

Stimulants May Help, Not Harm, Your Brain

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Disclaimers

- no pharmaceutical company affiliations or agreements
- YouTube channel @DrJohnKruse with 200+ free ADHD videos
- medium.com 250+ mental health / ADHD articles
- *Recognizing Adult ADHD* book signing 3:00 today
- not accepting new patients

Take Home Message

- Stimulants remain the most effective treatment for ADHD symptom reduction
- Stimulants have common (minor) side effects
- Stimulants have uncommon serious side effects
- Street stimulants can cause brain damage
- Therapeutic dosages of prescription stimulants NOT associated with damage
- Therapeutic dosages of prescription stimulants “normalize” brain structure

Risks of Stimulants

Amphetamine and Methylphenidate based products

- Nuisance side effects usually dose related and short term
 - agitation, insomnia, appetite suppression, sweating, nausea, bp
- Serious side effects
 - cardiac (more apparent over time)
 - addiction
 - psychosis

Brain Integrity and Drugs

- Street stimulants damage dopamine neurons in the striatum and beyond
- Antipsychotic medications associated with brain atrophy
- Antidepressants associated with neuroprotection (hippocampus, amygdala)
- Prescription stimulants?

Damage from Illicit Stimulants

Substance, dosage, and dosage timing all matter

- Case series from human meth and cocaine addicts
- Rodent models of stimulant abuse
 - inflammation, cell death
 - 50 mg/kg vs. 0.2- 2.0 mg/kg in humans
 - intraperitoneal injections (rapid surge) result in brain damage
 - drinking / gastric lavage of same doses don't cause damage

Acute Brain Effects of Stimulants

- Numerous studies
- While drug is on board, patterns of brain activation in those with ADHD look more like those without ADHD
- Normalization of connection strengths, brain activation
- Do these benefits persist?

Chronic Stimulant Effects on the Brain

2013 Meta-analysis Spencer, Biederman et al.

- 29 studies summarized
- 6 MRI, 20 fMRI, 3 spectroscopy
- Most naturalistic, not randomized/controlled
- Comparison to untreated ADHD subjects or to non-ADHD
- Variation in drug treatment duration, washout, structures examined

MRI studies from Meta-analysis

6 MRI studies analyzed

- Subjects age range 4-20
- 6/6 altered brain structures non-medicated ADHD vs controls
- 6/6 medication lessened abnormalities in at least some regions
- Normalization in rates of change of cortical thickness, multiple areas
- Gray matter, basal ganglion, cerebellar volumes no group differences
- 0/6 examples of brain deterioration relative to controls

fMRI Studies from Meta-analysis

20 functional MRI studies analyzed

- different brain regions studied, different tasks
- 20/20 ADHD brains showed different activation than controls
- 19/20 stimulant medications lessened ADHD vs. control differences
- increased differences compared to controls as compensatory
 - increased prefrontal activation with attention, reward tasks

Spectroscopy from Meta-analysis

3 studies examining functional connectivity

- ADHD subjects had hypo-connectivity compared to controls
 - ventral anterior cingulate to prefrontal cortex
 - amygdala to lateral prefrontal cortex
- Stimulant treatment increased connectivity strength

2021 Shaw et al Study

Cingulo-operculum network

- Network for error monitoring, initiating and adapting control
- Stimulants acutely strengthen this network
- Positive chronic response to stimulants, stable connectivity
- Poor response to stimulants, system overly strengthened
- No apparent change in DMN, striato-thalamic networks

Wu, Volkow 2024 Study

Part of large, multisite ABCD study

- Children 9-11
- MRI before and after
- 273 on Stimulants; 1002 ADHD off Stimulants; 5378 non-ADHD controls
- ADHD - structural abnormalities in brain regions for saliency, reward processing
- stimulant treatment improved ADHD symptoms, normalized brain structures
- naturalistic, not randomly assigned

Pretus et al. 2017 Study

Brain changes in drug naive adults with ADHD

- 25 ADHD + stimulant, 16 ADHD no treatment, 25 non-ADHD controls
- subjects not previously exposed to stimulants
- 3 years treatment with stimulants
- non-medicated subjects showed gray matter of putamen decreased
- normalizing (protective) effect of stimulants

Therapeutic Doses of Stimulants in ADHD

- No findings of damage, degradation, inflammation, gliosis
- Normalization of some brain structures relative to untreated controls
- Association only?
- Permanence of effects?
- Neuroprotective effects of ADHD? of stimulants?
- Are we consigning some kids to lifelong ADHD by not treating in childhood?

References

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