

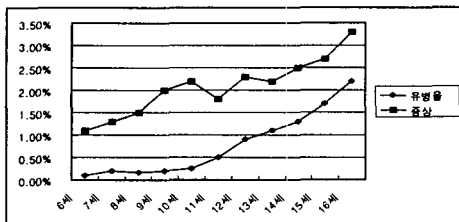
Different or Distinct? - Child & Adolescent OCD -

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Common or Rare ?

- Hollingsworth(1980): "소아-청소년에서의 강박장애는 성인에서 보다도 더욱 드물다"
- Nation wide child psychiatric epidemiologic studies from late 80's: 1.0-3.6% in child and adolescent period
- Onset age of adult OCD patient: retrospective studies: 약 반수 정도가 소아 및 청소년기 발병을 보인다
- Up-to-date field studies: pre-pubertal vs post-pubertal

Age and prevalence rate:meta-analysis



→ So, OCD in C & A period is not rare psychiatric disorder

Contents of Obsession/Compulsion

- Very similar contents of O-C symptoms with adult cases
- Obsession
 - Contamination fear > pathologic doubt > symmetry, perfection > sexual-aggressive theme
- Compulsion
 - Washing behavior > checking > rumination > counting > ordering

Distinct feature of Symptoms

1. Rare resistance
2. No ego alien feeling, esp, prepubertal
3. No insight
4. More frequent in compulsion only

Sex distribution

- 성인기 강박장애 환자연구
 - Overall sex ratio: 여>남 or 여=남
 - 발병연령별 sex ratio: 5세-18세 사이발병: 남성우위
25세 이상발병: 여성우위
- 소아-청소년기 강박장애 환자 연구
 - 임상군 대상 연구: 1.5-2.5 배 정도로 남아 우위
 - 지역 사회군 연구: 2배 이상 남아에서 많은 것으로 조사 (Heyman 2001)

→ Two peak onset age in OCD: bimodal distribution: early= boy ↑

Comorbidity

Study	Sample	Age	Measure	MDD+	ANX+	Any Psy+
Hanna(1995)	n=31	13.5	DICA	32	26	84
Douglass(1995)	n=37	14.3	DISC	62	73	84
Valleni(1994)	n=26	13	K-SADS	45	63	nc
Johnson(1993)	n=100	12.4	Case review	26	24	nc
Toro(1992)	n=72	12	K-SADS	22	41.6	72.8
Fiddle(1990)	n=21	12.2	K-SADS	10	60	71.4

- Selective review from 1990 –1995
- MDD: major depressive disorder
- ANX: social phobia, separation anxiety, simple phobia, overanxious disorder
- Any Psy: MDD + ANX + ADHD, ODD, Tic disorder etc

Comorbidity-tic disorder

- Child OCD F/U studies: 20-38% point prevalence & 30-60% Life time prevalence of tic disorder
- Adult onset OCD or Child onset adult OCD; no specific report
- General adult OCD: 12-19% tic lifetime prevalence

Comorbidity-tic disorder

- Atypical, tic-like compulsion in C & A OCD patients
 - Writing, vocalization, moving in 30% of Pts (Swedo et al)
 - Touching, vocalization like throat clearing
 - Breathing associated compulsion
 - More common in early onset(<10) patients
 - Associated with tourette's disorder in the future

→ high association with tic : distinct feature of C&A OCD

Family studies

- Adult OCD family studies
 - 149 relatives of 50 adult pts; only 1 OCD case(McKeon et al)
 - Comparative studies of primary relatives of 33 OC cases vs 32 control: no differences in OC and tic disorder(3% vs 2 %, 4% vs 7%: Black et al)

Family studies

- C & A OCD family studies
 - 71% of OC children's parents have OC symptoms(59%) or OCD(12%)
 - 141 relatives of C&A OC : 30% OCD, 44% tic disorder(친척에서의 틱 장애 유병은 강박장애 환자의 틱 동반여부와 무관)

Family studies

- 성인 강박장애 발병시기별 가족력 조사
 - 18세 미만 발병군 vs 18세 이상 발병군
 - 18세 미만군: 2배 이상의 OCD 가족력, 높은 틱장애 가족력
- Tic 장애 아동-청소년 가족력 연구
 - 강박장애의 높은 발생율

→ C & A OCD는 높은 OC 가족부하, 틱 장애와 높은 유전적 연관성을 보임

Molecular genetic studies

- Candidate gene studies for OCD
 - Positive findings only:
 - **5 HT 1 D beta** gene polymorphism (2 studies by same research group)(Mundo et al 2002)
 - **5-HT2A** gene polymorphism: specific association with female OCD(Enoch et al 2001)
 - **5 HTTLPR** gene insertion/deletion polymorphism: specific association with repetitive ritual(counting/repeating) and tic symptom(Gavallini et al 2002)
 - **5-HT transporter promoter regulatory region polymorphism /5-HT transporter coding gene polymorphism**(2 study group 1999, 2000)
- No specific C & A OCD or early onset OCD genetic studies

Neuroimaging studies

- Adult OCD :
 - Consistent findings:
 - Orbitofrontal and cingulate cortex hyperfunction
 - Normalization after adequate pharm Tx and CBT
 - Relatively, inconsistent and contradictory data from structural and functional studies in Basal ganglia(striatum(caudate, putamen), GP)
 - Meta-analysis result from many studies suggest no significant differences in caudate function or structures in adult OCD

Neuroimaging studies

- Adult onset OCD
 - Very few neuroimaging studies about adult onset OCD patient
 - Aylward et al: adult onset OCD 환자들만을 모아서 대조군과 비교연구- no differences in caudate, striatum & globus pallidus
 - Preliminary assumption: relatively few differences in basal ganglia structure or volume in adult onset OCD patients

Neuroimaging studies

- C & A OCD
 - Consistent findings in striatum abnormalities(volume reduction, hyperfunction)
 - relatively consistent finding in thalamus
 - OC symptoms severity : correlated with striatal volume reduction
 - OC symptom improvement: correlated with striatal functional decrease

Neuroimaging studies

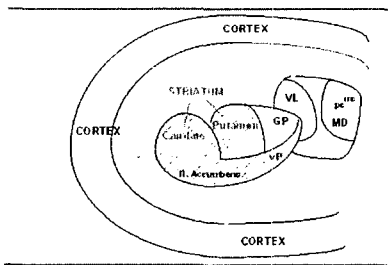
- Tourette or tic disorder
 - Volume reduction in striatum, thalamus
 - Reversed normal asymmetry in caudate
 - Functional impairment in thalamic area

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- C & A OCD has prominent subcortical abnormalities
 - In CSTC circuit, Subcortical abn may be primary
 - C & A OCD has shared feature with Tic in subcortical pathology

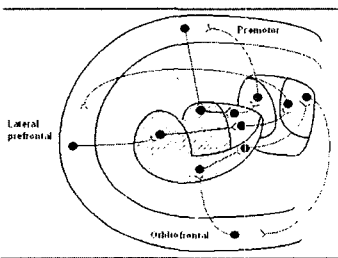
Shared common pathway?

- CSTC pathway:
 - Orbito-frontal cortex; 사회적-인지적 주제와 연관된 복잡한 인지과정 매개
 - Globus pallidus: 감각운동회로-감각 및 신체의 움직임 조절
 - Ventral striatum: limbic associated area-감정과 동기 조절
- C & A OCD / TS: shared CSTC pathology, 그러나 OCD는 일차적으로 ventral striatum, TS은 일차적으로 globus pallidus의 병리를 가질 가능성

Shared common pathway?



Shared common pathway?



Pediatric Autoimmune Neuropsychiatric Disorder
Associated Streptococcal infection

- 소아-청소년기 OCD, Tic or ADHD 일부(Yale)
- NIH에서 제안한 진단기준
 - 10세 이전에 발병한 OCD, Tic disorder
 - 수주이내 발병
 - Episodic wax and wane course
 - 발병/악화와 GABHS 감염간의 시간적 연관성
 - GABHS 감염을 시사하는 증거(pharyngitis, Culture, ASO titer)
 - 악화기에 나타나는 신경학적이상(tic, hyperactivity)

PANDAS-established ?

- ↑ anti-streptococcal antibodies / anti-neuronal antibodies
- ↑ basal ganglia volumes on MRI
- Significant correlation among Increased antibodies – increased basal ganglia volumes – Tic, OCD symptom severity or ADHD (Yale)

● NIH case report(1998):

- 10세 발병 OCD, 14세 PANDAS 진단 d/t course, high ASO titer, 치료저항성, BG swelling
- Plasmapheresis 치료 - 항체가의 허강 -MRI 상 basal ganglia volume 감소- 강박증상의 호전

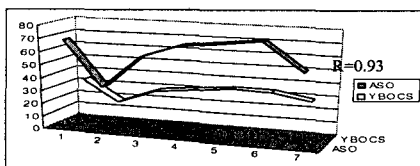
PANDAS-vulnerability factor ?

- Genetic vulnerability
 - Vulnerable to formation of antistreptococcal antibodies that cross-react with neuronal proteins
 - Vulnerable to immune dysregulation
 - Vulnerable to developing neurotransmitter dysfunction
- D8/17: monoclonal antibody that identifies a specific B lymphocyte cell-surface marker
 - elevated D8/17 marker in children with PANDAS, in subjects with early onset OCD and tic disorders, and autism with compulsive behavior
- Family studies of PANDAS cases: C & A OCD 및 Tic disorder의 빈도가 유의하게 높다는 보고

→ Unique cause of C & A OCD: linkage with genetic heritability

PANDAS-SNUCH case

- M/14, middle school boy
- Onset: 9 years old, episodic, wax and wane
- Recurrent OCD with tic disorder and/or recurrent URI infection with very high ASO titer
- ASO titer correlated with YBOC-C score
- Dramatic OC Sx remission after plasmapheresis(correlated with dramatic decrease of ASO titer)



Treatment

- First line Tx of C & A OCD: SSRI and CBT
- SSRI response rate
 - Adult OCD pts research:
 - 60-70% to single SSRI
 - Low response predictor: early onset in adult OCD patients
 - Early onset(<11) vs late onset(>17): SSRI response에 있어, 30% 차이
 - 소아연령 환아를 대상으로 한 연구
 - Sertraline, citalopram open trial; large sample and extended duration(52 weeks): usually 61-71% response rate (>20% symptom reduction)

Treatment

- C & A OCD
 - Relatively lower SSRI response
 - High comorbidity with tic
 - Consistent subcortical BG dysfunction

→ Suggest "Dopamine dysfunction" in C & A OCD

Treatment

- McDougle et al
 - Most of non-responder: early onset(C&A OCD)
 - Among SSRI non-responder OCD pts, haloperidol add on: "61% OC symptom reduction"
 - Comorbid tic pts: 92% of non-responder change to responder
 - Without tic pts: only 36% of non-responder change to responder

Treatment

- No systemic studies in C & A OCD with SSRI with atypical antipsychotics
 - Open trial: SSRI 에 반응하지 않는 OCD & OC related disorder 16명 환자에서 risperidone 병용 후 유의한 호전, 8명이 responder로 바뀜
 - Case series: SSRI 단독 및 병용 투여에 반응이 없던 4명의 소아 OCD 환자에서 risperidone 병용 후 모든 환자에서 유의한 호전반응 보고
 - 대개 저용량(1.0-2.0 mg)

→ low SSRI response / antipsychotics add on for C & A OCD

Treatment for PANDAS

- 1st line: Conventional SSRI, CBT, Neuroletics
- 2nd line: Special type of treatment
 - Penicilline IV or oral prophylactic therapy: no significant therapeutic effect on OC symptoms
 - 2 studies using immune-modulatory therapy
 - Plasmapheresis, IV gamma globulin, placebo for definite 21 PANDAS cases(usually OC symptoms): improvement in plasmapheresis and IV globlulin only
 - IV gamma globulin for childhood OC with tic disorder without streptococcal infection related Hx: no therapeutic benefit

C & A OCD as distinct subtype

- C & A OCD is closely related with tic disorder
- Supported by symptom feature, epidemiologic data, familial-genetic data, neuroimaging data, treatment response, PANDAS data

C & A OCD as distinct subtype-related tic ?

• Open questions to be answered

- 소아기 발병 강박장애 환자의 몇 % 정도가 틱 장애와 연관성을 갖는가?
- 소아기 발병 강박장애가 틱 장애와 동일한 병태생리를 공유한다는 확실한 증거가 있는가?—강박증상과 틱 증상이 동일한 뇌 병변을 공유하는가?
- 소아기 발병강박장애가 분자생물학적으로 동일한 유전 메커니즘을 틱장애와 공유하고 있는가?

C & A OCD as distinct subtype

• Clinical implications

소아-청소년기 발병군은 :

1. SSRI 단독요법에 반응율이 낮다
2. SSRI와 atypical antipsychotics의 병용투여가 필요한 경우가 많다
1. 틱장애의 과거력, 현병력, 또는 가족력을 가지는 경우가 많고, 그럴 경우 특히 더 atypical antipsychotics가 요구된다
2. 유전부하가 원동하게 더 크므로, 자녀들도 강박장애 및 틱장애의 고위험군이 될 수 있다

C & A OCD as distinct subtype

• Research implications

- 향후 강박장애에 대한 생물학적 연구(특히 유전연구와 뇌영상연구)에서는 환자의 발병연령에 대한 철저한 평가가 필요하며, 소아-청소년기 발병군은 하위군으로 따로 분류하여 평가할 필요가 있다
- 강박장애 관련 장애에 대한 연구에서 소아기 발병군을 구분하는 것이 매우 유용하다
 - AN: C & A onset OCD와 연관, 강박증이 AN 발병위험요인 작용
 - Trichotillomania: C & A OCD 및 tic 장애와 연관
- 소아기 강박장애의 특성(대한 정신약물학회지 2003)
- 소아기 난치성 강박장애의 치료(대한 소아청소년정신의학 2004)
- 소아기 강박장애 입원 환자 연구(대한 소아청소년정신의학2004)
