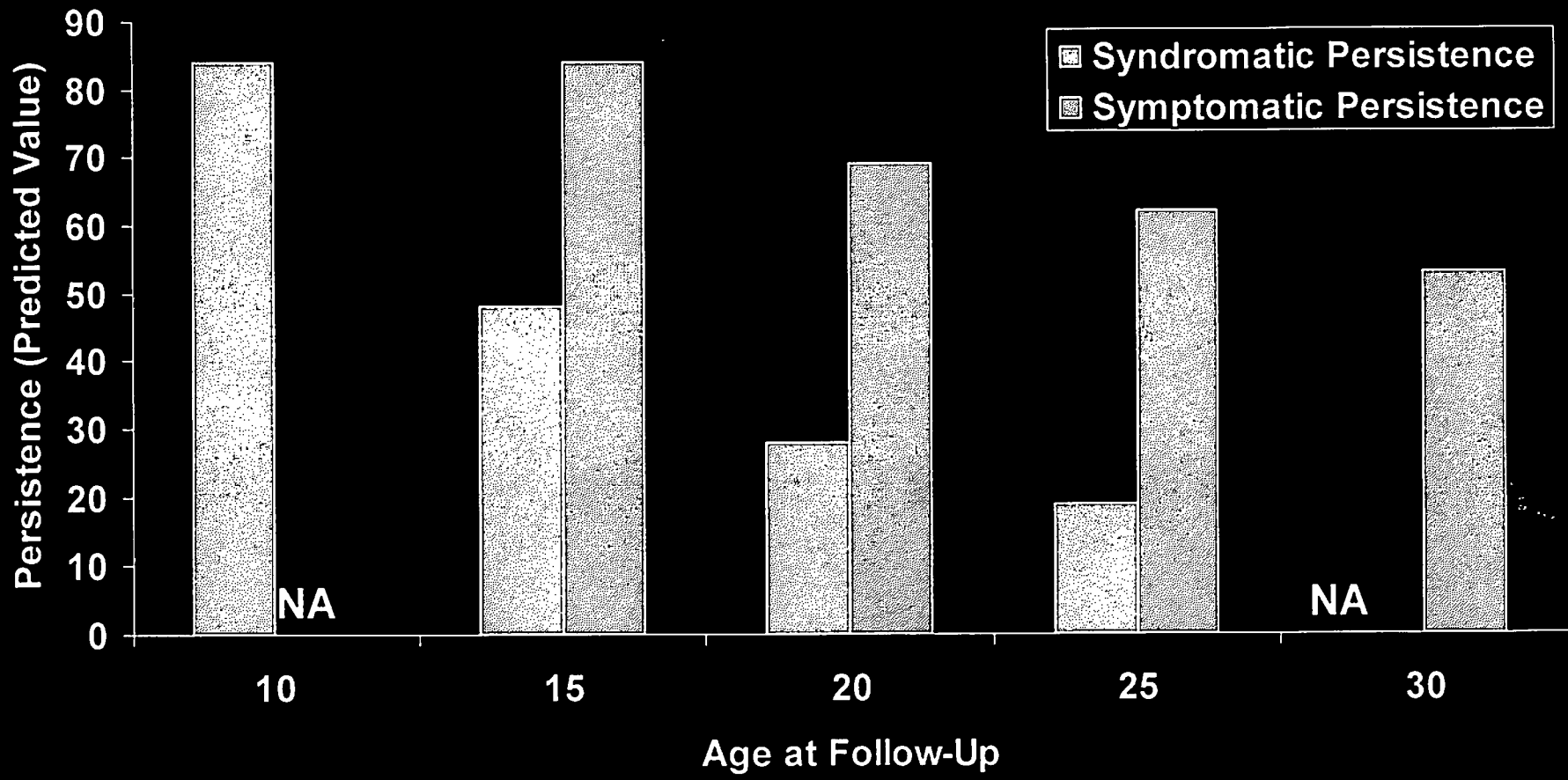
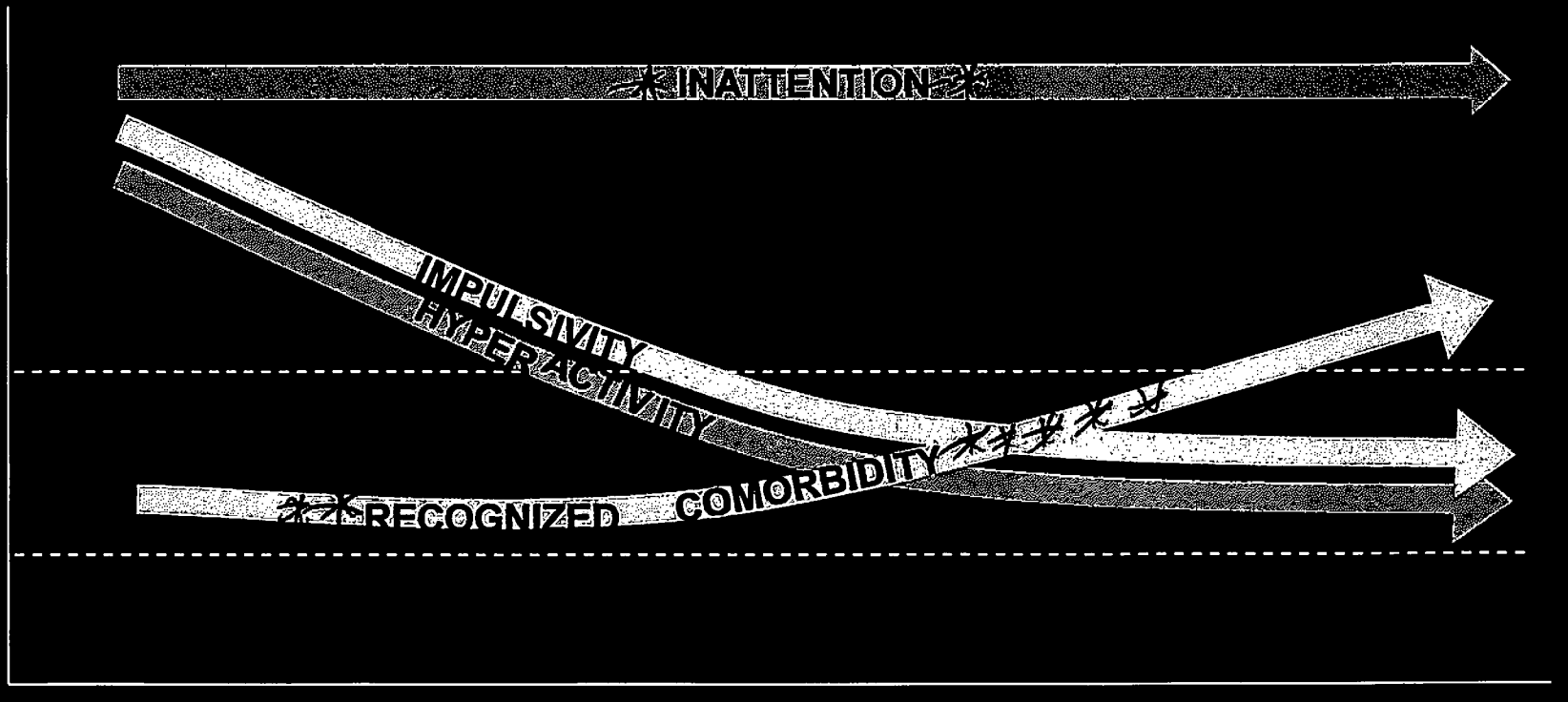
Persistence of ADHD Into Adulthood



Syndromatic: Loss of full diagnostic status Symptomatic: Loss of partial diagnostic status

Mick et al. Psychiatr Clin N Am 2004.

ADHD Developmental Trends by Age



Wasserstein. JCLP 2005. Mick et al. Psychiatr Clin N Am 2004.

ADHD Symptom Manifestation by Age

CHILDHOOD	ADOLESCENCE	ADULTHOOD
Hyperactivity	Easily distracted, inattentive	Inattentiveness
Low frustration tolerance	Easily bored	Poor organization of time/money
Aggression	Impatient	Missing deadlines or appointments
Easily distracted	Emotionally immature compared to peers	Poor bill tracking
Difficulty developing routines	Shifts activities	Restlessness
Impulsiveness	Poor driving	Emotional reactivity

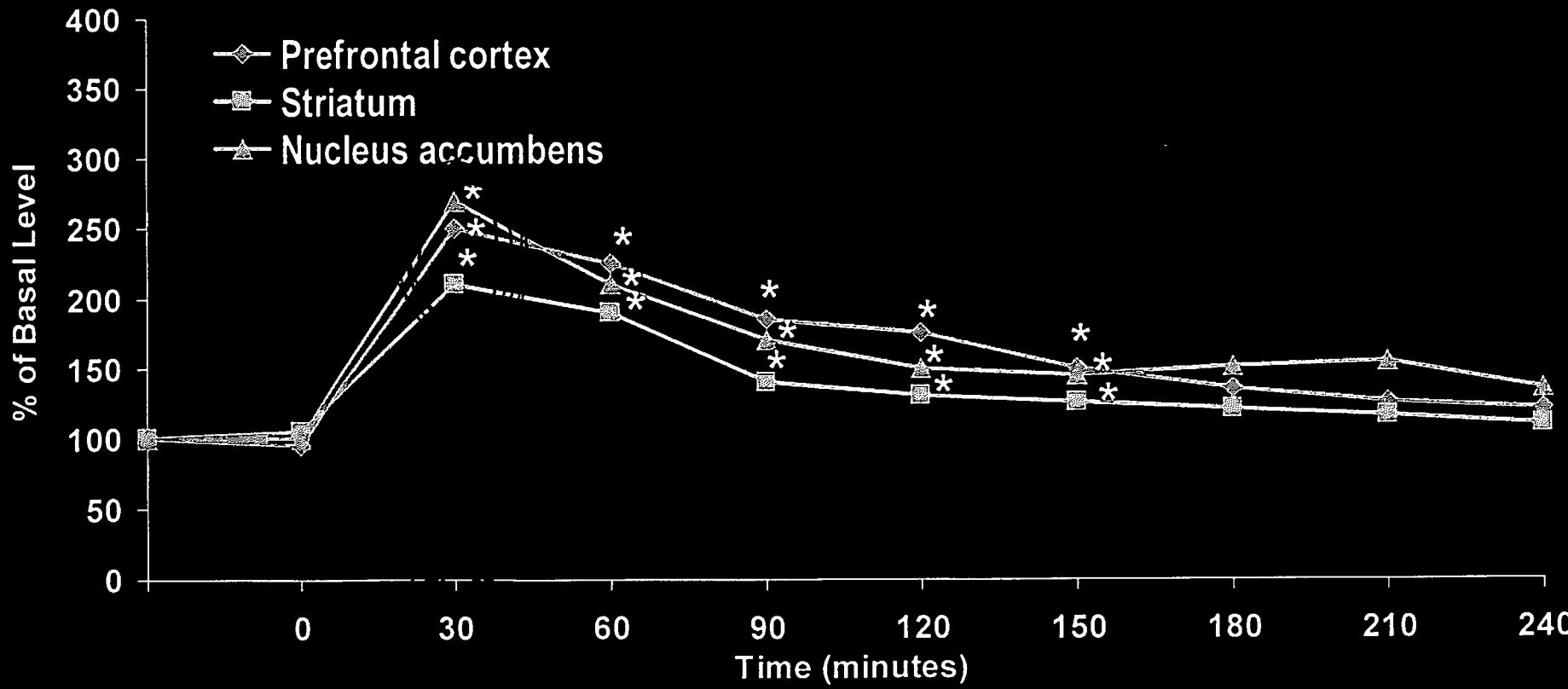
Wasserstein. JCLP 2005. Wilens et al. Ann Rev Psychiatry 1999. Millstein et al. J Atten Disord 1997.

MOA of Methylphenidate and Amphetamine

- Methylphenidate: dose-dependently blocks DAT in striatum
- Amphetamine: blocks vesicular monoamine transporters (VMATs) in cortex, releasing dopamine
- Both: increase spontaneously released dopamine responsive to environmental stimuli
  - Increases signal-to-noise ratio
  - Increases saliency of stimuli

Durston. Mental Ret Dev Disability Res Reviews 2003.
Volkow et al. Biol Psychiatry 2005.

Methylphenidate's Effects on Dopamine in PFC, Striatum, and Nucleus Accumbens

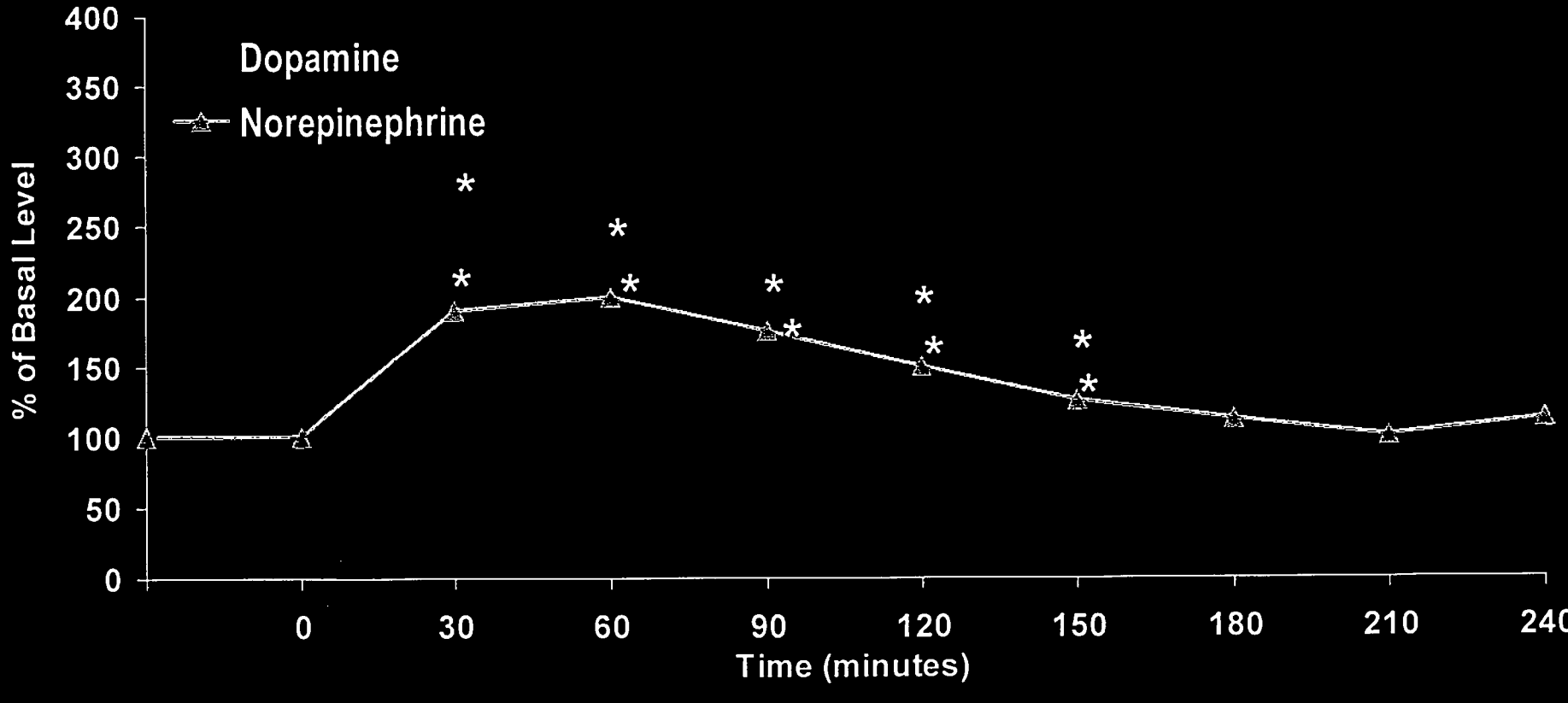


Effects of methylphenidate 3 mg/kg, i.p.

***p<0.05 vs. basal level**

Bymaster et al. Neuropsychopharmacol 2002.

Methylphenidate in Rat Prefrontal Cortex

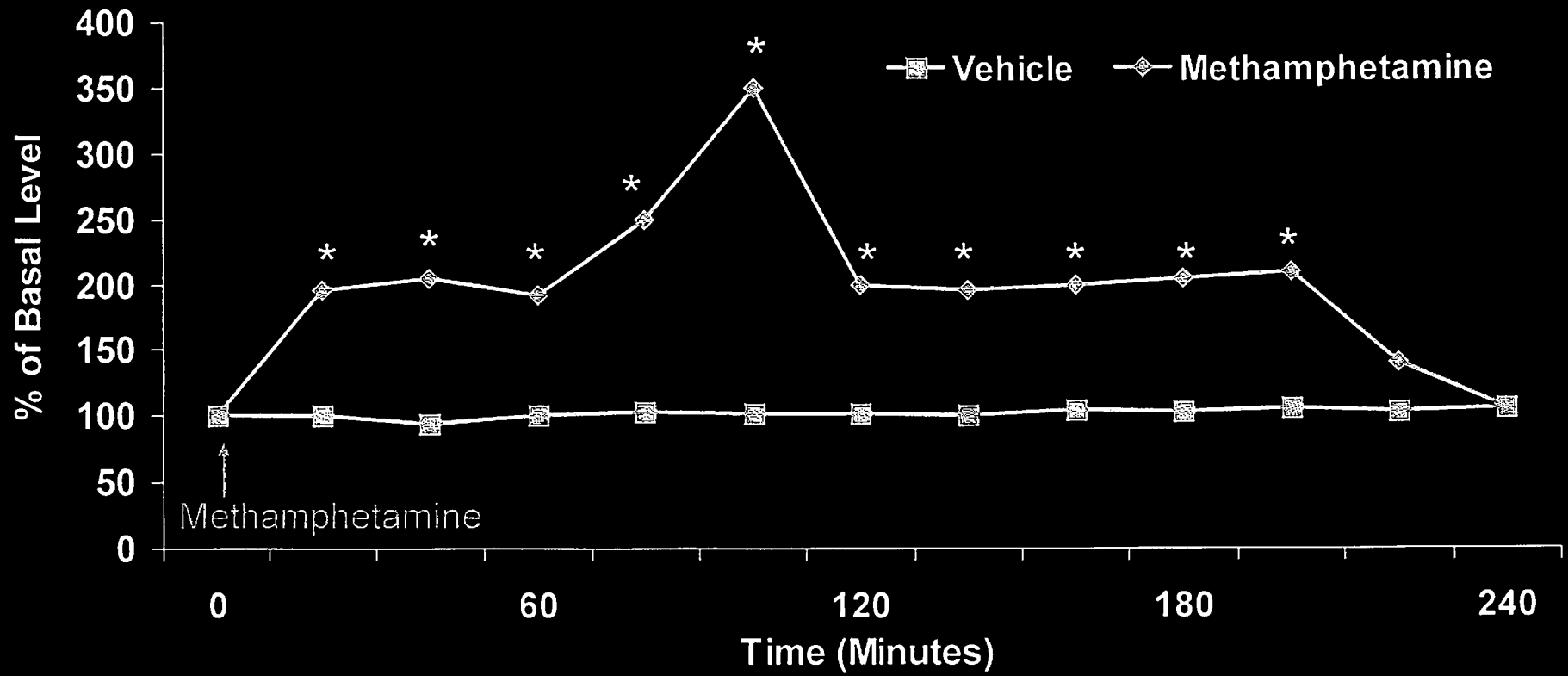


Effects of methylphenidate 3 mg/kg, i.p.

***p<0.05 vs. basal level**

Bymaster et al. Neuropsychopharmacol 2002.

Stimulant-Induced Histamine Release in the Rat Anterior Hypothalamus



Effects of methamphetamine 3 mg/kg, i.p.

***p<0.05 vs. basal level**

Ito et al. Psychiatry and Clinical Neurosci 1997.

Methylphenidate Formulations

Formulation	Peak, Duration	Profile
Immediate-release racemic *(Ritalin, Methylin, generic IR)*	Early peak, 2–4 hr duration	Lunch dosing; low risk for insomnia unless dosed at night
Immediate-release d-methylphenidate *(Focalin)*	Early peak, 2–4 hr duration	Lunch dosing; effective at half the racemic dose; possibly longer duration of action than racemic
Sustained-release racemic *(Ritalin SR, Methylin SR, Metadate ER, generic SR)*	Early peak, 4 hr duration	Lunch dosing; low risk for insomnia unless dosed at night
Time-release beads racemic *(Metadate CD)*	Strong early peak, 8 hr duration	Less risk for insomnia than OROS
SODAS microbeads racemic *(Ritalin LA)*	Two strong peaks (early and after 4 hrs), 8–12 hr duration	Less risk for insomnia than OROS
Oros technology racemic *(Concerta)*	Small early peak, 12 hr duration	Continued effects into evening
SODAS microbeads d-methylphenidate *(Focalin XR)*		

Amphetamine Formulations

Formulation	Duration	Profile
Immediate-release d-amphetamine *(Dexedrine)*	3–6 hr	Lunch dosing; low risk for insomnia unless dosed at night
Immediate-release d,l-amphetamine *(Adderall)*	5 hr	Lunch dosing; low risk for insomnia unless dosed at night
Sustained-release d-amphetamine *(Dexedrine Spansule)*	6–9 hr	No lunch dosing; low risk for insomnia unless dosed at night
Extended-release d,l-amphetamine *(Adderall XR)*	9 hr	Continued effects into evening

Stimulant Use and Substance Abuse

	Study	Protective Effect (OR)	
		OR	95% CI
Drug Studies	Lambert	0.47	0.22–1.0
	Biederman	3.9	1.8–8.1
	Huss	2.2	0.99–5.1
	Loney	1.1	0.46–2.8
	Molina	4.6	1.5–14.5
	Barkley	0.83	0.29–2.3
Alcohol Studies	Lambert	0.6	0.32–1.1
	Biederman	8.1	3.9–17.2
	Loney	3.6	1.7–7.4
	Molina	6.6	1.4–30.2
	Barkley	0.98	0.36–2.7

- Adverse effect (NS)
- Protective effect (NS)
- Protective effect (S)

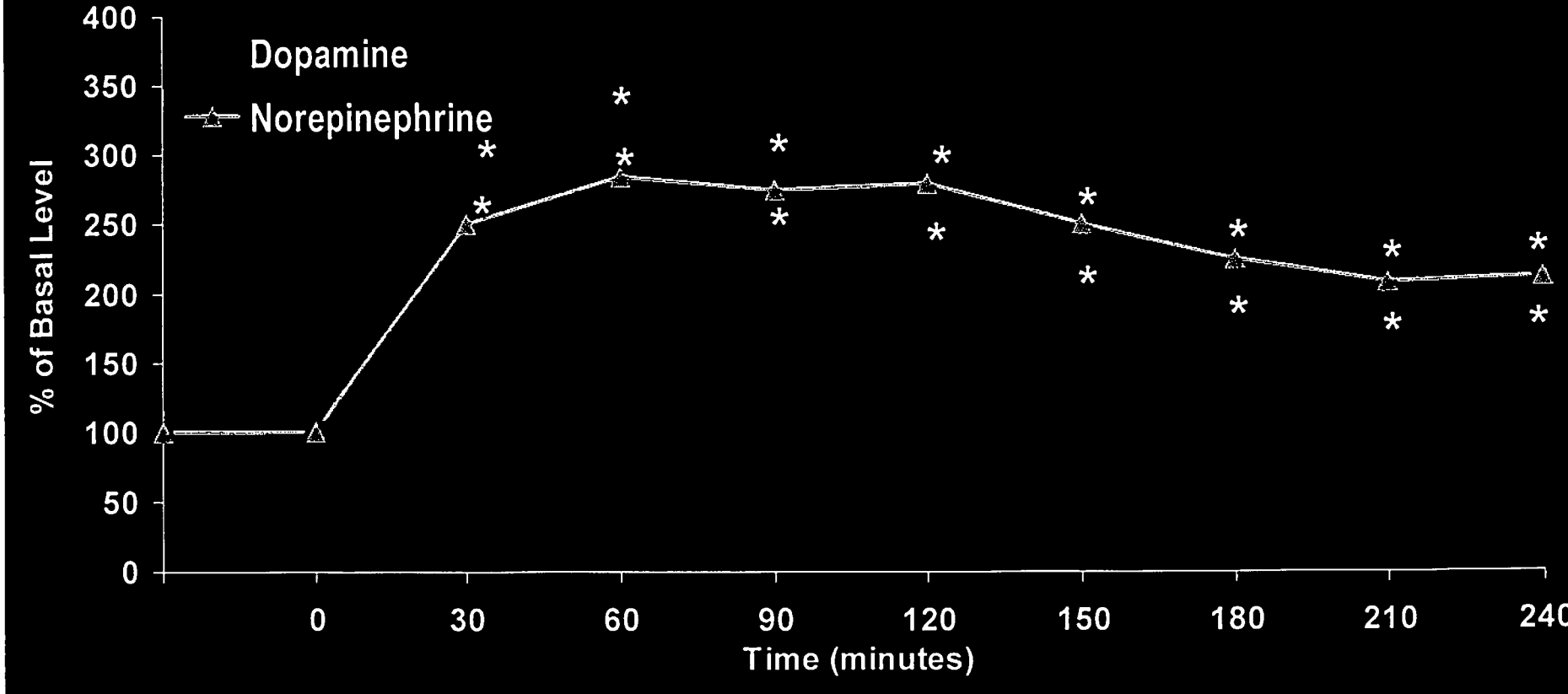
Wilens et al. Pediatrics 2003.

MOA of Atomoxetine

- Blocks norepinephrine transporter
- Throughout brain: increases extracellular norepinephrine
- In prefrontal cortex: increases both NE and DA

Stahl. J Clin Psychiatry 2003. Bymaster et al. Neuropsychopharmacol 2002.

Atomoxetine in Rat Prefrontal Cortex

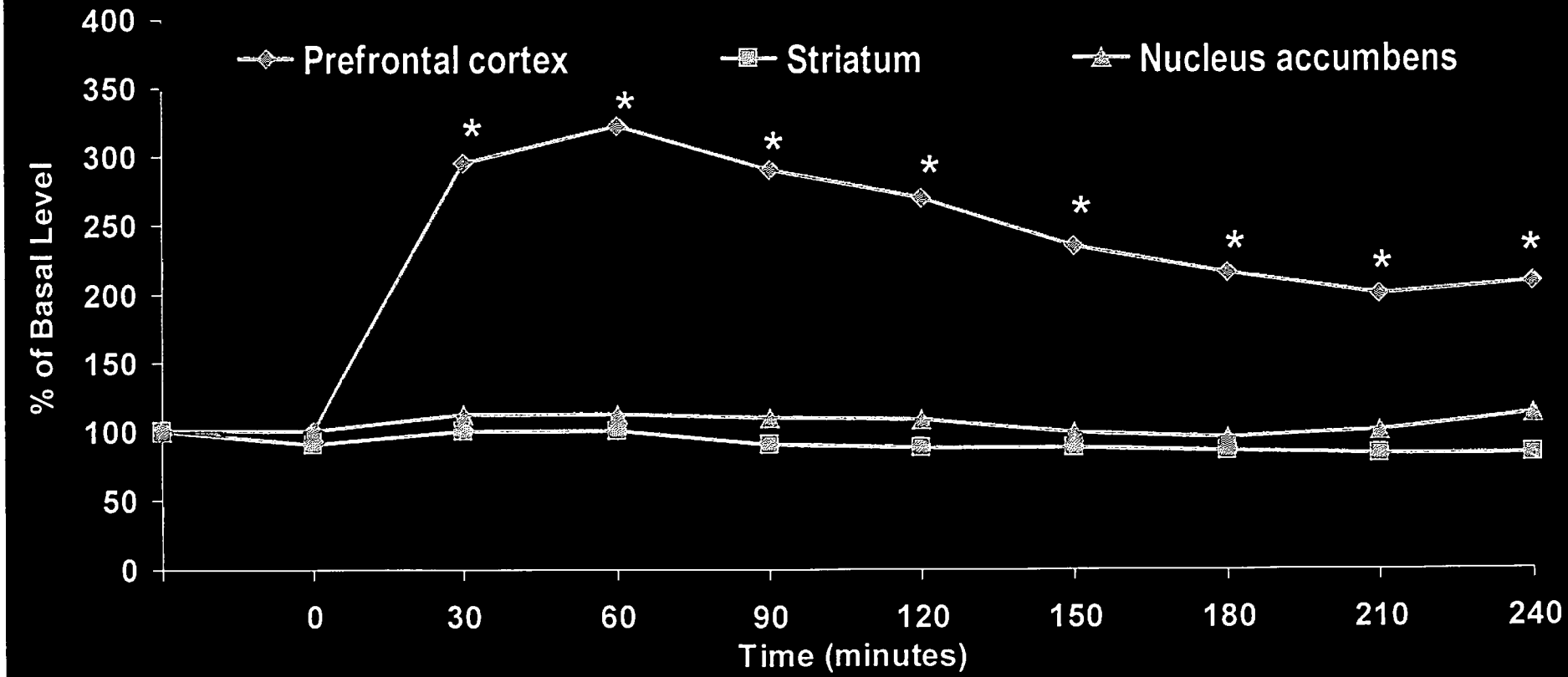


Effects of atomoxetine 3 mg/kg, i.p.

***p<0.025 vs. basal level**

Bymaster et al. Neuropsychopharmacol 2002.

Atomoxetine's Effects on Dopamine in PFC, Striatum, and Nucleus Accumbens



Effects of atomoxetine 3 mg/kg, i.p.

***p<0.05 vs. basal level**

Bymaster et al. Neuropsychopharmacol 2002.

Why Use Behavioral Treatment for ADHD?

- Has been shown to be effective
- Family may not want to use stimulant medications
- Reduces residual symptoms of ADHD
- Makes pharmacologic therapy more effective
- May reduce amount of medication
- Parent satisfaction is high

The MTA Cooperative Group. Arch Gen Psychiatry 1999.

Behavioral Management

- Strategies to simplify/shorten/emphasize tasks
- Positive and negative reinforcement
  - Use of token economies and time outs
- Home and school diaries
- Advantages
  - May be important as children reach adolescence and become less likely to continue their medication
- Disadvantages
  - More effort-intensive and more expensive than medication
  - Adherence rates are low
- Combination treatment: not more effective than pharmacotherapy alone, but may be more acceptable to parents/patients and may allow lower medication doses