

The Use of Medications to Treat Behavioral and Mental Health Problems in Children - When Do They Make Sense?

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2012 Through the Eyes of the Child Lecture Series

Talk Overview

- Development and the importance of prevention/early intervention
- Neurocircuitry, Neurotransmitters and Pharmacological Agents
- Neurobiology and Treatment of Disruptive Behaviors in Children
- Neurobiology and Treatment of Mood and Anxiety Disorders in Children

Mental Disorders and Development

- Mental Disorders as Developmental Disorders
- Prevalence of Mental Health Problems
- Normal Developmental Differences

The Origins of Mental Illnesses

“Mental illnesses are developmental disorders.”

Dr Insel,

Director, NIMH

Why developmental disorders?

- Genetics
- Vulnerability does not equal pathology
- Genes x Environment = Endophenotype

Normal Development

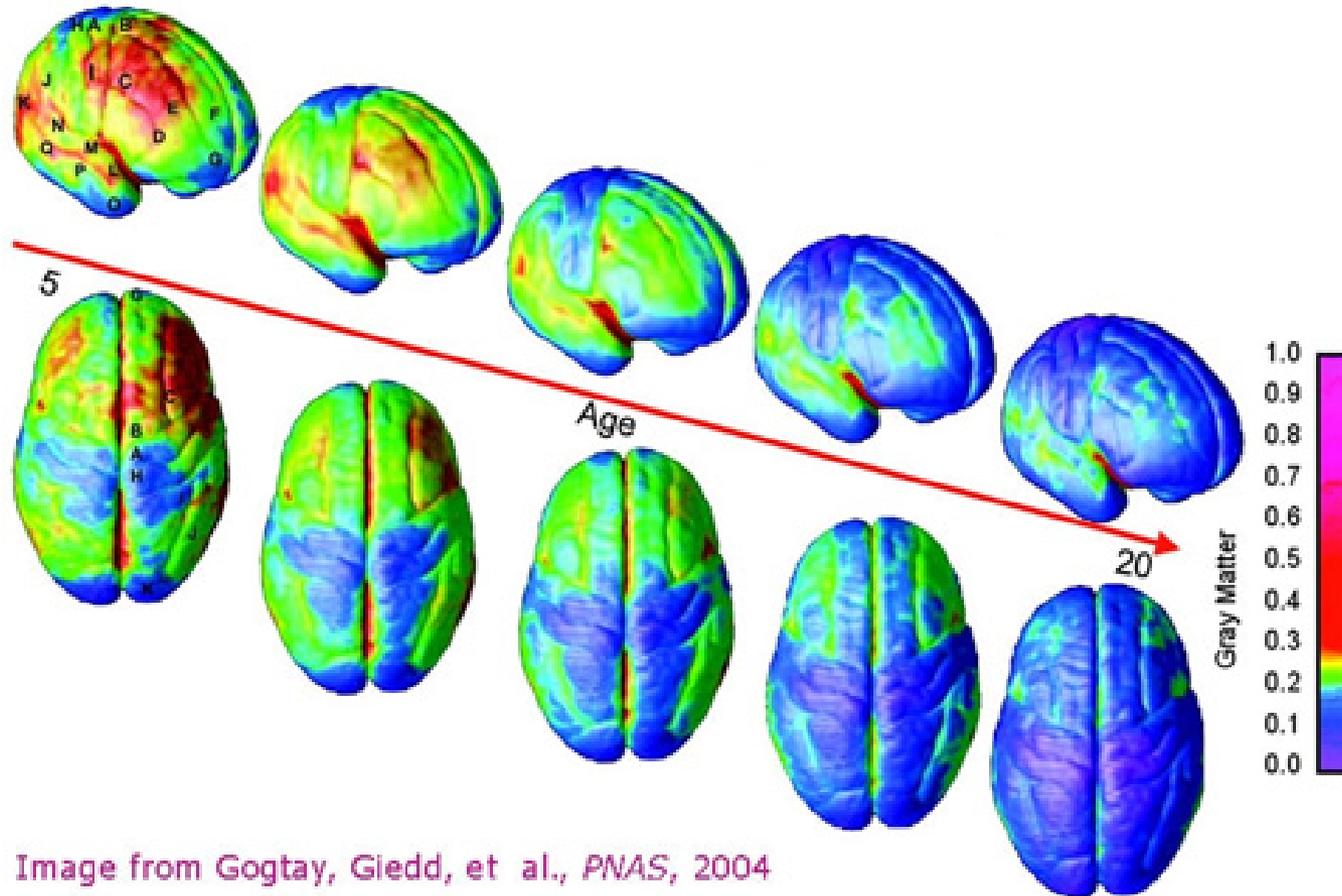


Image from Gogtay, Giedd, et al., *PNAS*, 2004

Plasticity vs Vulnerability

- Period of growth and change
- Circuitry being laid down
- Resilience vs pathology

Does early intervention work?

- Harlem Children's Zone
- Program designed for at risk kids- from prenatal period through college
- Community based with focus on integration of/partnership with schools, families and the medical and mental health community

Harlem Children's Zone

Results:

- 100% of pre-kindergarten kids ready for school
- 100% of 3rd graders at or above state scores for math
- 90% of high schoolers were accepted at one or more colleges

Prevention

- Importance of identifying children at risk
- Are we doing a good job?
 - Less than 50% of kids who attempt suicide received treatment in the prior year (Wu, et al, 2010)

School Based Mental Health Screening

- Wisconsin Based Study- comprehensive screening of 9th graders from 2005-2009 (Husky et al, 2011)
- Total of 2,488 students screened using DPS-8
- 19.6 % of students were deemed to be at risk
- Of those at risk, 73.6% were not receiving services

School Based Mental Health Screening

- Students referred for either school based or community based treatment
- Referral to school based less severe
- Of those referred, 74% referred to school had one or more visits, 57.3% referred to the community had one or more visits

School Based Mental Health Screening

- At risk but not previously identified:
 - Suicidal ideation N= 82
 - Depression N= 166
 - Anxiety N= 259

Neuroscience and Normal Development

- Structural MRI
- Functional MRI
- Behavioral Studies

Question: Is it safe to use MRI technology in conducting research with children?

- A. Structural MRI is safe but not fMRI
- B. Both are unsafe
- C. Both are safe

Normal Developmental Differences

- Executive Function:

Impulse control

Following through

Cognitive flexibility

Working memory

Attention

Normal Developmental Differences

- Emotional Reactivity and Behavioral Control:

Response to threat

Interpreting facial expressions

Understanding motives of self/others

Question: From adolescence to adulthood, cortical thickness...

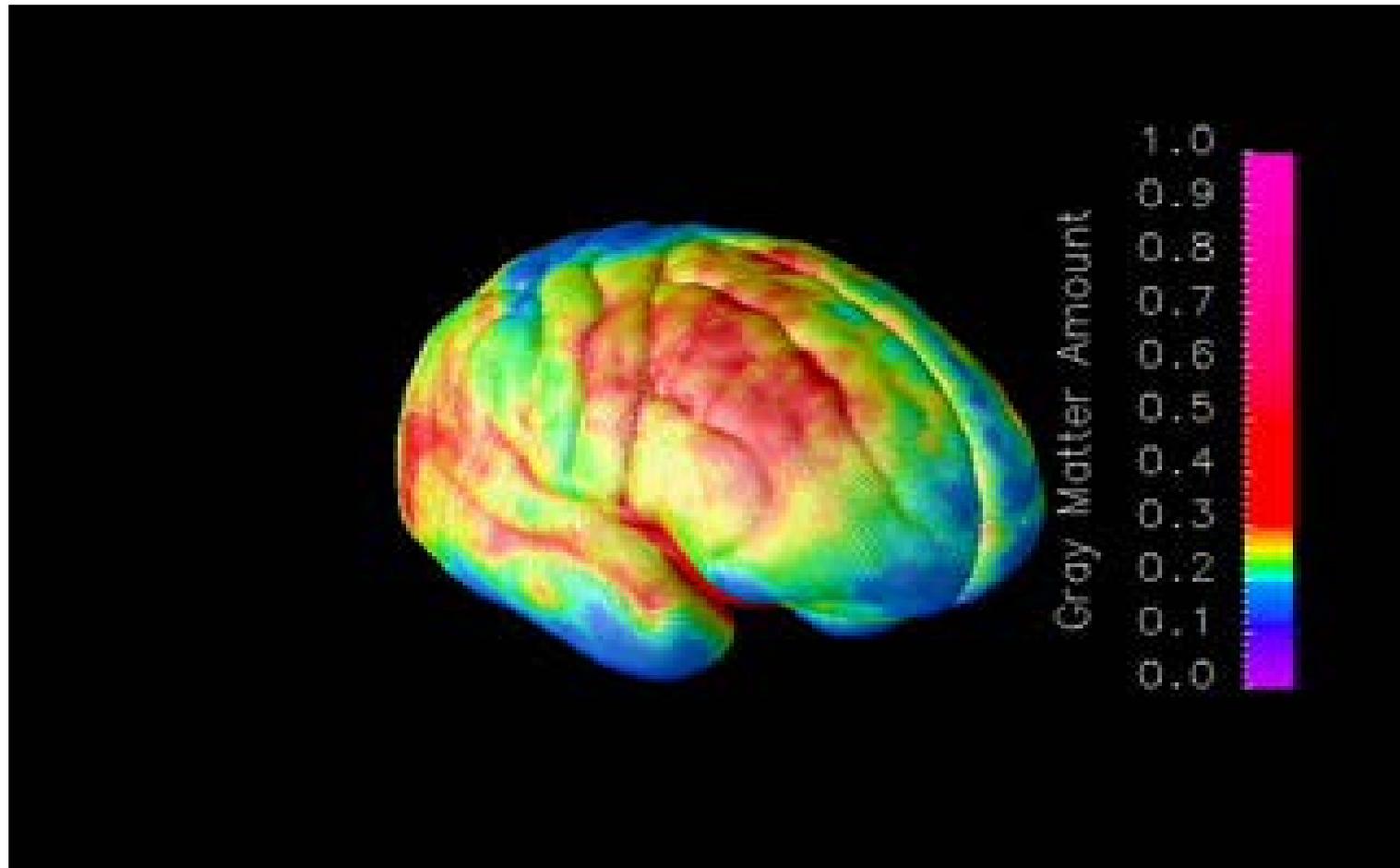
- Increases
- Decreases
- Remains unchanged

Structural Development

- Myelination
- Synaptic connections

Giedd et al, 2010; Giedd & Rapoport, 2010

Brain Development Age 4 to 22



Normal Development

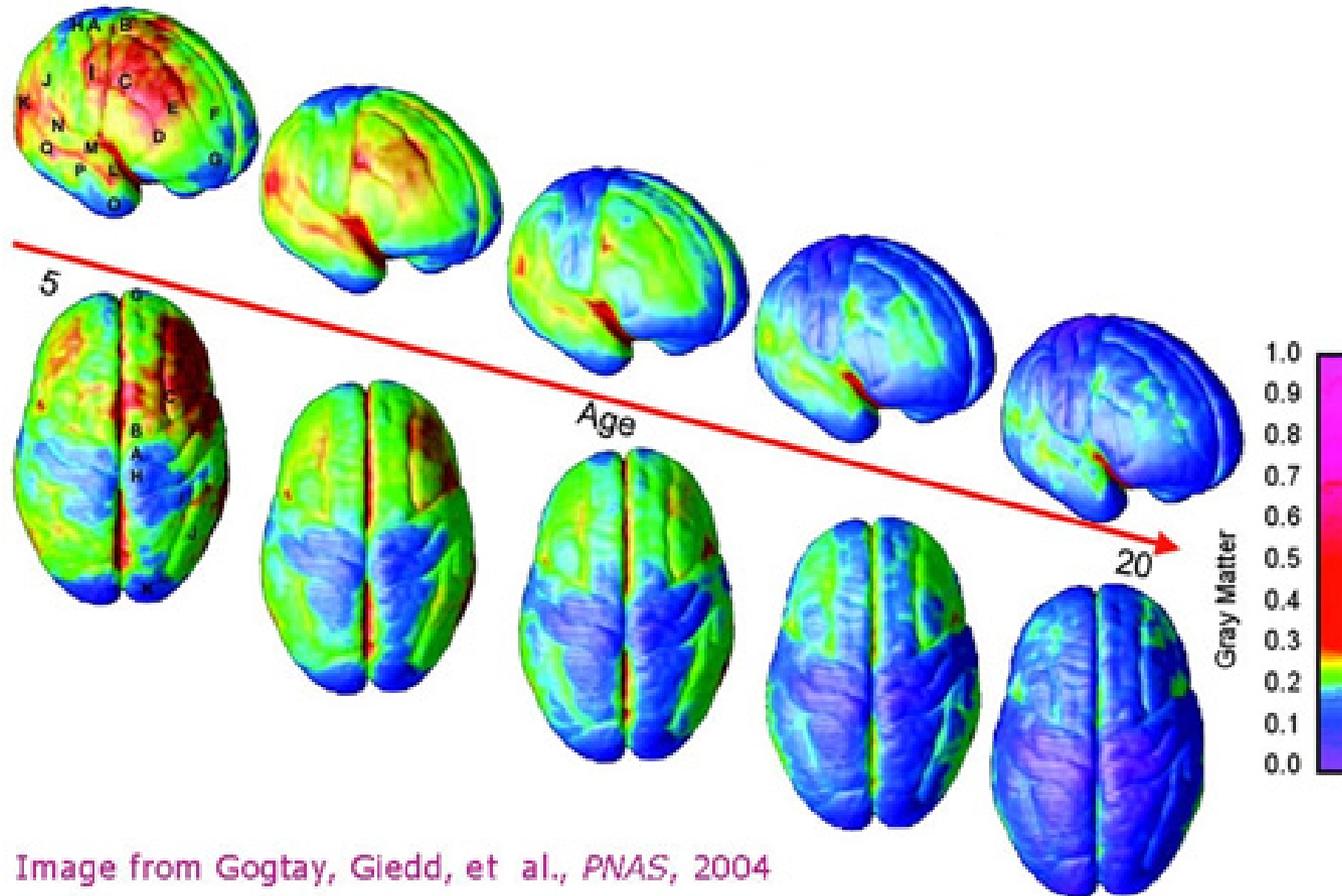


Image from Gogtay, Giedd, et al., *PNAS*, 2004

Diffusion Tensor Imaging (DTI)

- Measure of strength of connection between regions
 - Significant change in connections involved in impulse control between ages of 7 and 19
 - Liston et al, 2006
 - Significant change in areas involved in information integration between ages 9 and 23 (maximal change 9 to 15)
 - Casey et al, 2007

Functional MRI

- Changes in activity in a specific brain region
- Key Findings:
 - More areas of the brain are recruited in tasks requiring voluntary control (less efficient)
 - Luna et al 2001; Scherf et al, 2006; Geier et al, 2009)
 - More difficulty following task rules and changing their strategy when there is new information
 - Bunge & Wallis, 2007; Bunge & Zelazo, 2006

Functional MRI

- Emotion-
 - Adolescents 13 to 17 show exaggeration in area involved in flight, fight and desire.
 - (Galvan et al, 2006; Hare et al, 2008)
 - Less able to process and recognize fearful faces (Leppanen & Nelson, 2009)
 - Recruit more areas of the brain in understanding the emotions and thoughts of others and self-reflection (Burnett & Blakemore, 2009; Burnett et al, 2009)

Summary

- Childhood and adolescence is a time of significant growth and change in brain development
- Children at risk are often not identified despite early signs of significant pathology
- Early identification of children at risk and prevention strategies and can significantly alter outcomes

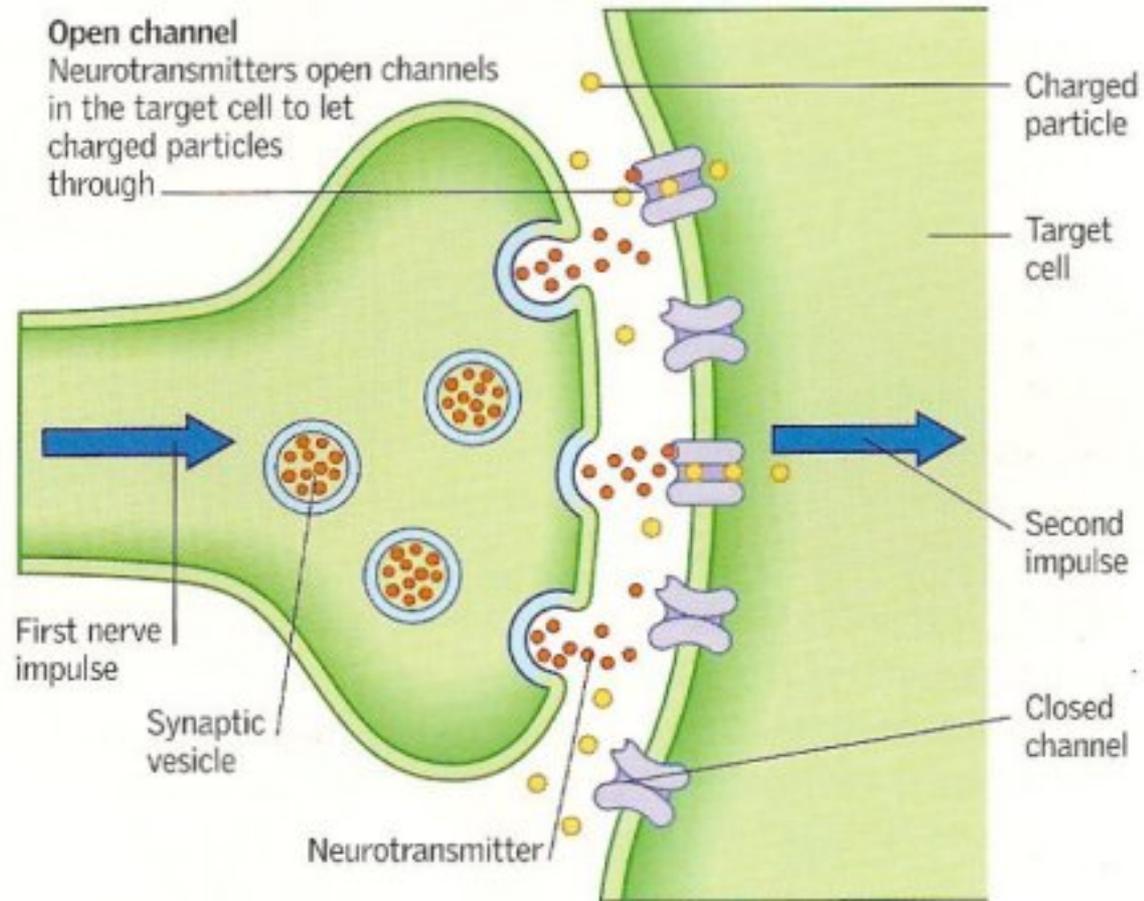
Recommendations

- Annual mental health check-up for all school aged kids (comprehensive screening)
- Referral for appropriate care – school vs community
- Better coordination between schools, health care providers and parents

Part II

Neurocircuitry, Neurotransmitters and Pharmacological Agents

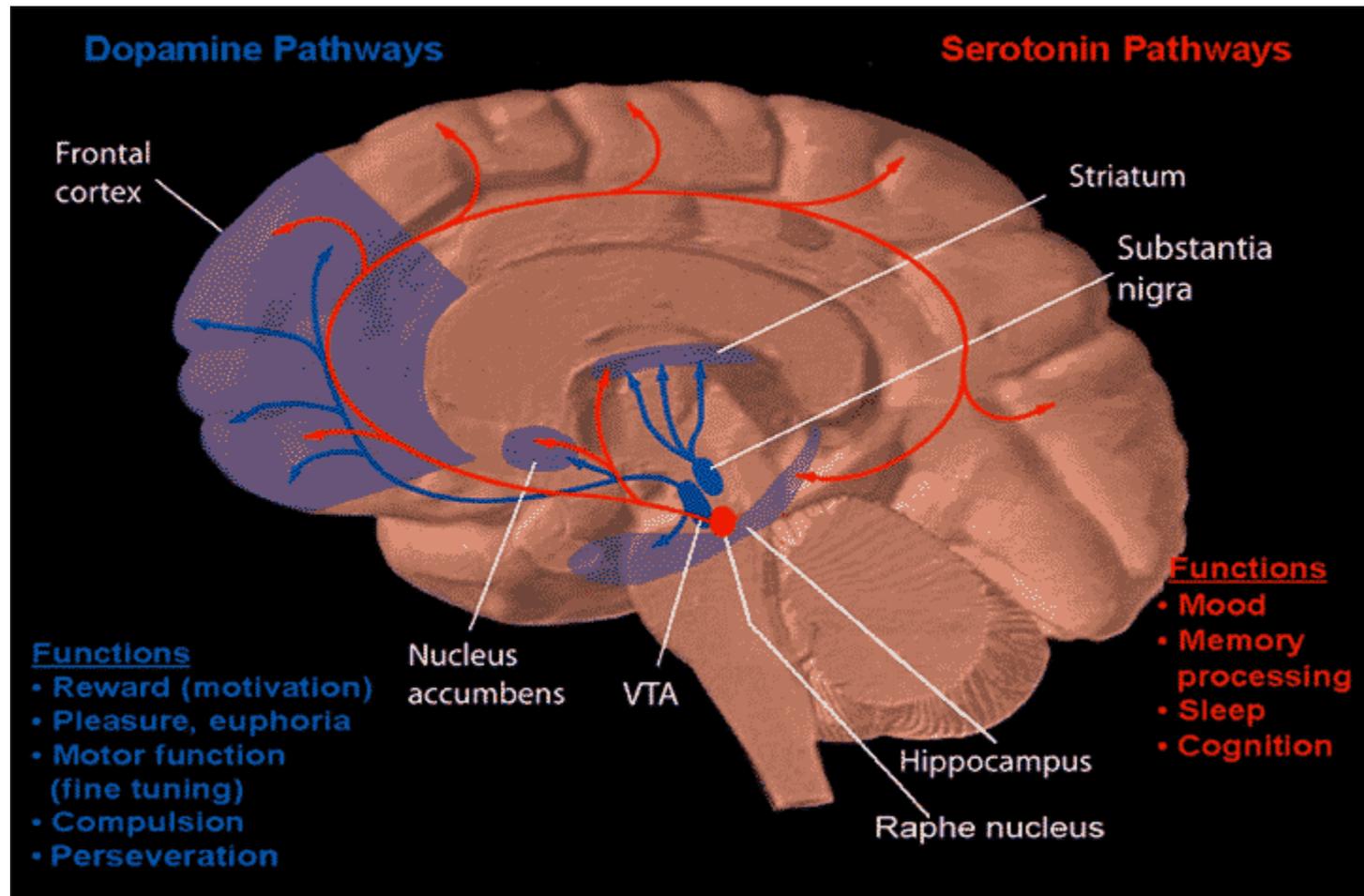
How Cells Communicate



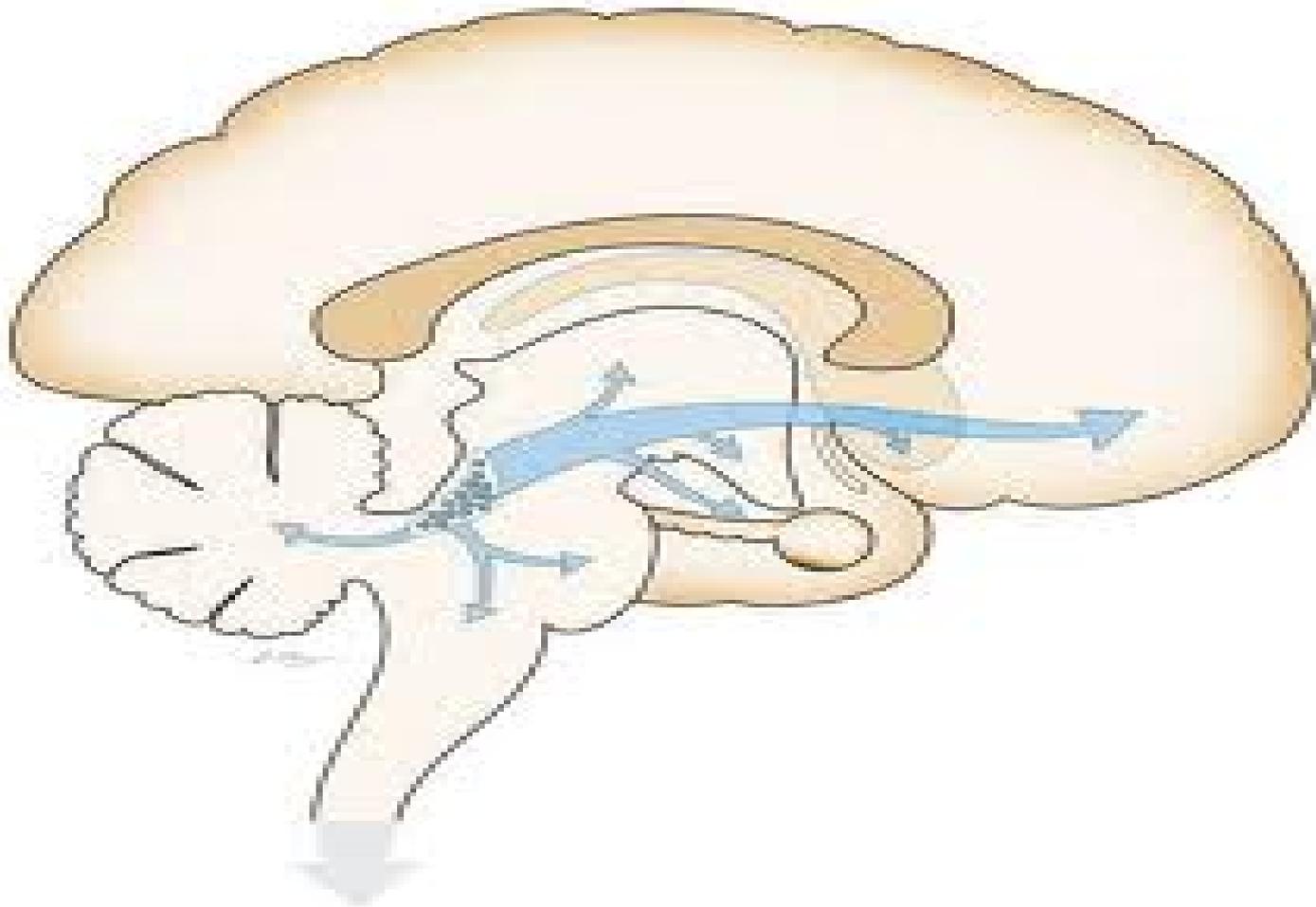
Neurotransmitters

- Dopamine- cognition, executive functioning, reward
- Serotonin- mood, anxiety
- Norepinephrine- arousal

Dopamine and Serotonin



Norepinephrine Pathway



Medications

- Dopamine Enhancers
 - Stimulants (Ritalin, Concerta)
 - Increase availability of dopamine
 - Enhance executive functioning
 - Atypical antidepressants (Wellbutrin, Zyban)
 - Increases dopamine and norepinephrine
 - Used for SA

Medications

- Dopamine Inhibitors
 - Typical and atypical antipsychotics
 - Decreases availability of DA
 - Used for psychotic symptoms
 - Increasingly used for aggression

Serotonin/Norepinephrine Enhancers

- SSRIs
 - Increases serotonin
 - Used for depression, anxiety

SNRIs

- Increases serotonin and norepinephrine
- Also used for depression

The Others

- Mood Stabilizers (lithium, depakote)
 - Unknown mechanisms
 - Also used to treat seizures
 - Increasingly used to treat aggression

Part III

Neurobiology and Treatment of Disruptive Behavior Disorders

Treating Children with Disruptive Behavior Disorders

- What are disruptive behavior disorders?
 - ADHD, ODD, CD
- Heterogeneous Group
- Co-morbidities

Question

- What percentage of youths detained have a psychiatric illness?
- a. 32%
- b. 48%
- c. 66%

Question

- Compared to youths in the juvenile system, youths in the adult system have
 - A. More psychiatric illnesses
 - B. Less psychiatric illnesses
 - C. Roughly the same

Prevalence of Mental Illness in Youths in Juvenile v Adult Court

- Any Disorder- 66 v 68% one or more psychiatric illnesses
- 64% v 66% excluding conduct disorder
 - (Washburn et al, 2008)
- We can treat (with a few caveats)

Disruptive Behavior Disorders Juvenile v Adult Court

- ADHD 9 v 8 %
- ODD 15 v 15%
- CD 37 v 38%
(Washburn et al, 2008)

Prevalence of Other Disorders Youths in Juvenile v Adult Court

Psychosis 1 v 2%

Mood Disorders 22 v 20%

Anxiety Disorders 24 v 22%

Substance Abuse 55 v 51%

(Washburn et al, 2008)

ADHD

- Delayed development of brain systems involved with executive functions
- Problems with:
 - Impulsivity
 - Organizing information
 - Carrying out tasks

ADHD

- Significant body of research that has outlined biological mechanism
- Dopamine implicated- and treatments are very effective
- Failure to treat has short term and long term implications

ADHD



ADHDDelayRtSideWeb.mp4

Treatments

- Stimulants
 - Both short acting and long acting available
 - Side effects most common are GI, weight loss
 - Less common are depression, psychosis
 - In cardiac history, EKG warranted

Treatments

- Straterra (SNRI)
 - Side effects include sedation, fatigue and decreased appetite
- Alpha 2 agonists (guanfacine, Tenex and Intuniv)
 - Original use was anti-hypertensive
 - Acts on the autonomic nervous system
 - Side effects include sedation, dizziness, fatigue, hypotension

Treatments

Let them run! Sports are a good thing



Disruptive Behavior Disorders

- Oppositional Defiant Disorder
- Conduct Disorder

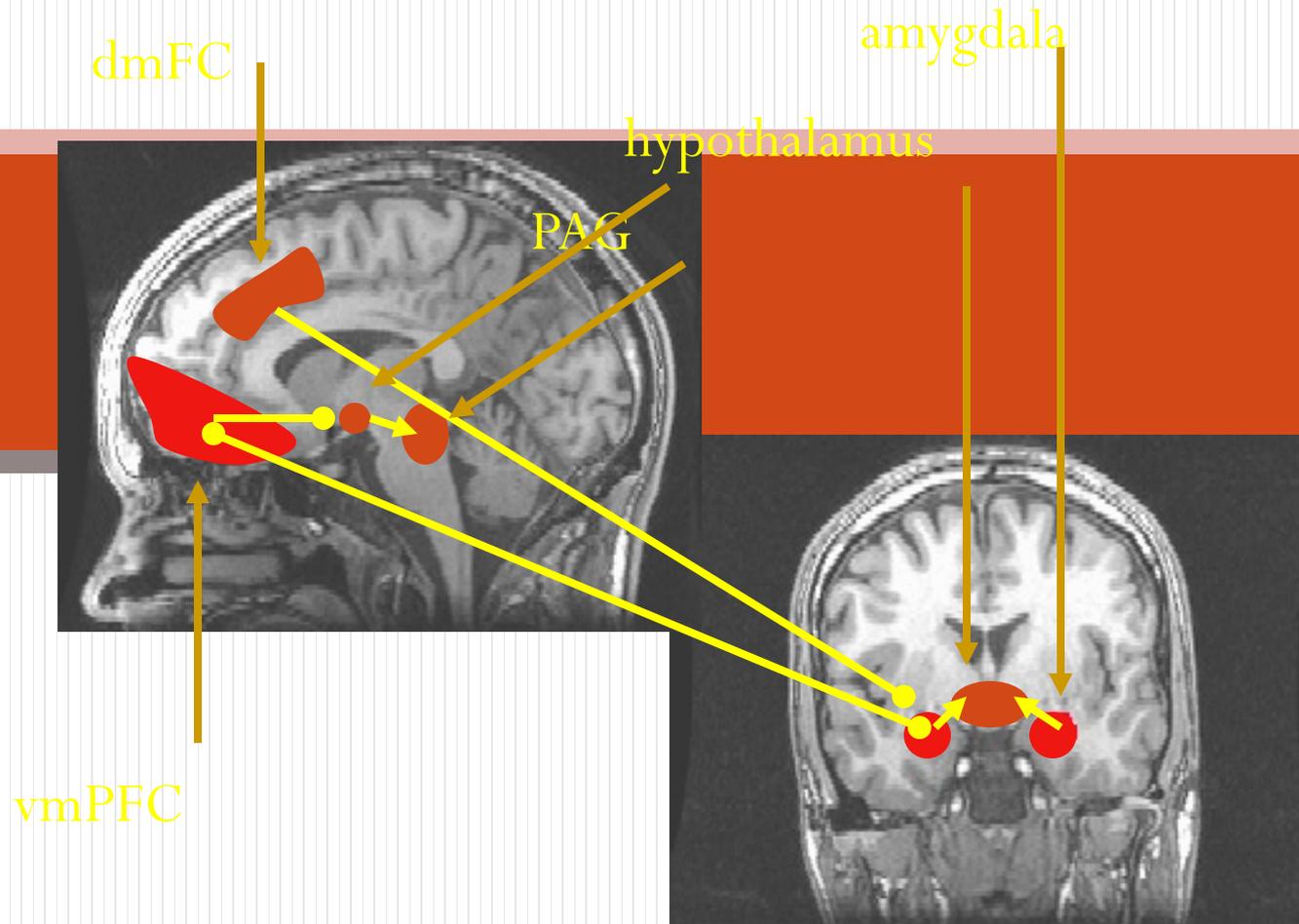
ODD and CD

- Highly co-morbid with ADHD- 70%
- What do we treat?
 - Aggression
 - Hyperactivity and inattentiveness

Circuitry of Conduct Disorder

- Heterogeneous group
- Ways to differentiate
 - Child v adolescent onset
 - Reactive v Instrumental
 - Callous unemotional traits

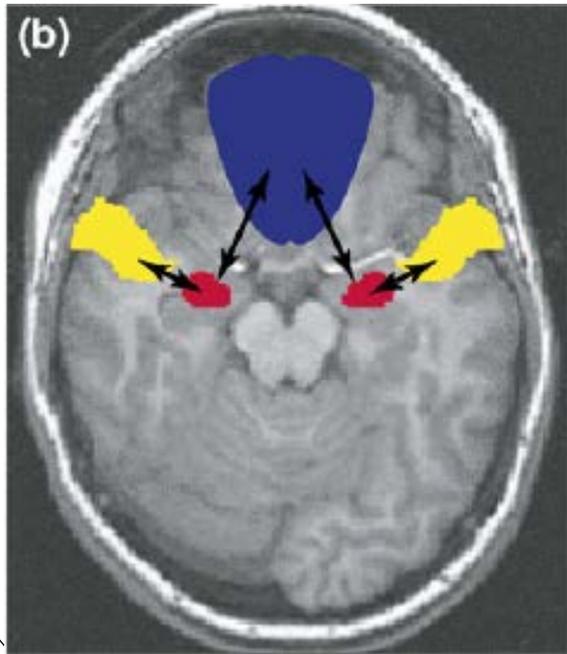
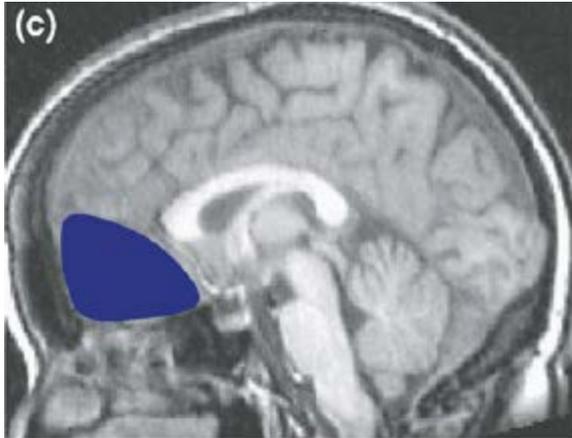
Emotional Volatility



Primed up basic threat system

Poor control

Callous-unemotional traits



Opinion

TRENDS in Cognitive Sciences Vol.11 No.9

Full text provided by www.sciencedirect.com

ScienceDirect

The amygdala and ventromedial prefrontal cortex in morality and psychopathy

R.J.R. Blair

Mood and Anxiety Program, National Institute of Mental Health, Department of Health and Human Services, 15K North Drive, MSC 2670, Bethesda, MD 20892, USA

The amygdala: stimulus-reinforcement learning

OFC: Representation of reinforcement value and prediction error sensitivity



Pharmacological Treatments

- Stimulants- used to treat co-morbid ADHD symptoms
- Atypical antipsychotics- increasingly being used to treat aggression
 - Problem- not clear whether they are effective
 - Significant side-effects

Non-Pharmalogical Interventions

- Psychotherapies
 - Cognitive-behavioral therapy (CBT)
 - Psycho-educational interventions
- Behavioral Interventions
- Multi-component treatments

CBT/Psycho-education

- CBT

- Explores the link between cognitions, behaviors and feelings
- Useful in helping to relieve anxiety and hostile attributions associated with reactive aggression
- Effective in treating trauma

- Psycho-education

- Useful in helping youth cope with stressful situations in appropriate ways
- Improves social skills and connectedness to peers and family
- Improves emotion regulation and reduces frustration, leading to fewer reactive outbursts
- Improves communication skills

Behavioral Interventions

- Behavioral Interventions rely on reward and punishment
- Most appropriate with younger or developmentally delayed individuals
- Examples:
 - Token economies
 - Time-out
 - Ignoring
- Most often fail due to lack of consistency or lack of generalizability to new situations

Multi-component Interventions

- Holistic interventions focusing on teens, their families and communities
- Involve traditional approaches, but include schools, communities, athletics and government services
- Effective with teenagers
- Expensive and difficult to successfully implement

Residential Treatments

- Insufficient research is conducted on treatment programs taking place inside facilities
- Evidence suggests that specialized treatment providers obtain better results than corrections “treatment as usual”
- There is very little evidence of rehabilitation in most US prisons (juvenile or adult)

Part IV

Treatment of Mood and Anxiety Disorders in Children

Mood and Anxiety Disorders

- Mood Disorders:
 - Depression
 - Bipolar Disorder
 - Severe Mood Dysregulation
- Anxiety Disorders
 - Generalized anxiety
 - Social phobia

Important Considerations

- Underdiagnosed
- Presentation often different in children than in adults
- Effective treatments do exist

Mood Disorders

- Major Depressive Disorder
 - Lifetime prevalence of 16.6%
 - Recurrent episodes is the norm- estimated 73%
 - Stronger the family history more likely recurrent episodes
 - With each additional episode, more likely that depression will occur spontaneously and not in response to life stressor

Depression is a progressive illness

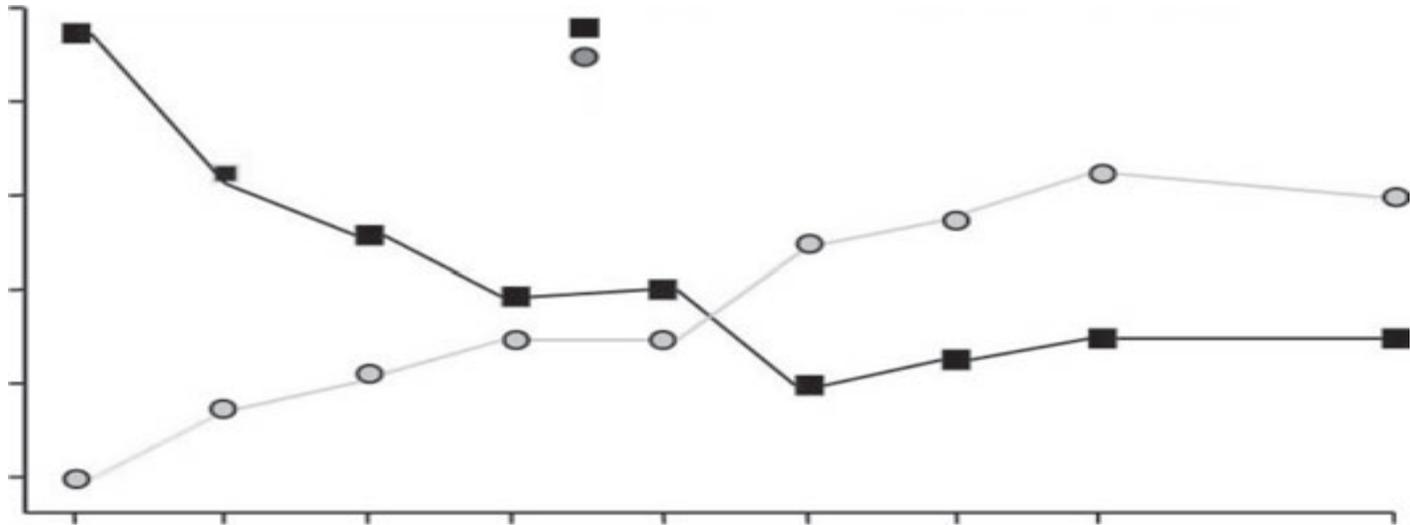


Figure 1 Major depression as a progressive illness. As the number of major depressive episodes increase, the risk for subsequent episodes is predicted more from the number of prior episodes and less from the occurrence of a recent life stress.

Depression

- As duration of a depressive episode increases, likelihood of a recovery decreases.
- Implications for treatment:
 - Early detection critical
 - Treat to full recovery

Depression: Treatment Recommendations

- AACAP Treatment Guidelines:
 - Mild depression: evidenced based therapy
 - Moderate: evidenced based therapy +/- SSRI
 - Severe: evidenced based therapy and SSRI

Depression: Treatment Recommendations

- Regular monitoring of symptoms- use of structured instrument
- Maintenance therapy – treatment should always be continued for 6 to 12 months. Longer may be warranted in multiple remissions.

Depressions: Treatment

- Therapeutic interventions: CBT, IPT
- Medications:
 - SSRIs most evidence, best tolerated
 - Choice of medication: family history, characteristics of depression, tolerability

Medication Choice: Key Considerations

- Family history of response
- Characteristics of depression- anxious vs lethargic
- Side effects and tolerability

Medications

- SSRIs- operate by increasing the amount of serotonin. Ex: Prozac, Zoloft
- SNRIs- increase both serotonin and norepinephrine. Ex: Effexor and Nefazadone
- Wellbutrin- dopamine and norepinephrine

Bipolar Disorder and Severe Mood Dysregulation

- Diagnosis of Bipolar Disorder in children very controversial
- Many children do present with dysregulation in multiple domains:
 - Sleep and diet
 - Emotion
 - Social regulation

From: Severe Mood Dysregulation, Irritability, and the Diagnostic Boundaries of Bipolar Disorder in Youths

Am J Psychiatry. 2011;168(2):129-142 doi:10.1176/appi.ajp.2010.10050766

Inclusion criteria

1. Current age 7–17 years, with onset of the syndrome before age 12.
2. Abnormal mood (specifically, anger or sadness), present at least half of the day most days, and of sufficient severity to be noticeable by people in the child's environment (e.g., parents, teachers, peers).
3. Hyperarousal, defined by at least three of the following: insomnia, agitation, distractibility, racing thoughts or flight of ideas, pressured speech, and intrusiveness.
4. Compared to his or her peers, the child exhibits markedly increased reactivity to negative emotional stimuli that is manifest verbally or behaviorally. For example, the child responds to frustration with extended temper tantrums (inappropriate for age and/or precipitating event), verbal rages, and/or aggression toward people or property. Such events occur, on average, at least three times a week.
5. The symptoms in 2, 3, and 4 are currently present and have been present for at least 12 months without any symptom-free periods exceeding 2 months.
6. The symptoms are severely impairing in at least one setting (home, school, or with peers) and are at least mildly impairing in a second setting.

Exclusion criteria

1. Exhibits any of these cardinal manic symptoms:
 - Elevated or expansive mood
 - Grandiosity or inflated self-esteem
 - Episodically decreased need for sleep
2. The symptoms occur in distinct periods lasting more than 1 day.
3. Meets criteria for schizophrenia, schizoaffective disorder, pervasive developmental disorder, or posttraumatic stress disorder.
4. Meets criteria for substance abuse disorder in the past 3 months.
5. IQ <70.
6. The symptoms are due to the direct physiological effects of a drug of abuse, or to a general medical or neurological condition.

Figure Legend:
Research Diagnost

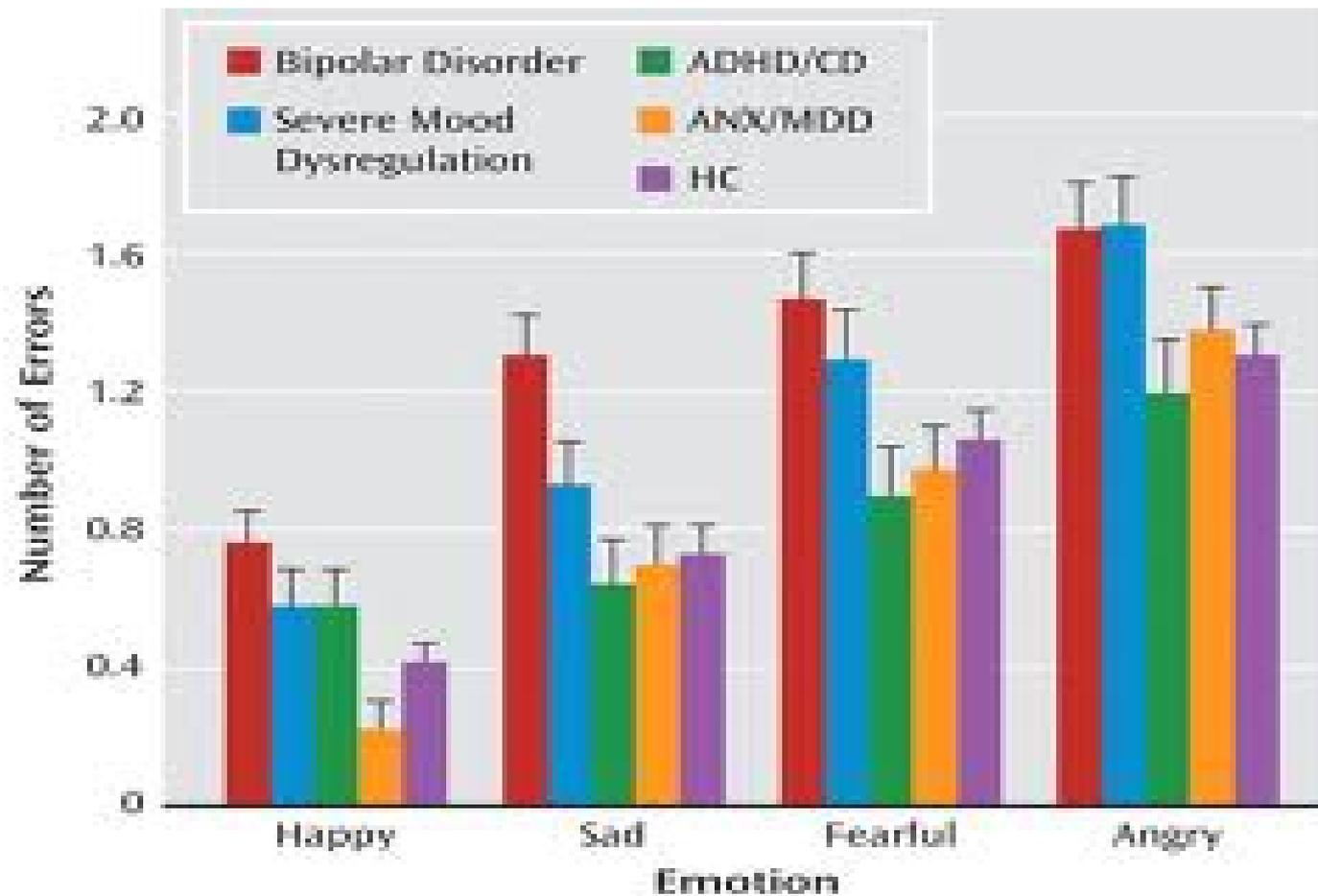
BPD vs SMD

- SMD- children have more frequent mood changes, often rapid cycling in a day
- Do not meet criteria for full blown manic episodes
- No clear treatment guidelines

SMD- Neurobiology

- Show increased emotional reactivity- increases in amygdala responsivity
- Show decreases in frontal lobe activation- less cognitive control over emotional responses

Imaging Task With Facial Expressions



Treatment of BPD/SMD in Children

- Lithium and depakote are gold standard for BPD
- Atypical antipsychotics frequently used- risperidone FDA approval for use with children with irritability (autism) and aggression (CD)

Anxiety Disorders

- Generalized anxiety disorder
- Social phobia

Generalized Anxiety Disorder

- Diagnostic criteria: 6 months of 3 or more of the following:
 - Feeling wound-up, tense, or restless
 - Easily becoming fatigued or worn-out
 - Concentration problems
 - Irritability
 - Significant tension in muscles
 - Difficulty with sleep

Generalized Anxiety Disorder

- Under-diagnosed in children
- Treatment recommendations from the AACAP:
 - Mild GAD- therapy (CBT or other evidenced based)
 - Moderate to severe- therapy and SSRI

Treatment of GAD with Sertraline

