



注意力缺陷多动症的認識

吳佑佑 醫師
宇寧身心診所

吳佑佑

現職：宇寧身心診所負責人, 宇寧心理衛生中心

財團法人長庚紀念醫院精神部兼任主治醫師

學歷：私立中國醫藥學院醫學系學士 (1987.06)

• 美國南康州州立大學特殊教育研究所碩士 2003.01

經歷：財團法人長庚紀念醫院精神科住院醫師

(1987.07--1990.06)

國立台灣大學附設醫院精神部兒童心理衛生中心研究員

(1990.07--1992.06)

• 長庚兒童醫院兒童心智科主任 (1995.06--2002.07)

• (2008.07--2011.08)

• 耶魯大學兒童研究中心研究員 (2001.09--2002.08)

一、注意力缺陷

1. 無法注意到小細節或因粗心大意使學校功課、工作或其他活動發生錯誤。
2. 在工作或遊戲活動中無法持續維持注意力。
3. 別人說話時似乎沒在聽。
4. 無法完成老師、家長或他人交辦的事務，包括學校課業、家事零工、或工作場所的職責（並非由於對抗行為或不了解指示）。
5. 缺乏組織能力。
6. 常逃避、不喜歡或拒絕參與需持續使用腦力的工作；如：工作或家庭作業。
7. 容易遺失或忘了工作或遊戲所須的東西；如：玩具、鉛筆、書等。
8. 容易被外界刺激所吸引。
9. 容易忘記每日常規活動，需大人時常提醒。

二、過動及衝動

• (過動)

1. 在坐位上無法安靜地坐著，身體動來動去。
2. 在課堂中或其它須乖乖坐好的場合，時常離席、坐不住。
3. 在教室或活動場合中不適當跑、跳及爬高等（在青少年或成人可僅限於主觀感覺到不能安靜）。
4. 無法安靜地參與遊戲及休閒活動。
5. 經常處於活躍狀態，或常像「馬達推動」般四處活動。
6. 經常說話過多。

• (衝動)

1. 問題尚未問完前，便搶先答覆。
2. 不能輪流等待(在需輪流的地方，無法耐心地等待)。
3. 常中斷或干擾其他人(如：貿然插嘴或打斷別人的遊戲)。

診斷準則

- ADHD目前將其症狀三個亞型:

不專心型、過動衝動型、混合型

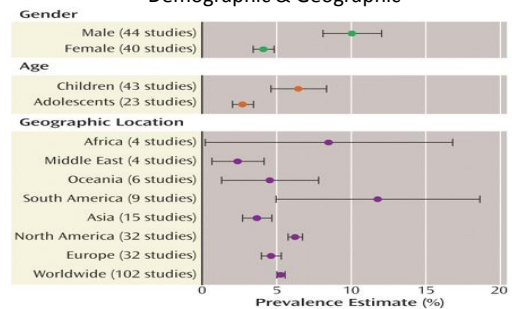
- 不專心包括九個症狀

- 過動包括六個症狀，衝動症狀則有三個

- 這些症狀在7歲以前即產生，且持續6個月以上，造成功能的影響至少出現在兩個場所以上。

- 在下診斷之前至少要先排除廣泛性發展疾患，精神分裂症、或其他精神疾病

ADHD Prevalence – Demographic & Geographic



5.3%, 102 studies, 171,756 children. Africa 8.5%, South America 11.8%, Asia 4.0%, Europe 4.6%, North America 6.2% Polanczyk et al. The Worldwide Prevalence of ADHD: A Systematic Review and Meta-regression Analysis. Am J Psychiatry 2007; 164:942-948.

盛行率 (prevalence)

- 宋維村(1984): 台灣ADHD盛行率的研究，在民國70-80年間以DSM-III-R 為診斷標準：發現在臨床門診的盛行率為5%
- 王雅琴,周文君,歐陽瑞琳(1990): 高雄市學齡兒童盛行率約為9.9%
- 趙家琛(1998): 臺北縣市國小二三年級男生7.5-9%
- 洪麗瑜(2001): 在台灣學齡兒童所做盛行率研究為4.9-5%
- 臧汝芬(2002): 北台灣社區樣本研究(根據DSM-IV)，盛行率為8.4%
- 高淑芬(2005): 國一學生為7.5%
- 高淑芬(2006): SNAP研究: 小一~國二學生為7.09-12.04%

盛行率 (prevalence)

- 性別差異: ♂:♀ = 2~9 : 1 (4~5 : 1)
- 在不同亞型方面:
 - 不專心型: ♂:♀ = 2 : 1
 - 混合型: ♂:♀ = 3~5 : 1
- 不同亞型的年齡分布:
 - 過動衝動型: 學齡前~ 小學低年級
 - 混合型: 小學中年級
 - 不專心型: 高年級~ 中學早期

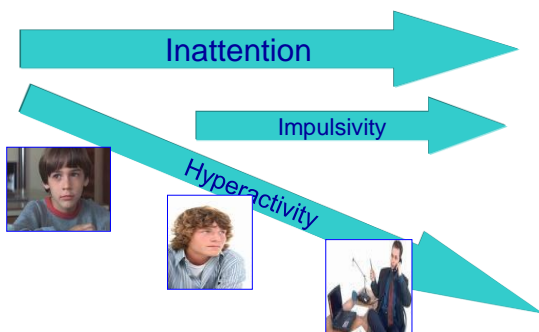
併發或衍生之問題

- (1) 課業學習及表現不理想
- (2) 人際關係不好，易受同儕排擠
- (3) 時常遭到父母或老師責罵，缺乏自信
- (4) 親子關係、學校及社會適應不良、學習障礙、及情緒問題

如果不治療，長大了會好嗎？

- 過動兒成長至青少年後，好動情形逐漸改善
- 自然緩解約發生在12-20歲之間
- 三分之一的個案在長大成人後無特殊症狀
- 三分之一的個案雖然好動現象消失，但注意力不集中及衝動仍然存在
- 三分之一的個案因無法適應學校及家庭，而淪為不良少年或發展出反社會行為、情緒障礙或藥物濫用等問題

ADHD: Decline in Hyperactivity Across the Timeline



小孩有這些情形，該怎麼辦？

- 專業人員評估、診斷
- 接受孩子的特質
- 充分利用相關資源
- 父母師長與孩子共同努力，針對問題，加以解決

臨床評估

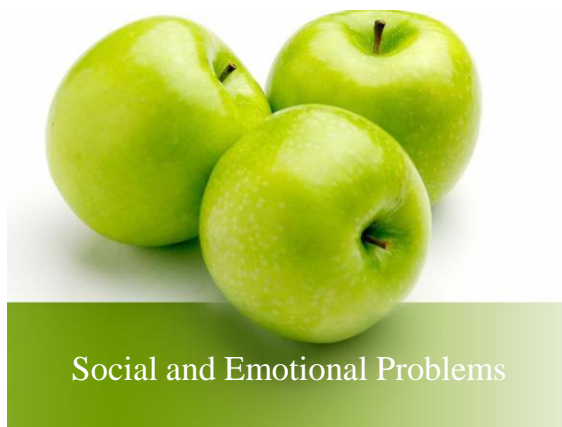
- 一、臨床晤談
 - 家長晤談
 - 兒童晤談
 - 老師晤談
 - 行為觀察
- 二、醫學檢查
 - 1. 身體檢查
 - 2. 醫技檢驗

三、行為量表

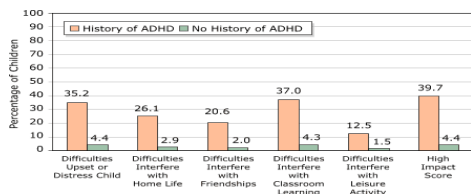
- | | |
|----------------------|----------------------|
| 父母量表 | 教師量表 |
| • 4-16歲兒童行為檢核表 (家長用) | • 4-16歲兒童行為檢核表 (教師用) |
| • SNAP量表 (家長用) | • SNAP量表 (學校版) |
| • 活動量量表 (家長用) | • 活動量量表 (教師用) |
| • 家庭情境量表 | • 學校情境量表 |
| | • 學業表現量表 |

四、心理測驗

- 1. 注意力測驗
 - (1).持續表現測驗 (CPT)
 - (2).刪除測驗 (Cancellation tasks)
 - (3).魏氏兒童智力測驗第三版--專心注意因素
- 2. 衝動控制
 - (1).持續表現測驗 (CPT)
 - (2).相似圖形比對測驗 (MFFT)
- 3. 神經心理功能

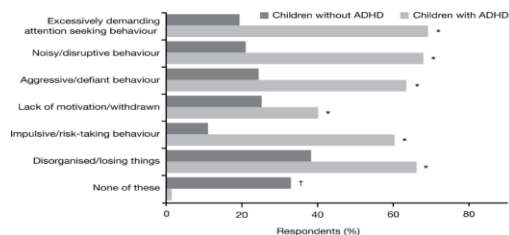


ADHD and the Impairment of Social and Emotional Behaviors



Strengths and Difficulties Questionnaire, based on the 2003 National Health Information Survey, USA, Strine et al., 2006, Preventing Chronic disease, http://www.cdc.gov/pcd/issues/2006/apr/05_0171.htm

Social and Emotional Behavioral Problems in Children with ADHD



European survey of parents of children with ADHD (n=910) and without ADHD (N=995). * $p < .0001$, (Coghill et al., Child and adolescent psychiatry and mental health, 2:31,2008)

Peer relation

- More than 50% of children with ADHD have significant problems in peer relationship (*Pelham 1982*)
- Less knowledge about
 - social skills, appropriate behavior with others (*Grenell 1987*)
- More likely to be engage in
 - Bullying, Victimized in bullying episode (*Unnever 2003*)
- Children with ADHD are stigmatized by their behavior
 - Troublemaking
 - Excessive talking
 - Breaking rules
 - Impulsive aggression (*Barkley 1991*)

Parent-Child relation

- ADHD affects the interaction of children with their parents (especially with mother)
 - Greater intrafamily conflicts (*Danforth et al. 1991*)
 - Children with ADHD (*Barkley 1985*)
 - More talkative, negative, and defiant
 - Less compliant and cooperative
 - Less able to play and work independently of their mother
- Mother of children with ADHD (*Hoza et al. 2000*)
 - Low self-esteem
 - Lower parenting efficacy
- Disturbance of interaction
 - Stem from the effects of a child's behavior rather than parent's behavior on the child (*Fischer 1990*)

ADHD的病因是...

基因學部分的證據

- 同卵雙胞胎(75%) > 異卵雙胞胎
- 手足: 為一般人口罹病風險的2倍
- ADHD孩子的原生父母, 較收養父母罹患ADHD的比率高
- ADHD 伴有行為障礙:
家族較常見有酒精濫用問題及反社會性人格違常

基因學部分的證據

- 多巴胺以及腎上腺素分泌系統的調節失衡
- 數種作用在相關神經內分泌系統的藥物, 對於ADHD症狀有改善效果
- Promoter region of DAT1 may be a risk factor
- 941G/T MAO-A polymorphism in the Taiwanese population.
- The DRD4 gene markers no associated with ADHD.
- DAT1 susceptibility among Asian populations.
- not support DRD2 in Taiwanese children with ADHD.
- evidence of *CLOCK* in susceptibility to ADHD

Environmental factors

- Perinatal stress, low birth weight, severe traumatic brain injury, maternal smoking, exposure to lead, severe early social deprivation
- Psychosocial adversity (maternal mental disorder, paternal criminality, chaotic home)
- Carrying the dopamine transporter gene, D4 receptor, nicotinic acetylcholine receptor

Enterovirus 71 central nervous system infection

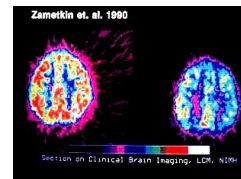
- affect long-term attention and emotion and cause hyperactivity-impulsivity in children.
- *Pediatrics* 2008;122:e452–e458

ADHD and the Brain

Diminished arousal of the Nervous System

Decreased blood flow to prefrontal cortex and pathways connecting to limbic system (caudate nucleus and striatum)

PET scan shows decreased glucose metabolism throughout brain

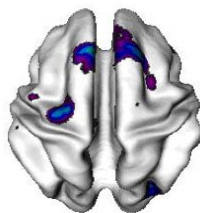


Comparison of normal brain (left) and brain of ADHD patient.

ADHD & Brain Arch Gen Psy 2006, 63(5):540-9

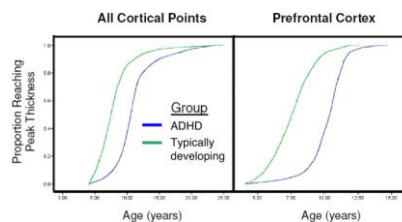
163 ADHD vs 166 control
Average at 9 y/o followed up 5.7 years later 60 % f/u rate
Thinner cortex, most prominently in frontal areas that control attention and motor activity

Best outcomes, an area of the cortex associated with attention (right parietal cortex) increased thickness resembled of health



Comparison of normal brain thinner cortex are part of circuitry that controls attention and motor activity

Kaplan–Meier curves illustrating the proportion of cortical points that had attained peak thickness at each age for all cerebral cortical points (Left) and the prefrontal cortex (Right). The median age by which 50% of cortical points had attained their peak differed significantly between the groups (all $P < 1.0 \times 10^{-20}$)

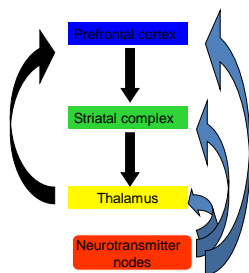


Copyright © 2007 by the Shaw, P. et al. (2007) Proc. Natl. Acad. Sci. USA 104, 19649-19654

PNAS

The cortico-striatal-thalamic-cortical loops

- Both of the striatum and thalamus are topographically organized to interact only with specific areas of the cortex
- These brain circuits allow information to be sent “downstream” and out of cortex, yet the cortex gets feedback on how that information was processed

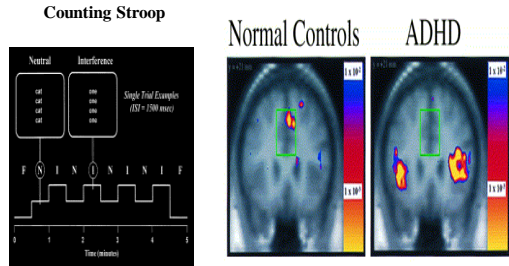
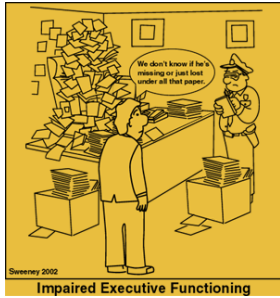


執行功能包括

- 動機 計畫 有目的的行動目標導向
- 抑制和抵抗分心
- 問題解決和策略發展選擇和監測
- 彈性的改變行動來滿足工作的要求
- 維持持續力來達到目標
- 隨時間自我察覺

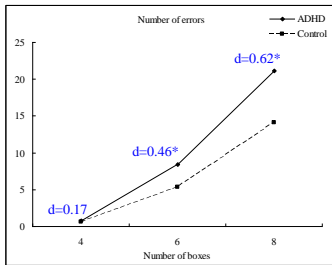
(Seidman, 2006)

Neurocognition in ADHD (Neuropsychological Functioning)

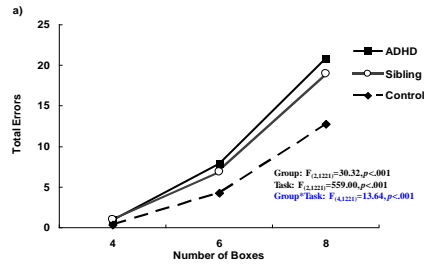


- Control: higher activity in the ACC during the interference blocks minus the neutral blocks (ACC: anterior cingulate cortex)
 - ADHD group: significant activity in a fronto-striato-insular-thalamic network
- Bush et al. AJP: 2001

Group Differences Increase with Increased Task Difficulties



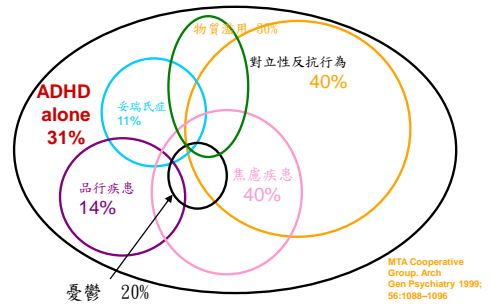
Spatial Working Memory: Group Differences Became Remarkable with Increased Task Difficulty



TOVA results pre & post MPH

	Before medication	After medication	Statistic
Omission			
Total	-0.66 ± 1.33	-0.49 ± 1.37	t (56) = -1.13, p = 0.3
First half	-0.49 ± 1.27	-0.50 ± 1.46	t (56) = -0.23, p = 0.98
Second half	-0.66 ± 1.33	-0.43 ± 1.28	t (56) = -1.58, p = 0.1
Commission			
Total	0.17 ± 1.00	0.45 ± 1.07	t (56) = -2.19, p = 0.033*
First half	-0.004 ± 0.94	-0.08 ± 1.17	t (56) = 0.46, p = 0.6
Second half	0.22 ± 1.08	0.74 ± 1.17	t (56) = -4.68, p < 0.001**
Response time			
Total	-0.62 ± 1.12	-0.34 ± 1.16	t (56) = -2.68, p = 0.003*
First half	-0.58 ± 1.01	-0.18 ± 1.10	t (56) = -3.64, p = 0.001**
Second half	-0.61 ± 1.16	-0.37 ± 1.16	t (56) = -2.10, p = 0.04*
Response time variability			
Total	-0.56 ± 1.03	-0.12 ± 1.10	t (56) = -3.60, p = 0.001**
First half	-0.56 ± 1.18	-0.42 ± 1.08	t (56) = -0.75, p = 0.5
Second half	-0.52 ± 1.08	-0.11 ± 1.13	t (55) = -3.12, p = 0.003*
Response sensitivity (d')			
Total	-0.43 ± 0.98	-0.34 ± 1.16	t (56) = -0.48, p = 0.6
First half	-0.46 ± 1.07	-0.39 ± 1.19	t (56) = -0.54, p = 0.6
Second half	-0.62 ± 0.93	-0.05 ± 1.31	t (56) = -5.75, p < 0.001**
ADHD score	-1.69 ± 1.86	-0.26 ± 2.29	t (45) = -5.76, p < 0.001**

其他可能伴隨ADHD出現的共病



其他可能伴隨ADHD出現的共病

• 睡眠障礙 (Sleep Disorders) :

社區大樣本研究發現，睡眠呼吸中止或是間歇性腿動症候群 (periodic leg movement disorder)，是和白天想睡覺、精神不濟、注意力不集中、過動、學業表現較差以及攻擊行為有關的。

臨床研究曾有報告: ADHD患童比起對照組有較高比例的睡眠呼吸中止(>25%) 或是間歇性腿動症候群 (10%)

藥物治療的考量

- 主要用在兒童症狀嚴重妨礙到學習、人際關係及人格發展時
- 學齡前兒童因環境要求較少，除非症狀特別嚴重，大多不用藥物治療
- 約70%~80%病童可因服用利他能而症狀改善
- 台灣家長或老師排斥用藥的理由：副作用、無法根治疾病、藥效沒有立即顯現
- 「藥物輔助治療」

Stimulants Found to Improve

Core Symptoms

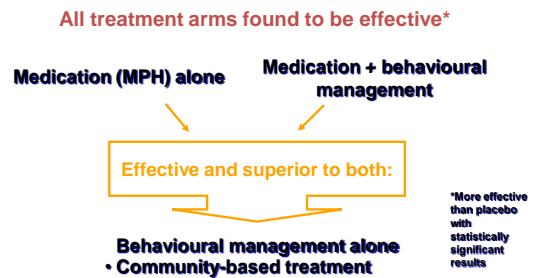
- Inattention
- Impulsivity
- Hyperactivity

AND

- Non-compliance
- Impulsive aggression
- Social interactions
- Academic progress

ADHD Practice Parameters. JAACAP 1997;36:858; Zamoikin and Ernst. N Eng J Med 1999;340:40

MTA Study Results



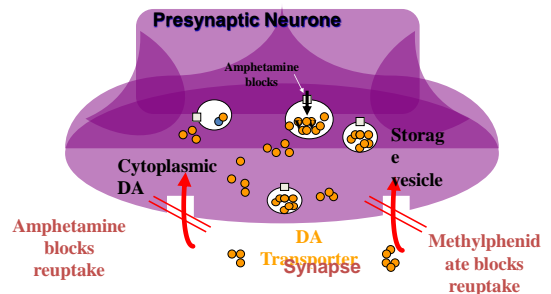
Pharmacological Agents Used in Treatment of ADHD*

Stimulants (Recommended first-line therapy)	Methylphenidate Amphetamine compounds Dextroamphetamine Pemoline
Antidepressants	Atomoxetine Bupropion
Antihypertensives	Clonidine Guanfacine

* Not all agents are available in some countries

Wilens T, et al. ADHD. In Annual Review of Medicine, 2002; 53.
Greenhill L. Childhood attention deficit hyperactivity disorder: pharmacological treatments. In: Nathan PE, Gorman J, eds. Treatments that Work. Philadelphia, PA: Saunders; 1998:42-64.

Mechanism of Action of Stimulants



Wilens T, Spencer TJ. Handbook of Substance Abuse: Neurobehavioral Pharmacology, 1998:501-513.

ADHD 的治療 Stimulant (中樞神經活化劑)

有效成分	商品名	藥效	適用對象
長效型 Methylphenidate	專思達 Concerta®	12小時 一天一劑	6歲以上
短效型 Methylphenidate	利他能 Ritalin®	一劑維持 3-4小時	Children with ADHD

CONCERTA® Multicentre Study: Adverse Events

Adverse Event*	CONCERTA® (n = 106)	Placebo (n = 99)
Headache	14%	10%
Stomach ache	7%	1%
Vomiting	4%	3%
Loss of appetite	4%	0%
Dizziness	2%	0%
Insomnia	4%	1%
Upper respiratory tract infection	8%	5%
Cough increased	4%	2%
Pharyngitis	4%	3%
Sinusitis	3%	0%

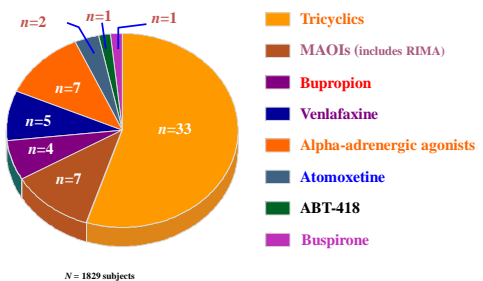
*Regardless of causality

Wolraich et al. Pediatrics 2001; 108: 883-892

TOVA results pre & post MPH

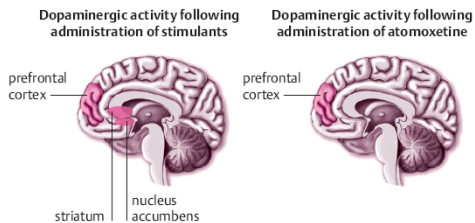
	Before medication	After medication	Statistic
Omission			
Total	-0.66 ± 1.33	-0.49 ± 1.37	t (56) = -1.13, p = 0.3
First half	-0.49 ± 1.27	-0.50 ± 1.46	t (56) = -0.23, p = 0.98
Second half	-0.66 ± 1.33	-0.43 ± 1.28	t (56) = -1.50, p = 0.1
Commission			
Total	0.17 ± 1.00	0.45 ± 1.07	t (56) = -2.19, p = 0.03*
First half	-0.004 ± 0.94	-0.08 ± 1.17	t (56) = 0.46, p = 0.6
Second half	0.22 ± 1.08	0.74 ± 1.17	t (56) = -4.68, p < 0.001**
Response time			
Total	-0.62 ± 1.12	-0.34 ± 1.16	t (56) = -2.68, p = 0.003*
First half	-0.58 ± 1.01	-0.18 ± 1.10	t (56) = -3.64, p = 0.001**
Second half	-0.61 ± 1.16	-0.37 ± 1.16	t (56) = -2.10, p = 0.04*
Response time variability			
Total	-0.56 ± 1.03	-0.12 ± 1.10	t (56) = -3.60, p = 0.001**
First half	-0.56 ± 1.18	-0.42 ± 1.08	t (56) = -0.75, p = 0.5
Second half	-0.52 ± 1.08	-0.11 ± 1.13	t (56) = -3.12, p = 0.003*
Response sensitivity (d')			
Total	-0.43 ± 0.98	-0.34 ± 1.16	t (56) = -0.48, p = 0.6
First half	-0.46 ± 1.07	-0.39 ± 1.19	t (56) = -0.54, p = 0.6
Second half	-0.62 ± 0.93	-0.05 ± 1.31	t (56) = -5.75, p < 0.001**
ADHD score	-1.69 ± 1.86	-0.26 ± 2.29	t (45) = -5.76, p < 0.001**

Studies of Nonstimulant Treatments in ADHD



Adapted from: Spencer et al. J Am Acad Child Adolesc Psychiatry 1996; 35: 409-432

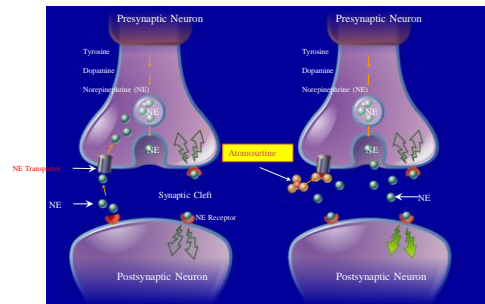
Dopaminergic Activity



*With Strattera, dopamine levels in the striatum (which controls movement) or the nucleus accumbens (implicated in drug abuse) of the brain are unaffected, as dopamine is not taken up by NE re-uptake transporters. This selectivity reduces side effects

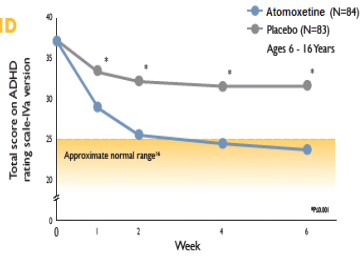
©Bymaster FP et al, 2002

Atomoxetine: a selective norepinephrine reuptake inhibitor

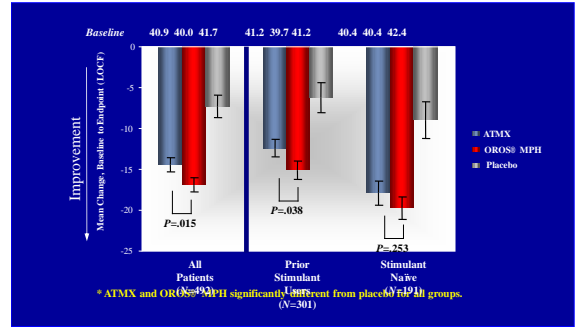


Atomoxetine effectively controls the core symptoms of ADHD

Change in ADHD rating scale⁸

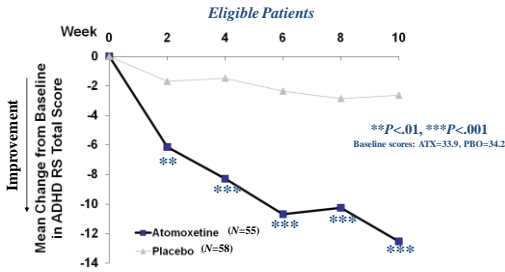


Adapted from Michelson D, et al. Am J Psychiatry 2002; 159: 1996-1901



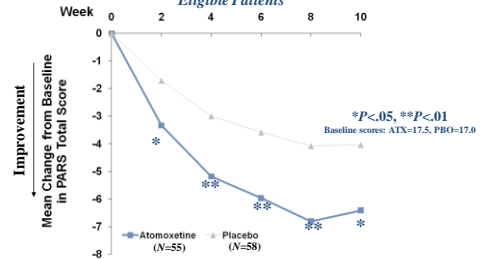
Michelson D. Results from a double-blind study of atomoxetine, OROS methylphenidate, and placebo. Paper presented at the American Academy of Child and Adolescent Psychiatry, October 21, 2004, Washington, DC. (Scientific Proceedings of the 31st Annual Meeting of the American Academy of Child and Adolescent Psychiatry, 2004:49, 202.)

ADHD and Comorbid Anxiety Disorder: ADHD Symptom Reduction Over Time



Data derived from Sumner C, et al. Paper presented at: The 158th Annual Meeting of the American Psychiatric Association; May 21-26, 2005; Atlanta, GA.

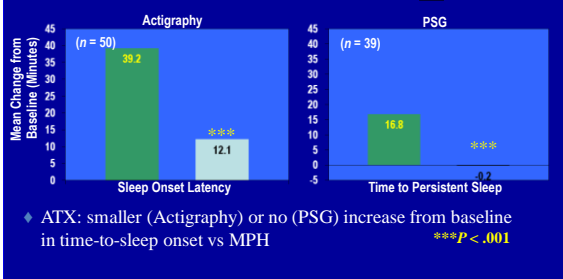
ADHD and Comorbid Anxiety Disorder: PARS Total Score Over Time



PARS: Pediatric Anxiety Rating Scale

Data derived from Sumner C, et al. Paper presented at: The 158th Annual Meeting of the American Psychiatric Association; May 21-26, 2005; Atlanta, GA.

Change in Sleep Onset Latency



♦ ATX: smaller (Actigraphy) or no (PSG) increase from baseline in time-to-sleep onset vs MPH

*** $P < .001$

Sangal RB, et al. Sleep. Vol. 29, No. 12, 2006

Event	Atomoxetine N=1597 n (%)	Placebo N=934 n (%)	P Value ^a
Headache	300 (18.8)	144 (15.4)	.035
Decreased appetite	257 (16.1)	39 (4.2)	<.001
Abdominal pain upper	211 (13.2)	81 (8.7)	<.001
Vomiting	168 (10.5)	53 (5.7)	<.001
Nausea	161 (10.1)	43 (4.6)	<.001
Somnolence	139 (8.7)	34 (3.6)	<.001
Fatigue	119 (7.5)	28 (3.0)	<.001
Cough	93 (5.8)	68 (7.3)	.152
Irritability	88 (5.5)	27 (2.9)	.002
Nasopharyngitis	88 (5.5)	60 (6.4)	.380
Dizziness	72 (4.5)	15 (1.6)	<.001
Weight decreased	48 (3.0)	3 (0.3)	<.001
Anorexia	47 (2.9)	11 (1.2)	.004
Abdominal pain	39 (2.4)	7 (0.7)	.002
Rash	39 (2.4)	10 (1.1)	.016
Stomach discomfort	36 (2.3)	10 (1.1)	.031

N=Patients who took at least one dose of study drug

Data on file, Eli Lilly and Company

^aTreatment difference, Fisher's exact test.

Overall Safety Summary

- Atomoxetine is **safe and generally well tolerated**.
- Patients who are started on therapy should be **monitored for suicidality** (suicidal thinking and behavior).
- Atomoxetine should be **discontinued in patients with jaundice or laboratory evidence of liver injury**, and should not be restarted. But routine LFT testing NOT recommended.
- **Modest elevations of pulse and blood pressure** over time; no statistically significant prolongation of QTc.
- Studies support **safety relative to growth** (weight and height) and development during long-term treatment.
- Atomoxetine **has less effect on sleep than MTP**.

- 要過動的孩子不要動，不要打架，倒不如教他動的方法，動的得當，及與同儕相處之道，高壓強迫的方式並不能真正解決孩子的問題。希望能提昇孩子學習時的專注力，改善學習效果，只有讓孩子在學習成長中獲得快樂，才是促進學習的最大動力。



Thank you for your attention!

Strattera 特點

- ◆ 唯一治療 ADHD 之非中樞神經興奮劑
 - 非管制藥，無藥物濫用之疑慮
 - 可治療 Tics 孩子的 ADHD
 - 可治療 焦慮孩子的 ADHD
- ◆ 全天持續的療效
 - 增進學習成效
 - 穩定情緒與人際關係
 - 改善家人互動

全面性及長遠性的治療：

1. 不能只靠單一介入方法，也不能只有兒童本身參與就好，周圍的人必須共同參與介入計畫。
2. 症狀、衍生問題、人際互動等會隨年齡增長而產生改變，對兒童的介入方式需考慮發展上的變化，並依此做相對的調整。