# ADHD a Valid Diagnosis?

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No conflicts of interest with regard to this presentation.

# ADHD a Valid Diagnosis?

- ADHD is in the boundaries of neurology and psychiatry.

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- Symptoms and diagnosis of ADHD validation.

- The importance of proper management.

- What and how to treat.

# ADHD, Questions

- Can the  phenomena of hyperactivity, impulsivity and attention deficit disorders be distinguished from other changes or normal variations in behavior?

- Are clinically significant  ADHD symptoms truly associated with psycho-social risks and disabilities?

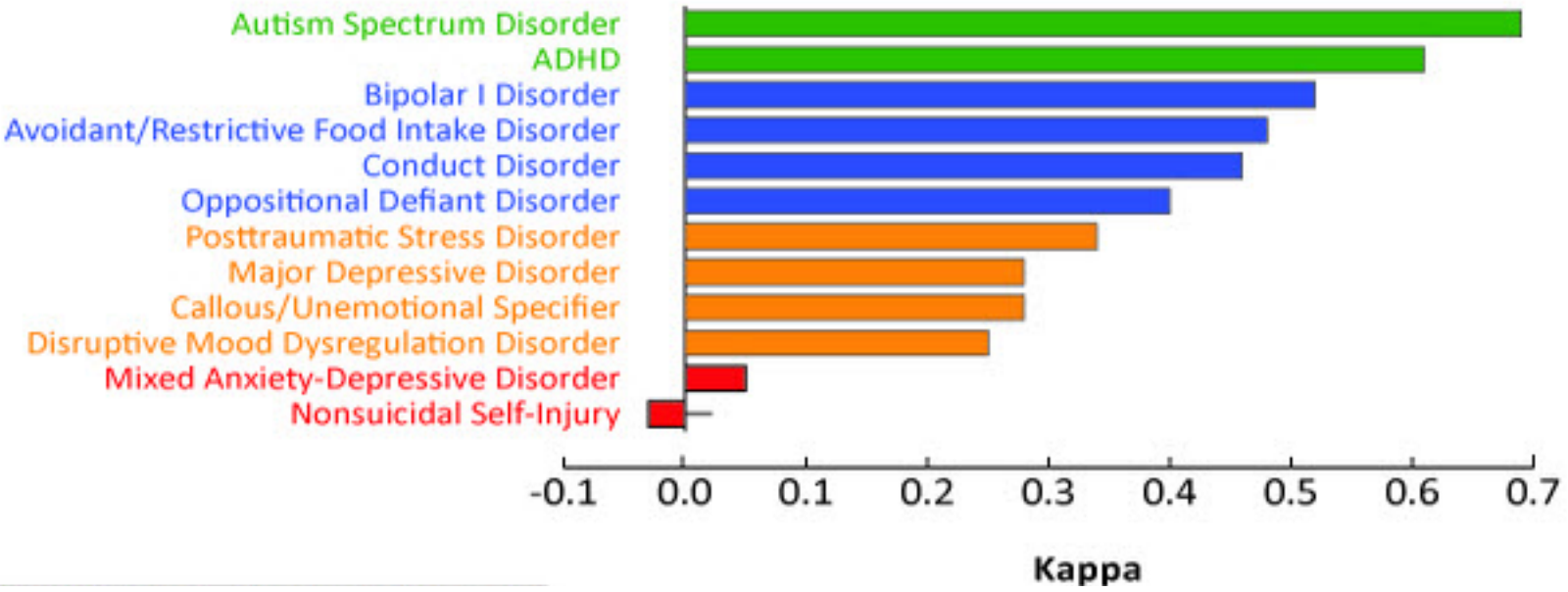
- Is there consistency in the neurobiological evidence of environmental and genetic factors associated to ADHD?

# ADHD, Questions

- Is the diagnosis of ADHD a predictor of behavioral and psychological disorders as well as  increased risk of illness or death?

- Does the treatment of ADHD reduce those risks?

# ADHD Symptoms by DSM-5




➡ ADHD symptoms are validated in DSM-5 with **very good agreement**

Very Good Agreement | Questionable Agreement
Good Agreement | Unacceptable Agreement

# ADHD Genetics

- Estimates of heredability are of around 0.76

(Faraone, 2005).

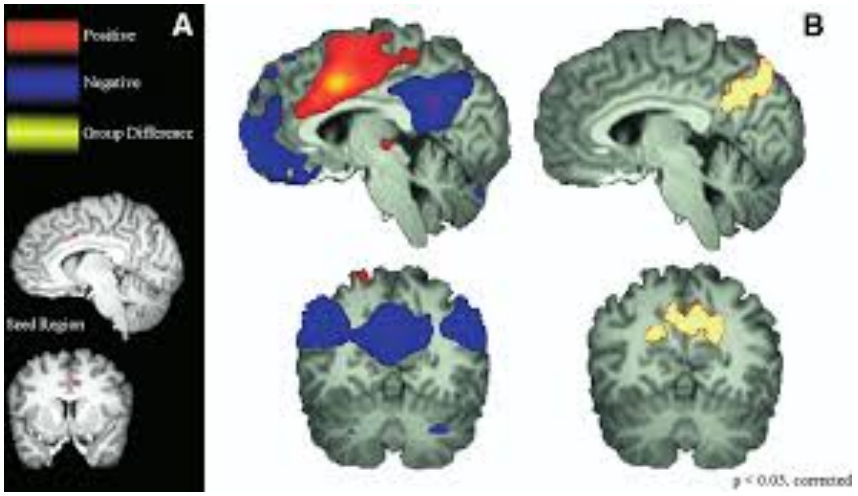
- Meta-analysis:  Polygenic risks for ADHD (higher in ADHD with conduct disorder).

(Hamshere et al., 2013).

# ADHD Neurobiology

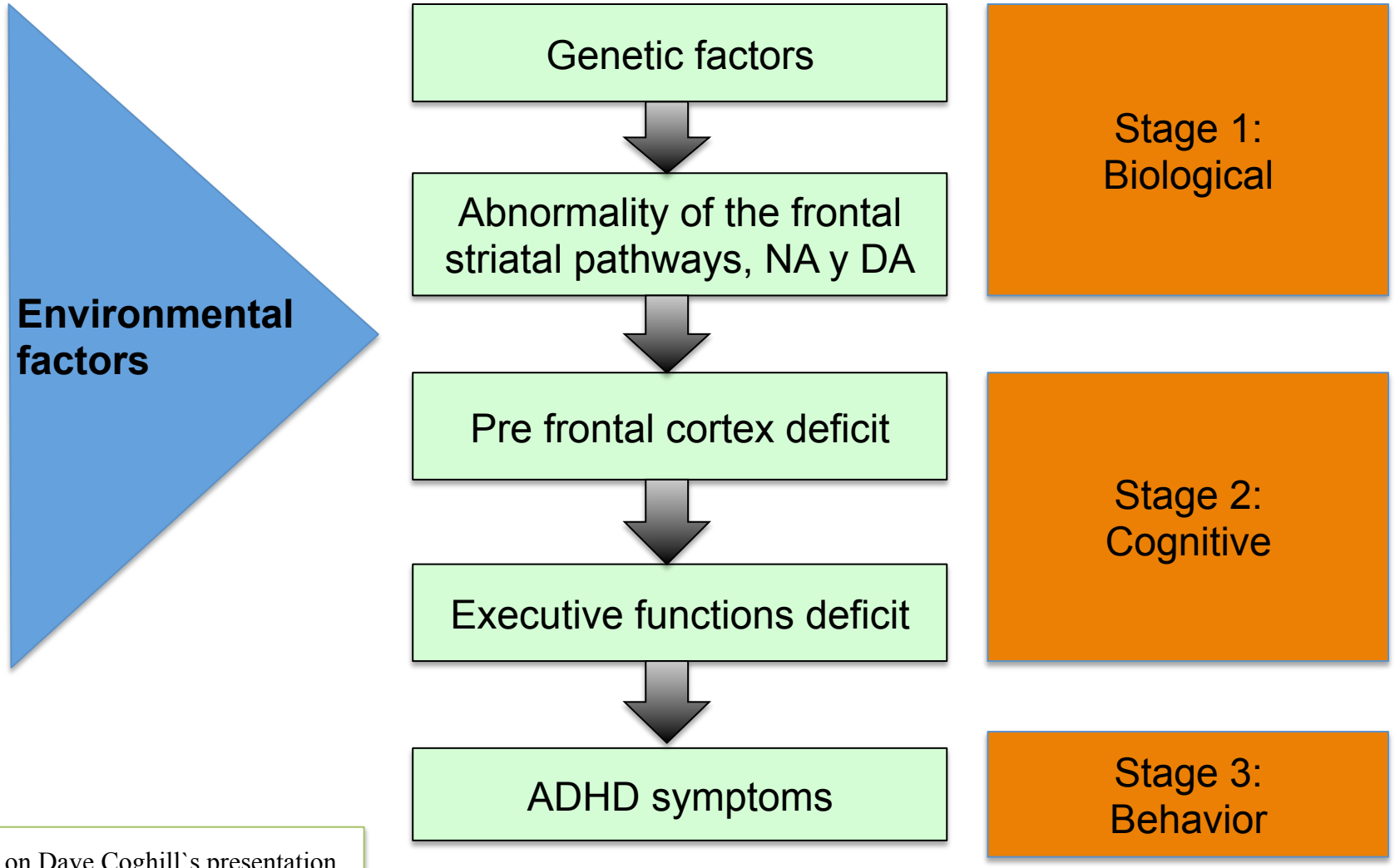
- Cingulate and Precuneus interaction is a new place of dysfunction for ADHD.
  (Castellanos et al, Biological Psychiatry 2008).

- Lack of attention in ADHD, results from interference or poor coordination between the default network and the executive control network.
  (Sonuga-Barke & Castellanos 2007).



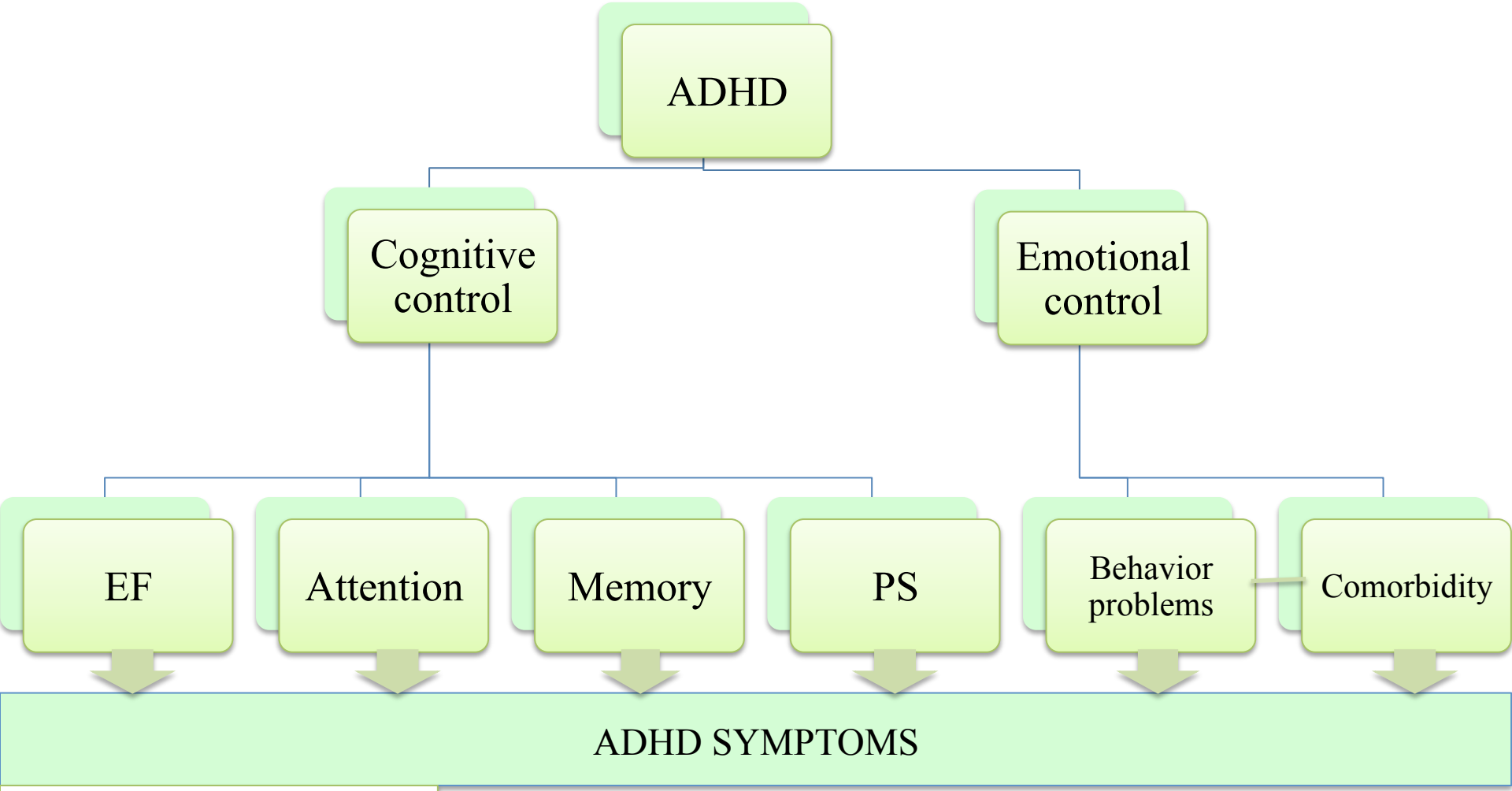
# Neurobiology

## Cause model of ADHD




Based on Dave Coghill`s presentation. World Congress of ADHD, 2015

# ADHD Neurobiology and Behavior

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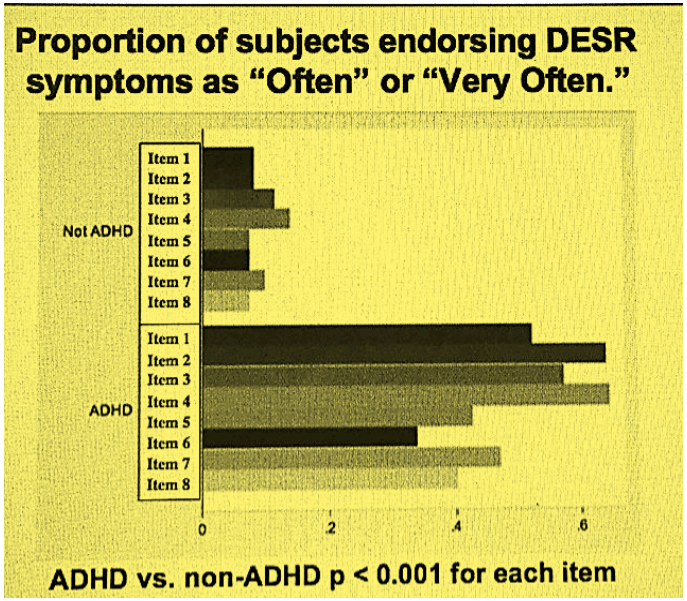
# ADHD Behavior:

## Deficient Emotional Self Regulation



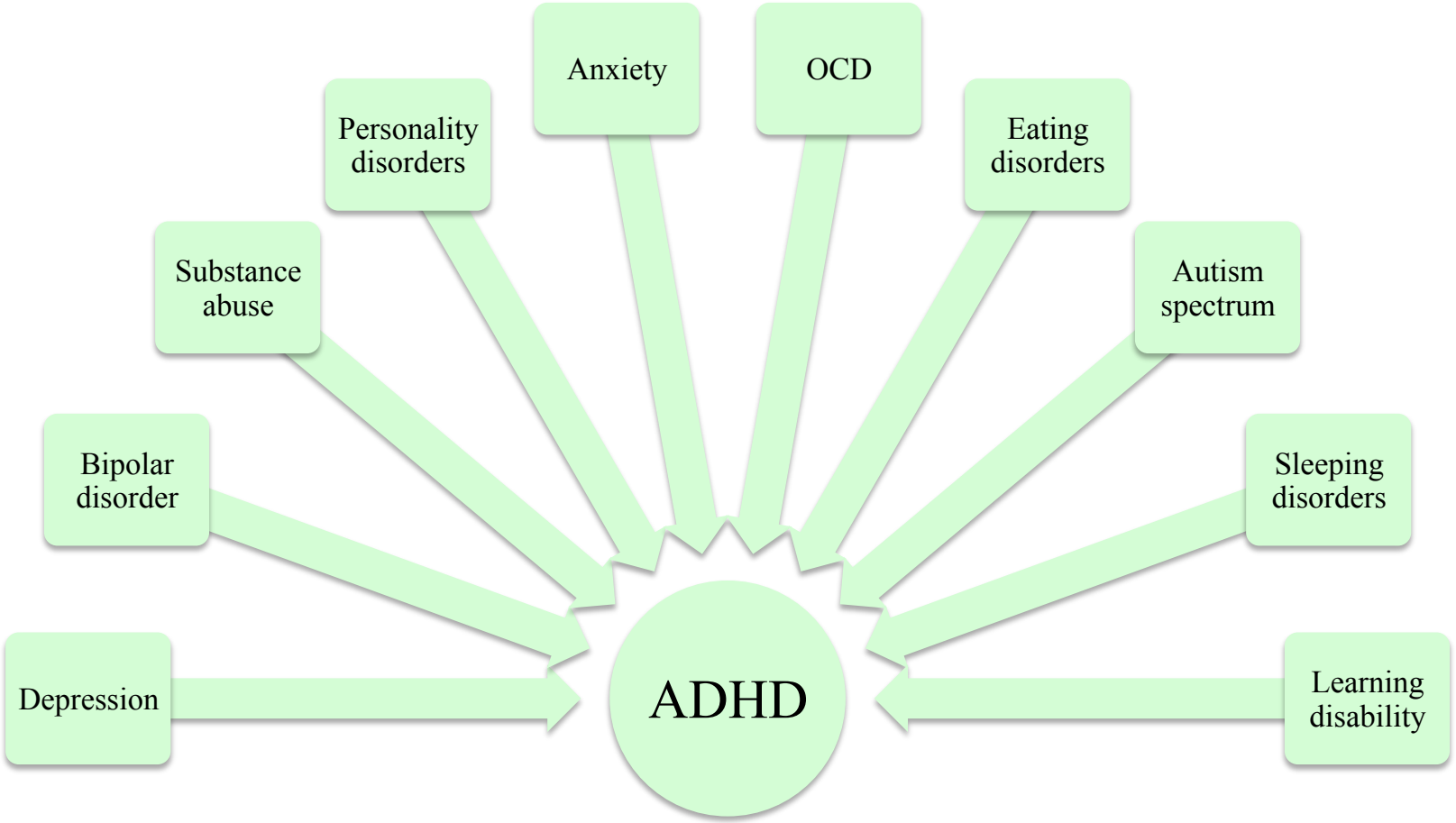

**Severity: None (0), Sometimes (1) Often (2), Very Often (3)**
**(Surman, Biederman, Spencer, Miller, Mc Dermott, Faraone ADHD Atten Def Hyp Disord,2013)**

1. Quick to get angry or become upset.
2. Easily Frustrated.
3. Emotionally over-reactive.
4. Easily excited by activities going on around them.
5. Lose temper.
6. Argue with others.
7. Are easily annoyed by others.
8. Are angry or resentful.

➡ **Deficient emotional self regulation is very important in ADHD behavior.**

# ADHD Behavior:

## Comorbidity



# ADHD Behavior,
## Risks and Consequences

- **15 year old adolescents** who were rated hyperactive as pre-schoolers displayed poorer reading ability and were more likely to be **reading-disabled.** (Mc Gee et al 1991)

- **Men** who were diagnosed **with ADHD** as children completed on **average 2.5 years less schooling** than men without ADHD, aproximately 25% of the ADHD group (2% of non ADHD) did not complete high school. (Mannuzza et al 1993)

- **Childhood ADHD predicted adolescent behavioral problems** (substance abuse, delinquency) and academic problems (leaving school with no qualifications). (Mc Gee et al 2002)

# ADHD, The Risk of Death

- *Followed a cohort study of all children born in Denmark 1981-2011 (1.9 mill).*
- *Identified 32.061 with ADHD.(%)*
- *Average age of ADHD diagnosis was 12,3 years.*
- *During follow-up 110 individuals with ADHD died.*
- *Unadjusted all-cause mortality rate per 100 person-year:*

***Individuals with ADHD=5.85***

***Individuals without ADHD = 2.21.***

*(Dalsgaard et al. Lancet.Published Online: 25 February 2015.)*

Mortality in children, adolescents, and adults with attention deficit hyperactivity disorder: a nation wide cohort study.

(Søren Dalsgaard, PhD, Søren Dinesen Østergaard, PhD, Prof James F Leckman, PhD, Prof Preben Bo Mortensen, MD, Marianne Giørtz Pedersen, MSc Lancet.Published Online: 25 February 2015.)

# ADHD, The Risk of Death

- **ADHD doubles mortality** rates. Higher risk in women.
- Comorbidity with ODD, conduct disorder, and substance abuse increase the mortality risk.
- Without these comorbid ADHD disorders, the relative risk of dying is 1:5.
- The diagnosis in adulthood leads to greater risk of dying.
- **Accidents were the most common cause of death**.

(Dalsgaard et al. Lancet feb, 2015 )

# ADHD and Criminal Activity

Adolescents diagnosed with ADHD (under 15 years old) using medication, reduce the risk of problems with the police by 17%.

(Dalsgaard, J. Health Econ 2014)

Adults diagnosed with ADHD using medication, reduce the risk of crime by 30-40%.

(Lichtenstein y Zellerqvist et al, New England J. Med. 2012)

# Treatment,

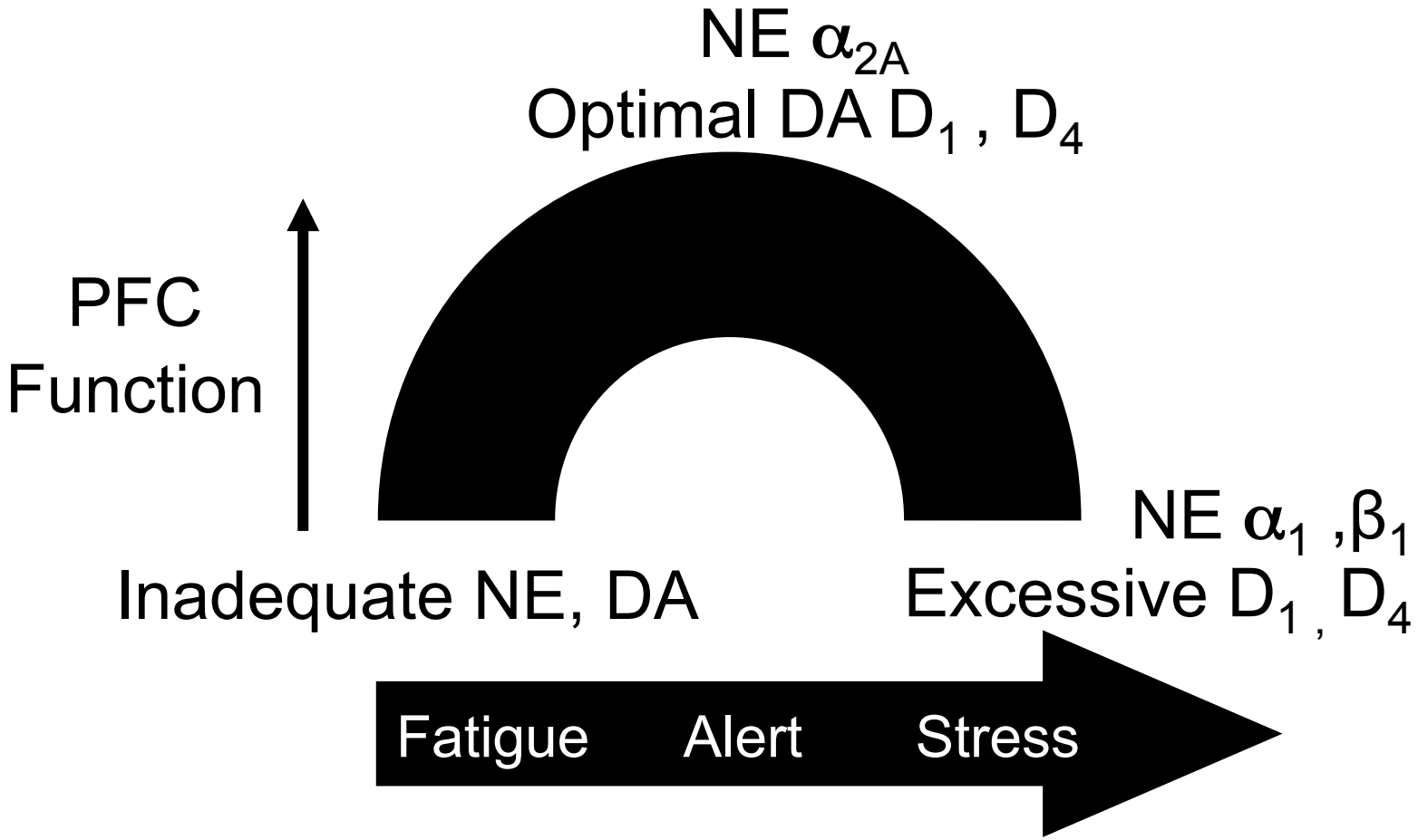
## Stimulant Medication

- More effective treatment for ADHD at all ages
  (Prince, Wilens, Spencer & Biderman, 2006)

- Higher doses increases vigilance, motor activity, euphoria and worsens cognition.
  (Arnsten and Dudley 2005; Berridge and Stalnaker 2002)

- Low doses block the reuptake of DA and NA with discrete action areas of the somatosensory cortex, hippocampus, subcortical areas, N accumbens and medial septum.
  (Kuczensky and Segal 2002 Berridg et al., Drouin et al, 2006)

# Treatment: PFC Function Effects




Inverted-U shaped modulation of prefrontal cortex (PFC) dependent function by norepinephrine (NE) and dopamine (DA) receptors. The PFC receives NE inputs from the locus.(Arnsten, 2007).(Image from book Translational Neuroscience.)

# Treatment
## Methylphenidate

- No increased incidence of addiction in patients receiving treatment with methylphenidate in ADHD.

- It does not produce dependance and may reduce the tendency to consume drugs.

(Biederman, 2003)

# Treatment
## New Drugs Explored

- MMDA antagonists
- H3 antagonists
- Catecholamine reuptake inhibitors
- Metadoxine

# Conclusions

- The symptoms which define the current criteria for ADHD can be distinguished from other disorders and from normal variation.
- There is consistent evidence of genetic, environmental and neurobiological factors associated with ADHD.
- ADHD is associated with significant clinical and psychosocial impairments.
- Stimulants are the  more effective treatment for ADHD at all ages.

# Bibliography


- Volkow ND, Wang GJ, Fowler JS *et al.* Therapeutic doses of oral methylphenidate significantly increase extracellular dopamine in human brain. *J. Neurosci.* 21, RC121 (2001).
- Spencer TJ, Adler LA, McGough JJ, Muniz R, Jiang H, Pestreich L. Efficacy and safety of dexmethylphenidate extended-release capsules in adults with attention-deficit/hyperactivity disorder. *Biol. Psychiatry* 61(12), 1380–1387 (2007).
- Spencer TJ, Adler LA, McGough JJ, Muniz R, Jiang H, Pestreich L. Efficacy and safety of dexmethylphenidate extended-release capsules in adults with attention-deficit/hyperactivity disorder. *Biol. Psychiatry* 61(12), 1380–1387 (2007)
- Medori R, Ramos-Quiroga JA, Casas M *et al.* A randomized, placebo-controlled trial of three fixed dosages of prolonged-release OROS methylphenidate in adults with attention-deficit/hyperactivity disorder. *Biol. Psychiatry*63(10), 981–989 (2008)
- Biederman J, Spencer TJ. Psychopharmacological interventions. *Child Adolesc. Psychiatr. Clin. N. Am.* 17(2), 439–458, xi (2008).
- Greenhill LL, Pliszka S, Dulcan MK *et al.* Practice parameter for the use of stimulant medications in the treatment of children, adolescents, and adults. *J. Am. Acad. Child Adolesc. Psychiatry* 41(2 Suppl.), S26–S49 (2002)
- Spencer T, Wilens TE, Biederman J, Faraone SV, Ablon S, Lapey K. A double blind, crossover comparison of methylphenidate and placebo in adults with childhood onset attention deficit hyperactivity disorder. *Arch. Gen Psychiatry* 52, 434–443 (1995)
- Wender PH, Reimherr FW, Marchant BK, Sanford ME, Czajkowski LA, Tomb DA. A one year trial of methylphenidate in the treatment of ADHD. *J. Atten. Disord.* 15(1), 36–45 (2010).
- Adler LA, Spencer T, McGough JJ, Hai J, Muniz R. Long-term effectiveness and safety of dexmethylphenidate extended-release capsules in adult ADHD. *J. Atten. Disord.* 12(5), 449–459 (2009).
- Biederman J, Mick E, Surman C *et al.* A randomized, 3-phase, 34-week, double-blind, long-term efficacy study of osmotic-release oral system-methylphenidate in adults with attention-deficit/hyperactivity disorder. *J. Clin. Psychopharmacol.* 30(5), 549–553 (2010).
- Greenhill L, Osman B. *Ritalin: Theory and Practice*. Mary Ann. Liebert Inc., New York, NY, USA (1999).