

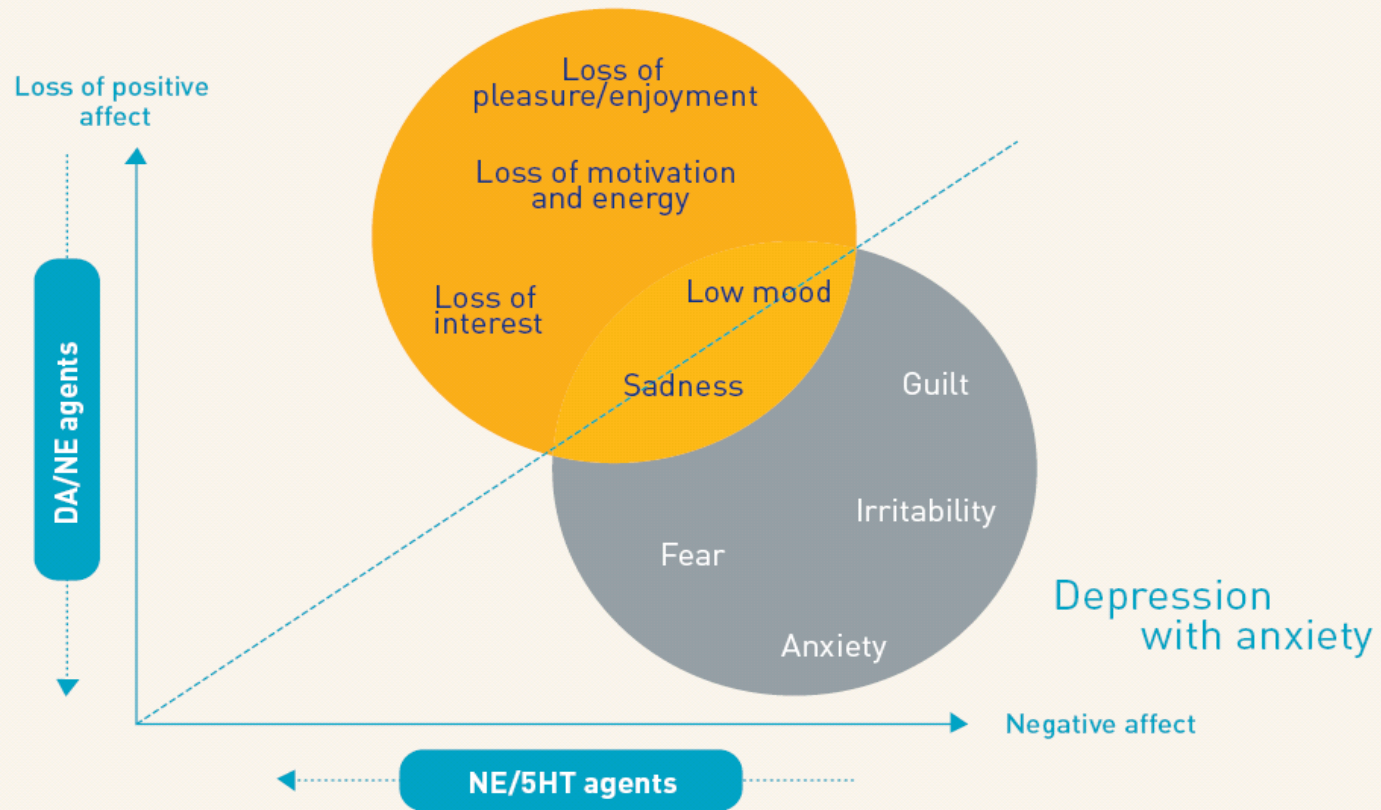
Escitalopram

NHIS Ilsan Hospital
Family Medicine
Sang Hyun Lee, MD, MPH, PhD

I. WHY?

왜 Escitalopram 인가?

Depression with loss of interest and energy



Hypothetical model showing differential actions of antidepressant agents on symptoms of positive and negative affect
Adapt from Nutt DJ et al. 2007⁴

Guideline

Comparison of clinical practice guideline recommendations

Table 2. Clinical practice guidelines for the pharmacological treatment of depression: Recommendations.

Recommendations/clinical practice guidelines	Chilean CPG ¹ [21]	Colombian CPG [22]	England CPG [23]	ICSI ² CPG [24]	APA ³ CPG [26]	CANMAT ⁴ CPG [25]
First-line drug choice	●	●	●	●	●	●
Selective serotonin reuptake inhibitors	●	●	●	●	●	●
Contraindication of tricyclics	●	-	-	●	-	-
Amitriptyline	-	●	-	-	-	-
Mirtazapine	-	●	-	●	●	●
Agomelatine, mianserin, and milnacipran	-	-	-	-	-	●

¹CPG = clinical practice guideline;

²ICSI = Institute for Clinical Systems Improvement;

³APA = American Psychiatry Association;

⁴CANMAT = Canadian Network for Mood and Anxiety Treatments.

● = CPG does contain topic; - = CPG does not contain topic.

전세계 여러 우울증 치료 가이드라인에서 SSRI를 First-line으로 권고 중

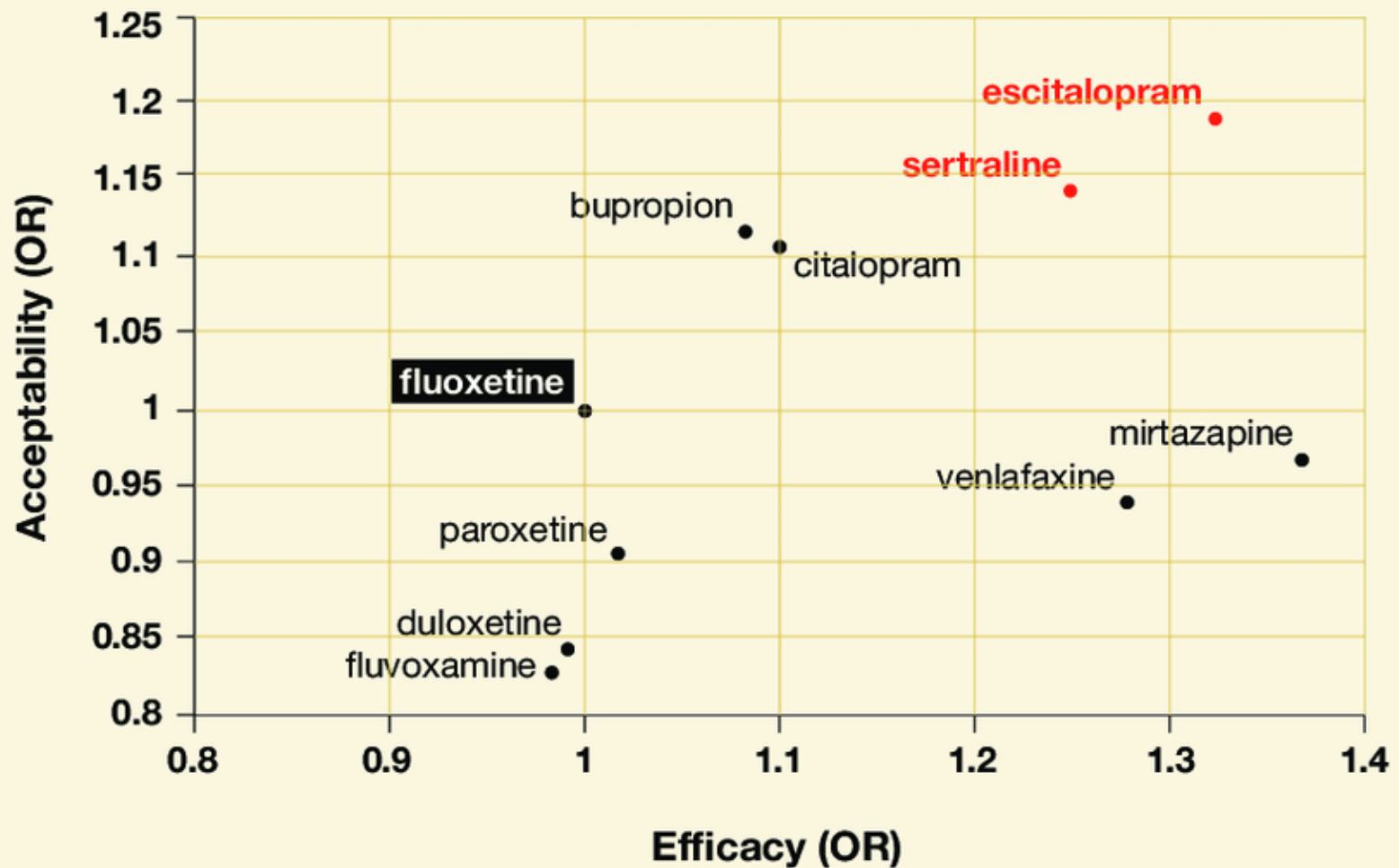
5-Hydroxytryptamine

5HT _{1A}	5HT ₂	5HT ₃
Antidepressant Anti-OCD property Anti-panic Anti-social phobia Anti-bulimia	Agitation Akathisia Anxiety Panic attacks Insomnia Sexual dysfunction	Nausea GI distress Diarrhea Headache

Assessing Different SSRIs



Drug	Characteristics	Advantages	Disadvantages	Applicable Cases
Fluoxetine	5-HT _{2C} antagonism	fewer withdrawal symptoms (longest half-life) Weight loss	Insomnia, agitation, anxiety, drug interactions due to long half-life	Obesity-comorbid depression, psychomotor retardation
Sertraline	DAT inhibition	Some dopamine reuptake inhibition, good for energy/motivation Less drug interaction	More GI side effects (diarrhea, nausea) Initial anxiety	Anhedonic depression, patients concerned about weight gain Cardiac problem Pt
Paroxetine	Anticholinergic effects	Effective for anxiety/OCD Sedation	Anticholinergic side effects, weight gain, sexual dysfunction	Anxiety/OCD-comorbid depression, elderly patients
Citalopram	Highly serotonin selectivity	Excellent tolerability, safe for elderly	QTc prolongation risk at high doses	Elderly depression, cardiovascular disease- comorbid depression
Escitalopram	Highly serotonin selectivity	More selective than citalopram; fewer side effects linear dose-response	Cost	Patients sensitive to side effects, patients with prior SSRI side effects
Fluvoxamine	Sigma-1 receptor affinity	High affinity for sigma-1 receptor , good for OCD	Initial anxiety/agitation, Drug interactions	Anxiety/OCD-comorbid depression



Using fluoxetine as the reference medication, the researchers analyzed various second-generation antidepressants. Sertraline and escitalopram had the best combination of efficacy and acceptability.

OR, odds ratio.

Source: Cipriani A et al. *Lancet*. 2009.¹

RESEARCH

Open Access



Escitalopram versus other antidepressive agents for major depressive disorder: a systematic review and meta-analysis

Juntao Yin^{1,2†}, Xiaoyong Song^{1†}, Chaoyang Wang³, Xuhong Lin^{4*} and Mingsan Miao^{2*}

- Escitalopram was significantly more effective than citalopram in achieving **acute response** (RR 0.67, 95% CI 0.50—0.87).
- Escitalopram was also more effective than citalopram in terms of **remission** (RR 0.53, 95% CI 0.30—0.93).
- **tolerability**, escitalopram demonstrated a statistically significant advantage over other SSRIs, with a risk ratio (RR) of **0.93 (95% CI 0.89 to 0.97)**
- When compared to **newer ADs**, **no significant differences** in tolerability were observed (RR 0.97, 95% CI 0.93 to 1.01)

Keywords Escitalopram, Antidepressant, Selective serotonin reuptake inhibitors (SSRI), Major depressive disorder (MDD), Meta-analysis

임상 삽화	1차 선택	2차 선택
경도 및 중등도 삽화	Escitalopram* Sertraline Desvenlafaxine Fluoxetine Venlafaxine Vortioxetine Duloxetine Mirtazapine Paroxetine	Milnacipran Agomelatine Bupropion Tianeptine
정신병적 양상이 동반되지 않은 중증 삽화	Escitalopram* Desvenlafaxine Venlafaxine Sertraline Mirtazapine Fluoxetine Duloxetine Paroxetine Vortioxetine	Milnacipran Esketamine Bupropion Agomelatine TCAs Tianeptine
정신병적 양상이 동반된 중증 삽화	Escitalopram* Venlafaxine Desvenlafaxine Sertraline Mirtazapine Fluoxetine Paroxetine Duloxetine	Vortioxetine Milnacipran Esketamine Agomelatine Bupropion TCAs Tianeptine

질문 2-1), 2), 3)

*최우선 선택

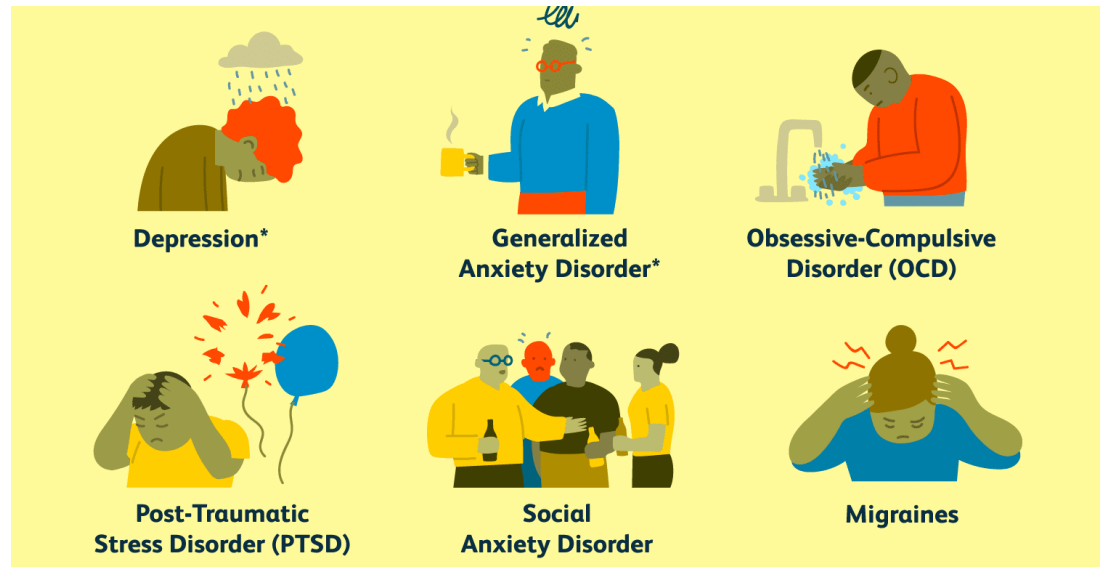
이탈릭체: 컨센서스 없음

II. WHAT?

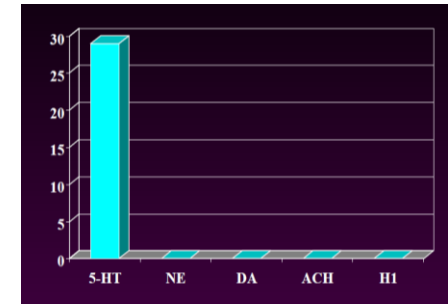
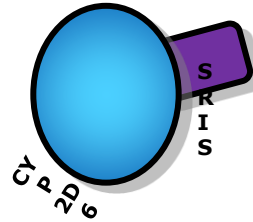
Escitalopram 무엇인가?

Indications

- Major Depressive Disorder (MDD)
 - Generalized Anxiety Disorder (GAD)
 - Cf. Panic Disorder or OCD
-
- It was approved for the indications in the US in 2002



Pharmacology



- Receptor selectivity:
 - Escitalopram, the S-enantiomer of citalopram, has an even higher selectivity for the serotonin transporter (SERT) than citalopram.
- Side effects:
 - Escitalopram's high SERT selectivity may contribute to its favorable tolerability profile, with lower rates of adverse effects compared to other SSRIs.
- Less drug interaction
- linear dose response

Metabolism and Elimination

- CYP2C19(major) & CYP3A4(minor) metabolism
 - CYP2D6 대사 영향이 적어 다중 약물 복용 환자에게 유리
 - cf. CYP2D6 대사 약물
 - 항우울제(Fluoxetine, Paroxetine), 항정신병제(Haloperidol, Risperidone, Aripiprazole), 진통제(Codeine → Morphine), β -차단제(Metoprolol, Propranolol)
- Half-Life: 27-32 Hours
- Primary Renal Excretion

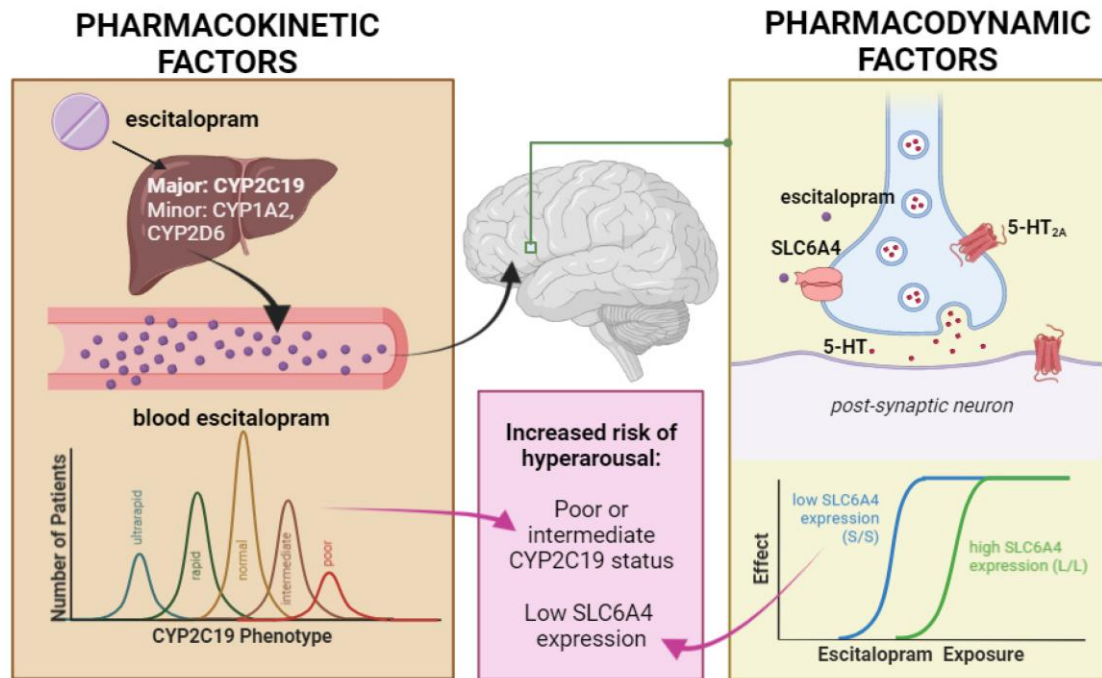


Table 2

Antidepressants: Recommended dosage adjustments in renal impairment

Medication	Mild renal impairment	Moderate renal impairment	Severe renal impairment	ESRD or dialysis
Escitalopram ¹⁷	None	None	(eCrCl <20 mL/min) No information available Use caution: Start at a reduced dosage and titrate slowly	
Citalopram ¹⁸	None	None	Use caution: Start at a reduced dosage and titrate slowly	
Paroxetine ¹⁹	None	None	Initial dosage: 10 mg/d Maximum dosage: 40 mg/d	
Venlafaxine ²⁰	(GFR 10 to 70 mL/min) Decrease dosage by 25% to 50%			Decrease dosage by 50% and withhold until dialysis is complete
Desvenlafaxine ²¹	None	50 mg/d (do not titrate)	50 mg every other day (do not titrate)	
Duloxetine ²²	None	None	(GFR <30 mL/min) Avoid use	
Milnacipran ²³	None	Use caution	Decrease dosage by 50%	Relative contraindication
Levomilnacipran ²⁴	None	80 mg/d	40 mg/d	Relative contraindication
TCAs ²⁵	None	Decrease by 50% in geriatric patients		
Bupropion ^{26,27}	(GFR <90 mL/min) Consider reducing the dosage or frequency	75 mg once daily		
	None	150 mg every 3 days		

eCrCl: estimated creatinine clearance; ESRD: end-stage renal disease; GFR: glomerular filtration rate; TCA: tricyclic antidepressants

Common Side Effects?

- Nausea, Headache, Insomnia, Fatigue
- Increased Sweating, Drowsiness
- Usually Transient



Fatigue



Dry Mouth



Headaches



Diarrhea



Indigestion



Somnolence



Yawning



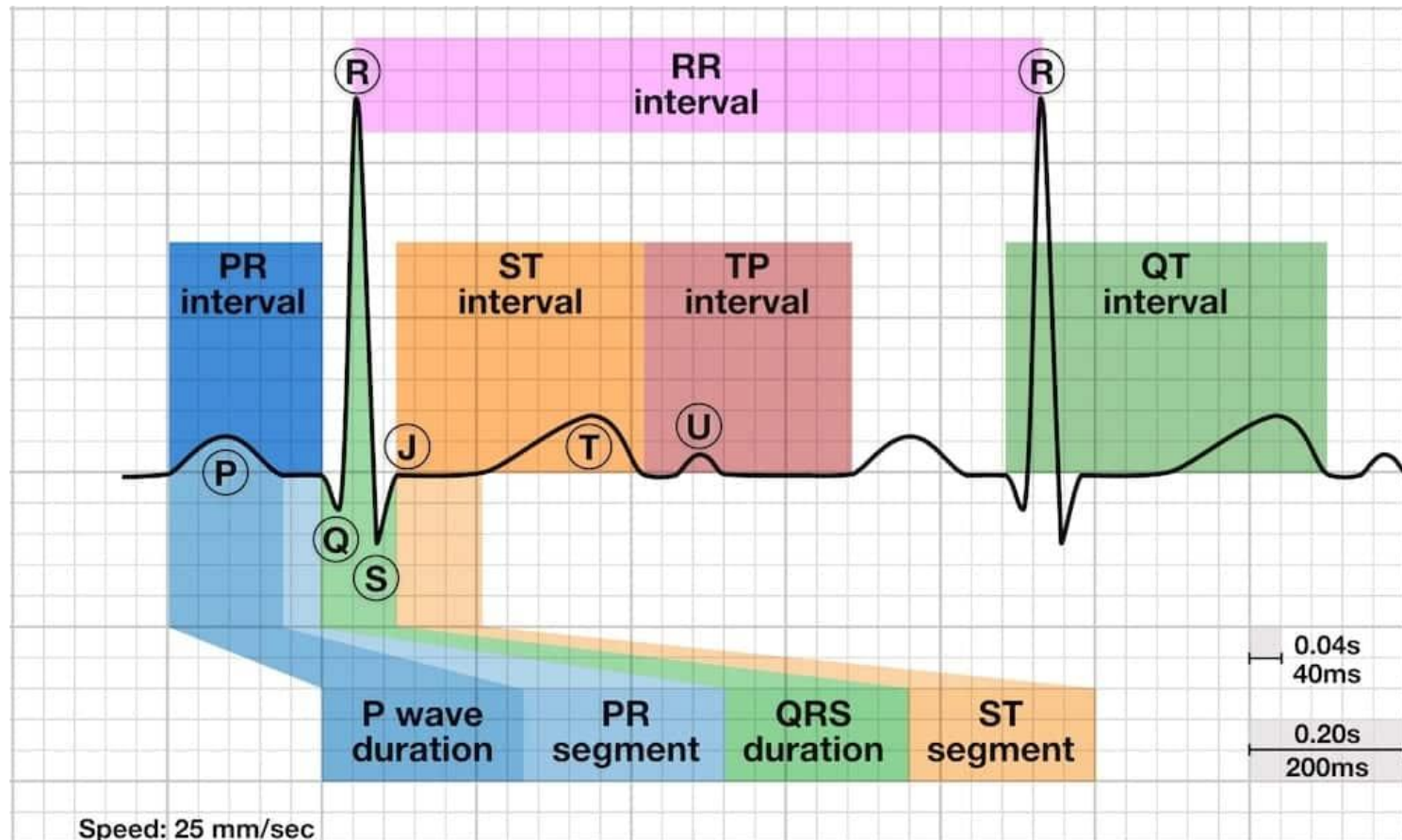
Impotence

Serious Side Effects?

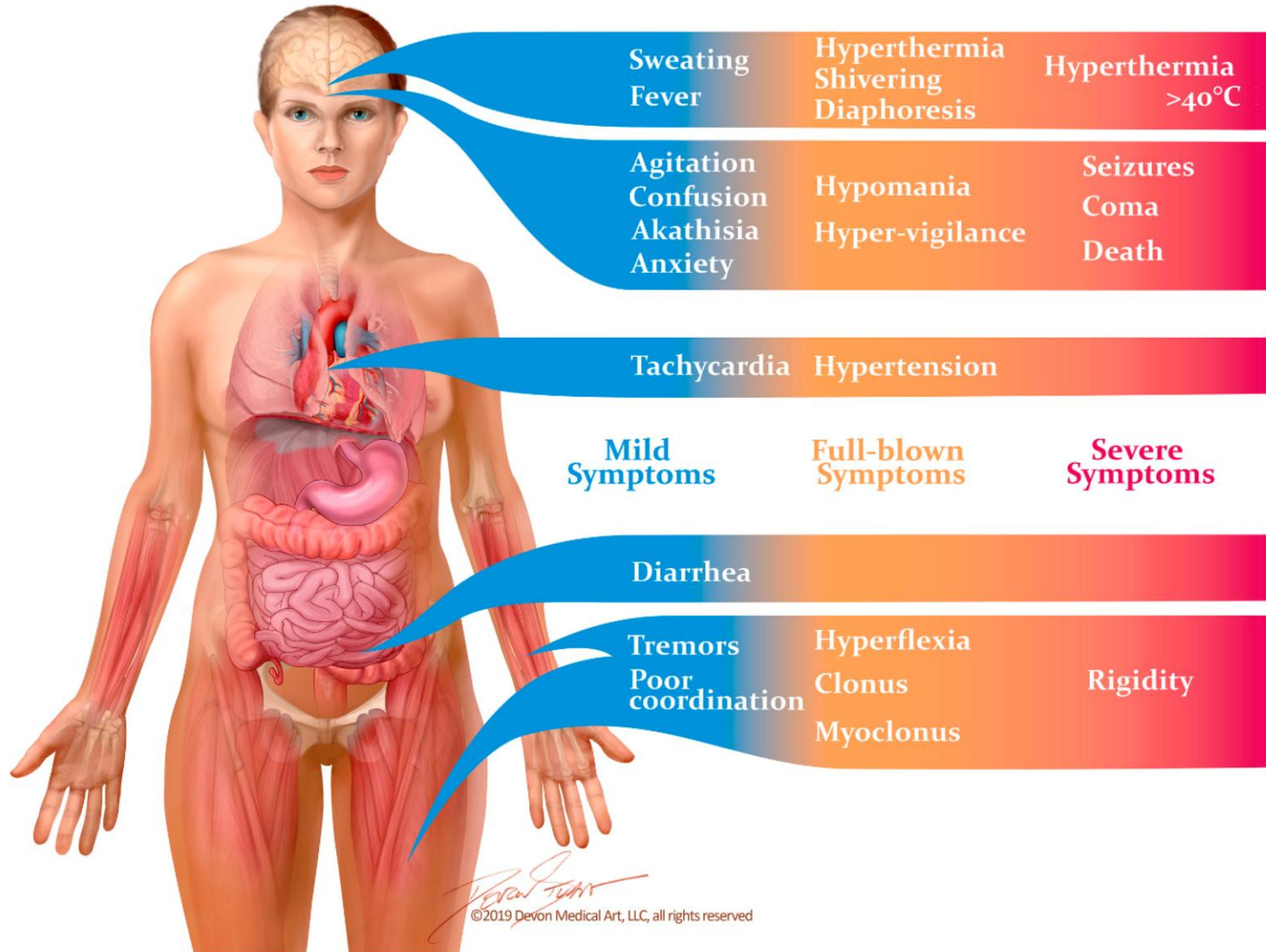
- **QT Prolongation**
 - **VPC** or serious heart issues such as **Torsades de pointes**.
 - **older age, existing heart conditions, and concurrent use of other medications that affect heart rhythm**
- **Serotonin Syndrome**
 - **life-threatening** condition occurs due to excessive serotonin levels in the brain.
 - confusion, agitation, rapid heart rate, high blood pressure, excessive sweating, shivering, muscle rigidity, and gastrointestinal distress.
 - when escitalopram is taken **with other serotonergic medications**
- **Increased Suicidal Ideation in Young Adults**
 - particularly in children, adolescents, and young adults (ages 18 to 24) during the initial treatment period or when doses are changed.

QT prolongation

- 정상 QT 간격(systole)은 해당 RR 간격의 $\frac{1}{2}$ 을 넘지 않는다.
 - Systole < Diastole (at normal state)
- QT 연장: 남성의 경우 440ms 이상, 여성의 경우 460ms 이상



Serotonin Syndrome



Drug Interactions

MAOIs:

- Serotonin Syndrome Risk

NSAIDs:

- Increased Bleeding Risk

Alcohol:

- CNS Depression

Safety profile

Drug interaction

■ Cytochrome P450 isozyme inhibition *in vitro/in vivo*

	3A	2D6	1A2	2C19	2C9
Escitalopram	0	+	0	0	0
Citalopram	0	0	+	0	0
Fluoxetine	+	+++	+	+ / ++	++
Paroxetine	+	+++	+	+	+
Sertraline	+	+	+	+ / ++	+

0=minimal or no inhibition, +=mild inhibition, ++=moderate inhibition, +++=strong inhibition

SSRI 계열 약물 中 Escitalopram, Sertraline 은 비교적 낮은 약물상호작용을 보임

신체 질환과 공존하는 우울증에서 항우울제의 선택

공존 질환	1차 선택	2차 선택	3차 선택
당뇨	Escitalopram	Sertraline	Bupropion
갑상선 질환	Escitalopram	Sertraline	Fluoxetine
간질환	Escitalopram	Sertraline	Tianeptine
신장 질환	Escitalopram	Sertraline	Tianeptine
고혈압	Escitalopram	Sertraline	Tianeptine
뇌전증	Escitalopram	Sertraline	Tianeptine
★ 심혈관 질환	Sertraline	Escitalopram	Tianeptine
파킨슨병	Escitalopram	Sertraline	Bupropion
★ 부정맥	Sertraline	Escitalopram	Fluoxetine
만성통증	Duloxetine	Milnacipran	Venlafaxine

III. HOW?

Escitalopram을 어떻게 사용하나?

Dosage and Administration

제형: 5, 10, 15, 20mg/day

- linear dose response

Standard Dosage: 10 mg/day

Maximum Dosage: 20 mg/day

여/41 김0주

S

- 잠을 자기 전에 숨이 막히는 느낌, 밀폐 공간에 들어간다는 생각만 해도 답답,
- 우울: 갑자기 우울감이 몰려온다
- 불안: 심하다
- SHx: 피부관리 운영

O

- BDI 36/ BAI 38 (2022.8.2)

Progress Note


- paroxetine 12.5 -> 20mg 증량 후에도 효과 없다
- escitalopram 15mg 교체 후 숨 쉬는 것이 호전
- escitalopram 20mg 증량 후 확실히 많이 좋아졌다. 짜증도 별로 안나고 우울하지도 않았다. 불안도 호전 숨막히는 증세, 밀폐공간도 괜찮았다. 불면도 호전 생각 자체가 치료 후 이어지는 것 같지 않다. Re) naming
- 호흡 도움이 된다. Re) 복식호흡, 누워서 잘 때와 일어날 때 호흡 -> 모음 호흡
- 간혹 우울 느낌 re) 손님처럼, 이름 붙이기
- 친한 친구 임파종 진단:
- 괜찮아서 약을 2-3일에 한번 복용하니 숨 차고, 가슴 두근거림, 불면증 증세 재발 -> 매일 복용 후 괜찮지만, 슬픈 감정, 짜증 간혹 -> 다 괜찮다. 사람 많은 곳 있으면 두근거림 약간 -> 좋았다
- BDI 26/ BAI 19 (2024.6.28)
- escitalopram 15mg 감량 후 분노, 별일 아닌데 스트레스 더 받는 것 같다, 우울
- escitalopram 20mg 재증량

Pregnant women

- **SSRIs** are typically the **preferred choice** for treating depression and anxiety in **pregnant women** due to their established safety profile.
 - Cf. neonates exposed to SSRIs, including escitalopram, late in the third trimester may experience complications at birth, necessitating prolonged hospitalization and respiratory support



Pediatric Use

- not approved for use in pediatric patients
 - under the age of 12 with MDD or
 - under 7 years with GAD
 - due to insufficient safety and effectiveness data in these populations
- 

소아 청소년

	1차 선택	2차 선택	3차 선택
항우울제 선택 (소아-초등학생까지)	Escitalopram* Fluoxetine	Sertraline Bupropion <i>Duloxetine</i> <i>Paroxetine</i>	Milnacipran TCAs Tianeptine Esketamine (nasal spray) <i>Desvenlafaxine</i> <i>Venlafaxine</i> <i>Agomelatine</i> <i>Mirtazapine</i> <i>Vortioxetine</i>
항우울제 선택 (청소년-중고등학생)	Escitalopram* Fluoxetine Sertraline	Venlafaxine <i>Duloxetine</i> <i>Bupropion</i> <i>Paroxetine</i> <i>Desvenlafaxine</i> <i>Agomelatine</i> <i>Vortioxetine</i> <i>Mirtazapine</i>	Milnacipran TCAs Tianeptine Esketamine (nasal spray)

질문 4-1)

*최우선 선택

이탈릭체: 컨센서스 없음

노인

	1차 선택	2차 선택	3차 선택
노인 주요우울장애 경도 및 중등도 삽화의 항우울제	Escitalopram* Sertraline Desvenlafaxine Vortioxetine Duloxetine Venlafaxine Fluoxetine Mirtazapine Milnacipran	Paroxetine Agomelatine Bupropion Tianeptine	TCAs <i>Esketamine (nasal spray)</i>

질문 15-3)

*최우선 선택. 이탤릭체: 컨센서스 없음

Laboratory monitoring?

Not require routine laboratory monitoring

in specific cases, some tests may be considered:

- **Electrolyte**
 - In **elderly** patients or those at risk for **hyponatremia**
- **ECG**
 - **High doses** of escitalopram (e.g., ≥ 20 mg/day) can prolong the QT interval.
 - Patients with **cardiac conditions, electrolyte imbalances, or those taking other QT-prolonging drugs**
- Liver and Kidney Function Tests
 - Patients with **hepatic impairment** or **severe renal dysfunction**

When Escitalopram Fails

1. Switching Medications

- **SNRI:** venlafaxine (Effexor) and duloxetine (Cymbalta)
- **Atypical Antidepressants:** bupropion or mirtazapine
- **Vortioxetine:**

2. Augmentation Strategies (Adding)

- **Atypical Antipsychotics:** aripiprazole or quetiapine
- **Buspirone**
- **Lithium**

To Change

현재 사용 약물	1차 교체 선택	2차 교체 선택
SSRIs	SNRIs Mirtazapine	Vortioxetine Another SSRIs Bupropion Agomelatine <i>Esketamine</i> Tianeptine TCAs
SNRIs	Mirtazapine SSRIs Another SNRIs	Vortioxetine Bupropion Agomelatine Tianeptine <i>Esketamine</i> TCAs
Mirtazapine	SNRIs SSRIs	Vortioxetine Bupropion Agomelatine <i>Esketamine</i> Tianeptine TCAs
Bupropion	SSRIs* SNRIs Mirtazapine Vortioxetine	Agomelatine <i>Esketamine</i> Tianeptine TCAs
Agomelatine	SNRIs* SSRIs Mirtazapine Vortioxetine	Bupropion Tianeptine <i>Esketamine</i> TCAs
Vortioxetine	SNRIs SSRIs Mirtazapine	Bupropion Agomelatine <i>Esketamine</i> Tianeptine TCAs

To Add

현재 사용 약물	1차 추가 선택	2차 추가 선택
SSRIs	Mirtazapine SNRIs Bupropion Agomelatine	Vortioxetine Another SSRIs Tianeptine TCAs <i>Esketamine</i>
SNRIs	Mirtazapine SSRIs Vortioxetine Bupropion	Agomelatine Another SNRIs Tianeptine <i>Esketamine</i> TCAs
Mirtazapine	SSRIs SNRIs Vortioxetine Bupropion	Agomelatine Tianeptine <i>Esketamine</i> TCAs
Bupropion	SSRIs SNRIs Mirtazapine Vortioxetine	Agomelatine Tianeptine <i>Esketamine</i> TCAs
Agomelatine	SSRIs SNRIs Mirtazapine Vortioxetine Bupropion	Tianeptine <i>Esketamine</i> TCAs
Vortioxetine	SSRIs SNRIs Mirtazapine Agomelatine	Bupropion Tianeptine TCAs <i>Esketamine</i>

Discontinuation Syndrome

- Withdrawal Symptoms typically emerge within **two to four days** after discontinuation





Management Strategies of Discontinuation Syndrome

- **Gradual Tapering:**

- over several weeks to months, rather than stopping abruptly.

- **Switching Medications:**

- switching to a longer-acting SSRI, such as fluoxetine

- **Reinstatement:**

- resuming the previous dose of escitalopram
- and then tapering more slowly

- **Supportive Care:**

- pain relievers for flu-like symptoms or
- antihistamines for nausea.



Escitalopram

Sang Hyun Lee
shleefm@nhis.or.kr