Welcome to M.I.N.D. Institute
Introduction & Overview of Research Projects
Space, Time & Numbers: Mind and Brain Issues
  • Tony Simon, Ph.D.
Behavior and Health Issues
  • Nicole Tartaglia, M.D.
Educational Issues & Open Discussion
  • Cheryl Dultz, M.A.
Requests

We’d like you to help us in the following ways:

1. Training, Media, Public Communications etc consent
   - Dysmorphology camera, teaching/training etc

2. M.I.N.D. Subject Tracking System Packet
   - Enrollment for current & future studies

3. Evaluation Form
   - Help us make future events better
The M.I.N.D. Institute

“The House that collaboration built”

The M.I.N.D. Institute is the only institution where scientists, clinicians, educators, parents, and community volunteers stand shoulder to shoulder under one roof in their effort to cure neurodevelopmental disorders.
The M.I.N.D. Institute

Medical Investigations of Neurodevelopmental Disorders

Conceived by five Sacramento families of children with autism

Multi-disciplinary clinical research program
• psychiatrists, neurologists, neuropsychologists, anatomists, immunologists geneticists, speech pathologists, educators, occupational therapists, pediatricians, cognitive neuroscientists and others

Research & Fee-for-Service Clinics for Treatment
Introduction & Overview

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What’s in a Name?

Much confusion about what name to use
We use chromosome 22q11.2 deletion syndrome

- DiGeorge syndrome
- Shprintzen syndrome
- Velocardiofacial syndrome
- Charge association
- Optiz GBBB syndrome
- Chromosome 22q11.2 deletion syndrome
What’s in a Name?

DiGeorge, 1960’s - DiGeorge Sequence
• Immune deficiencies from thymus hypoplasia,
• Hypocalcemia from hypoparathyroidism,
• Congenital cardiac anomalies

Shprintzen, 1980’s
• Velo - velopharyngeal, palatal abnormalities
• Cardio - congenital cardiac anomalies
• Facial - facial dysmorphisms
What’s in a Name?

Driscoll & others, Burn & others, 1990’s

DiGeorge, VCFS, Conotruncal face & other syndromes all arise from common deletion on long arm of chromosome 22, at q11.2 (DiGeorge Critical Region, DGCR)

So, DS22q11.2 is most complete label, but very clumsy!
What is CABIL?

Cognitive Analysis and Brain Imaging Laboratory

- Cognitive Analysis: how does the mind work?
- Brain Imaging: how is the brain constructed, connected, functioning

Together allow us to measure changes in mind and brain so we can explain (& fix) cognitive and behavioral impairments

What is different about what we do?
Psychometric Approach

Ma’am, this car

- can go 65 miles per hour
- runs badly in the rain
- goes better uphill than down
- has average gas mileage
- squeaks when turning left

“What it does” information

- describes strengths/weaknesses
Experimental Approach

Ma’am, this car

- runs badly in the rain BECAUSE this spark plug wire is frayed - we’ll replace it

- goes better uphill than down BECAUSE the fuel pump needs adjusting - we’ll tune it

- squeaks when turning left BECAUSE of the differential in the axle - we can lubricate it

“How it works” information

- leads to interventions
Intervention Plans

Cognition

- computer games to improve space, time & number abilities

Language Development

- “baby signs” to improve expressive language and cognitive development

Psychiatry

- early risk & treatment for schizophrenia, ADHD meds & DS22q11.2 clinical trial
Our Plan

We hope to build a long term relationship with you

• research projects with associated clinical care
• new results leading to novel interventions/treatments
• focus on several cognition, behavior, psychiatry issues
• from infancy to adulthood

More often you are willing to return, the more we all learn

• we from you (research), you from us (treatment)

More knowledge needs more studies, needs more funds
Acknowledgment

Thanks to parents and most especially your children

Without all of your co-operation we would not have learned what I am going to show you.

So, thank-you VERY much!!
Quantity, Space & Time

Quantity, space & time implicitly linked

3D space has “scale”

• width, height, distance ....

More “objects” occupy more space

Actions * rate => duration

Walsh, 2003
In typical adults the “frontoparietal” brain network plays a key role in processing this kind of information

- parietal lobe - space, time, quantity processing
- frontal lobe - control processes, working memory

In children, network likely similar but more diffuse

- focuses with age and experience
Prefrontal/Posterior Parietal Areas
Navigating Space

World is too full of information to “pay attention” to everything

- so must select (& ignore) information

Impairments will handicap effective use of information

PPL: spatial orienting and selection of relevant info

PFC: inhibition/ignoring irrelevant info
Navigating Space

White “pointer”/flashing box draws attention to one location

- Valid: alien appears in cued box so selection already done
- Invalid: alien appears in other box so must select new info
- Invalid cue requires “disengage” & re-select, pointer loads PPL more than flash

Prediction: invalid/pointer worst
Pointer condition much worse than flash condition
- horizontal vs vertical made little difference

Children with DS22q11.2 select & process information much better when they don’t have to search space to find it
Enumerating few objects (subitizing) does NOT require searching for each one

Enumerating ≥4 (counting) objects does require search

**Prediction**: counting, not subitizing, worse in DS22q11.2
Measuring Quantity

- 22q RT
- Con RT

Need to use search here

No need for search here
Navigating Space

Cue moves attention to part of display

- **Valid**: target box in same location - no need to search
- **Invalid-Within**: box in same object but new location
- **Invalid-Between**: box in new location & new object

Will objects structure space in a way that aids search for info?
Navigating Space

Box at different location to cue, inside same object

- children with DS22q11.2 perform better than controls

Box at different location to cue, inside different object

- children with DS22q11.2 perform far worse than controls

Children with DS22q11.2 use object boundaries to reduce search & improve selection & processing of information
Measuring Space

Decide if Kermit is closer to Fozzie Bear or Miss Piggy or in the center.

Requires accurate representation of space for “measurement”

Prediction: harder for DS22q11.2
Measuring Space

Center & edges easy to judge for everyone

Children with DS22q11.2 need bigger differences to be accurate

more error in middle area for DS22q11.2
Measuring Quantity

Comparing quantities involves spatial thinking

- bars - compare lengths
- numbers - position on “number line”

More similar magnitudes less easily distinguished

Prediction: “close” comparisons harder as are spatial
Measuring Quantity

Smaller differences much harder for DS22q11.2
Measuring Time

Time is a quantity we estimate and measure

- by itself - how much longer till the cookies are baked
- for other dimensions - “are we there yet?”, “aren’t we done with these sums yet?”

Estimating time affected by amount of “attention paid”

**Prediction:** Time estimation inaccurate, especially when hard (small differences, difficult task)
Measuring Time

Debbané et al, 2005

Time estimation:
Judge longer of two tones

- 400ms vs +/- 10ms steps (e.g. 400 vs 410ms or 420ms ...)

Just like other tasks DS22q11.2 need bigger differences to tell durations apart

Much bigger differences required by D22q11.2
Able to explain quite a lot about why children with DS22q11.2 have difficulties in these related domains

- hard to find information if have to search for it
- use objects not co-ordinates to “structure” space
- representation of “all” quantity has reduced resolution
  - space: like fewer, larger pixels in digital camera image
  - time: like clock that ticks less often with larger gaps
Brain/Behavior Relationships

Evidence for dysfunction in frontoparietal network

Predicts that changes in brain likely to most affect regions required for relevant cognitive functions

We use MRI to examine tiny cubes of brain tissue called voxels

• any voxel clusters that help explain differences?
Volumetric Findings - Gray

Areas with reduced gray matter in DS22q11.2

Areas with more gray matter in DS22q11.2
Areas with more fluid in children with DS22q11.2
Fractional Anisotropy Findings

Areas with strongest connections signal in controls

Areas with strongest connections signal in DS22q11.2
Corpus Callosum (CC) in VCFS shifted around dilated ventricles

b) control CC is in location of enlarged VCFS ventricles

c) VCFS CC is displaced around enlarged fluid filled ventricles

Changes in corpus callosum location/shape may affect connectivity/function of frontoparietal network
Control

DS22q11.2
Biggest Differences in Anterior CC!
Collaborators

CABIL Team (& Alumni) - M.I.N.D. Institute

• Dr. Joel Bish, Vy Nguyen, Kristine Strohbin, Samantha Ferrante, Heather Ferrante

University of Pennsylvania

• Dr. James Gee, Dr. Alexei Machado, Gary Zhang, Brian Avants

CHOP “22q & You” Center

• Dr. Elaine Zackai, Donna McDonald-McGinn
Inhibiting Information

Indicate direction of central “alien”

• single: nothing to ignore

• congruent: ignore “buddies” with correct information

• incongruent: ignore “buddies” with incorrect information

Ability to inhibit affects speed, accuracy of decision
Inhibiting Information

Controls - inhibit/ignore “cost” increases with conflict in info
DS22q11.2 do not inhibit/ignore irrelevant information well at all
• correct info improves performance, incorrect hurts performance

Alien+buddies may be perceived as single “object” (as in selection bias) - harder to ignore pieces of 1 object than info in 5 locations