# 소아청소년 정신과 영역에서의 새로운 약물치료: 새로운 장기작용형 중추신경자극제\*

## NEW DRUG THERAPY IN CHILD AND ADOLESCENT PSYCHIATRY-NEW LONG-ACTING PSYCHOSTIMULANTS

최 성 Sung-Ku Choi, M.D.\*\*† 요 약: 가 가 , 가 가 가 중심 단어: ADHD · 가 М 론 (Attention - deficit/Hyperac-3~7% <sup>2)</sup>, 가 tivity Disorder, 가 ADHD) psychostimulant

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3). methylphenidate amphetamine 7) 15 (NIMH)가 5). Ampheta-MTA(Multisite Multimodal Treatment Study of Children With Attention Deficit/Hyperactivity Disormine 60 der)<sup>8)</sup> methylphenidate 30 psychostimulant ADHD 가 가 , psychostimulant 가 psychosti-9-11) 가 mulant 가 ADHD psychostimulant methylphenidate amphetamine 가 4 psychostimulant 1 10 2 가 (Fig. 1). 2 , psychostimulant L(levo), D(dextro) . Amphetamine 가 d psychostimulant dextroamphetamine, levoam-가 50% amphetamine phetamine 가가 가 psychostimulant I psychostimulant CH<sub>3</sub> 본 론 Amphetamine 1. ADHD의 치료제로서 Psychostimulant의 위치 Psychostimulant 1937 amphetamine ADHD . 1937 1996 161 (randomized controlled trial)가 가 5,899 Methylphenidate (meta - analysis) , psychostimulant \*Asymmetric carbon center

**Fig. 1.** Chemical structure of amphetamine and methylphenidate.

65~75%

5~30%

**Table 1.** Immediate-release stimulants used for ADHD

Generic Name	Brand Name	Usual Daily Dose
Amphetamine		
Racemic(dextro-levo)	Benzedrine®(withdrawn)	10 - 40(0.3 - 1)
Day the amount of any in a	Dexedrine®	10 - 40(0.3 - 1)
Dextroamphetamine	Dextrostat®	5 - 30(0.2 - 0.7)
Levoamphetamine	Cydril®(withdrawn)	14 - 42(0.3 - 1)
Mixture 3/4 d-, 1/4 l-amphetamine	Adderall <sup>®</sup>	10 - 40(0.3 - 1)
Methamphetamine	Desoxyn®	5 - 25(0.2 - 0.7)
Methylphenidate		
	Ritalin®	10 - 60(0.3 - 1.5)
Racemic threo-methylphenidate	Methylin™	
Dextro-threo-methylphenidate	Focalin <sup>TM</sup>	5 - 30(0.2 - 0.7)
Pemoline	Cylert®	37.5 - 112.5(1 - 3)

 $\textbf{Table 2.} \ \ \textbf{Pharmacokinetics of drugs for the Treatment of Attention-deficit/hyperactivity disorder}$ 

Drug and preparation	Plasma half-life(hour)	Peak plasma concentration(hour)	Duration of effects on behavior(hour)
Methylphenidate, immediate-release form	3.3	1.6	1 - 4
Dextroamphetamine sulfate, immediate-release form	6.6	3 - 4	1 - 8
Pemoline	5 - 6	2 - 3	7 - 9

rac	emic amphetamine	psychostimulant	dopamine
. Levoamphetamine	dopamine	noradrenaline	axon terminal
·	иоранние	Horaurenanne	
Norepinephrine		transporter	dopamine
	•	noradrenaline	axon termi-
가		nal synaptic vesicle	transporter
levoamphetamine	. Am-	dopamin	e noradrena-
phetamine	racemic	line vesicle	vesicle
amphetamine dexti	roamphetamine, 1/4 le-	exocytosis가 ,	
voamphetamine 3/4	dextroamphetamine		
가 ADHD	. Methyl-	Psychostimulant	
phenidate	가 2 가	,	(Table
	2가 가	2) <sup>12)</sup> . P - hydroxylation, N - methyl	ation, deamination,
	d I, threo	conjugation	
erythro	. erythro	amphetamine 8	60%가
threo	,	, methylph	enidate
threo d I	racemic threo	de - esterification	n .
methyphenidate가	. dextro		
motify prioritiaato.	· GOATIO		
dextro de	extro - threo - methylphenidate		
		Dovobootimulant	
	(Table 1).	. Psychostimulant	

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가
                                                                                          psychostimulant
    13)
                         . Methylphenidate
        가
                                 가
        14)
                 psychostimulant가
                   가
                                                       가 20~65%
                                  psychostimulant
                                                                   James Swanson
                                       , U.S. Drug
Enforcement Administration
                                 psychostimulant
                                                        2. 장기 작용형 Psychostimulants (Table 3)
                                                        Psychostimulant
         methylphenidate
                                                                                              10
    가가
  1993
                           methylphenidate
  3
                            2.5 가 가
            1990
                                                                가
  15)
              psychostimulant가
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                                                                                                       Ri-
                                                       talin - SR® (MHH - SR20)
                                                                                      가
                                                                                                      Me-
    가
               가,
                             가
                                                       thylphenidate - SR, Metadate®, Methylin - SR®
                        DSM - <sup>2)</sup>
                                                                                     psychostimulant
                            10%가
  16)17)
            가<sup>1)</sup>,
                                         가<sup>18)</sup>,
                                                                                      Dexedrine Spanule®
                             18)
                  3)
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Table 3. Sustained/extended-release options for common stimulants

Stimulants	Preparations	Type/Form	Duration
Methylphenidate	Metadate™ CD	Encapsulated beads with different dissolution times	8 - 9hour
	Methylin™ ER	Tablets	Variable
	Retalin SR®	Coated tablets	Variable
d-Amphetamine	Dexedrine®	Encapsulated beads with	10 - 12hour
	Spanule	different dissolution times	10 - 12NOUr
3/4 d-Amphetamine, 1/4 l-Amphetamine	Adderall® XR	Encapsulated beads with different dissolution times	10 - 12hour

가

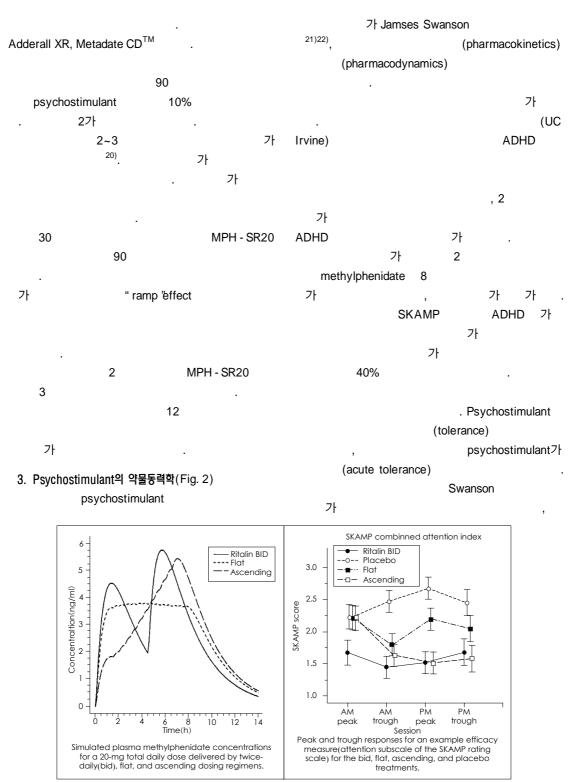


Fig. 2. Pharmacokinetic-pharmacodynamic relationship of methylphenidate in ADHD children.

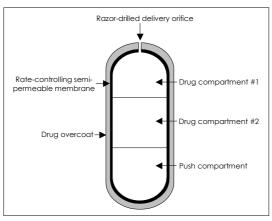


Fig. 3. Structure of OROS methylphenidate(Concerta®).

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methylphenidate

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23 - 25)

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methylphenidate , , , , psychostimulant7-

가 methylphenidate가 Psyhostimulant 60 methylphenidate가 , methylphenidate 20% ,

(Fig. 3). 12 ADHD 1

. multimodal treatment study

ADHD 1

methylphenide pemoline

#### **ADHD**

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Attention-deficit/Hyperactivity disorder (ADHD) is the most common psychiatric disorder of childhood and among the most prevalent chronic health conditions affecting school-aged children. Children with ADHD experience significant functional problems, such as school difficulties, academic underachievement, troublesome interpersonal relationships with family members and peers, and low self-esteem. The most widely used pharmacological treatments for ADHD are psychostimulants, such as methylphenidate and amphetamine salts. These medications provide clinical efficacy by increasing the availability of catecholamines, primarily dopamine, in the frontal lobe of the brain. Immediate-release (IR) formulations of sychostimulants were among the most effective psychotrophic medications in the psychopharmacological treatment. However, there are some limitations of IR formulations: the short half-life and duration of efficacy, which result in the need for multiple daily dosing and the poor compliance. These limitations have led to the development of once-daily, extended-release (ER) formulations of methylphenidate and amphetamine salts. However, these ER formulations may not be as immediately helpful to ADHD children due to delayed onset of action and the acute tolerance which is the failure to sustain the efficacy with the same concentration of drug as the initial stage of medication. OROS-methylphenidate (Concerta®) given once a day produces an ascending-pattern plasma drug level generated by the osmotically released, timed drug-delivery system. These new formulations of the psychostimulants have been shown to be a useful alternative to old stimulant medications through the evidence by the clinical trials.

KEY WORDS: ADHD · Psychostimulant · Concerta.