



Marijuana: Potency, Policy and Public Impact

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Marijuana and the Adolescent Brain

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How Marijuana Works

- Cannabis – THC - tetrahydrocannabinol – one of the active ingredients in marijuana plant – responsible for “high”
- Very different from cannabidiol – opposite mechanism of action

How Marijuana Works (cont.)

- THC binds preferentially to CB1 receptors
- Competes with anandamide (endogenous compound)

Brain alterations in Adolescents who use Marijuana

- Changes in volume of grey matter and white matter depending on region
- Reversible with Abstinence
- Degree of change correlates with age at first use and continual dose
- Mechanism?

Why do we have anandamide?

- Means “bliss”
- Poorly understood until recently
- Now we know that anandamide works in a complementary manner with glutamate (neurotransmitters.)

Why does anandamide matter?

- Glutamate is an “excitatory” NT
 - crucial for “learning” (LTP)
 - strengthens useful synapses
 - destroys weak/non-useful synapses

Why does anandamide matter? (cont.)

- Anandamide (CB1) receptors thought to work in a “feedback loop” with glutamate.
- Sends a “stop” signal to keep glutamate from going haywire (destroying good synapses and missing “bad” ones.)

What does all this have to do with Cannabis?

- Anandamide and cannabis activate the same receptor. Does this matter?

It depends...

Age and the Human Brain

2 “Critical Periods of Development” for the human brain:

- Conception to approximately 2 years of age
- Adolescence: 10-12 until 20-22 (10-22)

Critical Periods

- During these times, massive brain growth and changes are taking place. The first (infancy) period is obvious; but what is happening in adolescence?

Adolescent Brain Changes

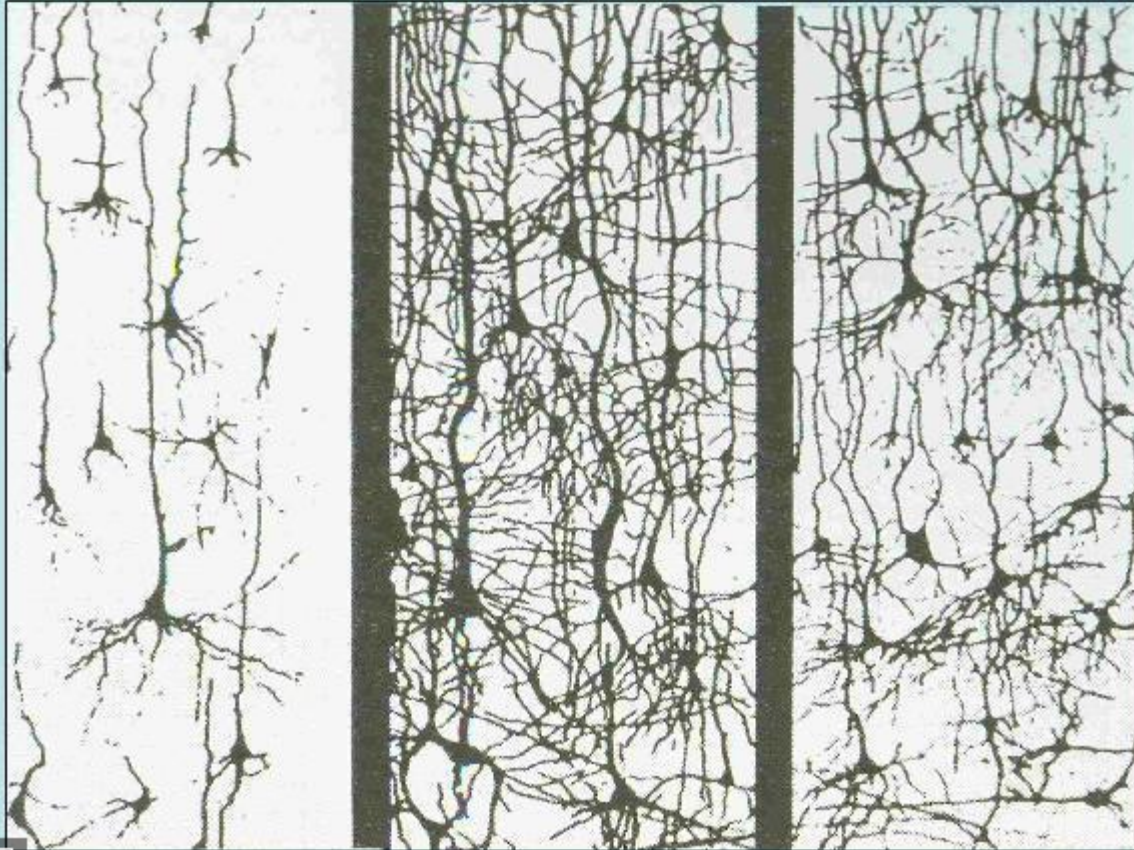
- “Older” regions are fully formed, and beginning secondary sex hormone expression – hypothalamus, pituitary, as well as amygdala (emotion, hormonal responses... “primitive”) Risk taking behavior /impulses.

Synaptic Density

At birth

6 years old

14 years old



Source: Rethinking the Brain, Families and Work Institute, Rima Shore, 1997; Founders Network slide

Adolescent Brain Changes

- Newer regions – prefrontal cortex (PFC) Higher executive function, decision making, impulse control, still not fully developed.
- 13 year old vs. 24 year old.

Pruning

- During adolescence, glutamate serves a very important function. Pruning is constant – synaptic connections related to behavioral outcomes are either strengthened or discarded.
- Result of consequences/outcomes.

Pruning

- Recall that anandamide, via CB1R, monitors/mediates/inhibits glutamate (and other NT).
- Anandamide sends “stop” signal via CB1 receptor.

Anandamide, THC and CB2

- THC activates the same receptor that anandamide does. Why is this a problem? More pruning? How does the brain respond to frequent heightened activation of a receptor by a drug?
- Downregulation

What is “Downregulation?”

- Maintain homeostasis – frequent peaks of any NT activity (unusual) result in either elimination or reduction in sensitivity of receptors.
- CB1 receptors can be downregulated by frequent cannabis (THC) use in adolescence.

Conclusion

- While there is little evidence to support negative outcomes in adults, evidence is emerging that adolescents should be strongly discouraged from heavy use of marijuana.
- Frequency of use and age of first use are of importance, in that order.

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