Brain Mechanisms for the Perception, Experience, and Regulation of Emotion in Autism

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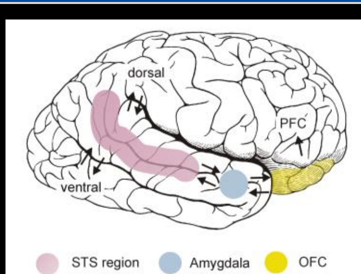
Brain Mechanisms for Social Perception

- Humans, in response to the unique computational demands of highly social environments, have evolved specialized brain mechanisms supporting abilities including:
  - Individuating others
  - Perceiving agents and their actions
  - Perceiving the emotional states of others
  - Analyzing the intentions and motivations of others
  - Sharing attention and intentions
  - Representing another person's perceptions and beliefs

Yale SCHOOL OF MEDICINE SLIDE 1

Brain Mechanisms for Social Perception



From Allison et al. (2000) *Trends in Cognitive Sciences*

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Autism Spectrum Disorder (ASD)

- Qualitative impairments in social interaction
  - Impairment in eye contact and social reciprocity
- Qualitative deficits in communication
  - Delay in or lack of spoken language
- Restricted, repetitive, and stereotyped patterns of behavior
  - Persistent preoccupations with parts of objects
  - Self-stimulatory behavior

Yale SCHOOL OF MEDICINE SLIDE 3

Detecting Other Agents: Biological Motion and its Disruption in Autism

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Behavioral Training for fMRI

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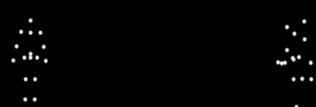
Participant Characteristics

	Typically Developing (TD)	Unaffected Siblings (US)	Autism Spectrum (ASD)
Number of Subjects:	17	20	25
Mean Age in Years:	10.9	11.3	11.8
Age Range in Years:	4 - 17	6 - 17	4 - 17
Gender (male : female):	12 : 5	9 : 11	20 : 5
Differential Ability Scale-II:	116.0 (16.7)	114.2 (7.7)	100.2 (19.7)
Amount of Movement (mm):	0.9 (0.7)	1.4 (0.9)	1.1 (0.6)
Social Responsiveness Scale:			
Raw scores	23.7 (14.5)	18.9 (15.3)	98.7 (23.5)
T-scores	46.3 (6.7)	43.9 (7.5)	83.0 (13.1)
Vineland Adaptive Behavior Scales:			
Communication	102.5 (15.8)	102.0 (12.9)	78.3 (10.5)
Daily Living	93.1 (10.4)	93.6 (10.9)	78.5 (11.0)
Social	102.7 (9.0)	99.6 (11.3)	73.5 (9.8)

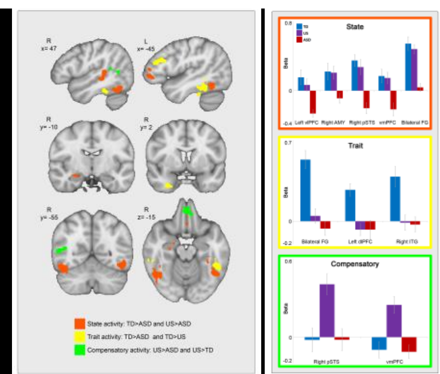
Neural Signatures of Autism

- State markers are defined as regions of dysfunction in children with ASD relative to US and TD children.
- Trait markers are defined as regions of activity reflecting shared dysfunction in US and children with ASD.
- Compensatory mechanisms are defined as enhanced differential activity unique to US relative to TD and ASD.

Biological vs. Scrambled Biological Motion



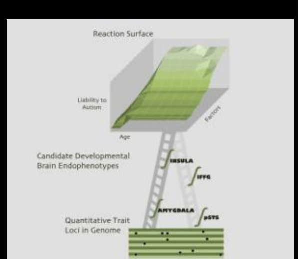
Kaiser et al. (2010) *Proceedings of the National Academy of Sciences*



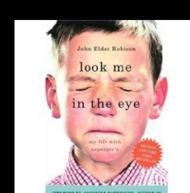
Kaiser et al. (2010) *Proceedings of the National Academy of Sciences*

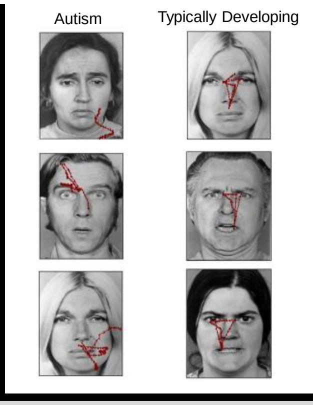
Next Steps: Using Neuroendophenotypes

1. Identifying brain mechanisms underlying the moderating effects of common polymorphisms.
2. Whole-genome analyses using the functional brain phenotype as a quantitative trait.
3. Selecting maximally divergent sibling pairs for selective whole-exome analysis.



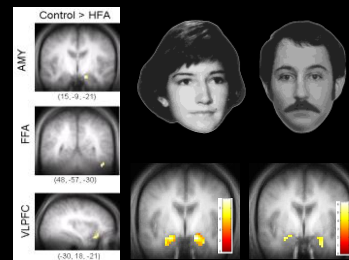
Can we normalize face-related activity in participants with autism by experimentally modifying visual scanpaths?





Pelphrey et al. (2002) *Journal of Autism and Developmental Disorders*

Amygdala Dysfunction in Autism

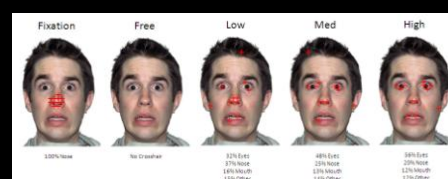


Pinkham et al. (2008) *Schizophrenia Research*

Amygdala and Visual Scanpaths

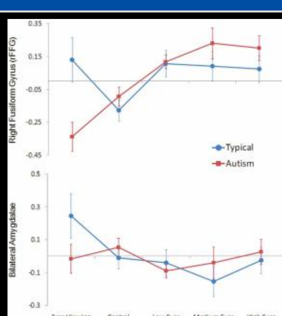
Adolphs et al. (2005) *Nature*

Manipulation of Scanpaths



Perlman et al. (2010) *Social Neuroscience*

Effects of Scanpath Manipulation by Group



Perlman et al. (2010) *Social Neuroscience*

The skin as a social organ: Do abnormal responses to social and affective stimuli in autism generalize beyond the visual and auditory domains?

Properties of C-Tactile Afferents

- Low-Threshold Unmyelinated Mechanoafferents
- Slow conduction velocity (around 1 m/s)
- Respond vigorously to slowly moving stimuli but poorly to brisk movements and vibration
- Easily fatigued
- Not present in glabrous skin
- Poorly designed for discriminative aspects (timing and intensity) of touch

Hypothesis: C-tactile afferents signal affective touch.

Gentle Brushing of the Arm and Palm

Gentle Brushing of the Arm and Palm

Arm	Rest	Palm	Rest	Arm	Rest	Palm	Rest
6 sec	*12 sec*	*6 sec*	*12 sec*	*6 sec*	*12 sec*	*6 sec*	*12 sec*
X 8		X 8		X 8		X 8	

Total experiment duration = 10 minutes 12 seconds (there are 8 additional seconds of "rest" between each run).

Each child experienced the arm and palm touch prior to the experiment and rated the pleasantness. Overall ratings did not differ across groups or area of touch.

Participants

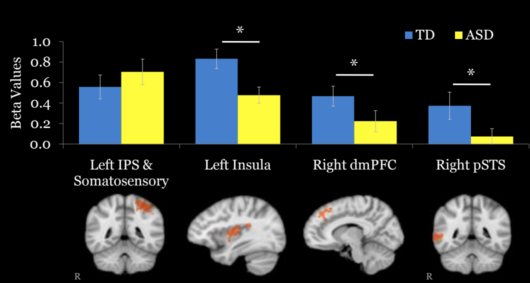
Child Study: (N=23) Groups matched on age and IQ.

Typically Developing (n=10)
5 females
Mean Age = 12.2 years
Range = 6-15 years
DAS Overall = 104 (SD = 16.9)

ASD (n=13)
3 females
Mean Age = 10.8 years
Range = 6-15 years
DAS Overall = 99 (SD = 15.9)
Dx = ADOS, ADI-R, clinical evaluation

Typically Developing versus ASD – Independent ROIs

Response to Affective Touch in adult Arm > Baseline Regions



Group × Condition Interaction

Arm – Palm in TD > Arm – Palm in Autism; $q < .05$, $k = 8$

Development of brain mechanisms for emotion regulation in children with and without autism

Munch, *Anxiety* (1894)

Emotion Dysregulation in Autism Spectrum Disorder

- Emotional volatility is common among individuals with autism spectrum disorder (ASD), detrimentally impacting the quality of life for those affected and their families.
- For many higher-functioning children with ASD, maladaptive emotional responses (e.g., behavioral outbursts associated with changes in routines or violation of expectations) are often the first concerns noted by parents or caregivers.
- Despite the importance of this area, the behavioral and neural underpinnings of emotion dysregulation in ASD remain poorly understood.

Objectives

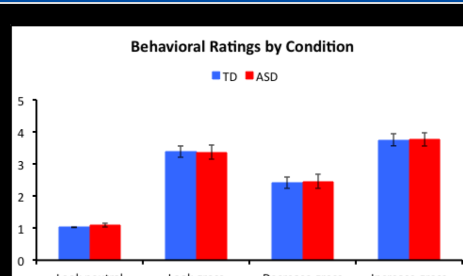
- We sought to examine activity associated with cognitive reappraisal of negative reactions to disgusting images in children and adolescents with and without ASD. Our hypotheses centered on:
  - regions involved in the experience of disgust
  - the regulation of emotion in regions involved in the processing of disgust, particularly the amygdala and insula
  - regions in which activity covaried with severity of social impairments

Cognitive Reappraisal of Experienced Disgust

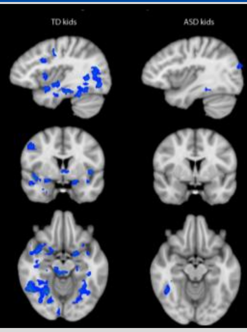
Participants

- Participants:
  - Two IQ- and age-matched groups: typically developing children (TD), *n* = 15, mean age = 13.03, range = 9-18 years; children with autism spectrum disorder (ASD), *n* = 16, mean age = 13.82 years, range = 9-17 years

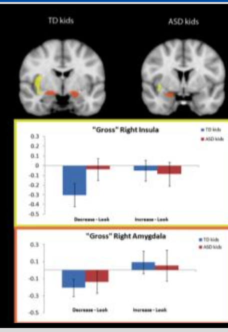
Behavioral Results



“Gross Regions” Modulated During Decrease Trials



Insula and Amygdala Regions of Interest



Conclusions

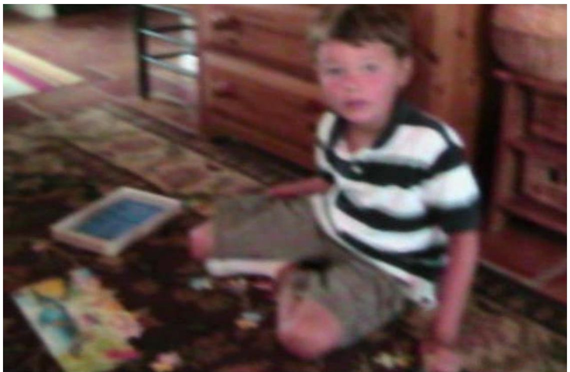
- TD and ASD children exhibited similar behavioral profiles indicating successful cognitive reappraisal.
- TD and ASD children exhibited robust gross > neutral activity in the right insula, right amygdala, and bilateral fusiform gyri.
- TD children down-regulated “gross” regions when decreasing to a much greater degree than did ASD children.

Childhood Disintegrative Disorder

- Normal development for at least 2 years with a subsequent regression of a mixture of:
  - expressive or receptive language
  - social skills or adaptive behavior
  - bowel or bladder control
  - play
  - motor skills
- Followed by:
  - social Impairments
  - communication Impairments
  - restricted, repetitive, and stereotyped patterns of behavior

Childhood Disintegrative Disorder

- Rare: 1-2/100,000 (Fombonne, 2005)
- Age of regression 3-4yo (Volkmar, 1989; Malhotra, 2001)
- Distinguishing Characteristics from other ASDs
  - Natural History
  - Lower Function (Volkmar, 1995)
    - IQ < 40
    - Mutism
    - Residential Placement
  - Anxiety prodrome (Kurita, 1998)
- The severity, low population frequency and apparently sporadic transmission seen in the vast majority of cases points to the involvement of either rare *de novo or rare recessive mutations of large effect.*



Yale Child Study Center Sample

- 32 children seen between 1992 and 2010
  - 28 Male, 4 Female
  - From across the world

	Mean (Mode)	Range
Age at Evaluation	7y 4m	3y 6m – 12y
Age at Regression	3y 4m	2y – 7y 6m
Regression Duration	3.9m	1-9m
NVIQ	42 (<30)	<30-71

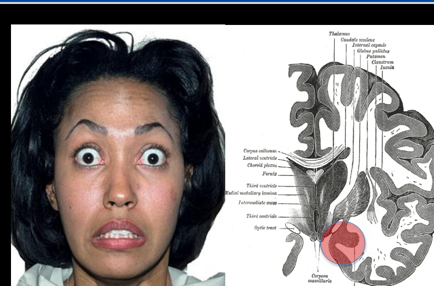
Clues: Prodrome

- "crying, sobbing, unable to talk about what was wrong except that he was scared"
- "wake up several times a night in an anxious state… [and take] an hour or longer to fall back asleep,"
- "crying virtually inconsolably"
- "episodes of appearing terrified and confused"
- "talk to herself and scream and cry that she was scared for no apparent reason"
- "crying constantly and saying isolated words such as 'blood,' 'death,' or 'skeleton'"
- "waking up in the middle of the night terrified and confused"

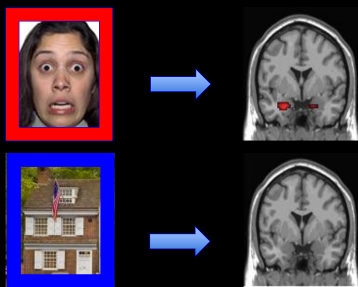
Clues: Prodrome

Characteristic	# Reported	% Cohort
Terrors and Extreme Anxiety	19	70
Social Withdrawal	19	70
Severe Tantrums	13	48
Aggression	12	44
Sleep Interference	10	37
Motor Changes	7	26
Labile Mood	6	22
Staring Episodes	6	22
References to Head Sensation	6	22
Hallucinations	6	22
Inappropriate Laughter	5	19
Noise Sensitivity	4	15

Amygdala



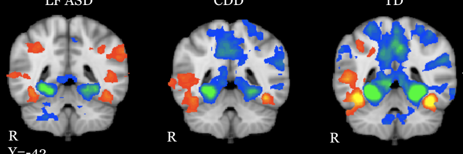
Faces vs. Houses



Faces vs. Houses

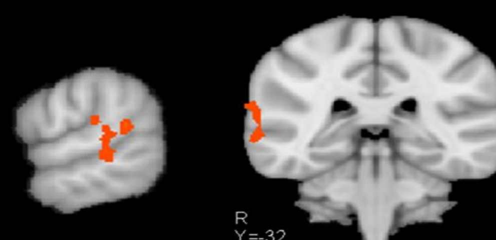
Results of the Faces > Houses Contrast in children with low-functioning ASD (n=6), CDD (n=6), and typical controls (n=12). $q<0.05$, $k>12$. Children with CDD exhibit a more typical pattern than their ASD counterparts in bilateral amygdalae.

Faces vs. Houses



Results of the Faces > Houses Contrast in children with low-functioning ASD (n=6), CDD (n=6), and typical controls (n=12). $p<0.05$, $k>12$. Children with CDD exhibit a more typical pattern of rSTS, and bFFA than their ASD counterparts. ***The PPA was equally responsive in each group.***

CDD > Low Function ASD without Regression



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