Understanding how cognition-emotion interactions affect risk and protection for mental health diagnoses

Tony J. Simon Ph.D.
Director, 22q11.2 Research Center & Clinic
Assoc. Director, MIND Institute & IDDRC
University of California, Davis
http://mindinstitute.ucdavis.edu/research/cabil
tjsimon@ucdavis.edu

UC DAVIS MIND INSTITUTE

Neuropsych/Cognitive Profile

Standardized tests show a stable pattern for 22q11.2DS

Full Scale IQ: 70-85 (±15)

- Verbal Domains (VCI) > Nonverbal (PRI/WMI) (in <u>most</u> people)

- etc ….

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Very familiar, but what does this mean for a person with 22q?

- most things will be more difficult for you than your peers
- some things won't be that hard, others are just "*mind-boggling*"
- being *mind-boggled* is stressful and makes you feel <u>bad</u>
- knowing you will be *mind-boggled* next time creates anxiety about it
- NOBODY is at their best when *mindboggled*, stressed and anxious
- even worse, people who are not you don't get why you are like that!
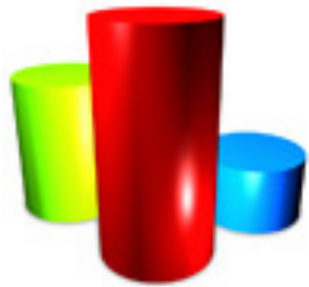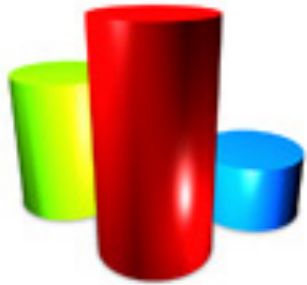
Cognition/ Behavior
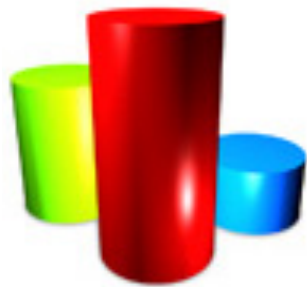
Everyday
Demands

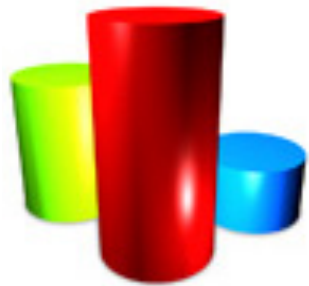Cognition/
Behavior

Everyday
Demands

Cognition/
Behavior

Coping
Resources

Everyday Demands

Cognition/Behavior

Coping Resources
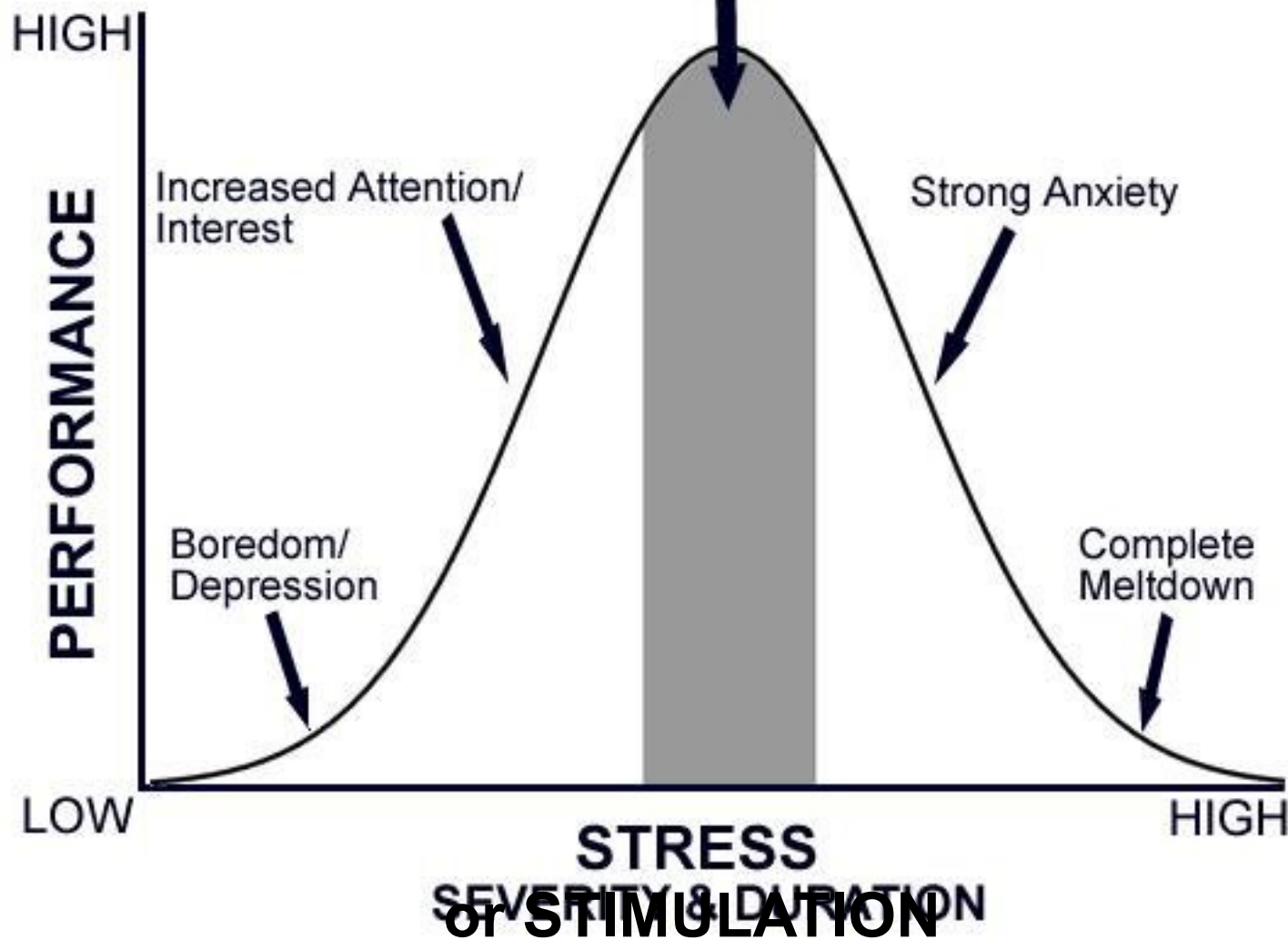
Everyday Demands

Cognitive Behavior

Optimal Performance

PERFORMANCE

HIGH

Increased Attention/Interest

Strong Anxiety

Boredom/Depression

Complete Meltdown

LOW

HIGH

STRESS SEVERITY & DURATION or **STIMULATION**
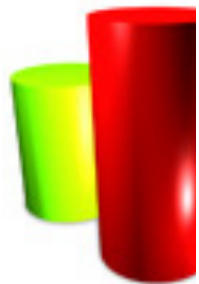
Resources

Anxiety Not IQ Predicts Adaptive Function
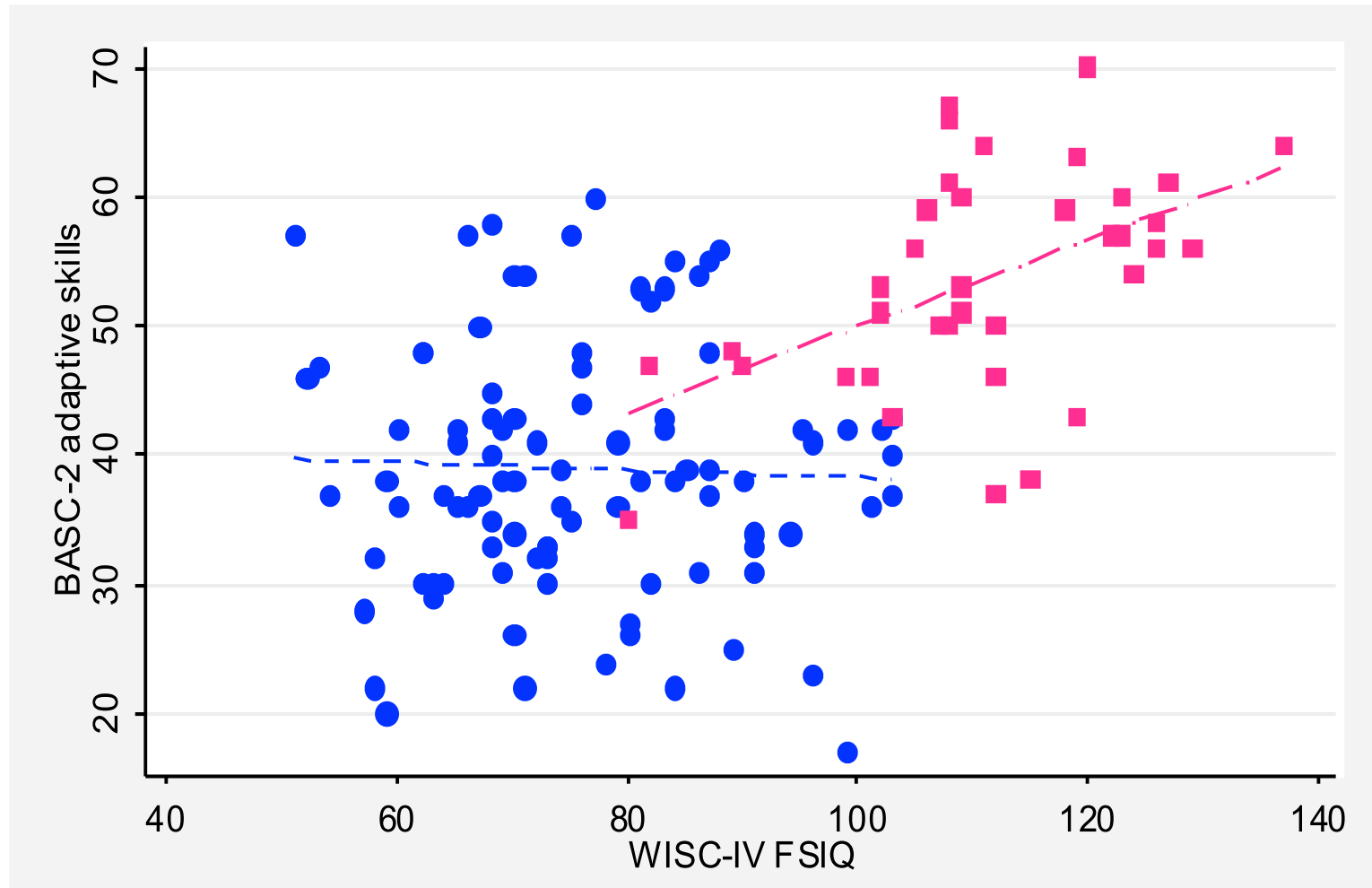
22q: N=99; r=-0.04; p=0.71   TD: N=45; r=0.5; p=0.002

Unlike TD children, FSIQ is NOT related to adaptive function in children with 22q11.2DS aged 7-14 years

Angkustsiri et al., J. Dev. Beh, Peds., 2012

Anxiety Not IQ Predicts Adaptive Function

Angkustsiri et al., J. Dev. Beh, Peds., 2012

Anxiety Not IQ Predicts Adaptive Function

22q11.2, N=62; r=-0.34, p=0.007

Copers

Strugglers

ABAS-II General Adaptive Compostie

Total Spence Anxiety (parent)
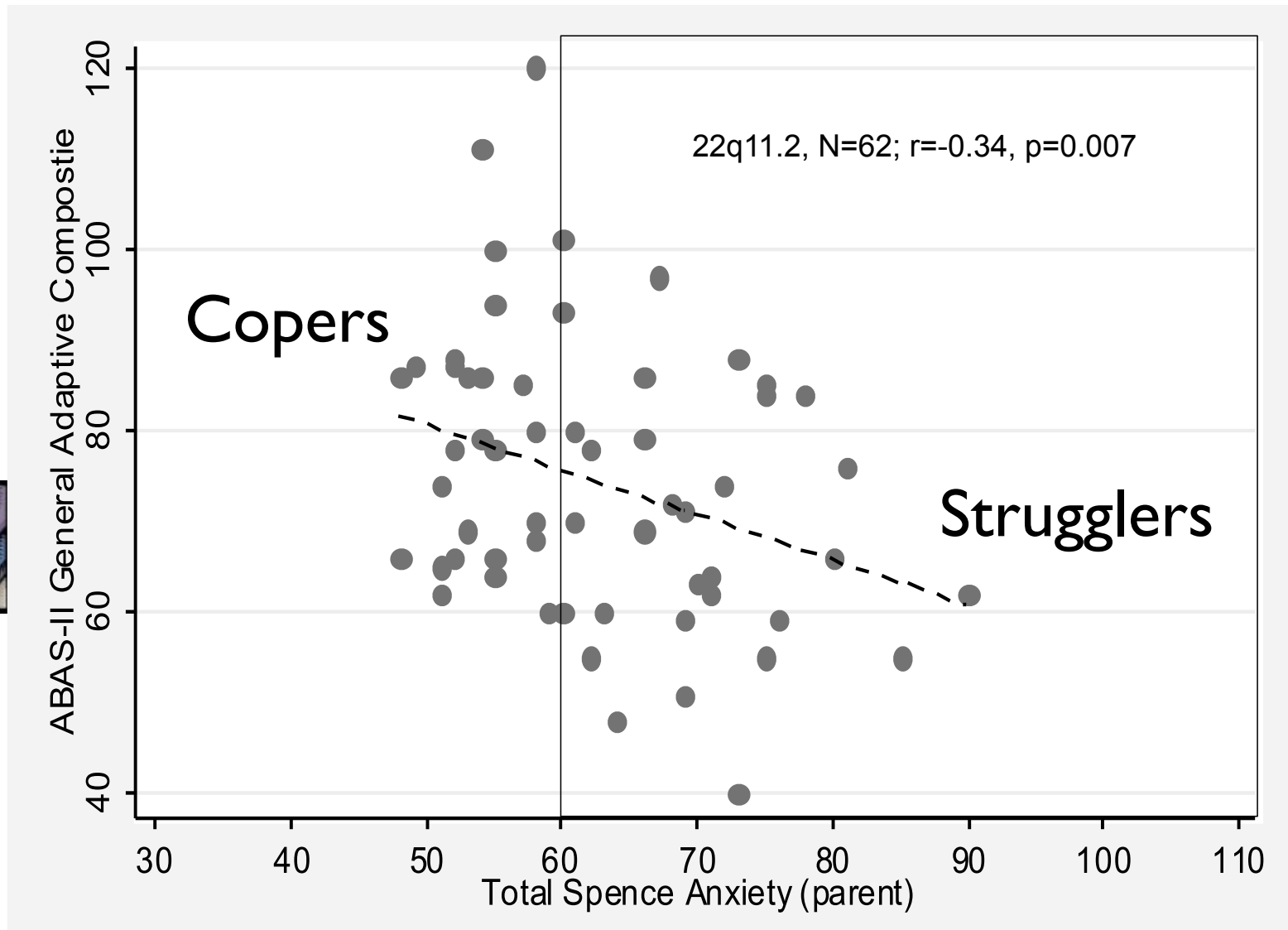
In children with 22q11.2DS aged 7-14 years, adaptive function is strongly and negatively related to anxiety levels

Angkustsiri et al., J. Dev. Beh, Peds., 2012

Core Working Hypothesis

Cognitive impairments limit competence in numerous domains

- but vary widely among people, activities, situations

Despite cognitive limitations some outperform predictions from IQ testing while others fall very short

- "copers" show lower anxiety, higher real world functioning and often achieve in academics far beyond what cognitive testing would predict

- "strugglers" show the reverse pattern - more anxiety poorer adaptive functioning and worse academics

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■ "strugglers" show the reverse pattern - more anxiety poorer adaptive functioning and worse academics

"Strugglers" experience more worry, stress & maybe psychiatric risk

"Copers", by being less stressed & anxious, may gain protection instead

If so, we can help target cognitive, emotional and environmental factors for intervention to improve academics, mental health, family dynamics

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Attention - Selection & Filtering

Attention: manage competition among things in memory & world
Switching (selecting) what the brain processes can be driven:

- 🟪 internally - controlled by goals or plans
- 🟪 externally - driven by objects/events in the world

Corbetta, Patel & Shulman, Neuron, 2008

Goal Driven: Endogenous

Event Driven: Exogenous

Figure 1. Focusing Attention and Reorienting Attention Recruit Interacting Networks

(Left panel) Focusing attention on an object produces sustained activations in dorsal fronto-parietal regions in the intraparietal sulcus, superior parietal lobule, and frontal eye fields, as well as visual regions in occipital cortex (yellow and orange colors) but sustained deactivations in more ventral regions in supramarginal gyrus and superior temporal gyrus (TPJ) and middle and inferior prefrontal cortex (blue and green colors). (Right panel) When an unexpected but important event evokes a reorienting of attention, both the dorsal regions and the formerly deactivated ventral regions are now transiently activated.

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Salience usually provided, using "cold" stimuli in experiment instructions
- but, what captures a child's attention in real world "hot" cognition?

Menon & Uddin 2010 "Increased anxiety […] may be the consequence of [the insula] misattributing emotional salience to mundane events"

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" Cold" Distractor Target

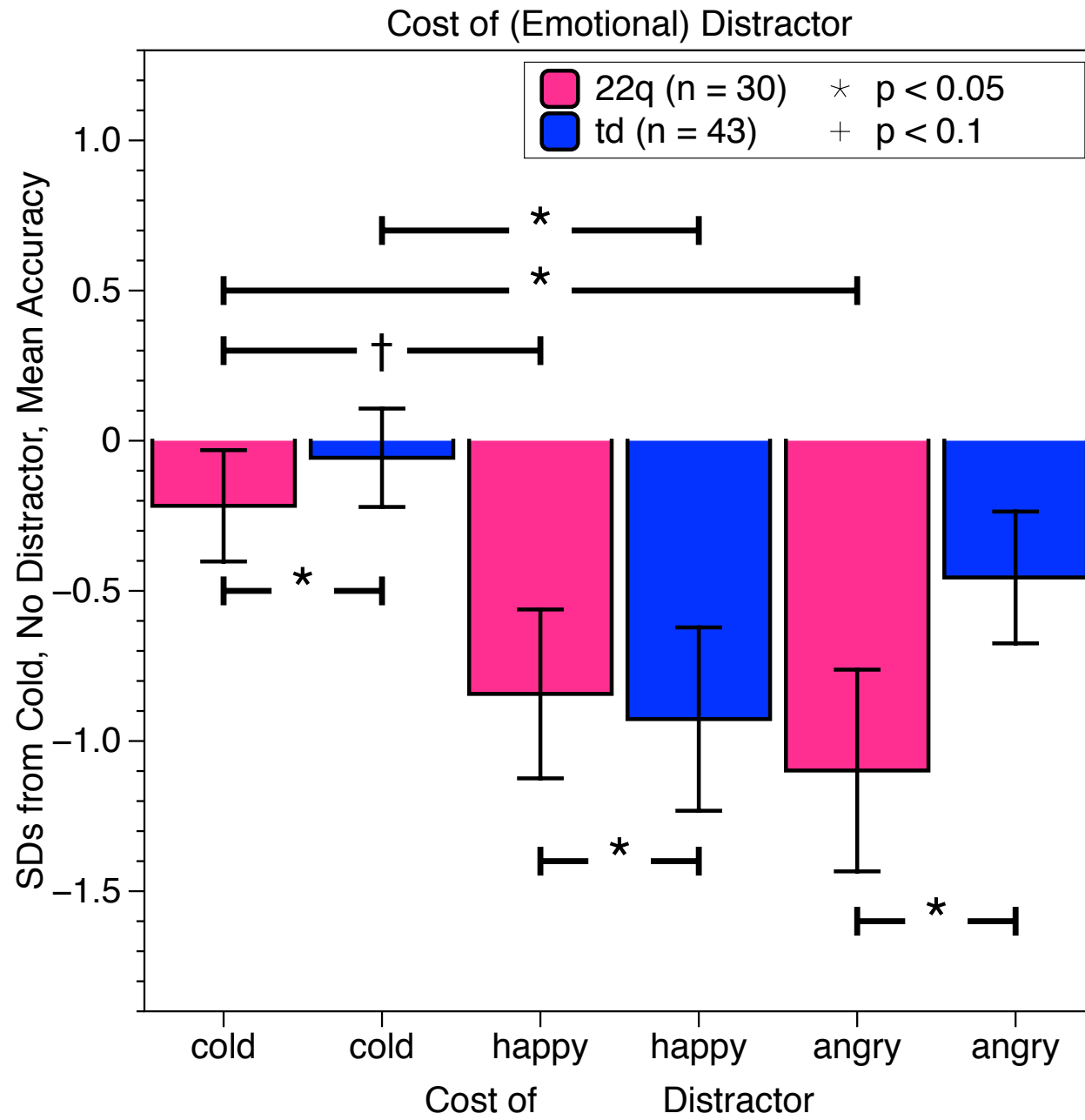Adapted from Sawaki, Geng & Luck,2012 by Abbie Popa & Steve Luck

- Stimulus 200 ms
- Respond to a specific color (red, green, or blue) in the center of the screen
- Center 70% gray, 10 % green, 10% blue, 10% red
- Lateral 33% green, 33% blue, 33% red

"Hot" Emotional Distractor Target

- Respond to specific emotion (happy, calm, angry)

- Center 70% scrambled, 10 % happy, 10% calm, 10% angry
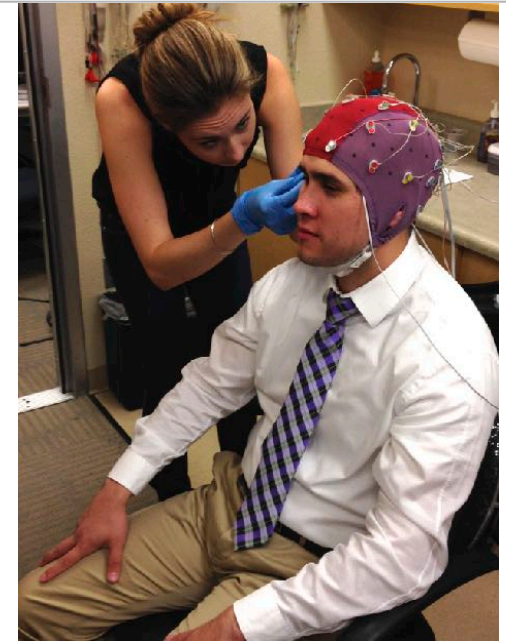
- Lateral 33% happy, 33% calm, 33% angry
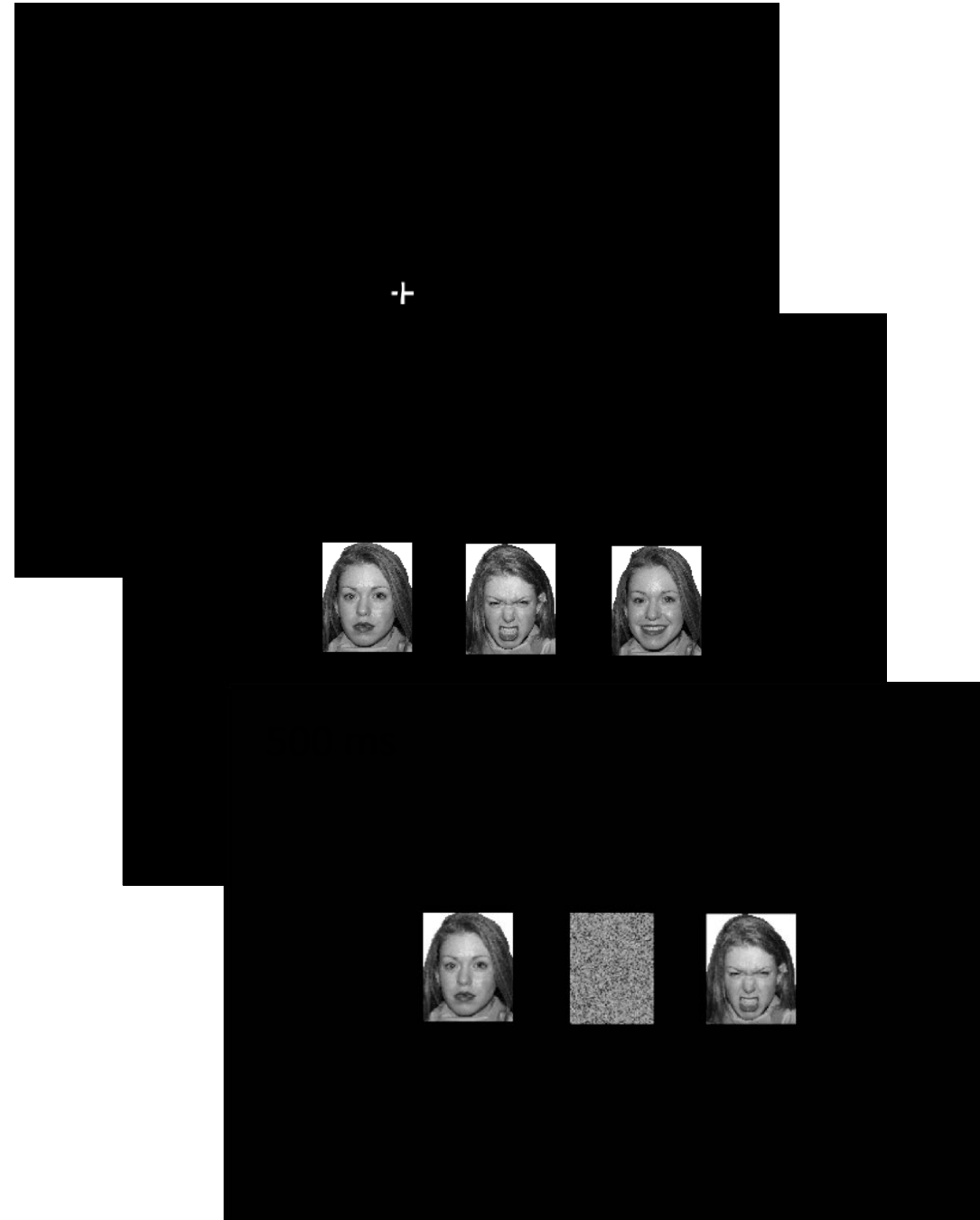
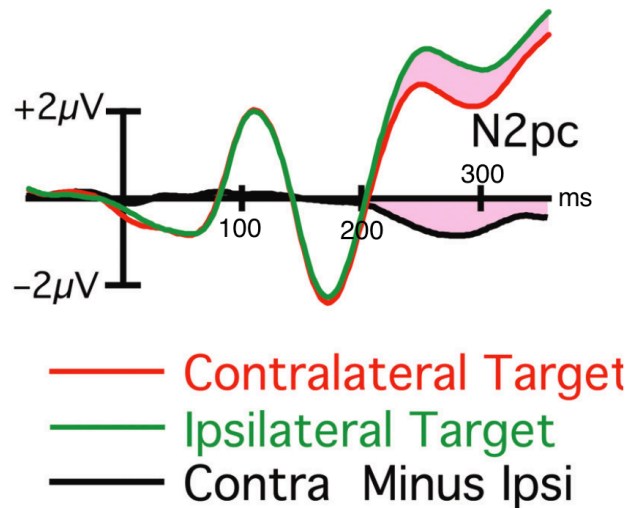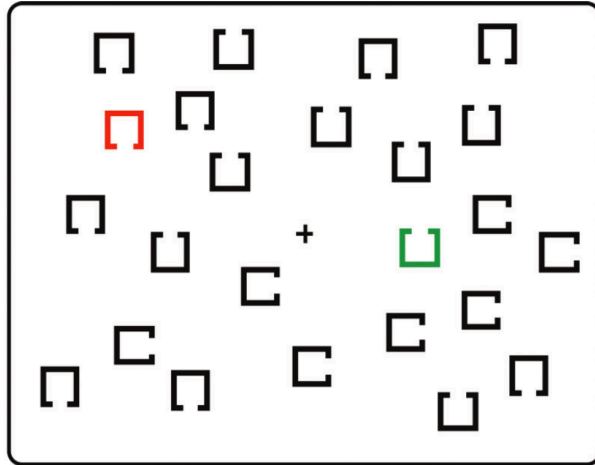# (e)DT - Emotional Distractor "Cost"

Cost of (Emotional) Distractor
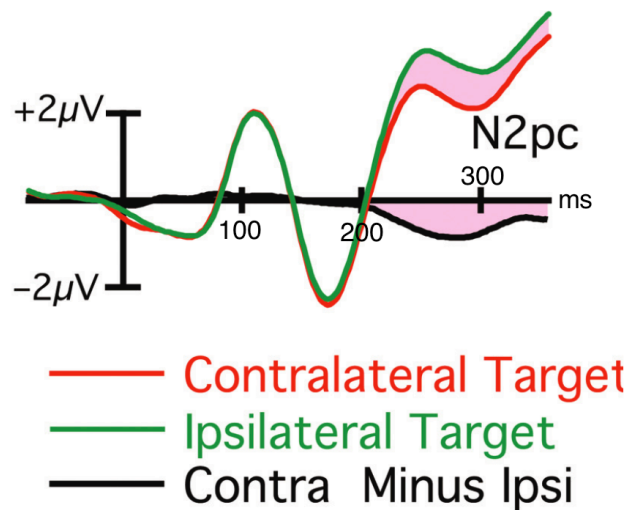
Acquiring ERP Data

Attention Related ERPs

N2PC – FIND TARGET

+2μV
N2pc
300
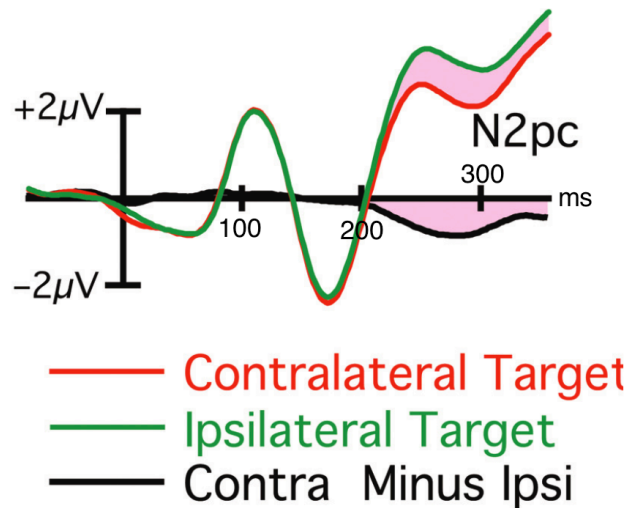100   200   ms
−2μV

— Contralateral Target
— Ipsilateral Target
— Contra Minus Ipsi

Attention Related ERPs

N2PC – FIND TARGET

Contralateral Target
Ipsilateral Target
Contra Minus Ipsi
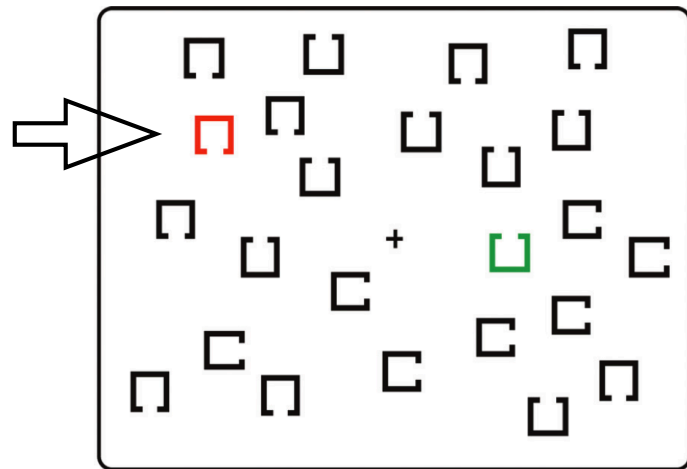
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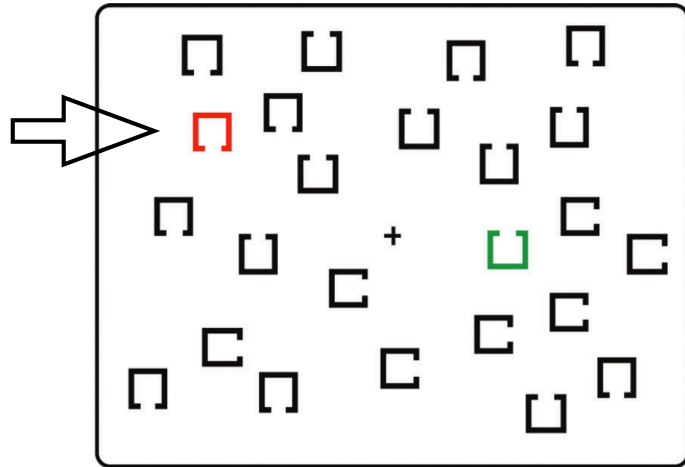
N2PC – FIND TARGET   Pd – SUPPRESS DISTRACTOR
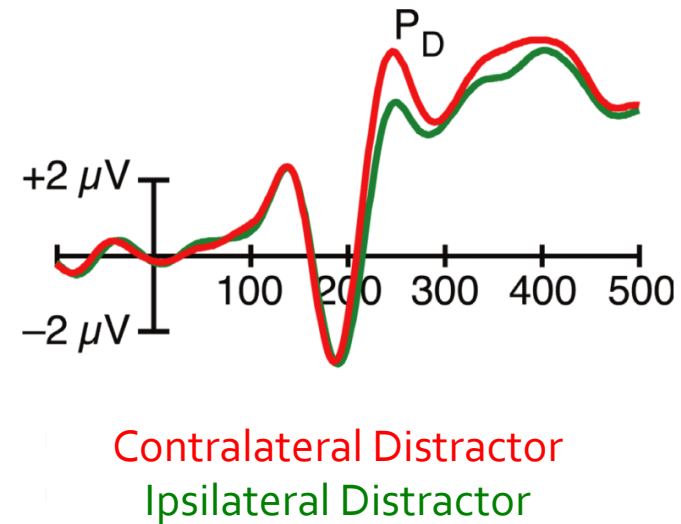
"Cold" DT ERPs
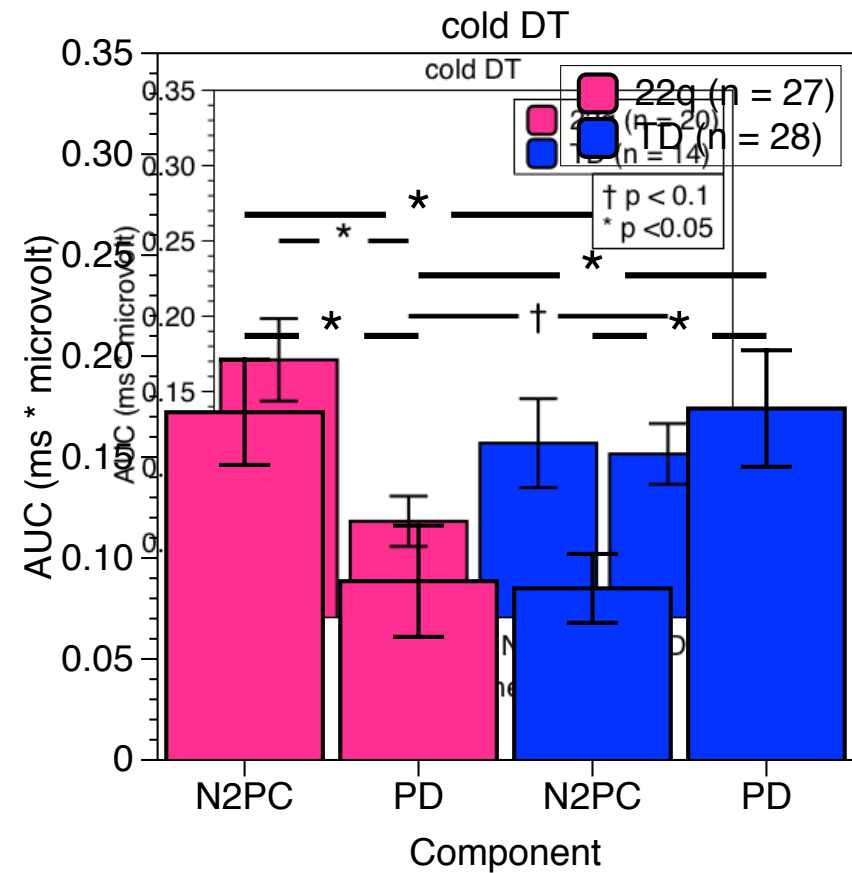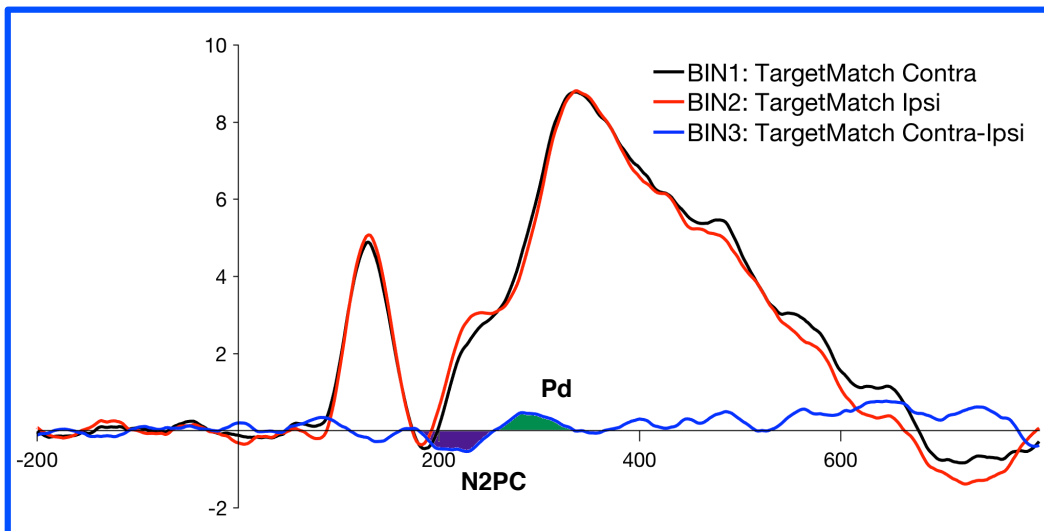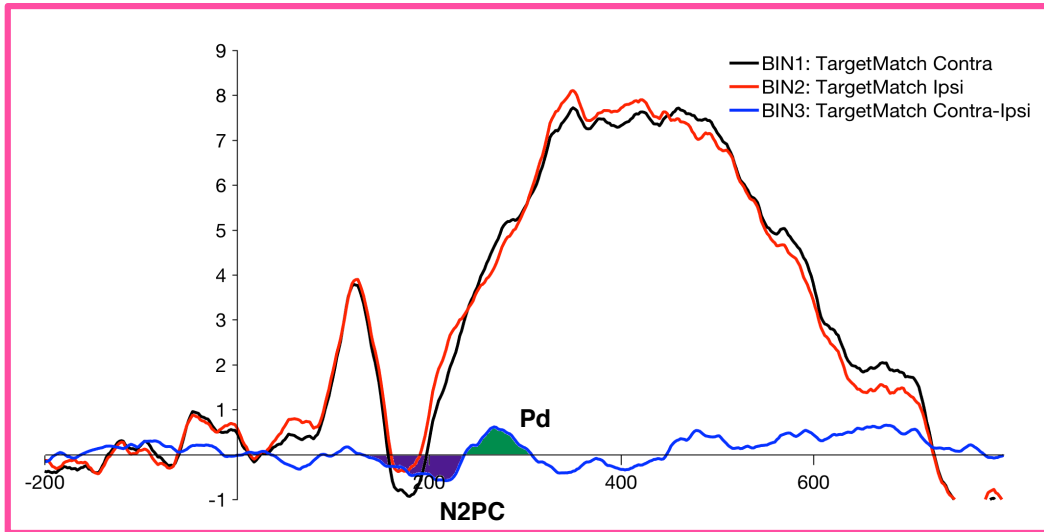
"Cold" vs "Hot" DT ERPs
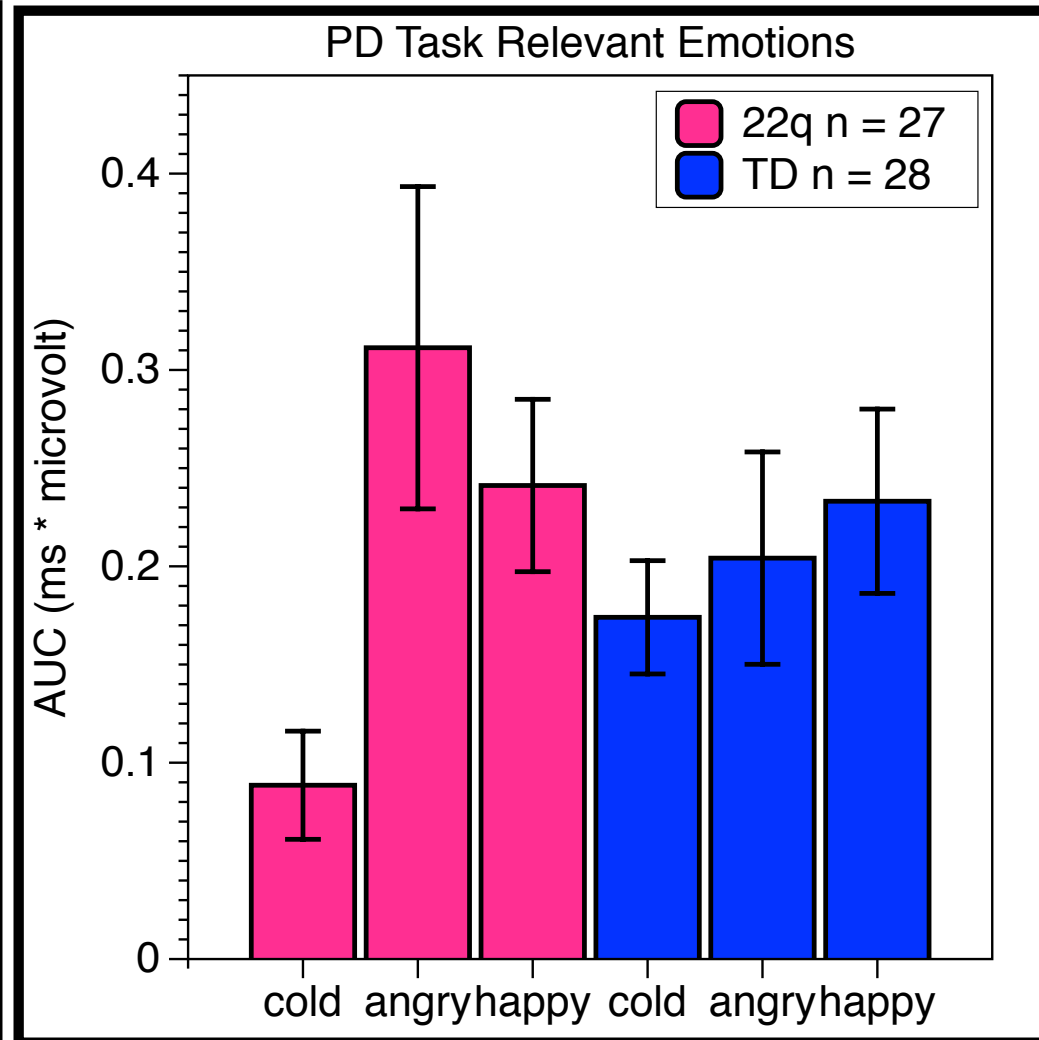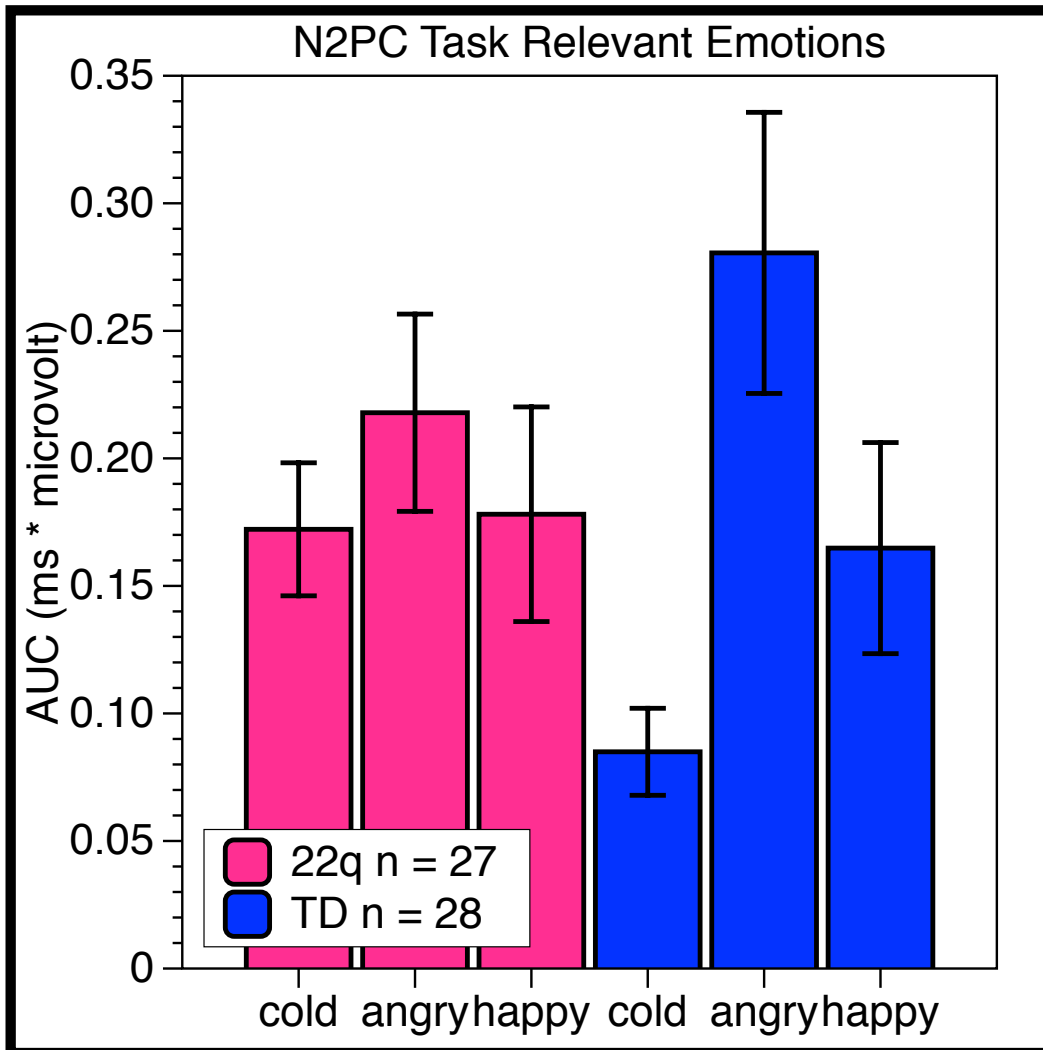
"Cold" Cognitive (Inhibitory) Control

Tests ability to withhold/inhibit in-appropriate responses

- "Go" trials (75%): press a button to "whack" the mole
- "No-Go" trials (25%): do NOT press for vegetable
    - Preceded by 1, 3, or 5 "Go" trials

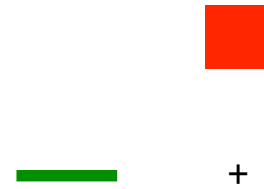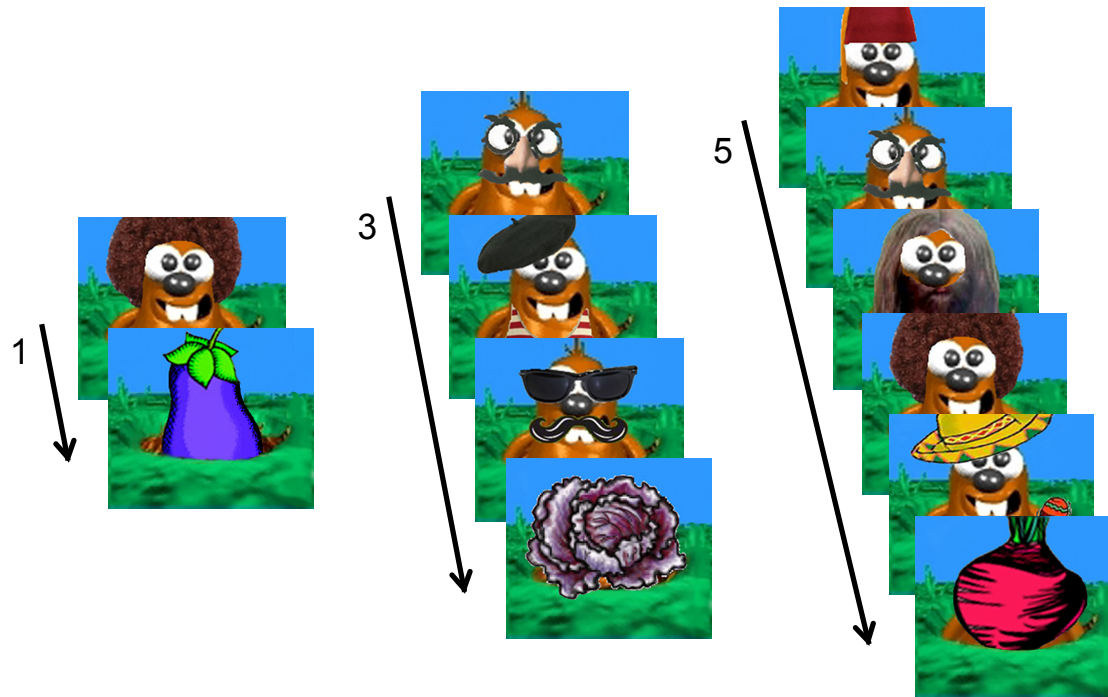# "Hot" Cognitive (Inhibitory) Control

Do emotionally salient stimuli affect the ability to withhold responses?

- "Go" trials (%): respond to Happy (50%) or Angry (50%) face
- No-Go (25%): do NOT respond to calm face
  - Preceded by 1, 3, or 5 "Go" trials

15
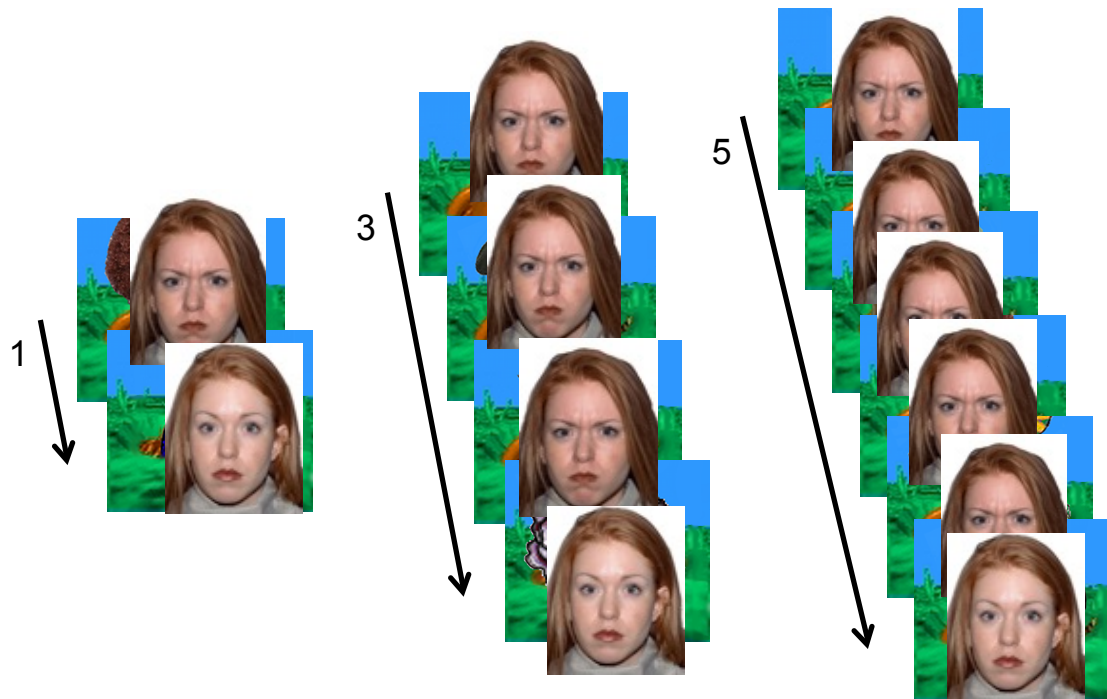
E(GNG) – Emotional NoGo "Cost"

Cost of Emotional NoGo (5 Go Trials)

Legend:
- 22q (n = 26)
- TD (n = 39)
- ★ p < 0.05
- + p < 0.1

y-axis: SDs from Cold Mean

x-axis: angry, angry, happy, happy — Cost of...
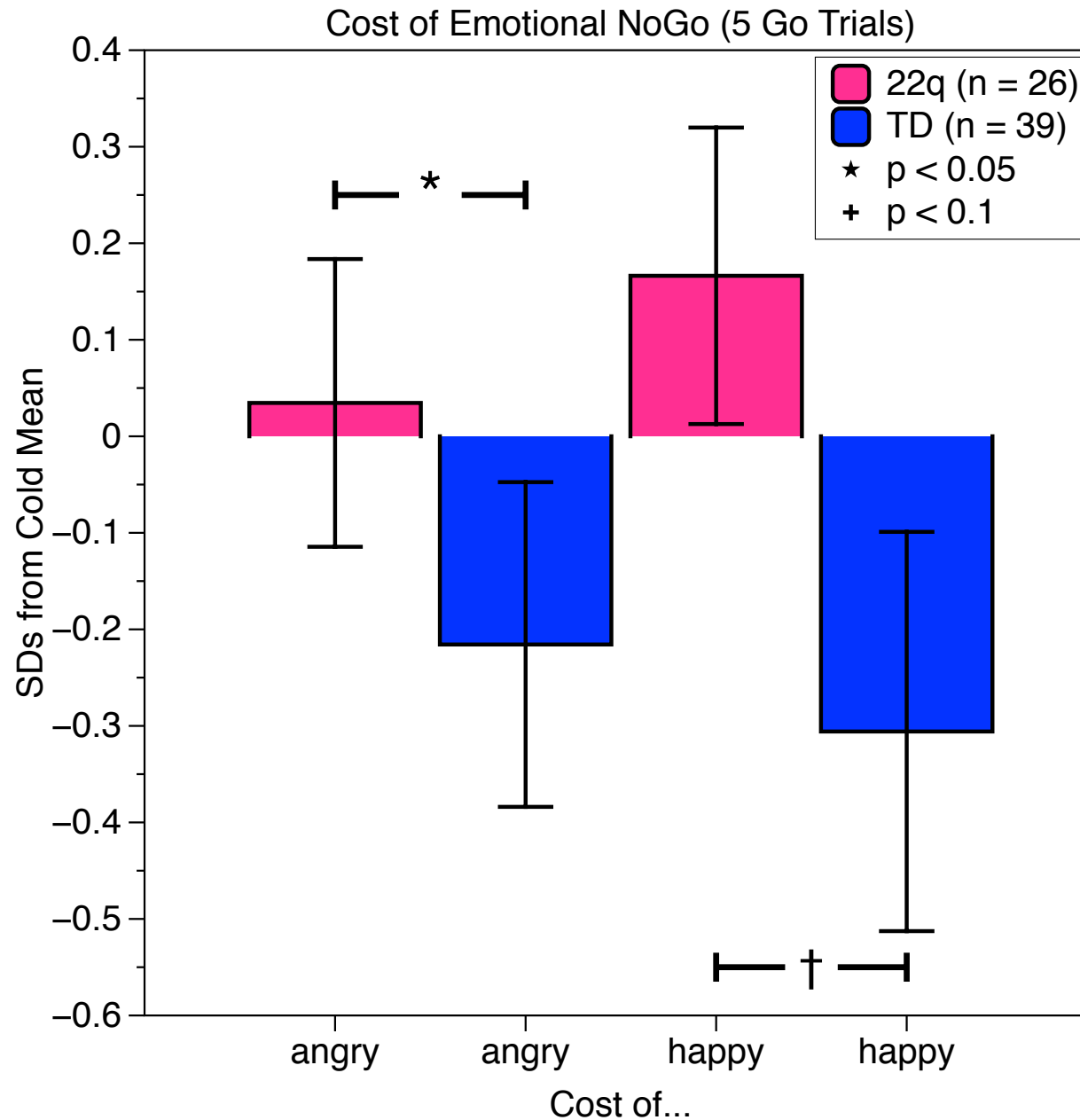
GNG ERP: N2 - Detect Conflict (NoGo)

Average Anterior Sites

BIN1: NoGo
BIN2: Go

microvolts

-200   200   400   600   ms
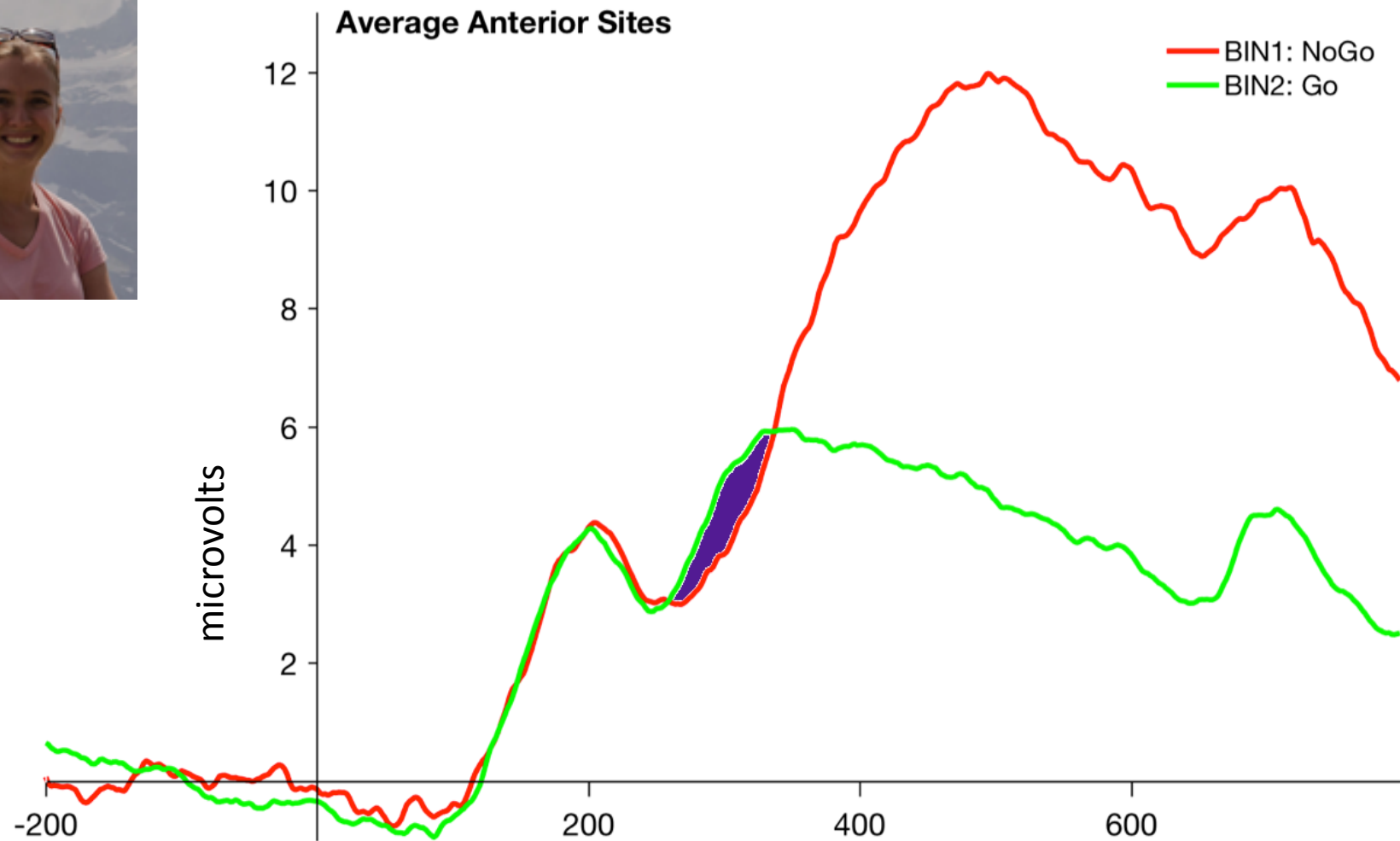
Anterior N2 is the negative portion of the difference wave (difference in NoGo – Go) between 150 and 350 ms

"Cold" vs "Hot" (e)GNG N2 ERPs
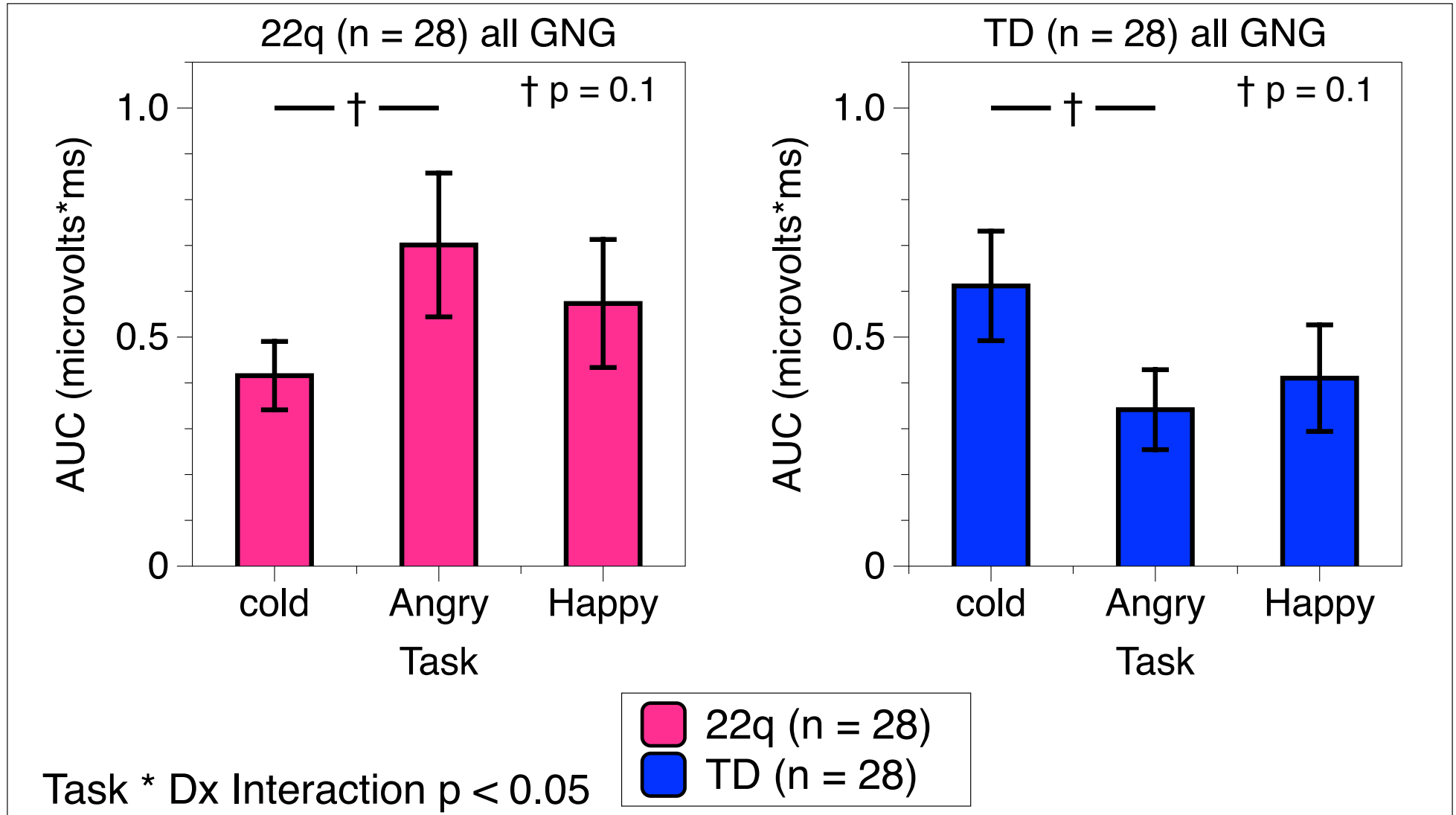
22q (n = 28) all GNG — TD (n = 28) all GNG

† p = 0.1

Task * Dx Interaction p < 0.05

22q (n = 28)
TD (n = 28)

Affective (Hot) Stimuli Impact Summary

Affective distractors impact attention differently in the 2 groups

BOTH groups, much less accurate in HOT than Cold task

■ but 22q group much worse than TD for Angry distractors

Opposite *capture* vs *suppress* brain signals to the Cold task

■ 22q group more captured by & less suppression of distractors

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Opposite *capture* vs *suppress* brain signals to the Cold task

- 22q group captured by hot & cold but suppress emotions most
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Affective stimuli impact inhibition differently in the 2 groups

- emotional faces improve 22q group performance but impair TD
- more conflict detection to faces in 22q group, opposite for TD

Stress, Anxiety & Psychiatric Diagnoses

IQ of 75 creates significant, ongoing, uneven challenge patterns

- 50-60% of children with 22q11.2DS have significant anxiety

- 20-50% of children with 22q11.2DS get a diagnosis of ADHD (mainly Inattentive or Combined type) and take medications

  - "ADHD" Sx = hyperarousal/hypervigilance from anxiety?

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Mismatches between capabilities and demands induce stress, which can lead to anxiety, avoidance and reduced motivation and self esteem

- reducing childhood *struggling load* may protect against psychosis

Prognostic Power of Anxiety

Gothelf et al. 2013 3-5 year longitudinal study 125 with 22q
"The predictive value of having an anxiety disorder at baseline for later development of psychosis was quite robust, as 9 of 10 patients with emerging psychotic disorder in our sample were diagnosed with an anxiety disorder at baseline".

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Tang et al. 2013 cross-sectional study 112 with 22q 8-45 years
"We also found that those with psychotic features were more likely to have a lifetime diagnosis of mood or anxiety disorder"
"Perhaps individuals with significant anxiety are at even higher risk than the 22q11DS population at large".

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Psychosis Proneness in 22q11.2

FIGURE 2. Prevalence of Schizophrenia Spectrum Disorders and Distribution of Specific Disorders by Age in Participants With 22q11.2 Deletion Syndrome[a]

out of 1402 or 17%
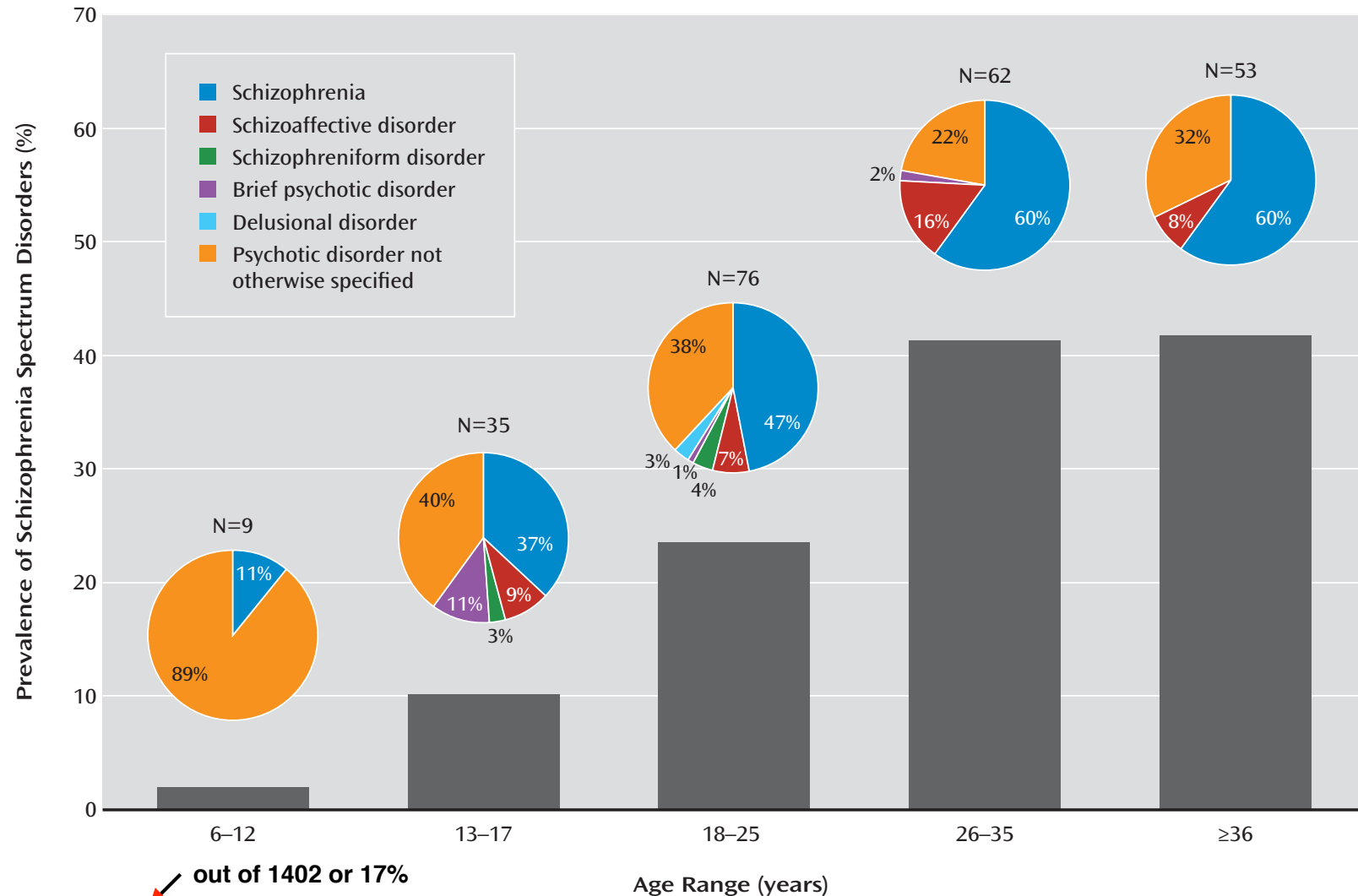
[a] Among the 235 subjects with schizophrenia spectrum disorders, the prevalence of a schizophrenia diagnosis increased significantly over the age groups (χ^2=12.54, df=4, p=0.01), whereas the diagnosis of psychotic disorder not otherwise specified decreased (χ^2=17.17, df=4, p=0.002).
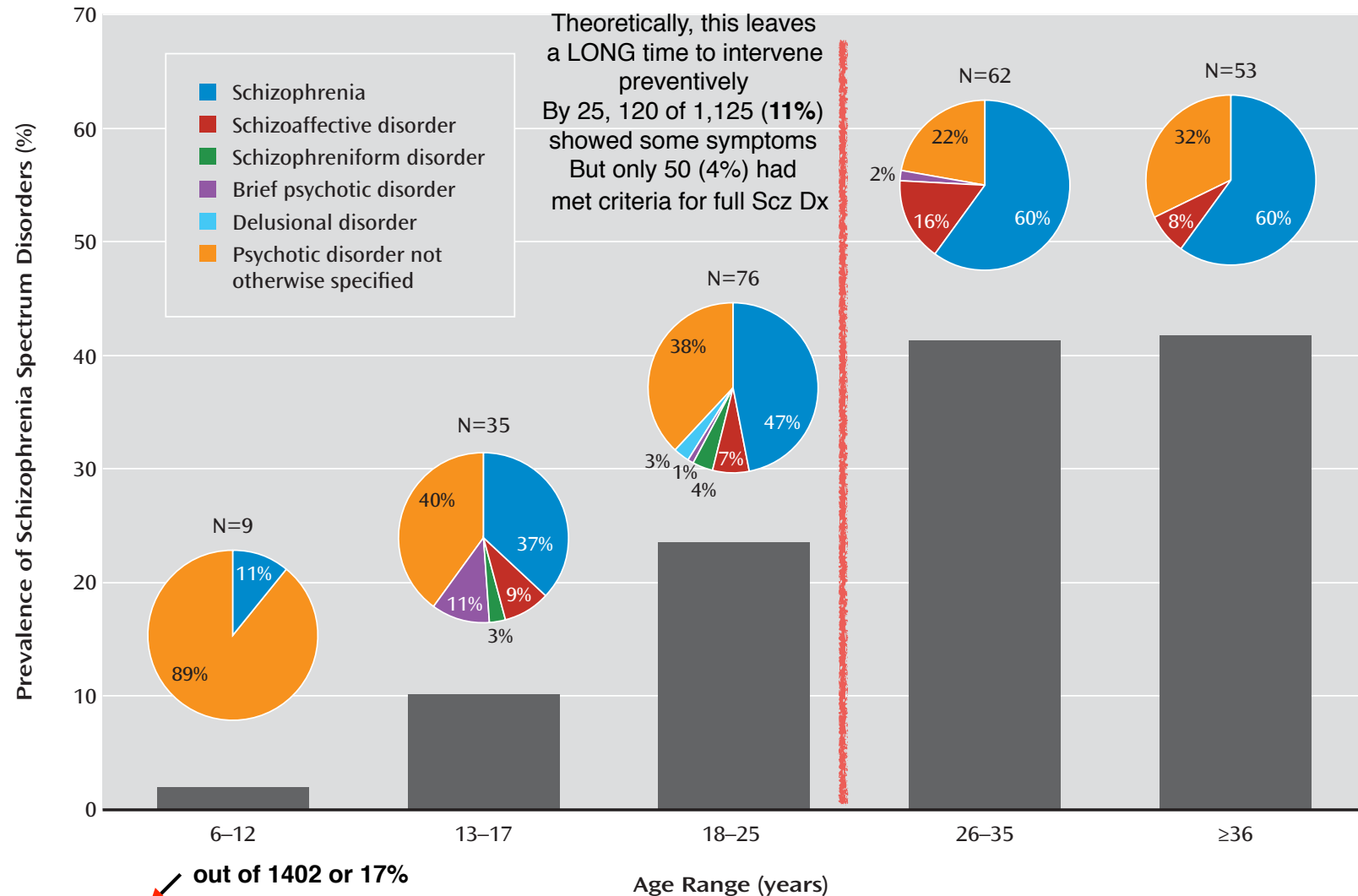
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Conclusions I

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Psychopathology risk only partly genetic, suitable experience matters!

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INTERVENTION IMPLICATIONS

Family/School/Community supports further modulate this interaction & influence "coper/struggler" trajectory

Strugglers can be converted to copers with child, school, family change
■ not with stem cells or brain surgery but commonly available therapy

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🟪 not with stem cells or brain surgery but commonly available therapy

Child: cognitive behavioral/behavioral therapy, SSRI, cognitive training

School: effective IEP, careful calibration of challenge based on testing

Family: coping strategies for parents, matching parent/child expectations
🟪 reduced parental psychological control, negative expressed emotion

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Thanks

MOST important: Kids who participated & their families!!

Majority of the work presented here was done by:

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