10일까지 진행된 연구이다. 연구 대상자는 150명이며, 그 중 여성 환자는 75명(50%)이었다. 연구 결과, 여성 환자는 남성 환자에 비해 발병 연령이 늦고, 증상 발현 전의 스트레스 사건이 더 빈번하게 보고되었다. 또한, 여성 환자는 남성 환자에 비해 치료 반응이 더 좋았다. 이러한 결과는 성별이 OCD의 임상적 특성과 치료 반응에 영향을 미칠 수 있음을 시사한다. 또한, 성별에 따른 유전적 취약성의 차이를 시사하는 성적 이형성 패턴이 존재할 수 있다.

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임상 증상 및 동반질환



유전연구



9% 25% , (pene-
trance) (30)
가 (5HT_{1D} gene) 여성 생식 주기와 광박장애
(female reproductive cy-
cle) (gonadal steroid)
(allele)가 (32,33) G cle) (42) (44,45) (46) (47)
(Africaner population of South Africa)
가 G861C (variant) C (42,48)
(allele) (homozygous) (49)
가
MAO - A 가
EcoRV (variant) MAO - A 3.4~33.3%
EcoRV (variant) 12~40%
(28) Camarena (34) 가 (44,50 - 52)
T 가 (45)
C 가
Fun4HI (35) (46,48)
Catechol - O - Methyltransferase gene
(COMT) Monoamine Oxidase A gene(MAO - A)
(polymorphism) 가 (43,46,48)
(SLC6A4) (36 - 68) (5 - HTTLPR) 가
가 (39) (53)
(gonadal hormone)
1/4 가
가 (43)
lamus - pituitary - adrenal, HPA axis) (hypotha-
(54) 가
(55)
가
(40,41) (55)
가 (40) 가 (56)
가
(45,47,48)

45,57)

치료적 접근

가

가

가

가

에스트로겐과 강박장애

가

가?

가? Zohar⁵⁸⁾

가

가

가

가

가

^{59,60)}

(corpus callosum),⁶¹⁾ (axon) (my-
elinization),⁶²⁾ preoptic area⁶³⁾
가

가

가

10

가 가

(neuromodulatory effect) (D2),
5-HT₂, NMDA, GABA
⁶⁴⁻⁶⁶⁾

가

1993

(Food

and Drug Administration)

가

⁷⁰⁾

가

⁶⁶⁻⁶⁹⁾

가 가

가

- and comorbid obsessive-compulsive disorder. *J Am Acad Child Adolesc Psychiatry* 1994;33:795-804.
- 22) Lochner C, du Toit PL, Zungu-Durwayi N, Marais A, van Kradenburg J, Seedat S, et al. Childhood trauma in obsessive-compulsive disorder, trichotillomania, and controls. *Depress Anxiety* 2002;15:66-68.
 - 23) Skoog G. Onset of anancastic conditions. A clinical study. *Acta Psychiatr Scand. Suppl.* 1965;184:1-82.
 - 24) Swedo SE, Rapoport JL. Phenomenology and differential diagnosis. In: Rapoport JL editor. *Obsessive-Compulsive Disorder in Children and Adolescents*. Washington DC: American Psychiatric Press;1989.
 - 25) Fischer DJ, Himle JA, Hanna GL. Age and gender effects on obsessive-compulsive symptoms in children and adult. *Depress Anxiety* 1997;4:237-239.
 - 26) Fahy TA, Oscar A, Marks I. History of eating disorders in female patients with obsessive-compulsive disorders. *Int J Eating Disord* 1993;14:439-443.
 - 27) Perugi G, Akiskal HS, Pfanner C, Presta S, Gemignani A, Milanfrachi A, et al. The clinical impact of bipolar and unipolar affective comorbidity on obsessive-compulsive disorder. *J Affect Dis* 1997;46:15-23.
 - 28) Lochner C, Hemming SMJ, Kinnear CJ, Moolman-Smook JC, Corfield VA, Knowles JA, et al. Gender in obsessive-compulsive disorder: clinical and genetic findings. *Eur Neuropsychopharm* 2004;14:105-113.
 - 29) Nestadt G, Lan T, Samuels J, Riddle M, Bienvenu OJI, Liang KY, et al. Complex segregation analysis provides compelling evidence for a major gene underlying obsessive-compulsive disorder and for heterogeneity by sex. *Am J Hum Genet* 2000;67:1611-1616.
 - 30) Cavallini MC, Pasquale L, Bellodi L, Smeraldi E. Complex segregation analysis for obsessive compulsive disorders and related disorders. *Am J Med Genet* 1999;88:38-45.
 - 31) El Masari M, Bouchard C, Blier P. Alteration of serotonin release in the guinea pig orbito-frontal cortex by selective serotonin reuptake inhibitors. Relevance to treatment of obsessive-compulsive disorder. *Neuropsychopharmacology* 1995;13:117-127.
 - 32) Mundo E, Bareggi SR, Pirola R, Bellodi L. Effect of acute intravenous clomipramine and antiobsessional response to proserotonergic drugs: is gender a predictive variable. *Biol Psychiatry* 1999;45:290-294.
 - 33) Mundo E, Richter MA, Zai G, Sam F, McBride J, Macciardi F, et al. 5HT1Dbeta Receptor gene implicated in the pathogenesis of Obsessive-Compulsive Disorder: further evidence from a family-based association study. *Mol Psychiatry* 2002;7:805-809.
 - 34) Camarena B, Rinetti G, Cruz C, Gomez A, de Jr LF, Nicolini H. Additional evidence that genetic variation of MAO-A gene supports a gender subtype in obsessive-compulsive disorder. *Am J Med Genet* 2001;105:279-282.
 - 35) Karayiorgou M, Altemus M, Galke BL, Goldman D, Murphy DL, Ott J, et al. Genotype determining low catechol-O-methyltransferase activity as a risk factor for obsessive-compulsive disorder. *Proc Natl Acad Sci USA* 1997;94:4572-4575.
 - 36) Karayiorgou M, Sobin C, Blundell ML, Galke D, Murphy DL, Malinova L, et al. Family based association studies support a sexually dimorphic effect of COMT and MAOA on genetic susceptibility to obsessive-compulsive disorder. *Biol Psychiatry* 1999;45:1178-1189.
 - 37) Alsobrook JP, Zohar AH, Leboyer M, Chabane N, Ebstein RP, Pauls DL. Association between the COMT locus and obsessive-compulsive disorder in females but not males. *Am J Med Genet* 2002;114:116-120.
 - 38) Kinnear CJ, Niehaus DJ, Seedat S, Moolman-Smook JC, Corfield VA, Malherbe G, et al. Obsessive-compulsive disorder and a novel polymorphism adjacent to the oestrogen response element (ERE 6) upstream from the COMT gene. *Psychiatr Genet* 2001;11:85-87.
 - 39) Kinnear DJ, Niehaus DJH, Moolman-Smook JC, du Toit PL, van Kradenburg J, Weyers JB, et al. Obsessive-compulsive disorder and the promoter region polymorphism (5-HTTLPR) in the serotonin transporter gene (SLC6A4): a negative association study in the African population. *Int J Neuropsychopharmacol* 2000;3:327-331.
 - 40) Behar D, Rapoport JL, Berg CJ, Denckla MB, Mann L, Cox C, et al. Computerized tomography and neuropsychological test measures in adolescents with obsessive-compulsive disorder. *Am J Psychiatry* 1984;141:363-369.
 - 41) Baxter Jr LR, Schwartz JM, Mazziotta JC, Phelps ME, Pahl JJ, Guze BH, et al. Cerebral glucose metabolic rates in nondepressed patients with obsessive-compulsive disorder. *Am J Psychiatry* 1988;145:1560-1563.
 - 42) Weiss M, Baerg E, Wisebord S, Temple J. The influence of gonadal hormones on periodicity of obsessive compulsive disorder. *Can J Psychiatry* 1995;40:205-207.
 - 43) Labad J, Menchon JM, Alonso P, Segalas C, Jimenez S, Vallejo J. Female reproductive cycle and obsessive-compulsive disorder. *J Clin Psychiatry* 2005;66:428-435.
 - 44) Diaz SF, Grush LR, Sichel DA, Cohen LS. Obsessive-compulsive disorder in pregnancy and the puerperium. In: Pato MT, Steketee G, editors. *OCD Across the Life Cycle*. Washington, DC: American Psychiatric Press;1997. p.97-112.
 - 45) Neziroglu F, Anemone R, Yaryura-Tobias J. Onset of obsessive-compulsive disorder in pregnancy. *Am J Psychiatry* 1992;149:947-950.
 - 46) Williams K, Koran L. Obsessive-compulsive disorder in pregnancy, the puerperium, and the premenstrual. *J Clin Psychiatry* 1997;58:330-334.
 - 47) Altshuler LL, Hendrick V, Cohen LS. Course of mood and anxiety disorders during pregnancy and the postpartum period. *J Clin Psychiatry* 1998;59:29-33.
 - 48) Sichel DA, Cohen LS, Dimmock JA, Rosenbaum JF. Postpartum obsessive compulsive disorder: a case series. *J Clin Psychiatry* 1993;54:154-150.
 - 49) Rodopman-Arman A, Yazgan MY. Obsessions associated with hormone therapy. *J Am Acad Child Adolesc Psychiatry* 1998;37:1244-1245.
 - 50) Pollitt J. Natural history of obsessional states. *Br Med J* 1957;9:133-140.
 - 51) Ingram IM. Obsessional illness in mental hospital patients. *J Ment Science* 1961;107:382-402.
 - 52) Lo WH. A follow-up study of obsessional neuritics in Hong Kong Chinese. *Br J Psychiatry* 1967;113:823-832.
 - 53) Leckman JF, Goodman WK, North WG, Chappell PB, Price LH, Pauls DL, et al. The role of central oxytocin in obsessive-compulsive disorder and related normal behavior. *Psychoneuroendocrinology* 1994;19:723-749.
 - 54) Steiner M, Dunn E, Born L. Hormones and mood: From menarche to menopause and beyond. *J Affect Disord* 2003;74:67-83.
 - 55) Freeman MP, Smith KW, Freeman SA, McElroy SL, Kmetz GE, Wright R, et al. The impact of reproductive events on the course of bipolar disorder in women. *J Clin Psychiatry* 2002;63:284-287.
 - 56) Miller FD, Ozimek G, Milner RJ, Bloom FE. Regulation of neuronal oxytocin mRNA by ovarian steroids in the mature and developing hypothalamus. *Proc Natl Acad Sci USA* 1989;86:2468-2472.
 - 57) Buttolph ML, Holland AD. Obsessive-compulsive disorder in pregnancy and childbirth. In: Jenike MA, Baer L, Minichiello WE, editors. *Obsessive-compulsive disorder: Theory and Management*. Chicago: Year Book Medical Publishers Inc;1990. p.89-95.
 - 58) Zohar J, Gross-Isseroff R, Hermesh H, Weizman A. Is there sexual dimorphism in obsessive-compulsive disorder? *Neurosci Biobehav Rev* 1999;23:845-849.
 - 59) Beyer C. Estrogen and the developing mammalian brain. *Anatomy and Embryology* 1999;199:379-390.
 - 60) Hutchison JB, Wozniak A, Beyer C, Karolczak M, Hutchison RE. Steroid metabolism enzymes in the determination of brain gender. *J Steroid Biochem Mol Biol* 1999;69:85-96.
 - 61) Kawata M. Roles of steroid hormones and their receptors in structural organization in the nervous system. *Neuroscience Research* 1995;24:1-46.
 - 62) Aboitiz F, Rodriguez E, Olivares R, Zaidel E. Age-related changes in fibre composition of the human corpus callosum: sex differences. *Neuroreport* 1996;7:1761-1764.
 - 63) Swaab DF, Fliers E. A sexually dimorphic nucleus in the human brain-a review of the literature. *Fortschritte der Neurologie-Psychiatrie FDN* 1996;64:382-389.
 - 64) Sumner BEH, Fink G. Oestradiol-17B in its positive feedback mode significantly increases 5-HT2a receptor density in the frontal, cin-

- gulated and piriform cortex of the female rat. *J Physiol* 1995;483:52.
- 65) FinK G, Sumner B, McQueen JK, Wilson H, Rose R. Sex steroid control of mood, mental state and memory. *Clin Exp Pharmacol Physiol* 1998;25:764-765.
- 66) Shughrue PJ, Lane MV, Merchenthaler I. Comparative distribution of estrogen receptor and X and B mRNA in the rat central nervous system. *J Compr Neurol* 1997;388:507-525.
- 67) Casas M, Alvarez E, Duro P, Pinet MC, Tejero A, Udina C, et al. Use of antiandrogens in the treatment of obsessive compulsive neurosis. *Acta Psychiatrica Scand* 1986;73:221-222.
- 68) Casas M, Alvarez E, Duro P, Pinet MC, Tejero A, Udina C, et al. Use of antiandrogens in the treatment of obsessive compulsive disorders: theoretical considerations. In: Lerer B, Gershon S, editors. *New directions in affective disorders*, New York: Springer;1989. p.438-440.
- 69) Feldman JD, Noshirvani H, Chu C. Improvement in female patients with severe obsessions and/or compulsions treated with cyproterone acetate. *Acta Psychiatr Scand* 1988;78:254.
- 70) Merkatz RB, Temple R, Subel S, Feiden K, Kessler DA. Women in clinical trial of new drugs: a Change in Food and Drug Administration policy. *N Engl J Med*;1993. p.329-292-296.
- 71) Rubinow DR, Schmidt PJ, Roca CA. Estrogen-serotonin interactions: implications for affective regulation. *Biol Psychiatry* 1998;44: 839-850.

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