

# Psychiatric Issues in Adolescents and Young Adults with 22q11 Deletion Syndrome

**Joe Cubells, MD, PhD**

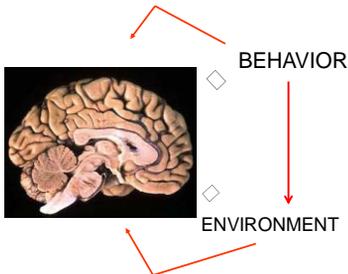
Department of Human Genetics,  
and Emory Autism Center,  
Department of Psychiatry and Behavioral Sciences,  
Emory University School of Medicine

## Outline

- Overview of the complex determinants of human behavior
  - What determinant differs in 22q11DS?
- Psychiatric diagnosis vs. target symptoms.
- Vulnerability to psychiatric symptoms in 22q11DS.
- Psychotropic medications as tools for improving quality of life.
- Discussion and questions.

## Determinants of Human Behavior

- GENES
- NUTRITION
- EXPERIENCE
- CULTURE
- SOCIAL MILEAU
- EDUCATION
- DRUGS



Picture: Williams, et al., 2003: The Human Brain: Dissections of the Real Brain  
<http://www.vh.org/adult/provider/anatomy/BrainAnatomy/BrainAnatomy.html>

### **What do we mean by “psychiatric illness?”**

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A pathological pattern of thoughts, feelings and behaviors that interferes with psycho-social function and degrades the quality of life for the patient (and usually, the patient’s family too).

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### **How do we establish a “psychiatric diagnosis?”**

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We look for specific combinations of observable behaviors, and reports of thoughts and feelings, and compare them to criteria for syndromes established by expert consensus.

*Diagnostic and Statistical Manual  
of the APA (DSM-V)*

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### **Example: Major Depressive Disorder**

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- At least 2 weeks of depressed mood
  - Reduced capacity for pleasure
  - Impaired social fxn.
- Changes in sleep/eating/sex drive
- Poor concentration
- Suicidal thoughts or behavior

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## **At present, *ALL* psychiatric diagnoses are *DESCRIPTIVE***

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Classify patients based on observable characteristics.

- cross sectional
- developmental
- longitudinal
- familial

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## **Descriptive vs. Etiologic Diagnosis**

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• **Descriptive diagnoses:** Classify patients based on observable characteristics.

- cross sectional
- developmental
- longitudinal
- familial

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## **Descriptive vs. Etiologic Diagnosis**

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• **Etiologic diagnoses:** Classify patients based on causative factors.

- infectious
- metabolic
- exposure-related
- genetic

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## Descriptive vs. Etiologic Diagnosis

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- Both approaches are essential for research and for good clinical practice.
- Descriptive diagnosis necessarily precedes etiologic diagnosis.
- Progressing from description to etiology is **essential** for improving therapeutic approaches.

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## Historical example: General Paresis of the Insane

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- First described by Antoine Laurent Jessé Bayle in 1822
  - males >> females
  - initial presentation: depression
  - progression to grandiose psychosis
  - Argyll-Robertson pupil (“prostitute’s pupil”)
  - progression to seizures, dementia, paresis and death
  - contemporary authorities attributed GPI to “weak character”




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## Historical example: General Paresis of the Insane

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- **Esmarck and Jessen, 1857:** note association between GPI and past history of syphilis.
- **Hideyo Noguchi, 1913:** cultures *Treponema pallidum* from the brain of a GPI patient, establishing **etiology**.
- **Julius Wagner-Jauregg, 1917:** first effective biological therapy for **neurosyphilis**:
  - **infect the patient with malaria!**
  - First psychiatrist to win the Nobel Prize (1927).




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## Psychiatric Diagnoses in 22q11DS

- Autism Spectrum Disorders 15-45%
- ADHD 40+ %
- Schizophrenia (adulthood) 25-30%
- Anxiety (including social anxiety) 50+ %
- Depression 20+ %

## Axis-I diagnoses (DSM-IVR) in Young Adults with 22q11DS

**Table 1**  
Sex, age, and psychiatric diagnoses of adolescents and young adults with 22q11 deletion syndrome.

ID	Male	Female	Age	Schizophrenia spectrum	Autism spectrum	Depressive disorder	Anxiety disorder
1		X	21	Schizotypal, prodromal			
2	X		17	Schizotypal			
3	X	X	27	Schizoaffective			
4		X	17		FDD-NOS-CFEA		
5		X	18		FDD-NOS-CFEA		
6	X		19		Autism-CFEA		
7	X		20		Autism-CFEA		
8		X	16		FDD-NOS-DSM-IV		
9		X	20			Depressive disorder NOS	
10		X	22			Depressive disorder NOS	
11		X	20			Depressive disorder NOS	
12		X	17			Major depressive disorder	
13		X	22			Bipolar disorder	
14	X		15				Specific phobia
15	X		21				OCD
16	X		19	Schizoaffective	FDD-NOS-CFEA		OCD, specific phobia
17	X		20	Prodromal	FDD-NOS-DSM-IV		
18	X		26	Schizoaffective, schizotypal	FDD-NOS-DSM-IV		
19	X		17	Schizotypal	FDD-NOS-DSM-IV	Depressive disorder NOS	
20	X		24	Prodromal	FDD-NOS-DSM-IV	Major depressive disorder	Social phobia
21		X	15	Prodromal	FDD-NOS-DSM-IV		Social phobia
22	X	X	15	Prodromal		Major depressive disorder	OCD
23		X	21				Specific phobia
24-31	3	6	18.1 (4.6)	Criteria not met for any axis I diagnosis or prodromal syndrome			

Ousley et al., 2013, Eur. Psychiatry 28: 417-422.

## Pts with NO Axis-I Dx

- 2 Males
- 6 Females
- Age: 18.1 ± 4.6

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Is there a practical alternative to psychiatric diagnosis in patients with 22q11DS?

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***TARGET SYMPTOMS***

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**Basic principles of neuro-pharmacology, and strategies for addressing target symptoms**

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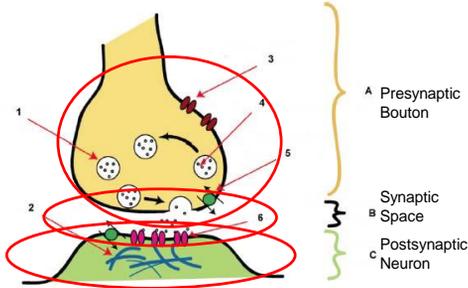
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The synapse is the basic “relay” in the circuitry of the brain




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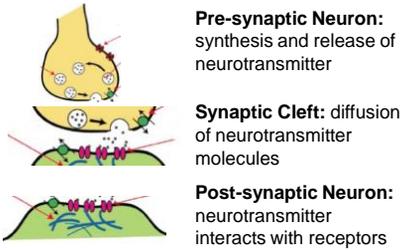
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Basic scheme for transmitting information between neurons (brain cells):




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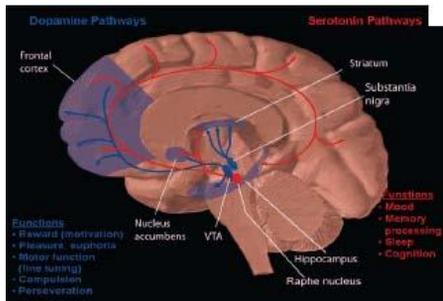
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Dopamine and Serotonin




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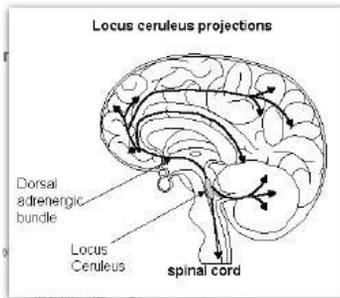
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## Norepinephrine




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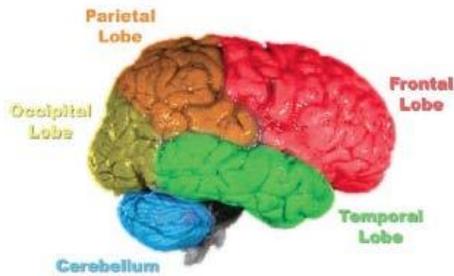
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## GABA and glutamate function *locally* throughout the brain




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People with 22q11 DS often exhibit symptoms and behaviors that worsen their difficulties

- Anxiety (shyness)
- Depression
- Challenging behaviors (e.g., “melt-downs,” impulsivity)
- Obsessions and compulsions
- Disturbances of sleep
- Attention difficulties
- Psychosis

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### Target Symptoms

- Anxiety
  - enhance serotonin: SSRIs (Prozac-like medications)
  - enhance GABA: benzodiazepines (Valium-like medications)
- Depression
  - serotonin: SSRIs, MAO inhibitors
  - norepinephrine: Tricyclics (imipramine and others), SNRIs (Cymbalta and others)
- Challenging Behaviors
  - block dopamine:
    - first-generation antipsychotics (Haldol and others)
    - second-generation antipsychotics (Risperdal and others)
    - enhance GABA
    - benzodiazepines (Valium-like medications)
    - anti-convulsants (Depakote, Tegretol and others)

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### Target Symptoms

- Obsessions and Compulsions
  - enhance serotonin: SSRIs (Prozac-like medications)
  - block dopamine (1st and 2nd-generation APMs)
- Attention difficulties
  - enhance dopamine: psychostimulants (Ritalin and others)
- Psychosis
  - block dopamine (1st and 2nd-generation APMs)
- Sleep
  - enhance GABA, NE, or serotonin
  - enhance melatonin

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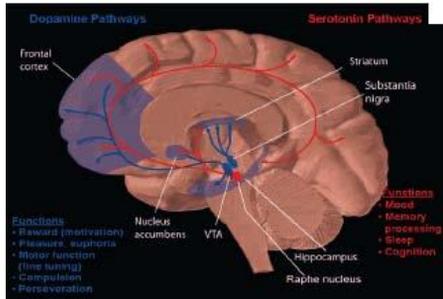
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### Dopamine and Serotonin




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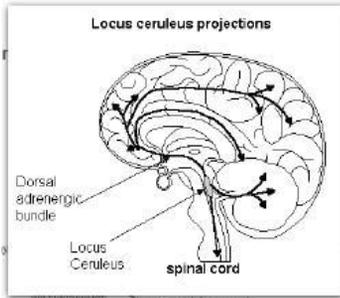
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## Norepinephrine




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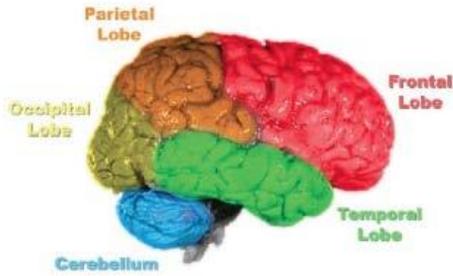
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## Psychotropic medications targeting Dopamine (DA)

- **Dopamine (DA)**
  - attention
  - organization and focus
  - psychosis, agitation, aggression
- **Anti-psychotic medications** (haldol, risperdal, seroquel, etc): block DA receptors
  - lessen aggression (but akathisia can complicate this)
  - improve organization and focus (sometimes)
- **Psychostimulants** (Ritalin, Concerta, etc): enhance DA release and increase action of DA at receptors.
  - improve attention, organization, and focus
  - lessen aggression (sometimes, but sometimes worsens aggression).

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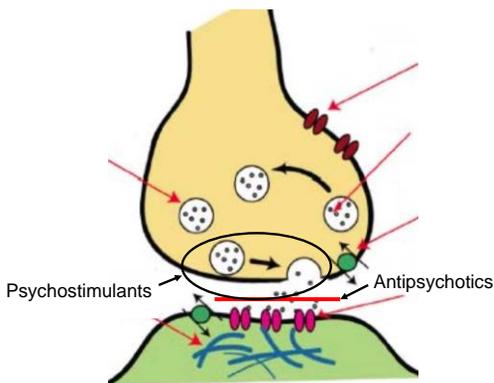
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## Practical Issues in Approaching Medication Treatments for Target Symptoms in 22q11DS

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- **Calcium:** abnormalities in serum *ionized calcium* levels are common in 22q11DS (due to parathyroid issues).
- Low calcium can lead to seizures, and possibly to other changes in brain function.
- Many psycho-tropic medications can lower the seizure threshold.
- Monitor ionized calcium at least annually in patients with 22q11DS who are taking psychotropic medications.

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## Practical Issues in Approaching Medication Treatments for Target Symptoms in 22q11DS

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- **Polypharmacy:** Targeting symptoms can lead to using more than one medication.
  - **Example:** Treatment of psychotic symptoms and depression may require a combination of an anti-psychotic and an anti-depressant.

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## Practical Issues in Approaching Medication Treatments for Target Symptoms in 22q11DS

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- **Some combinations of medications make sense, others don't!**
  - Antipsychotic + antidepressant– usually reasonable.
  - Antipsychotic + psychostimulant- usually unreasonable.

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