Physiology and Psychosocial Functioning in Autism: Examining the Unique Role of the Autonomic Nervous System

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Outline

1. Define the Autonomic Nervous System (ANS) and its role in Autism Spectrum Disorder (ASD).
2. Describe the relationship between stress, physiological functioning, and social behavior in ASD.
3. Discuss possible clinical implications and critical avenues for future research.

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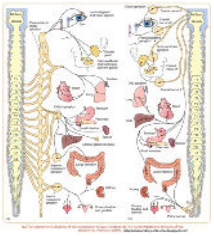
The Autonomic Nervous System (ANS)

- Sympathetic (SNS):
  - "Fight or flight"
  - Increases heart rate
  - Raises blood pressure
  - Increases respiration

↑SNS = ↑Arousal/ "Stress"



Parasympathetic (PNS):
- "Rest and Digest"
- Slows heart rate
- Lowers blood pressure
- Slows respiration
- Increases intestinal activity

↑PNS = ↓Arousal/ "Stress"

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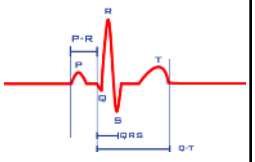
Measuring the ANS: Heart Rate Variability

- Changes in beat-to-beat variability
- Provides insight into contribution of PNS and SNS branches
- Respiratory Sinus Arrhythmia (RSA)
  - Cardiac measure of parasympathetic regulation
  - Elevated RSA = ⇑ PNS regulation
- Pre-ejection Period (PEP)
  - Indicator of sympathetic cardiac control
  - *Lower* PEP = ⇑ SNS activation



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Relevance of the ANS in the Context of Social Functioning

- Neurovisceral Integration (Thayer and Lane, 2000)
- Central Autonomic Network (Benarroch, 1993; 1997)
- Polyvagal Theory (Porges, 1995)
- Calm, restful visceral states promote interconnected social behaviors (e.g., eye contact, social orienting), whereas aroused states inhibit the Social Engagement System.

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Given the hypothesized connection with autonomic arousal and social engagement, understanding atypical functioning of the ANS may be particularly relevant for youth with ASD (Porges, 2005).

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DSM-5 Criteria for Autism Spectrum Disorder (ASD)

A. Persistent deficits in social communication and interaction
B. Restricted, repetitive patterns of behavior, interests, or activities
C. Symptoms present in early childhood
D. Symptoms limit and impair everyday functioning

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ASD

Physiology

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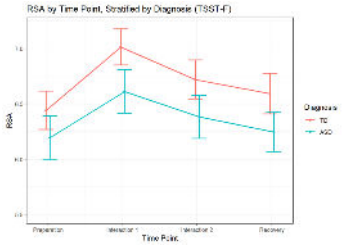
Reduced Parasympathetic Regulation in Adolescents with ASD



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Other Important Variables to Consider – Body Mass Index (BMI)

- Autonomic functioning and BMI highly correlated (e.g., Eyre et al., 2014)
- Weight loss associated with increased parasympathetic control and reduced sympathetic activation (Arone et al., 1995)
- High rates of overweight (18.0 – 42.0%) and obesity (10.0 – 30.4%) in autism (e.g., Corbett et al., 2020; Criado et al., 2018; Curtin et al., 2010).

Table 2 Percentage of ASD and TD participants falling into each BMI category

BMI category	TD (N = 103)	ASD (N = 126)	Total
Underweight	3.0% (n = 3)	4.5% (n = 6)	3.8% (n = 9)
Healthy weight	69.9% (n = 69)	53.8% (n = 71)	60.2% (n = 142)
Overweight	12.9% (n = 12)	13.6% (n = 18)	13.1% (n = 31)
Obese	16.0% (n = 16)	28.0% (n = 38)	22.9% (n = 54)
Total	100%	100%	100%

Underweight, <5th percentile; Healthy weight, 5th to <85th percentile; Overweight, 85th to <95th percentile; Obese, ≥ 95th percentile

Corbett, Muscatello, et al., 2021, *JADD*

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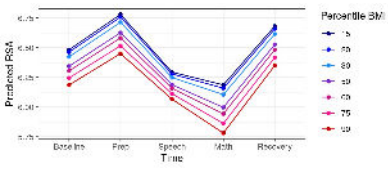
Elevated BMI and Reduced RSA



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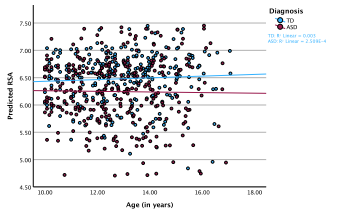
Parasympathetic regulation is stable over adolescence in ASD and NT youth



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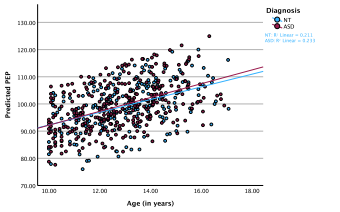
Sympathetic control decreases (PEP increases) over advancing age and puberty



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Primary Findings

1. Some diagnostic differences in PNS regulation, but no evidence for differences in sympathetic activation.

2. Diagnostic differences may be driven by BMI and psychotropic medication use.

3. Autistic and neurotypical youth show similar autonomic developmental trajectories- stable parasympathetic regulation and reduced sympathetic control over time.

4. While autonomic differences appear to be present in ASD, there is a need to embrace a trait-based approach.

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Social Interactions and Stress

- Social interactions may be:
  - Significant source of anxiety (Bellini et al., 2006)
  - Significant source of stress (e.g., Corbett et al., 2010)
- Psychological stress occurs when environment is perceived as too demanding and is often context- and experience-dependent.

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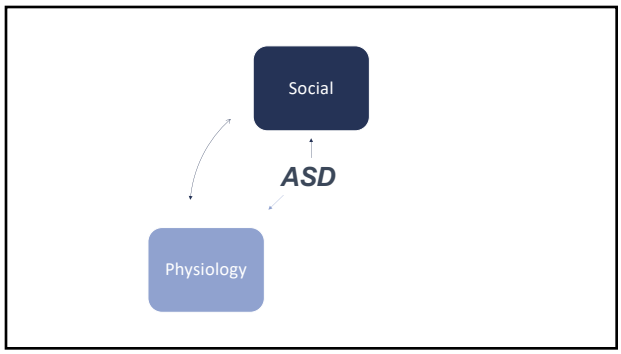

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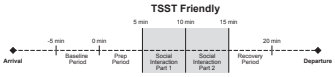
Social Interaction: Trier Social Stress Test-Friendly (TSST-F)

- Adapted from original TSST (Kirschbaum, 1993) to be a more friendly interaction.
- Twenty-minute social paradigm with a novel peer.



TSST-F adapted from: Wiemers et al., 2013, *Stress*

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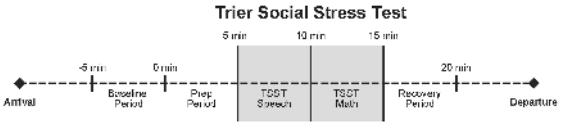
Social Evaluation: Trier Social Stress Test (TSST)



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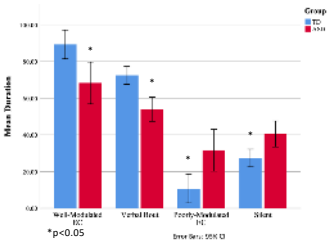
Children with ASD engage in less verbal interaction and less eye contact



Muscatello et al., unpublished data

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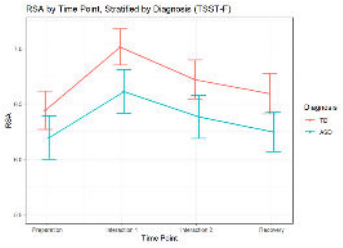
Lower RSA mean but not reactivity during TSST-F



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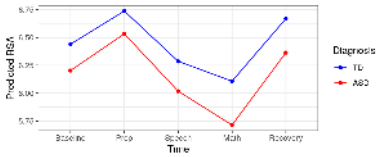
Lower RSA mean but not reactivity in ASD during TSST



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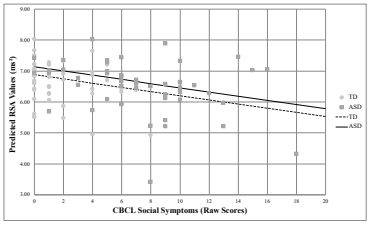
Reductions in Mean RSA Correlated with Increased Social Severity



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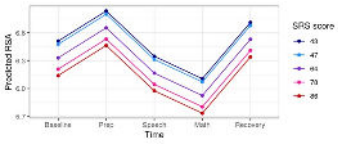
Social Symptom Severity Associated with Lower Mean RSA



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Social Function and the ANS

Autistic youth demonstrate similar parasympathetic reactivity patterns to social stressors, regardless of context.

Increased severity of parent-reported social symptoms were associated with lower overall RSA.

Research to this point has focused on parasympathetic system. Extent to which sympathetic activation differs in autistic youth remains under studied.

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Clinical Implications – Physiology and Internalizing Symptoms

- Anxiety and depression, the statistics:
  - Estimated 20.1% of youth ages 12 to 17 reported at least one major depressive episode in 2021 (Substance Abuse and Mental Health Services Administration, 2022).
  - Estimated 31.9% of any anxiety disorder (National Comorbidity Survey Adolescent Supplement, 2009).
- In ASD:
  - Recent surveys reported 4.8% prevalence of depression in children ages 4 to 8 and 20.2% in adolescents 13 to 17 (Greenlee et al., 2016, *Pediatrics*).
  - Lifetime depression prevalence estimated to reach 40.2% by adulthood (Hudson et al., 2019, *J Abnorm Child Psychol).*
  - One in two individuals with ASD may have an anxiety disorder (Hofvander et al., 2009, *BMC Psychiatry).*

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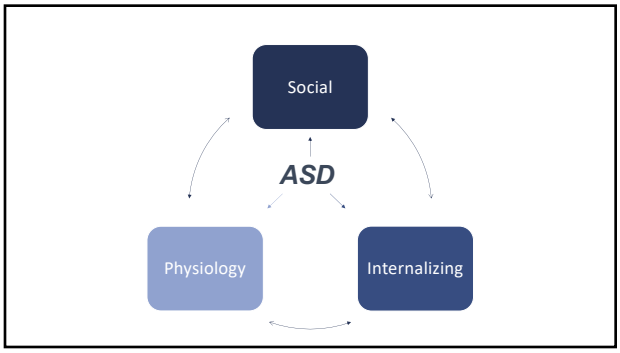

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The Autonomic Nervous System and Internalizing Disorders

- Neurovisceral Integration and Central Autonomic Control: Overlap of brain regions regulating executive attention, emotion regulation, and autonomic activity
- Lower resting-state PNS regulation in:
  - Depression (e.g., Koenig et al., 2016)
  - Anxiety (e.g., Chalmers et al., 2014)
  - Conduct Disorders (e.g., Beauchaine et al., 2007)
  - Non-suicidal Self-injury (e.g., Crowell et al., 2005)

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Worsening Internalizing Symptoms Associated with Social Withdrawal

	Well-Mod EC	Poor-Mod EC	Reciprocal Verbal Bout	Silent	Involvement	Rapport
Parent-Report						
CBCL Affective	-0.08	0.08	**-0.23***	**0.23***	**-0.20***	**-0.21***
CBCL Anxiety	-0.14	0.14	**-0.28***	0.16	**-0.21***	**-0.23***
MASC-P	-0.16	0.16	**-0.29***	0.19	-0.16	-0.14
MASC-SA	-0.07	0.07	-0.13	0.11	-0.07	-0.02
Self-Report						
MASC-S	**-0.31***	0.31	-0.17	**0.20***	**-0.30***	**-0.33***
MASC-SA	-0.14	0.14	-0.08	0.08	**-0.22***	**-0.28***
CDI	-0.18	-0.18	-0.13	0.05	-0.13	-0.10

Muscatello et al., unpublished data

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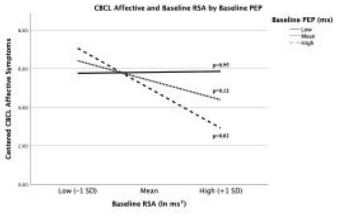
In ASD, Low SNS and High PNS Predict Lowest Affective Symptoms



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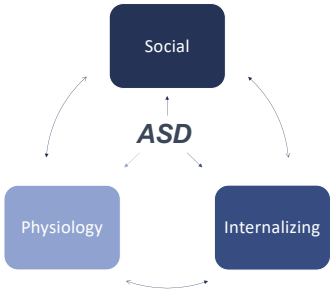

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Future Directions

- Focus has largely been on parasympathetic nervous system, while less is known about sympathetic activity in ASD
- Utility of HRV as a biomarker in ASD
- Transdiagnostic autonomic response profiles
- Identifying possible areas of intervention

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Key Takeaways

- Growing evidence supports differences in autonomic function in autistic individuals
- Individual characteristics matter– Influence of BMI, medication usage, social functioning
- Physiological differences may have implications for psychological function (e.g., internalizing conditions)
- More work is needed to understand if HRV can be utilized as a transdiagnostic versus ASD-specific biomarker

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