Neurobehavioral Differences: Everyday Challenges & Optimal Development

Tony J. Simon Ph.D.
Cognitive Analysis and Brain Imaging Lab
http://cabil.mindinstitute.org
tjsimon@ucdavis.edu

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Center for Excellence in Developmental Disabilities
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Cognitive Abilities
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Everyday Demands
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Coping Resources
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Coping Resources
Stimulation
Spatial Resolution & Comparison

Tests ability to mentally represent & compare quantity information

Tasks adapts to child’s ability, like a video game, to find “threshold”

- spatial magnitudes & auditory pitch to test "crowding"
- first or second blue bar longer? (first or second pitch higher?)

Almost all of our data comes from 7-15 year old children
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For Bars, 22q group needs a larger difference (smaller ratio) to accurately choose the bigger bar.
For Pitch, there is no difference between the groups.

So, the problem is not “comparing”, it is representing length.
The same is true for duration
Bigger differences were need by the 22q group to judge “longer”

So, the problem is not “comparing”, it is representing time
Cognitive Control

Can you dynamically choose “good”/inhibit “bad” behaviors?

- “Go” trials (75%): press a button as quickly as possible to “whack” the mole
- “No-Go” trials (25%): do NOT press button to avoid “squashing” the vegetable
  - Preceded by 1, 3, or 5 “Go” trials
Cognitive Control - Overall Results

Children with 22q DO predict “don’t do it” event BUT, they were much less able than TD children, to “not do it”!

Both groups monitor appropriately

# preceding Go trials

**Go trials: in order following No-Go**

- **TD N=23**
- **22q N=32**
Cavum Septum Pellucidum

Introduced new “extreme” category of CSP >10mm length
- 83% of TD no/normal CSP
- 34% of 22q abnormal CSP
- 18% extreme (0% in TD)

Indicates common middle of brain anomaly

CSP volume correlated with Devel. Delay (IQ)
- FSIQ -.31, p=.02
- VIQ -.27, p=.03
- PIQ -.30, p=.0018

Beaton et al., 2010

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Ventricles

Another common middle of brain is enlarged ventricles

No relation to developmental delay but unusual change with age
Ventricles

Another common middle of brain is enlarged ventricles.

Lateral Ventricle and Age

| Coefficients | Estimate | t value | Pr(>|t|) |
|--------------|----------|---------|----------|
| Age_in_month_TD | 49.94 | 2.201 | 0.03 |
| Age_in_month_22q | 80.56 | 1.969 | 0.05 |

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| TD_M | Estimate | t value | Pr(>|t|) |
|------|----------|---------|----------|
| TD_F | 16.83 | 0.62 | 0.54 |
| 22q_M | 136.58 | 2.66 | 0.01 |
| 22q_F | 26.68 | 0.474 | 0.64 |
Another common middle of brain is enlarged ventricles. No relation to developmental delay but unusual change with age.

| Coefficients       | Estimate | t value | Pr(>|t|) |
|--------------------|----------|---------|----------|
| Age_in_month_TD    | 49.94    | 2.201   | 0.03     |
| Age_in_month_22q   | 80.56    | 1.969   | 0.05     |

Lateral Ventricle and Age

|              | Estimate | t value | Pr(>|t|) |
|--------------|----------|---------|----------|
| TD_M         | 70.37    | 1.901   | 0.07     |
| 22q_M        | 136.58   | 2.66    | 0.01     |
| TD_F         | 16.83    | 0.62    | 0.54     |
| 22q_F        | 26.68    | 0.474   | 0.64     |
Fornix connection types

Type 1

Type 2

Type 3

(StT) ant. ROI

(StT) pos. ROI

(ConTrack)
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Mock MRI scanner designed to reduce anxiety of MRI scan. 95% of kids complete the scan.

BUT, as a group, they show much higher levels of a stress hormone before and after the familiarization experience.

So, they “cope” with the MRI scan, but they are more stressed.

*Beaton et al. submitted*
Anxiety & Functional Abilities

Adaptive function NOT related to overall IQ.
Unlike TD/most other NDDs

Adaptive function IS related to anxiety levels
Angkutsiri et al., submitted

Anxiety levels related to stress hormone level & maybe psychosis risk
Beaton et al., submitted; Beaton & Simon, 2011
Anxiety Not IQ Predicts Adaptive Function

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Anxiety and Cognitive Control

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Anxiety and Attention

Very new tasks (happening today!) gently manipulate emotional content with different faces to see if “threat” changes functioning.

- Anxious children switch attention to “threat” losing some control.
Anxiety and Attention

Very new tasks (happening today!) gently manipulate emotional content with different faces to see if “threat” changes functioning anxious children switch attention to “threat” losing some control.
Anxiety and Attention

Very new tasks (happening today!) gently manipulate emotional content with different faces to see if “threat” changes functioning in anxious children switch attention to “threat” losing some control.
Anxiety and Attention/Control

Pilot data suggest emotional stimuli alter attention more in 22q group:
- Behavior more strongly biased by emotions in 22q group.
- Typical group avoids angry (& less so happy) faces in favor.
- Angry/Happy faces impair attention in opposite ways for groups.
- Cognitive control more affected by angry face in 22q group.

Positive values indicate bias towards emotional face
Negative values indicate bias away from emotional face

TD kids faster when cued to happy face location but MUCH slower when cued to Angry. No diff when on other side
Opp pattern in 22q & stays that way when on other side

TD (n=4) 22q (n=9)

TD  22q

Group

Mean bias score (ms)

DotProbe threat bias

DotProbe happy bias
Anxiety and Attention/Control

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Behavior more strongly biased by emotions in 22q group.
Typical group avoids angry (and less so happy) faces in favor of neutral.

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IQ of 75 means operating as a 9-year-old in a 12-year-old’s world. 

- 35-50% of children with 22q11.2DS get a diagnosis of ADD (mainly Inattentive or combined type) and take medications.
  - distinct from hyperarousal/hypervigilance from anxiety?
- Many children get diagnosed with OCD (part of anxiety ~60%) and most likely anxiety-drive “coping” behaviors.
- Mismatches between capabilities and demands induce stress, which can lead to anxiety, avoidance and reduced motivation and self-esteem.
  - reducing “allostatic load” might protect against psychosis.
- Mismatched cognitive and social demands & resulting anxiety and avoidance might explain frequent “Autism” diagnoses.
Children with 22q11.2DS have social and communication impairments, sometimes along with repetitive behaviors, but is it really autism?

Many (20-50%) children screen positive for ASD symptoms or meet criteria based on the ADI-R, which is only one part of the gold-standard assessment for ASD diagnosis (Antshel et al., 2007; Kates et al., 2007; Vorstman et al. 2006) as is the case for CABIL cohort (N=90).

No one has looked at ASD diagnoses using gold-standard assessments. This requires BOTH

- Autism Diagnostic Interview-Revised (ADI-R) or (Social Communication Questionnaire-SCQ based on ADI-R)
- Autism Diagnostic Observation Schedule (ADOS)
Autism? Or Anxiety & Cognitive Delay?

- 29 children with 22q11.2DS ages 7-14, 16 boys; 13 girls
- using only one assessment, 7-18% demonstrated concerns for ASD, but no child met strict diagnostic criteria for ASD using *both* ADI-R/SCQ and ADOS

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<th>total</th>
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<td>1 (3%) Autism</td>
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<td>SCQ+ADOS</td>
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Summary & Plan

We are planning a longitudinal study of neurocognitive, emotional environmental & psychiatric growth:

- interaction of cognitive, social-emotional, neurobiological & environmental factors to identify risk and protective factors for psychiatric symptoms

We plan to re-recruit, at least twice, ALL nearly 100 children (7-14 years seen between 2005-2013 “Time 0”) for a 5 year NIH grant

- “Time 1”: 75-85 children with 22q11.2DS 13-20 years

Then we will apply for further funding to extend the study

- “Time 2”: 75-85 children with 22q11.2DS (TD?) 18-25 years

Not only would results better explain “modulators” of psychiatric health and disorders, it would also point directly to targets for intervention
Summary & Plan

This entire novel approach developed from the integrated team in our “22q Healthy Minds Clinic

integrating pediatric, psychological and psychiatric assessments, and the team discussions that followed, led to new understanding

This led to new directions in our neuroscience research, which has led to new clinical assessments being included

While we do actually plan to explore gene therapy, stem cell programming, video games and other “high tech” treatments, the clinic is pointing to powerful tools, widely available now

pediatric, psychological and psychiatric assessments of the child

IEP’s and analysis of family dynamics

Classroom changes, CBT, SSRIs, Child and Family Therapy ......
Thanks

**MOST important:** Kids who participated & their families!!

Majority of the work presented here was done by:

- Margie Cabaral, Josh Cruz, Freddy Bassal, Heather Shapiro, Ling Wong, Elliott Beaton Ph.D., Siddarth Srivastava Ph.D., Michelle Deng Ph.D., Joel Stoddard, M.D., Danielle Harvey, Ph.D., Kathy Angkustsiri M.D., Nicole Tartaglia M.D., Ingrid Leckliter Ph.D., Janice Enriquez Ph.D.

With important contributions from:

- Brian Avants Ph.D., Tracy Riggins Ph.D., Yukari Takarae Ph.D., Gary Zhang Ph.D., Marisol Mendoza