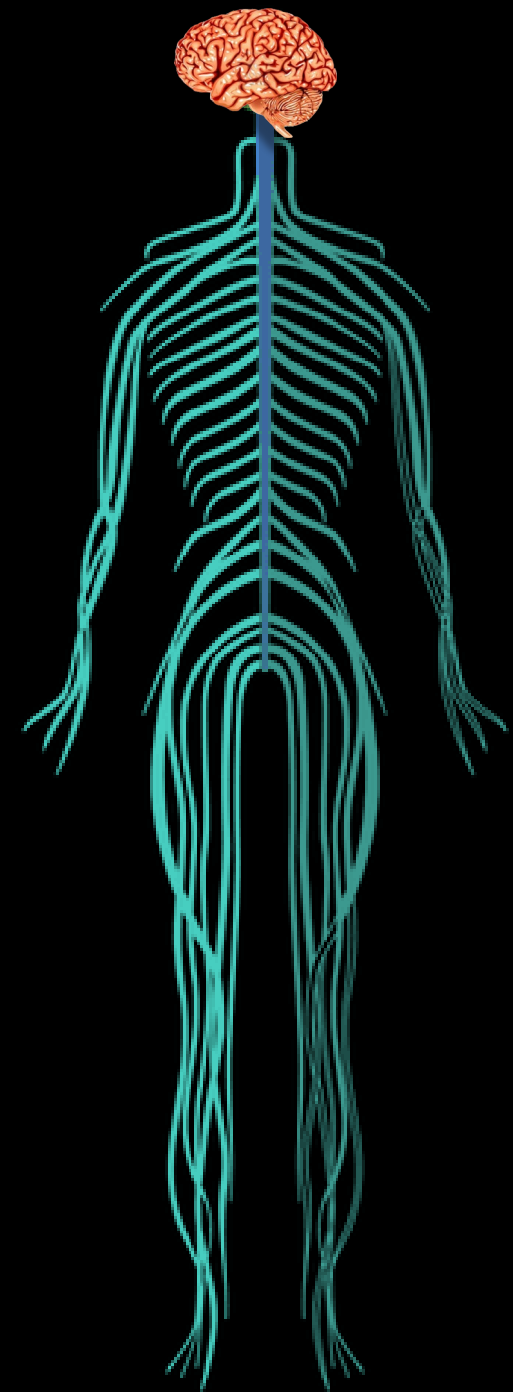
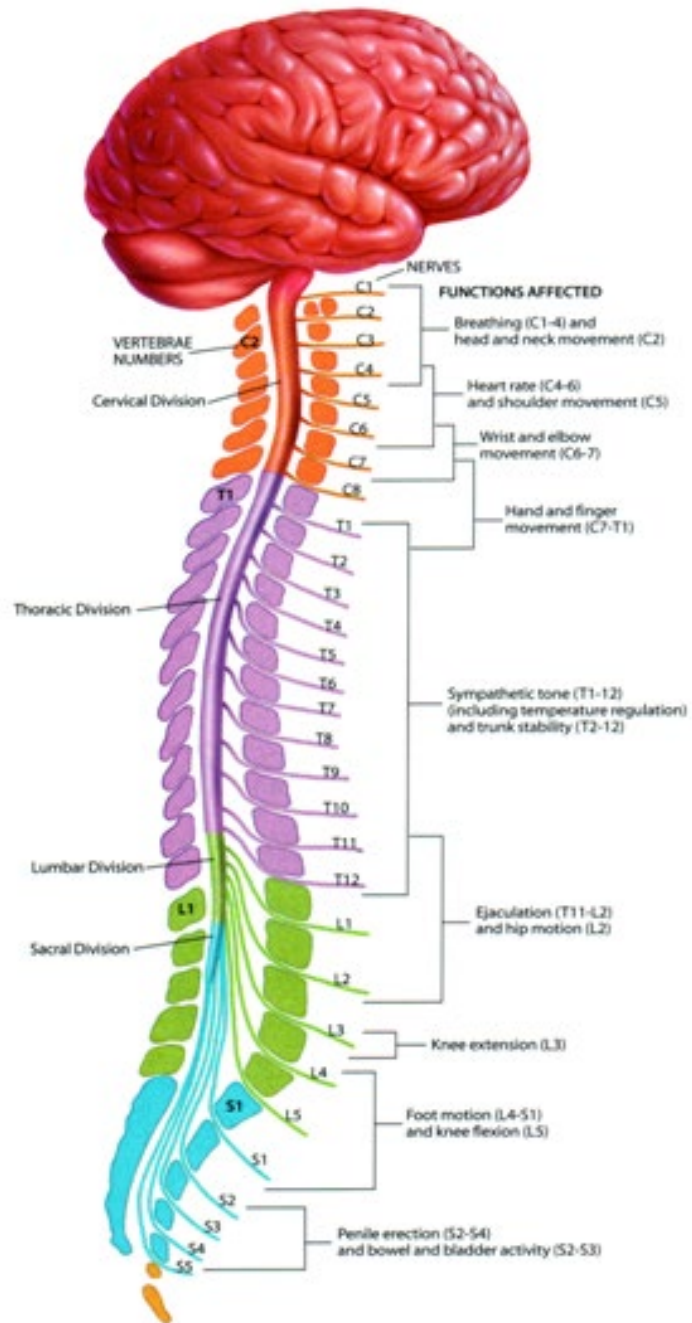


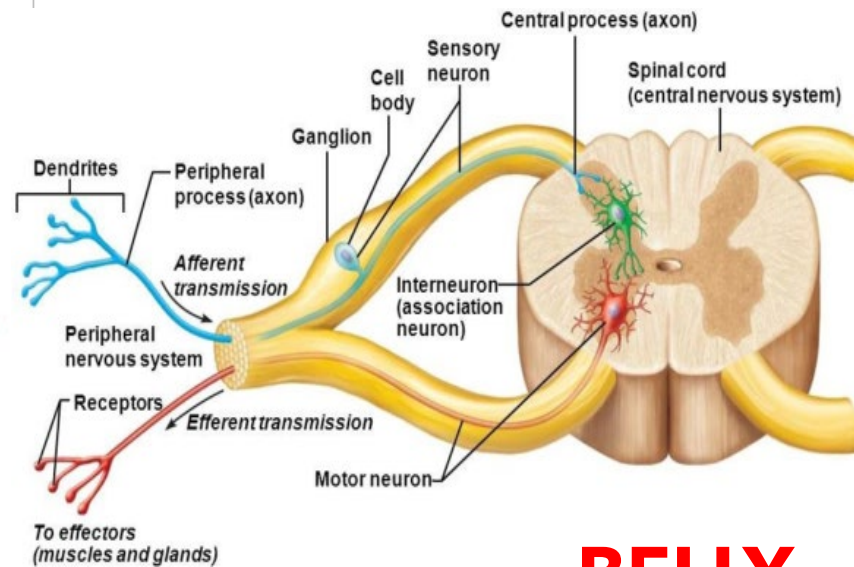
HOW THE AUTONOMIC NERVOUS SYSTEM MAY GOVERN ANXIETY IN AUTISM

Emily L. Casanova, PhD
Manuel F. Casanova, MD



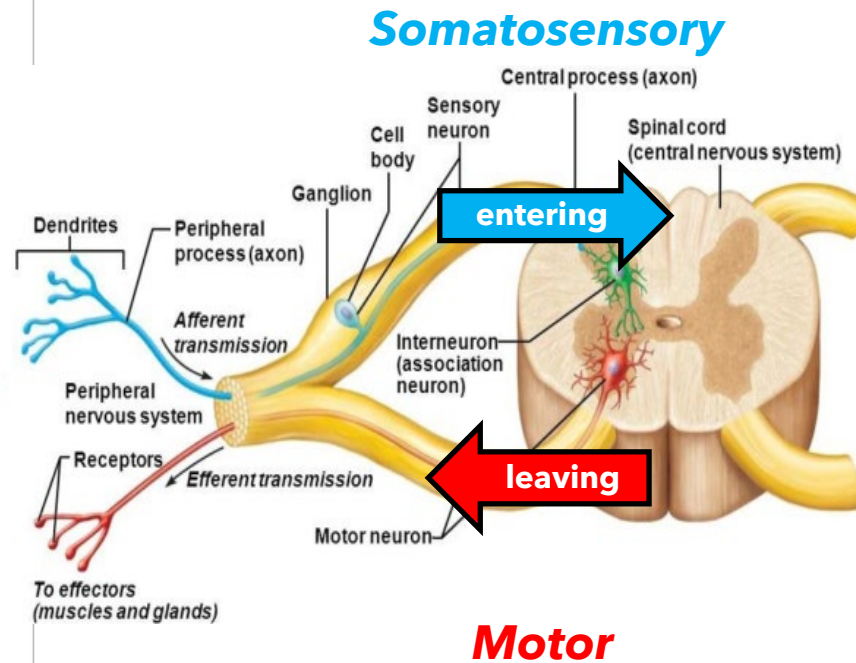
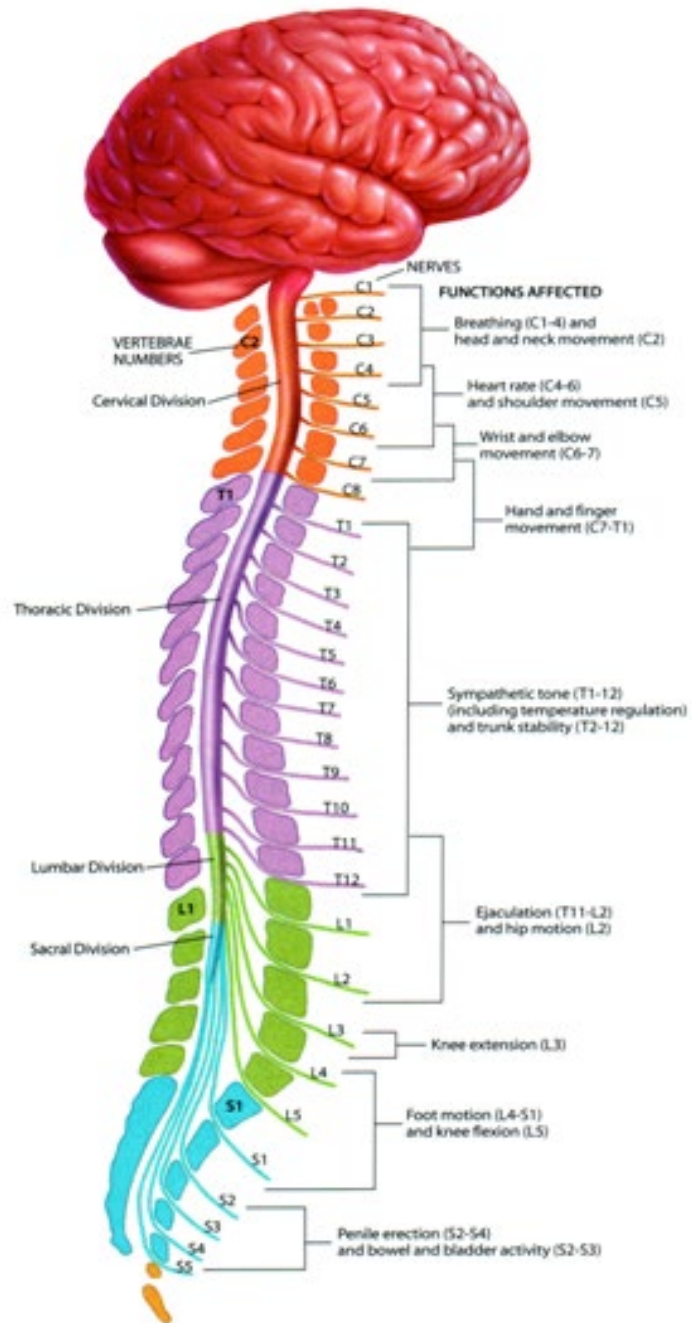


BACK
(aka "dorsal")



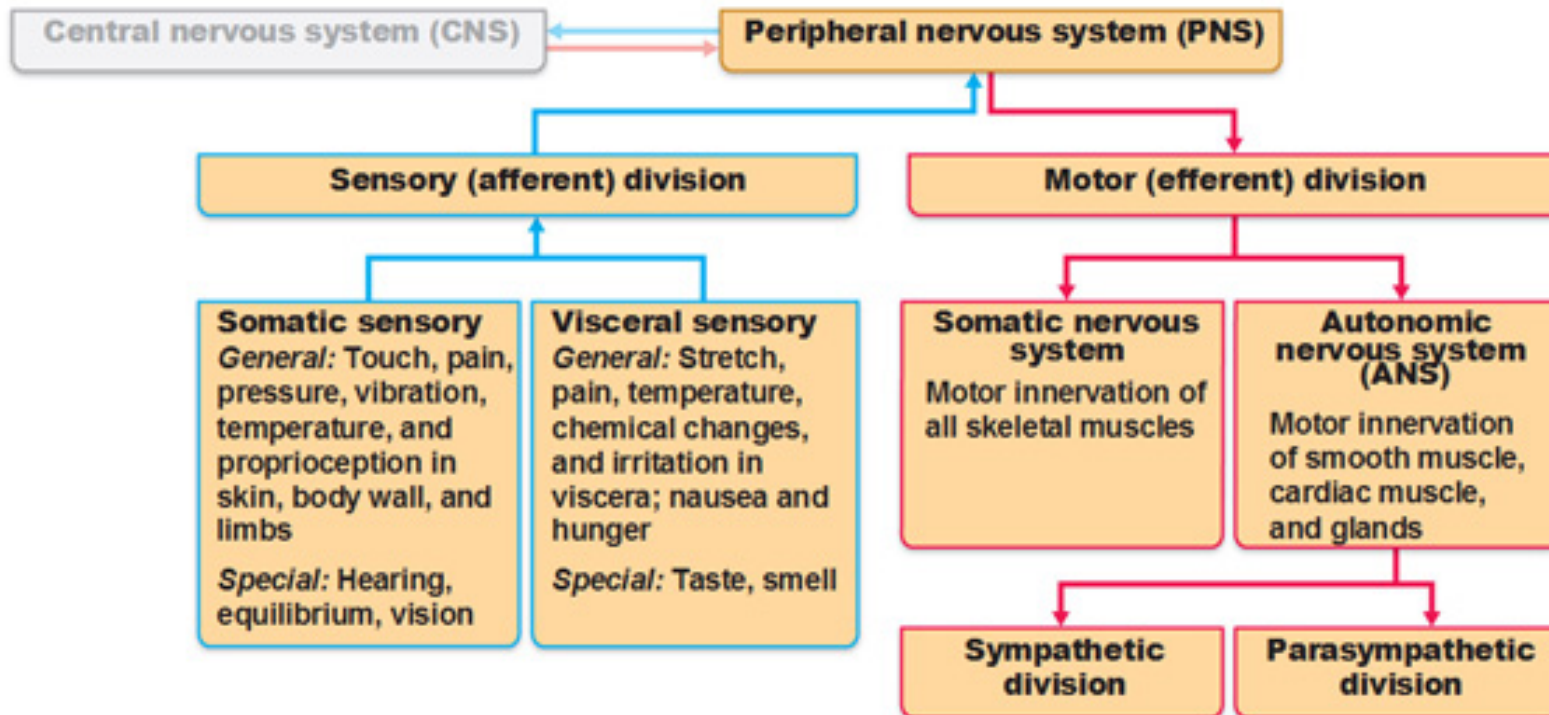
BELLY
(aka "ventral")

THE CENTRAL NERVOUS SYSTEM



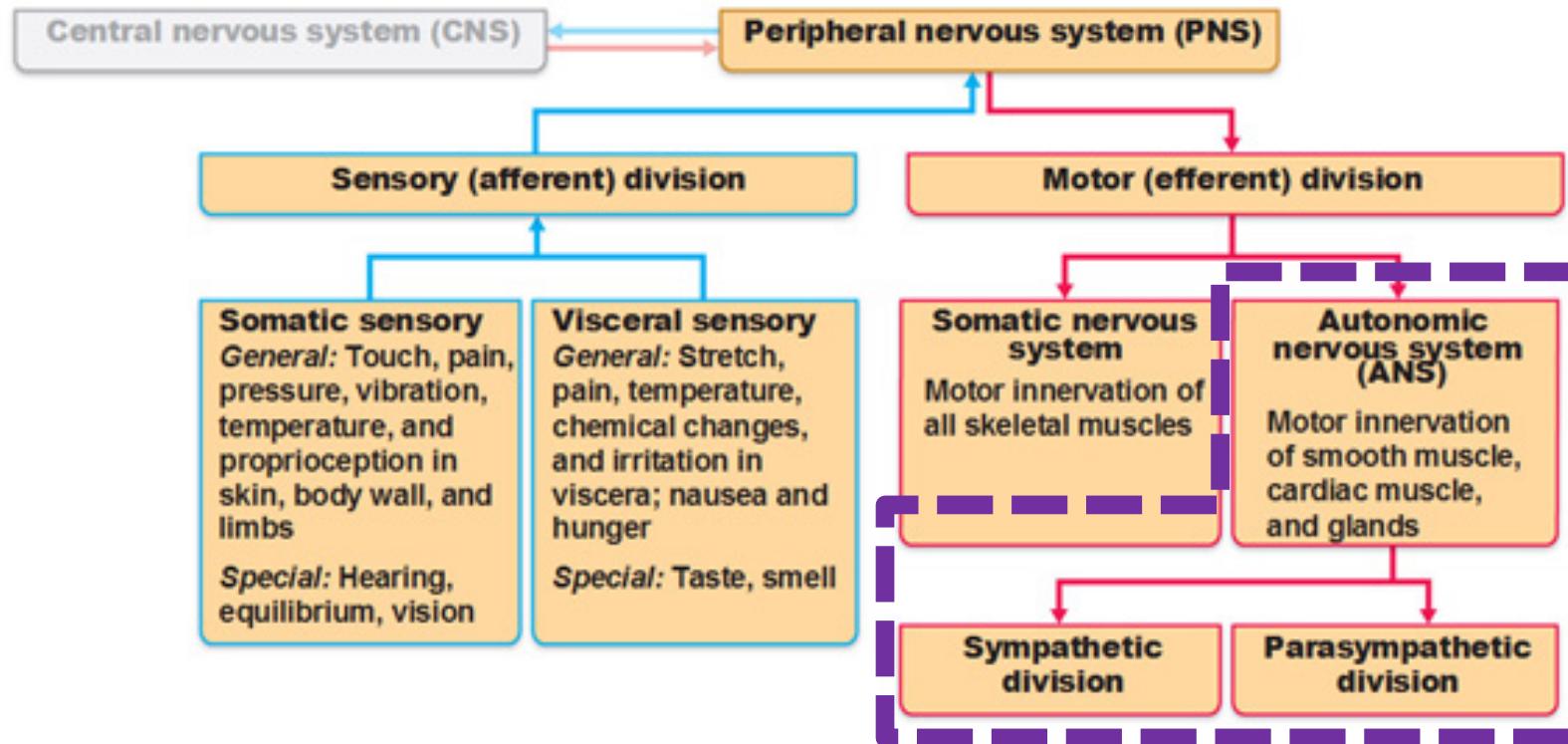
THE CENTRAL NERVOUS SYSTEM

Functional Organization of the PNS



THE PERIPHERAL NERVOUS SYSTEM

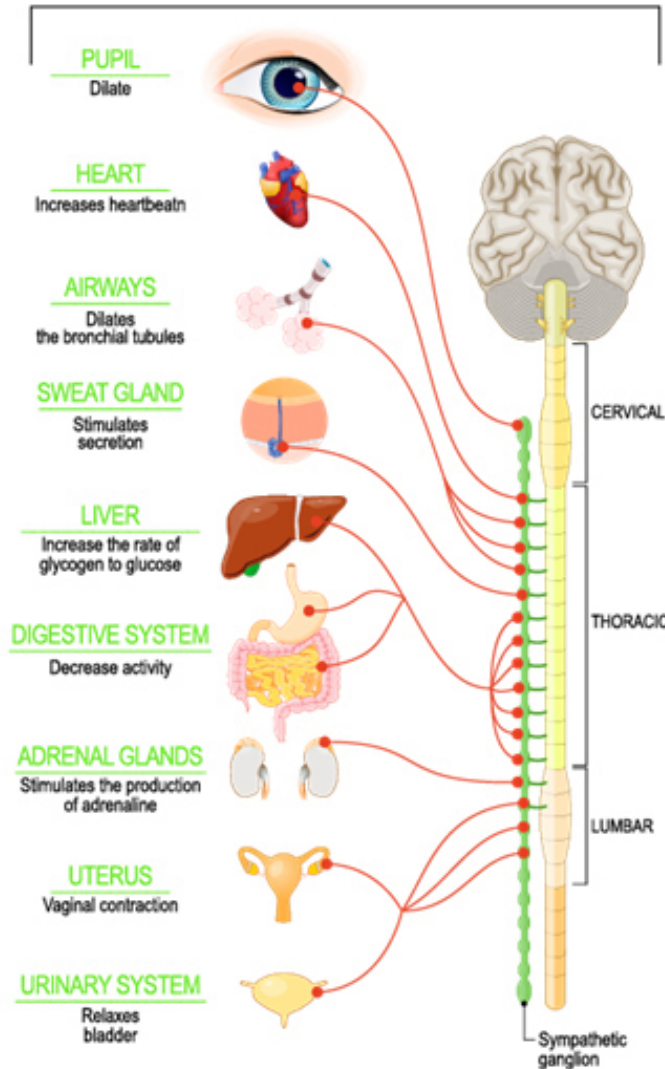
Functional Organization of the PNS



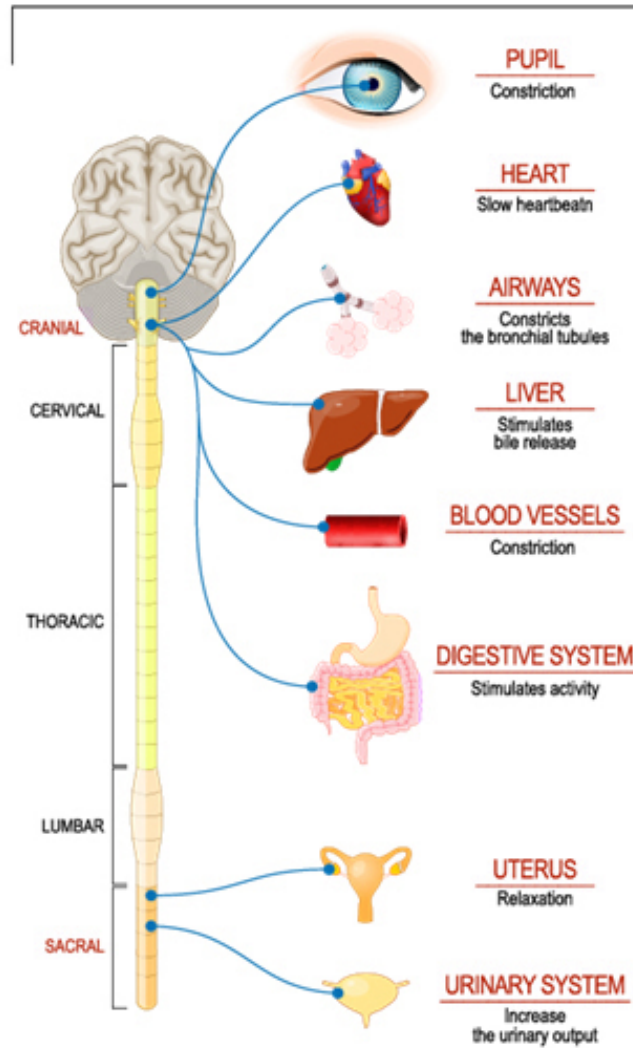
THE PERIPHERAL NERVOUS SYSTEM

Autonomic Nervous System

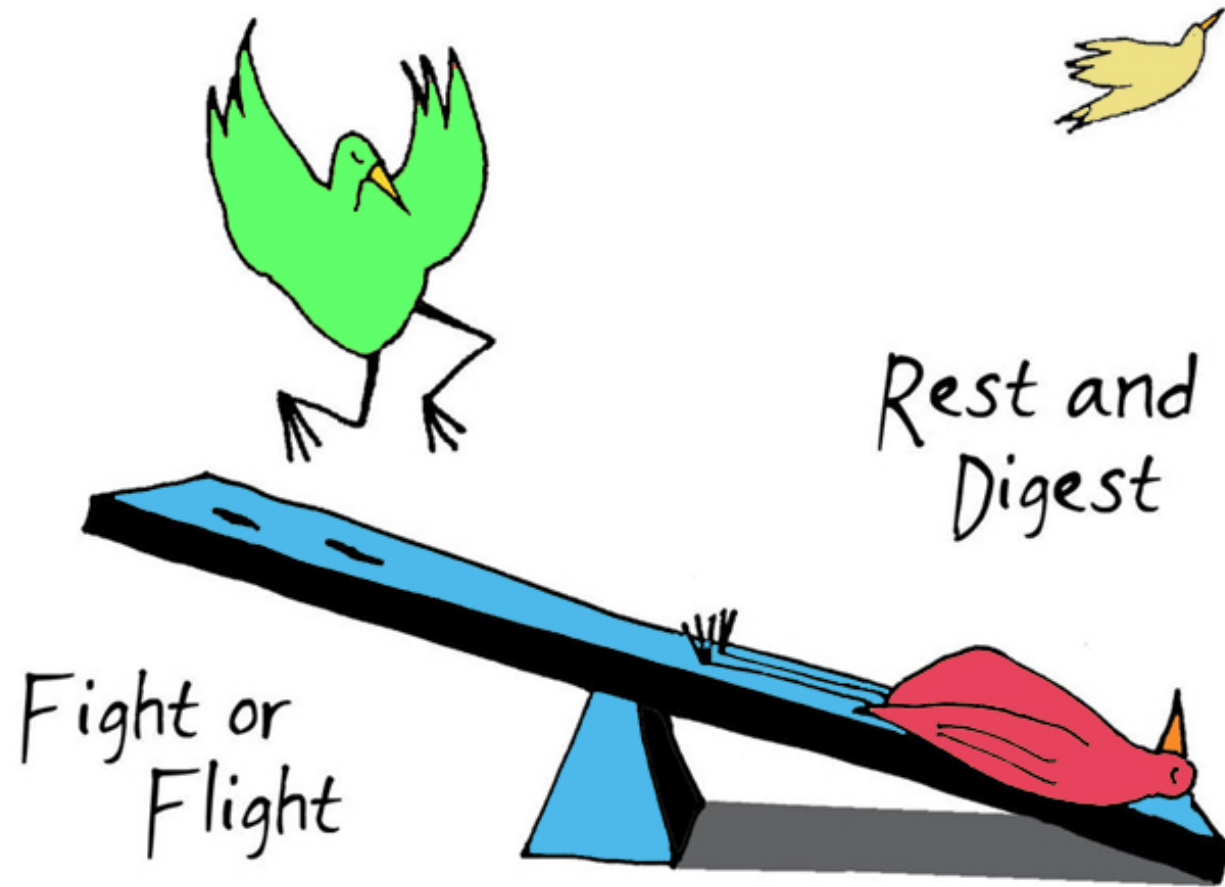
"Fight or Flight"
Sympathetic



"Rest and Digest"
Parasympathetic



THE PERIPHERAL NERVOUS SYSTEM





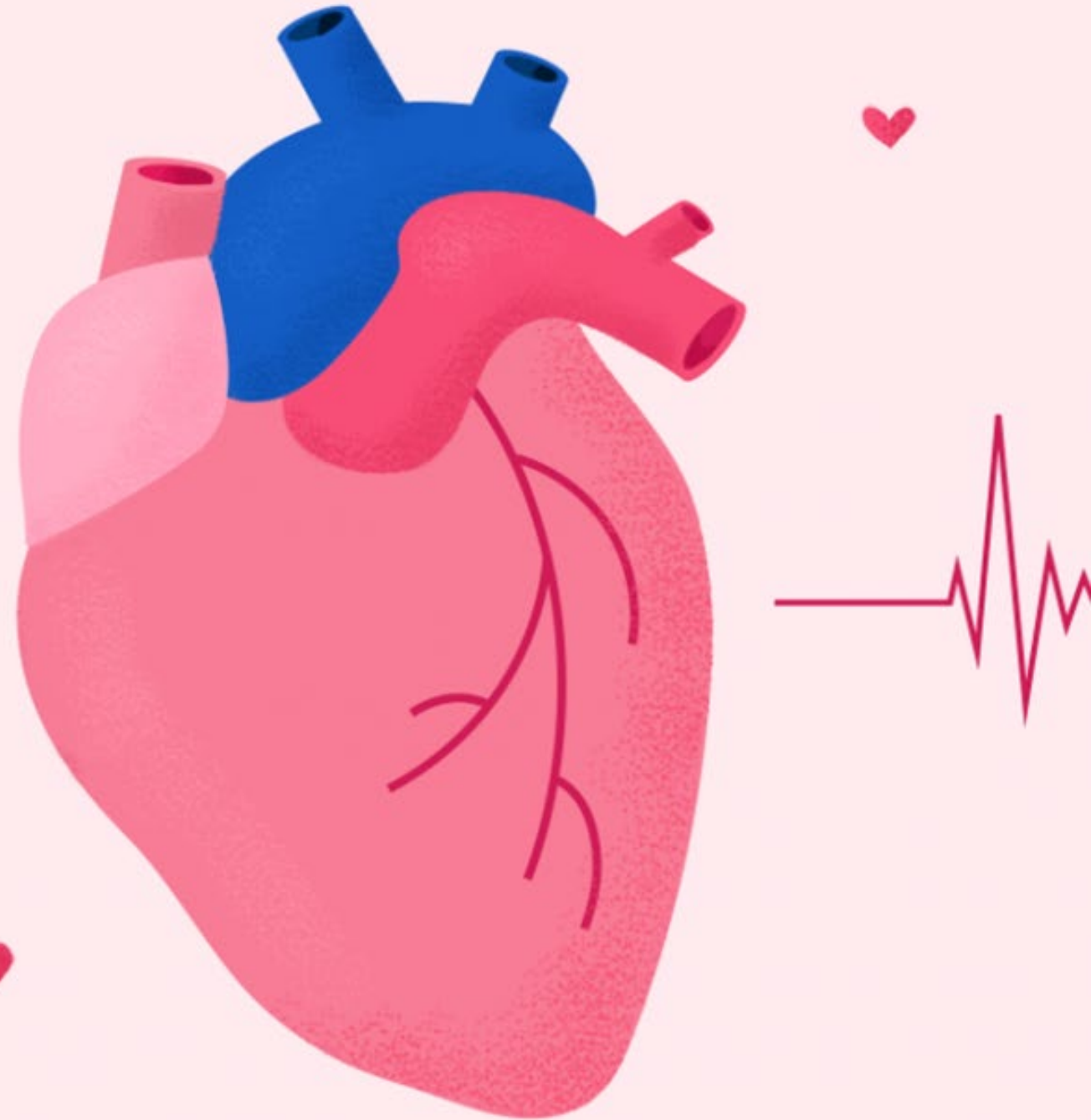
Sympathetic

Parasympatheti

C

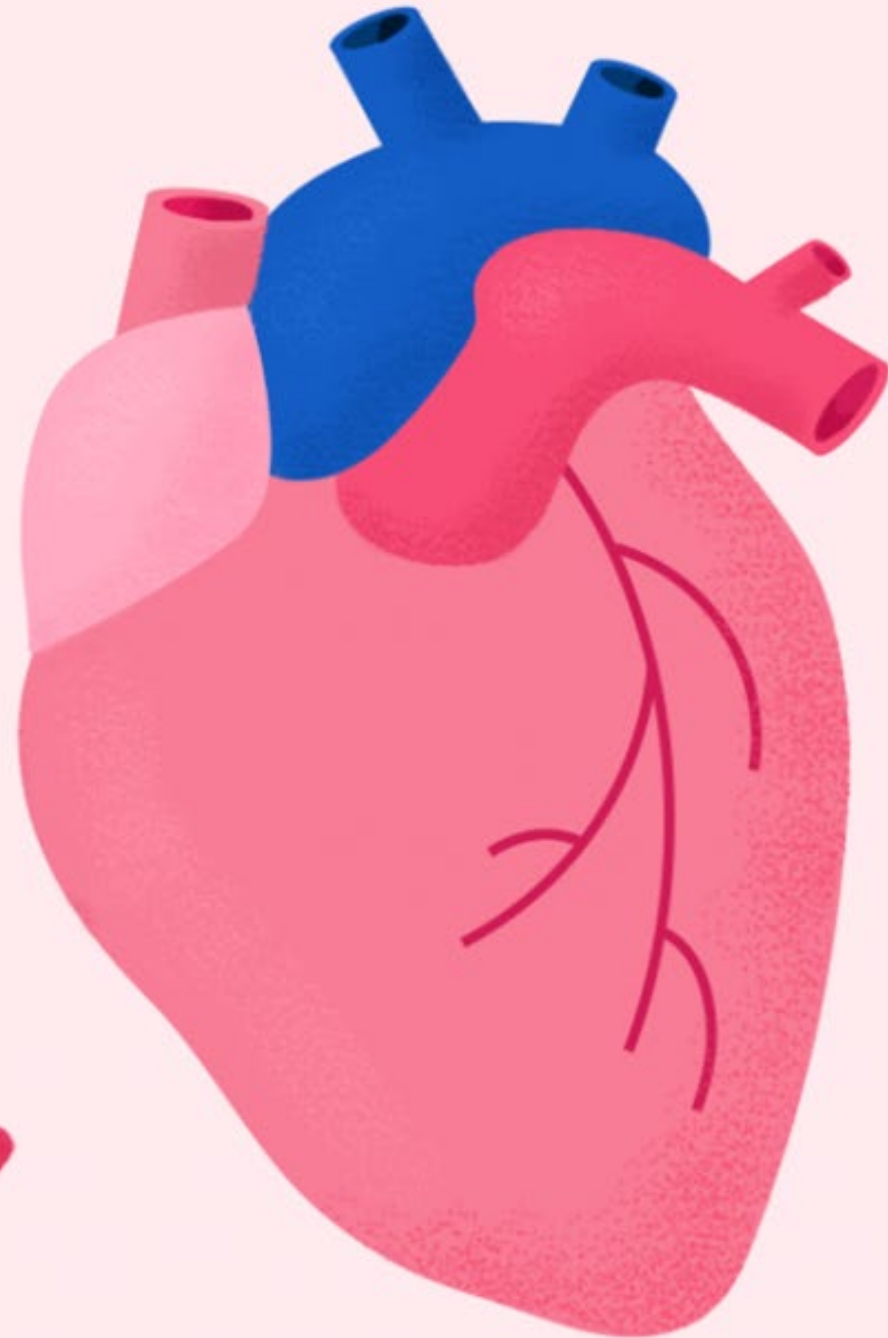
Autonomic Dysregulation in Autism

- **Autistic people tend to exhibit:**
 - Higher at-rest **sympathetic (fight or flight)** activation, as evidenced by:



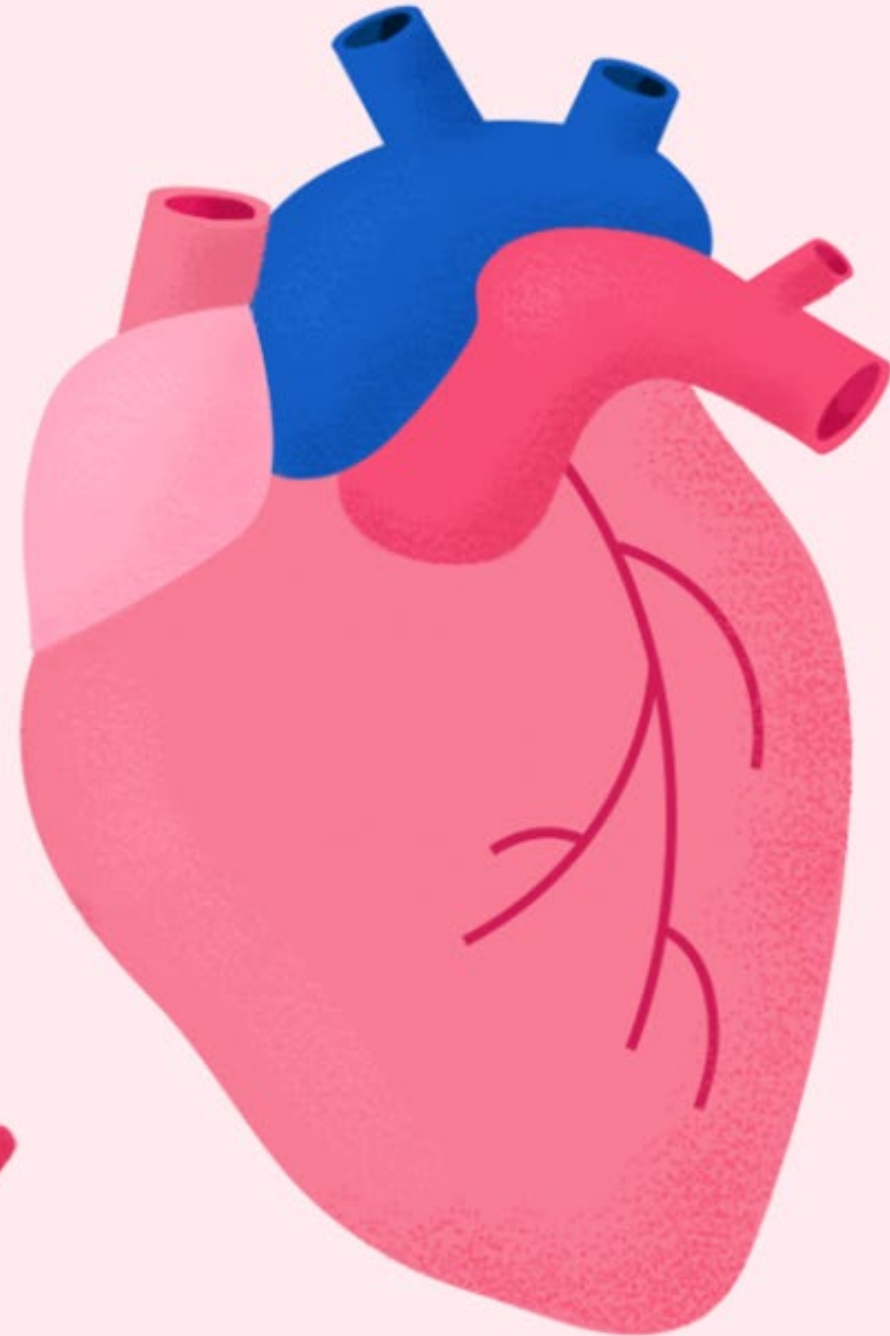
Autonomic Dysregulation in Autism

- **Autistic people tend to exhibit:**
 - Higher at-rest **sympathetic (fight or flight)** activation, as evidenced by:
 - Higher resting heart rate^{1,2}



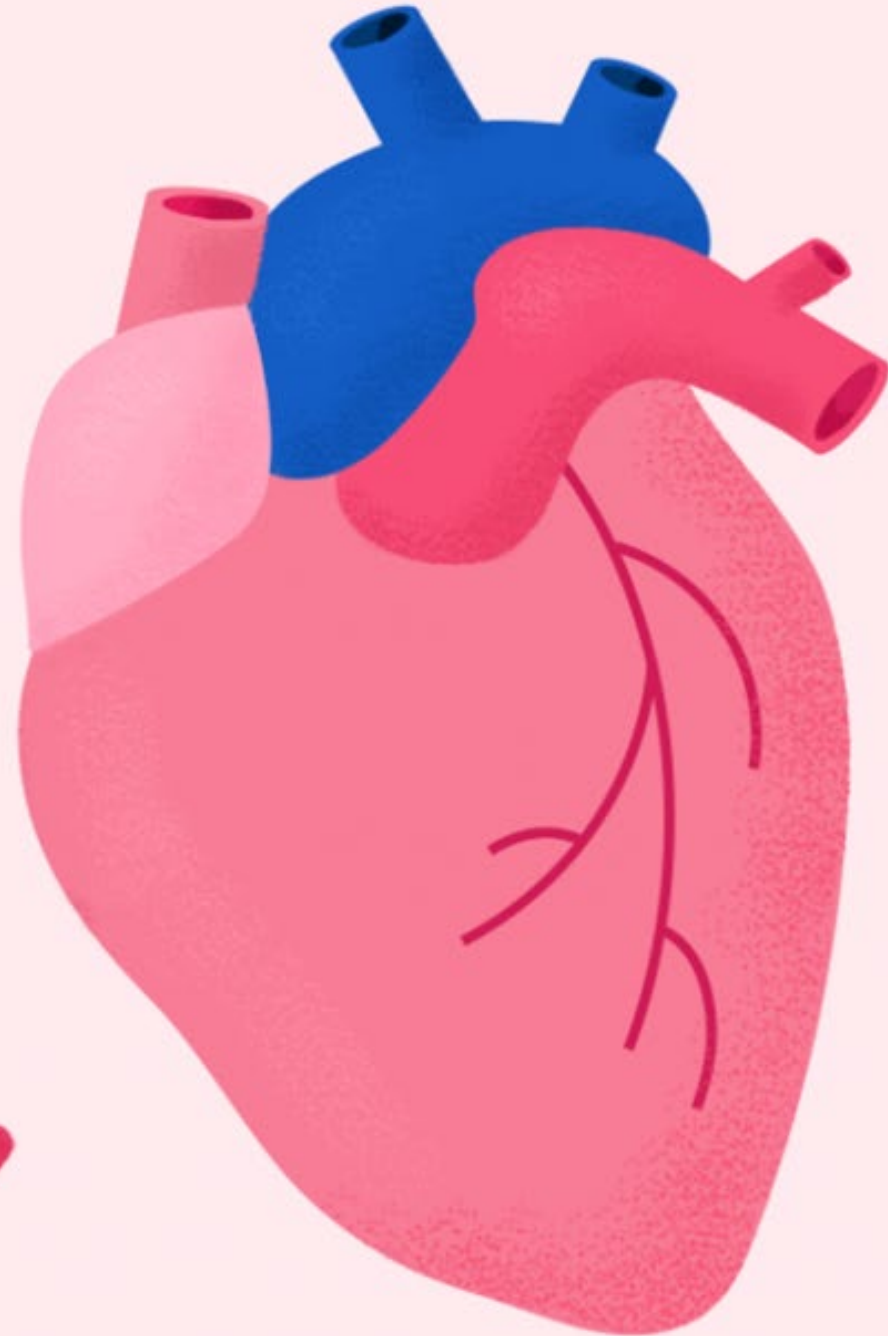
Autonomic Dysregulation in Autism

- **Autistic people tend to exhibit:**
 - Higher at-rest **sympathetic (fight or flight)** activation, as evidenced by:
 - Higher resting heart rate^{1,2}
 - Increased pupil size³



Autonomic Dysregulation in Autism

- **Autistic people tend to exhibit:**
 - Higher at-rest **sympathetic (fight or flight)** activation, as evidenced by:
 - Higher resting heart rate^{1,2}
 - Increased pupil size³
 - Higher respiration rate⁴



The 4 Stages of Sleep



NREM Stage 1

- transition period between wakefulness and sleep
- lasts around 5 to 10 minutes



NREM Stage 3

- muscles relax
- blood pressure and breathing rate drop
- deepest sleep occurs



NREM Stage 2

- body temperature drops and heart rate begins to slow
- brain begins to produce sleep spindles
- lasts approximately 20 minutes



REM Sleep

- brain becomes more active
- body becomes relaxed and immobilized
- dreams occur
- eyes move rapidly

Autonomic Dysregulation in Autism

- **Autistic people tend to exhibit:**
 - Higher **sympathetic** (fight or flight) activation during:
 - Certain stages of sleep (N2, N3, REM)⁵

The 4 Stages of Sleep



Autonomic Dysregulation in Autism

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Autonomic Dysregulation in Autism

- **Autistic people tend to exhibit:**
 - Higher **sympathetic (fight or flight)** activation during:
 - Certain stages of sleep (N2, N3, REM)⁵
 - Social interaction with peers⁶

**Animals lower arousal in ASD
during peer interactions!**



Autonomic Dysregulation in Autism

- **Autistic people tend to exhibit:**
 - Higher **sympathetic (fight or flight)** activation during:
 - Certain stages of sleep (N2, N3, REM)⁵
 - Social interaction with peers⁶

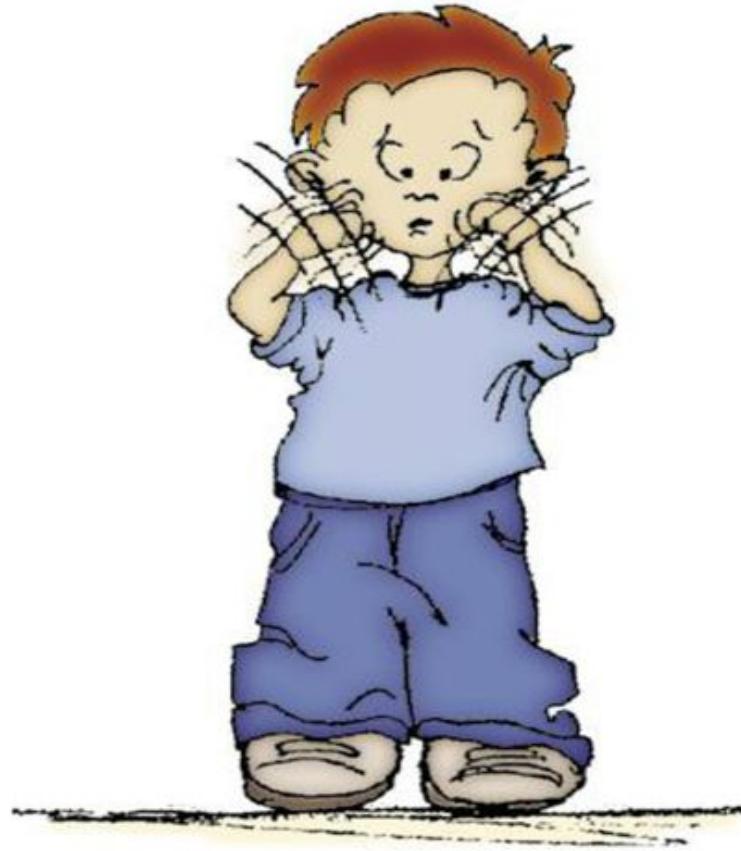
BUT...

Spinning and hand flapping



And... autistic people often use **stimulatory behaviors** to reduce sympathetic hyperarousal.⁷

Spinning and hand flapping



In fact, these probably shouldn't be called "stimulatory" behaviors but "calming" behaviors.

**But a small percentage
of autistic people have
low sympathetic
activation, except
during self-injurious
behavior.⁷**



These may more accurately be called "stimulatory" behaviors.





Autonomic Dysregulation in Autism

- **Autistic people tend to exhibit:**
 - Lower **sympathetic (fight or flight)** activation during:
 - Fear-eliciting responses (toddlers)⁸



Autonomic Dysregulation in Autism

- **Autistic people tend to exhibit:**
 - Lower **parasympathetic (rest and digest)** activity during the morning⁹



Autonomic Dysregulation in Autism

- **Autistic people with lower *parasympathetic tone* tend to:**
 - Have greater symptoms of anxiety^{10, 11}



Autonomic Dysregulation in Autism

- **Autistic people with lower *parasympathetic tone* tend to:**
 - Have greater symptoms of anxiety^{10, 11}
 - Poorer social skills¹²



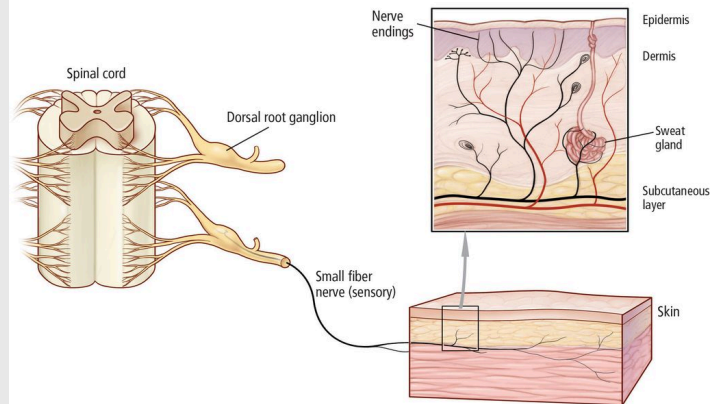
Autonomic Dysregulation in Autism

- **Autistic people with lower *parasympathetic tone* tend to:**
 - Have greater symptoms of anxiety^{10, 11}
 - Poorer social skills¹²
 - Lower GI tract problems (e.g., constipation), common with regression¹³

Nerve Fiber Loss in Some Kids with Autism

Small fiber neuropathy affects sensory nerves

Small fiber neuropathy is a major cause of pain in the hands and feet, especially in the elderly. Diabetes mellitus is the most common identifiable cause, but there are many others. The nerve fibers affected are small-diameter myelinated A-delta fibers and unmyelinated C fibers, which mediate pain, thermal sensation, and autonomic function. Large fibers that innervate muscles are not affected. Skin biopsy may show a paucity of nerve fibers. Quantitative sudomotor axon reflex testing may show a lack of sweating in response to acetylcholine.

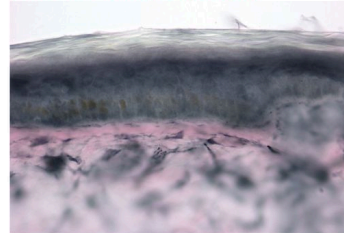


Normal skin biopsy



Normal innervation with small nerve fibers seen in the epidermis (arrows). Skin biopsy specimens with protein gene product 9.5 immunostaining.

Small fiber neuropathy biopsy



A specimen from a patient with small fiber neuropathy shows denervation, with no small nerve fibers seen in the epidermis.

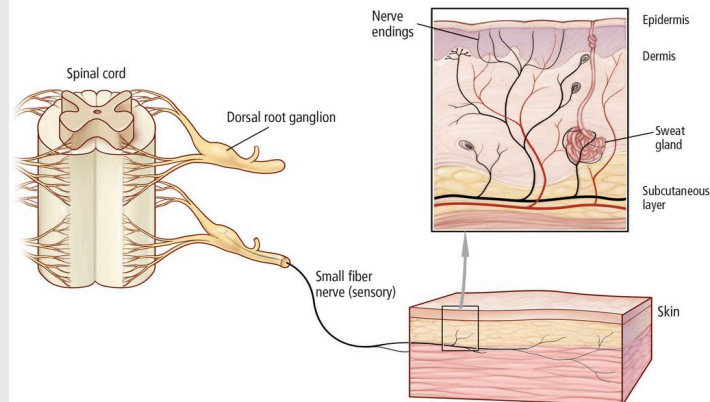
Tavee J, Zhou L. Small fiber neuropathy: a burning problem. *Cleve Clin J Med* 2009; 76(5):297-305. doi:10.3949/ccjm.76a.08070

- Loss of small unmyelinated C-fibers in the skin in autistic children with reduced sensation (including pain)¹⁴
- This type of small fiber is also involved in the **autonomic nervous system**

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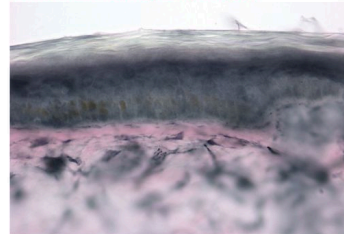


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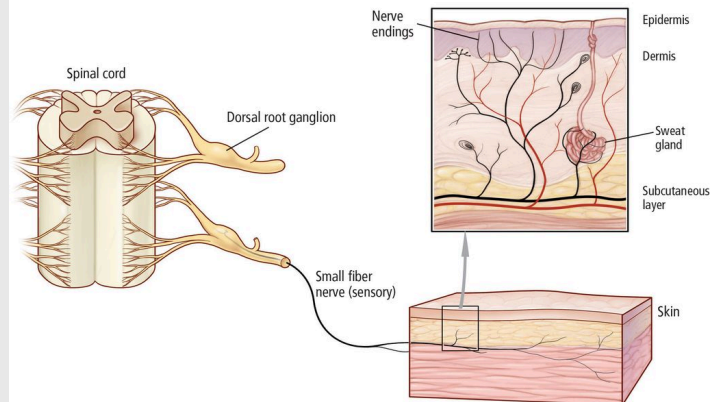
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- Loss of small unmyelinated C-fibers in the skin in autistic children with reduced sensation (including pain)¹⁴
- This type of small fiber is also involved in the autonomic nervous system
- **Small Fiber Neuropathy has been implicated in:**
 - GI motility disorders
 - Sleep disorders
 - Pain disorders
 - Altered temperature perception

Nerve Fiber Loss in Some Kids with Autism

Small fiber neuropathy affects sensory nerves

Small fiber neuropathy is a major cause of pain in the hands and feet, especially in the elderly. Diabetes mellitus is the most common identifiable cause, but there are many others. The nerve fibers affected are small-diameter myelinated A-delta fibers and unmyelinated C fibers, which mediate pain, thermal sensation, and autonomic function. Large fibers that innervate muscles are not affected. Skin biopsy may show a paucity of nerve fibers. Quantitative sudomotor axon reflex testing may show a lack of sweating in response to acetylcholine.

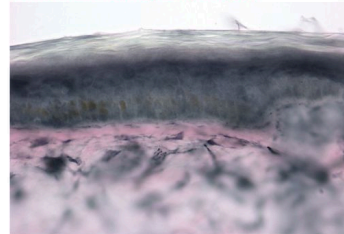


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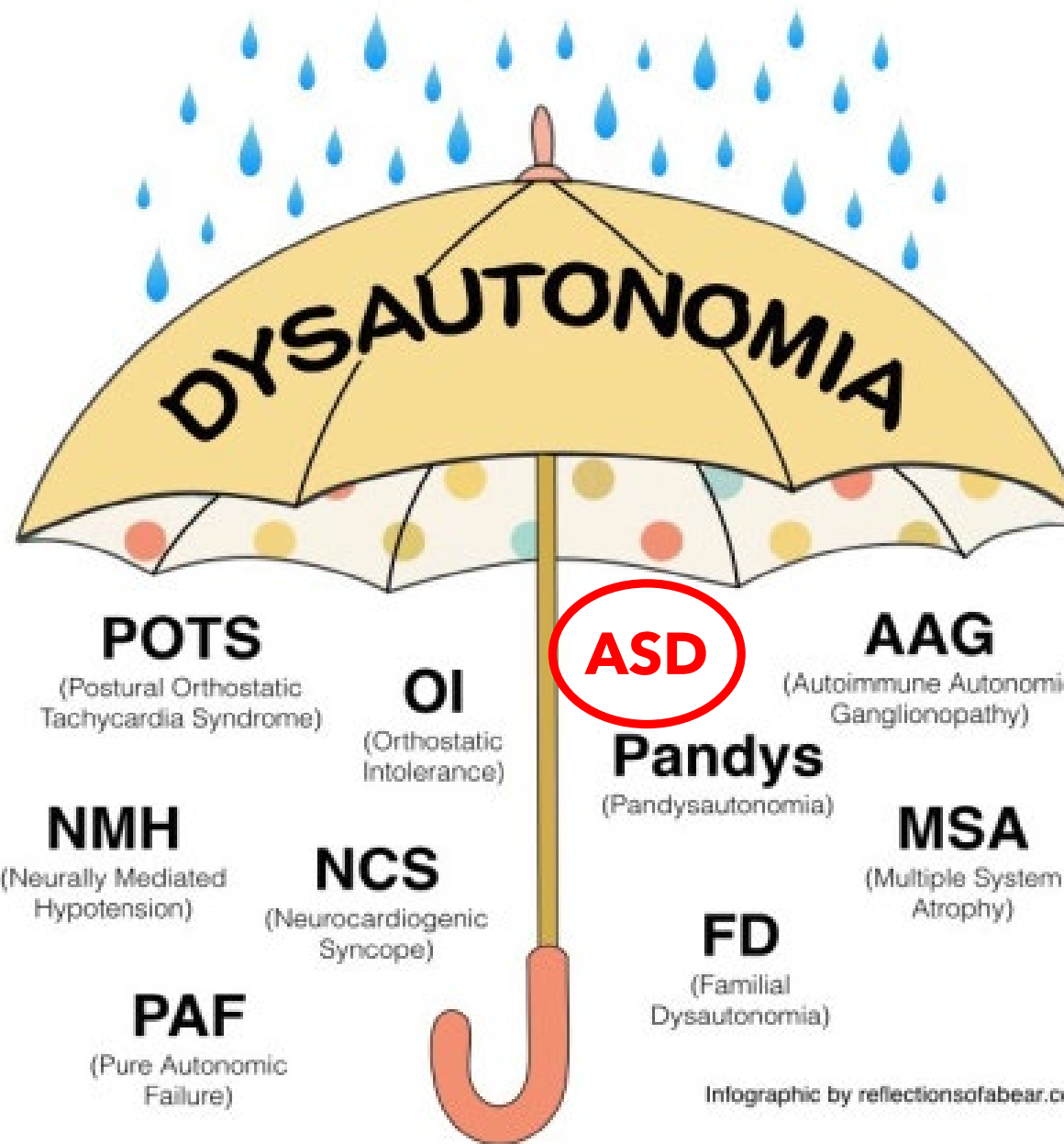
- Loss of small unmyelinated C-fibers in the skin in autistic children with reduced sensation (including pain)¹⁴
- This type of small fiber is also involved in the autonomic nervous system
- **We see this same kind of small fiber loss in Ehlers-Danlos syndrome/hypermobility spectrum disorders.**
- Previous ARI webinar on autism and hypermobility-related disorders:

<https://www.autism.org/hypermobility-asd/>

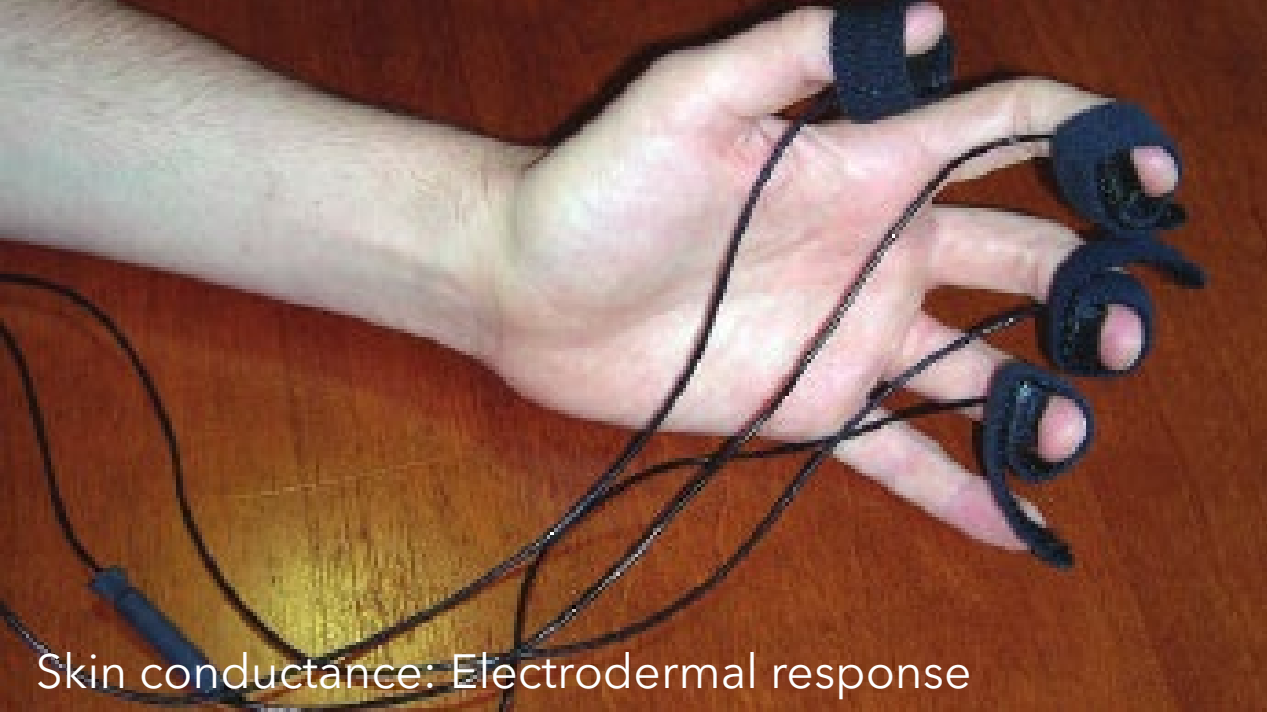
Other Materials on EDS & Autism:

- **"What Ehlers-Danlos Syndrome Can Teach Us About Autism" - Spectrum News**
<https://www.spectrumnews.org/opinion/viewpoint/what-ehlers-danlos-syndrome-can-teach-us-about-autism/>
- **"Researchers Have Identified a Relationship between Ehlers-Danlos Syndrome and Autism" - Autism Research Institute**
<https://www.autism.org/researchers-have-identified-a-relationship-between-ehlers-danlos-syndrome-and-autism/>
- **"Sensory Issues in Ehlers-Danlos Syndromes and Hypermobility Spectrum Disorders" - TheMighty**
<https://themighty.com/2020/10/overlap-ehlers-danlos-syndrome-autism/>
- **Emily's Blog: "Science Over a Cuppa" -**
<https://scienceoveracuppa.com/>

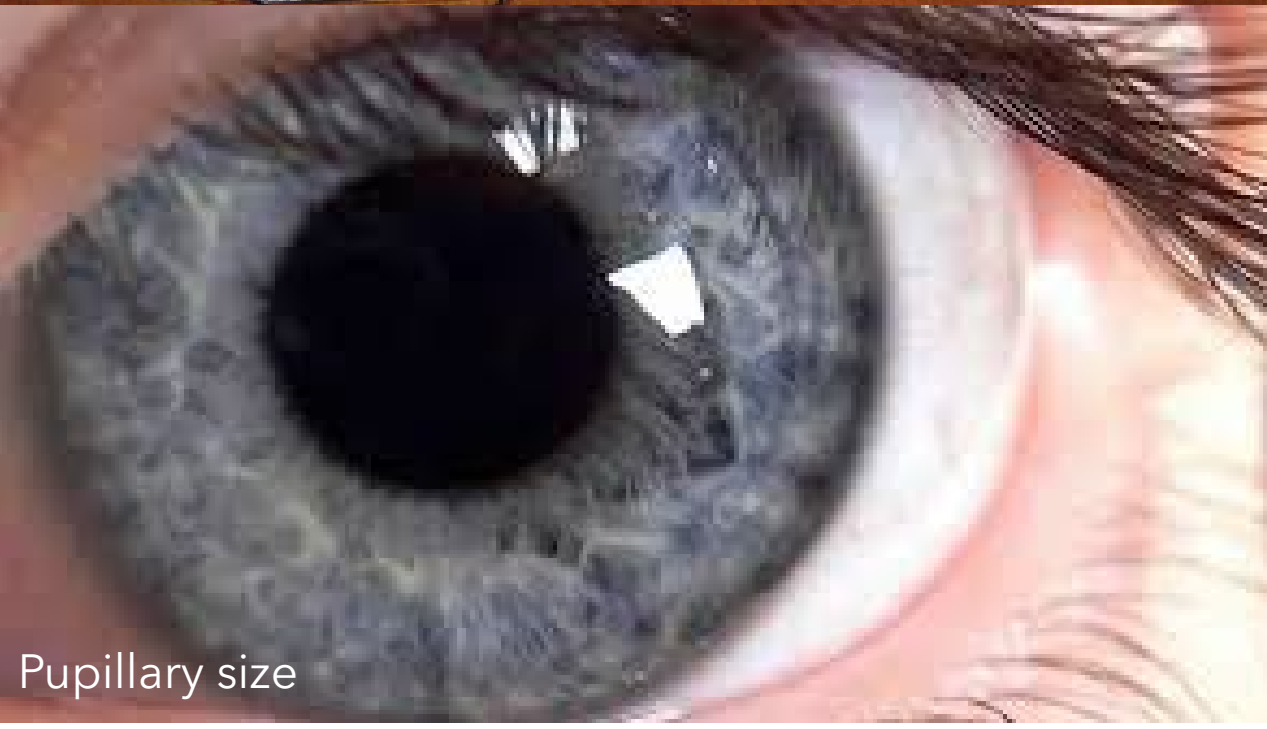
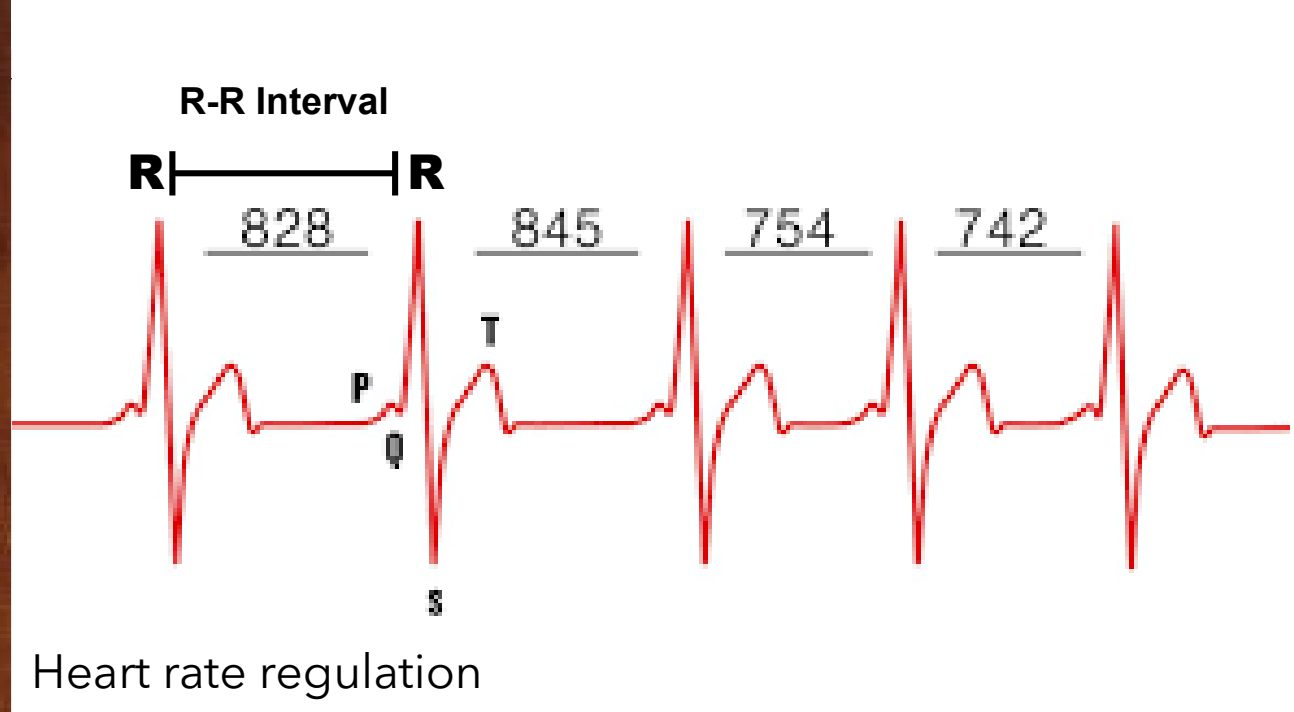




DYSAUTONOMIA IN AUTISM: PART 2



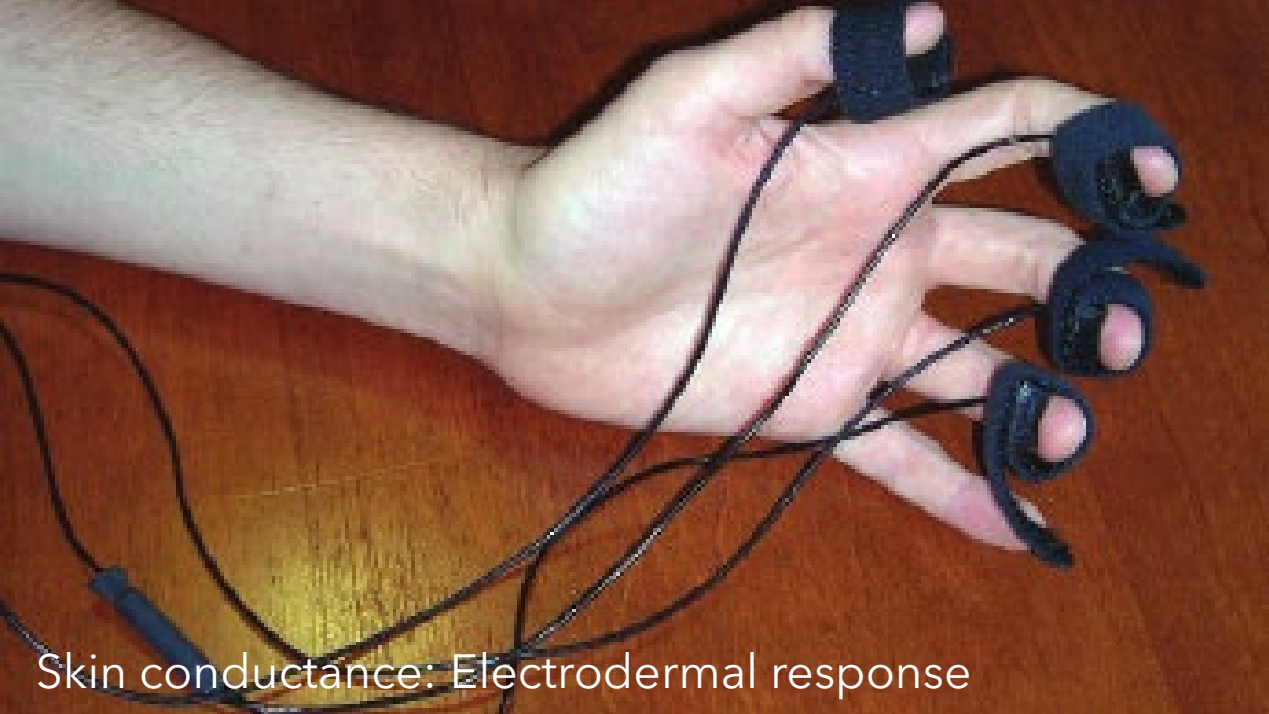
Skin conductance: Electrodermal response



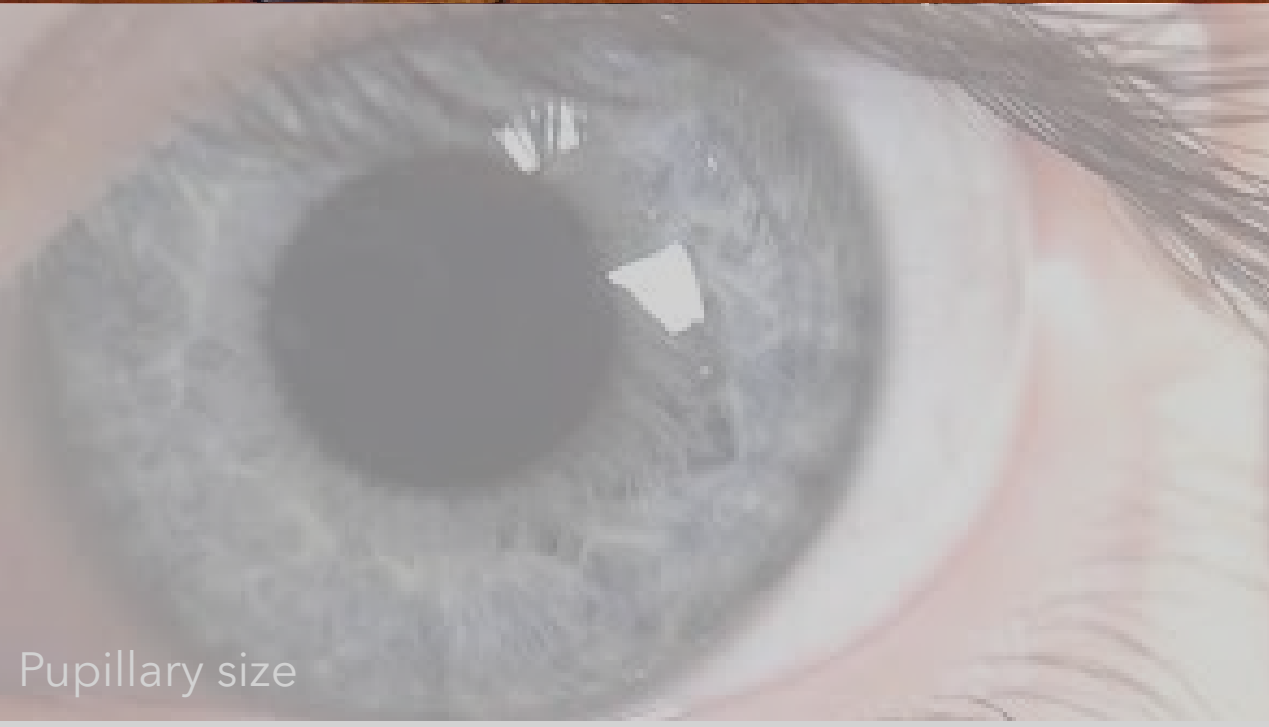
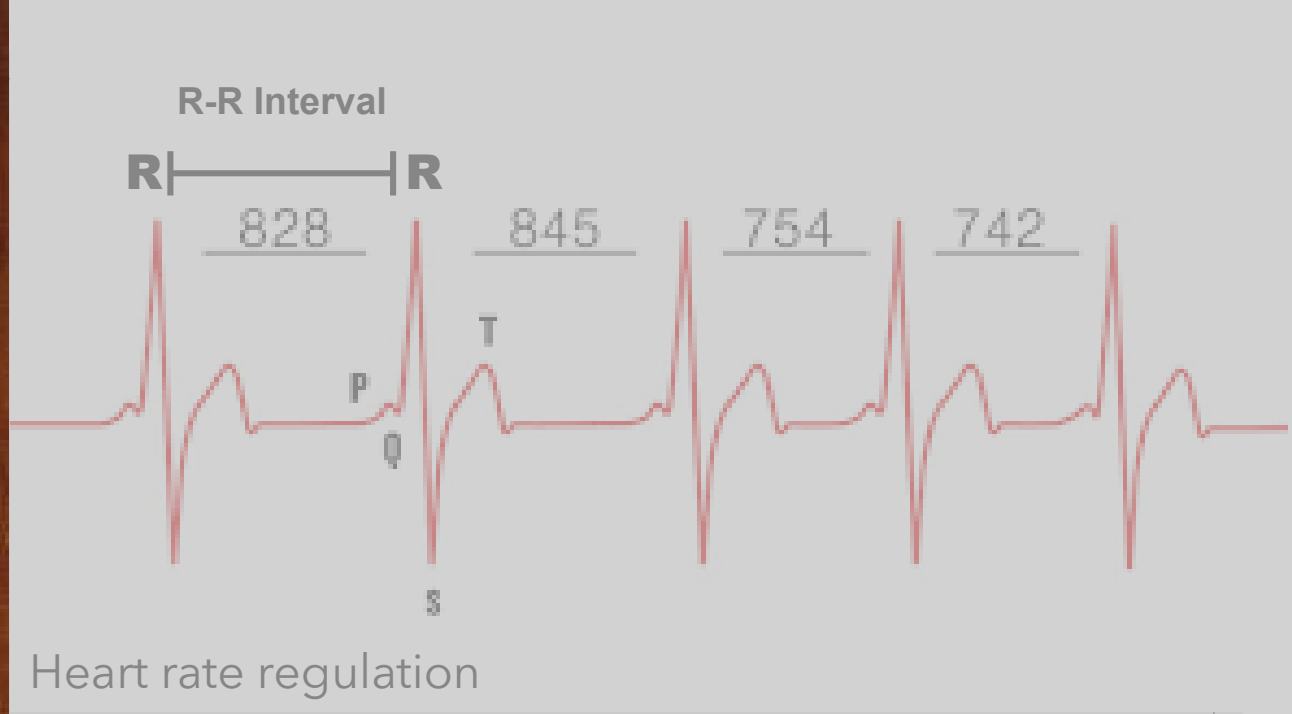
Pupillary size



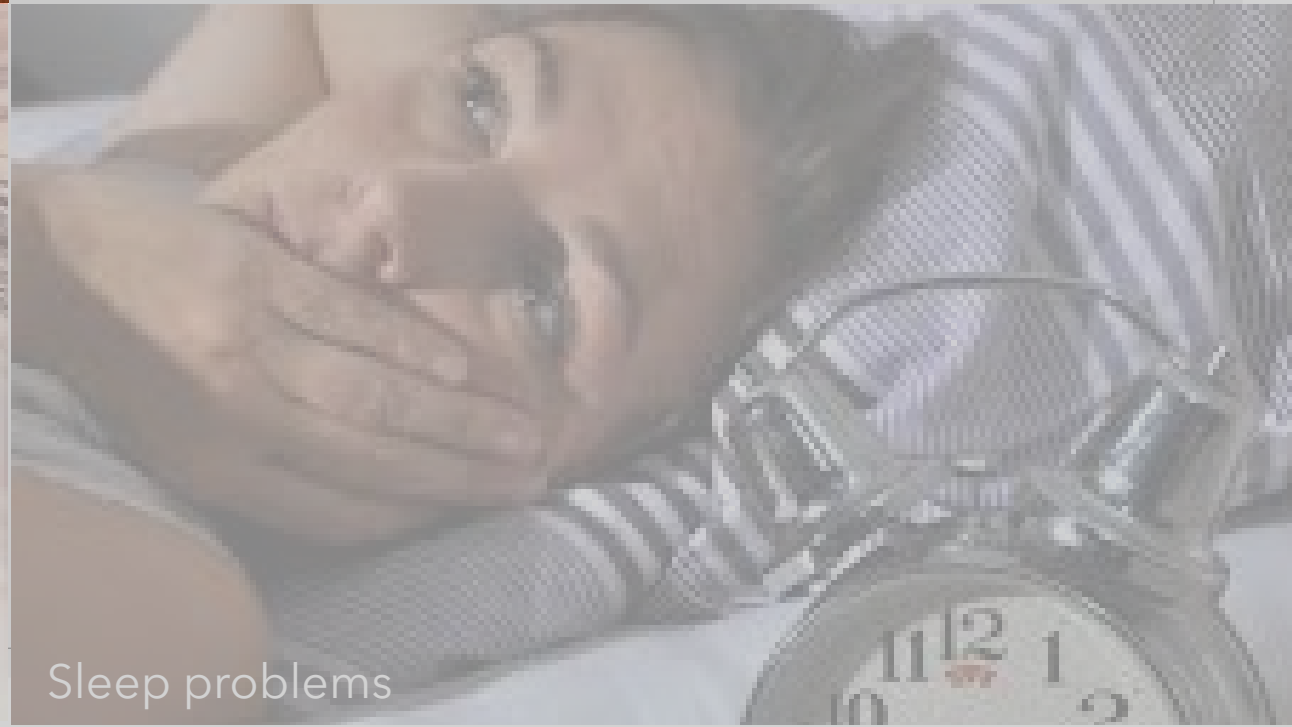
Sleep problems



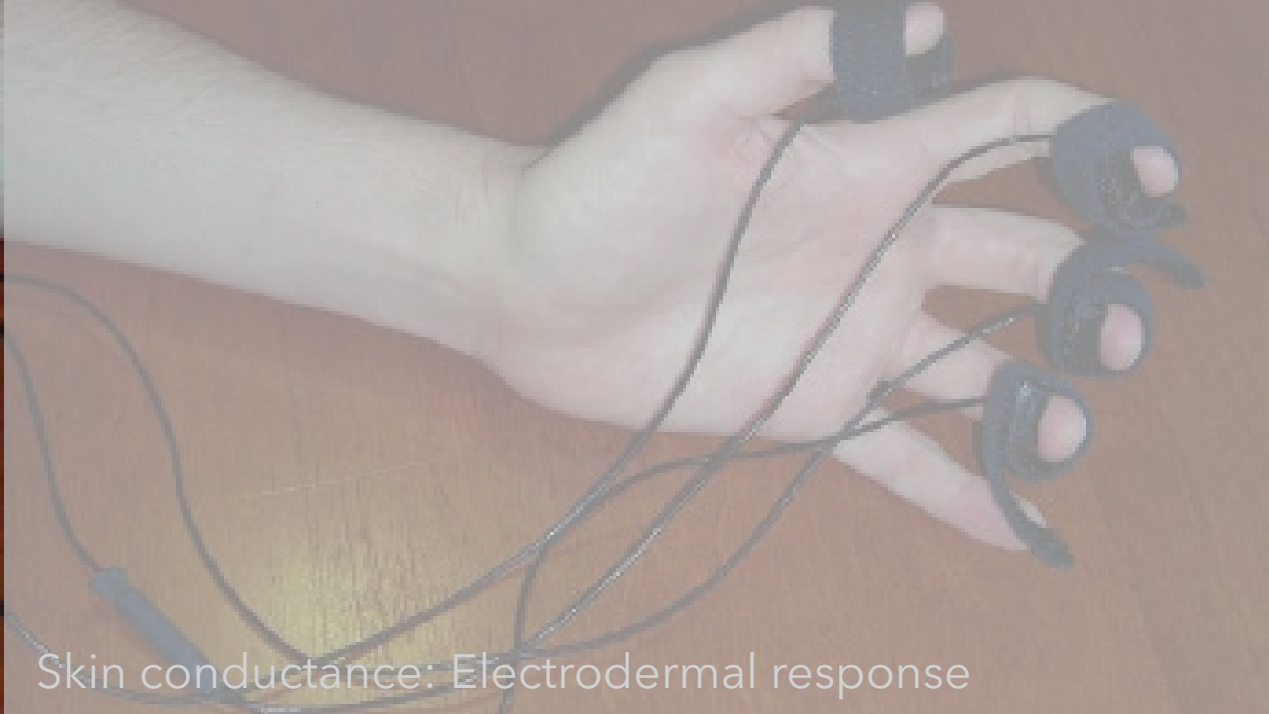
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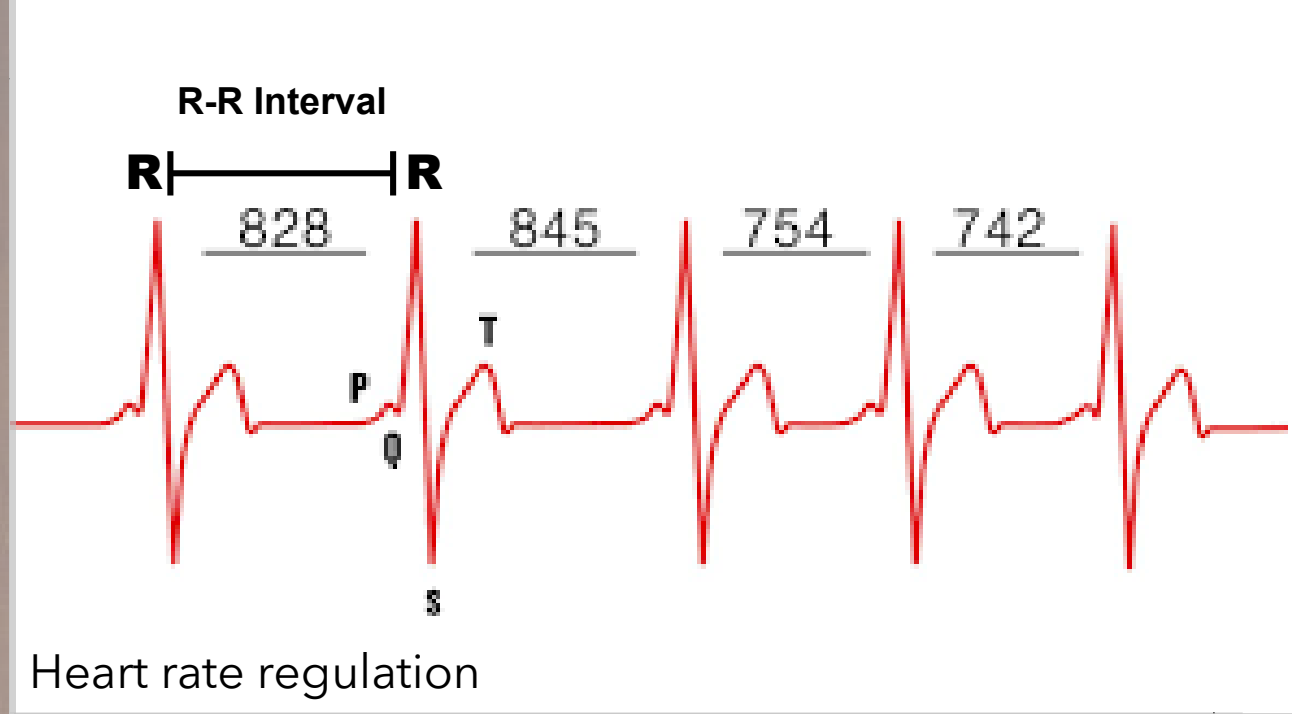
Pupillary size



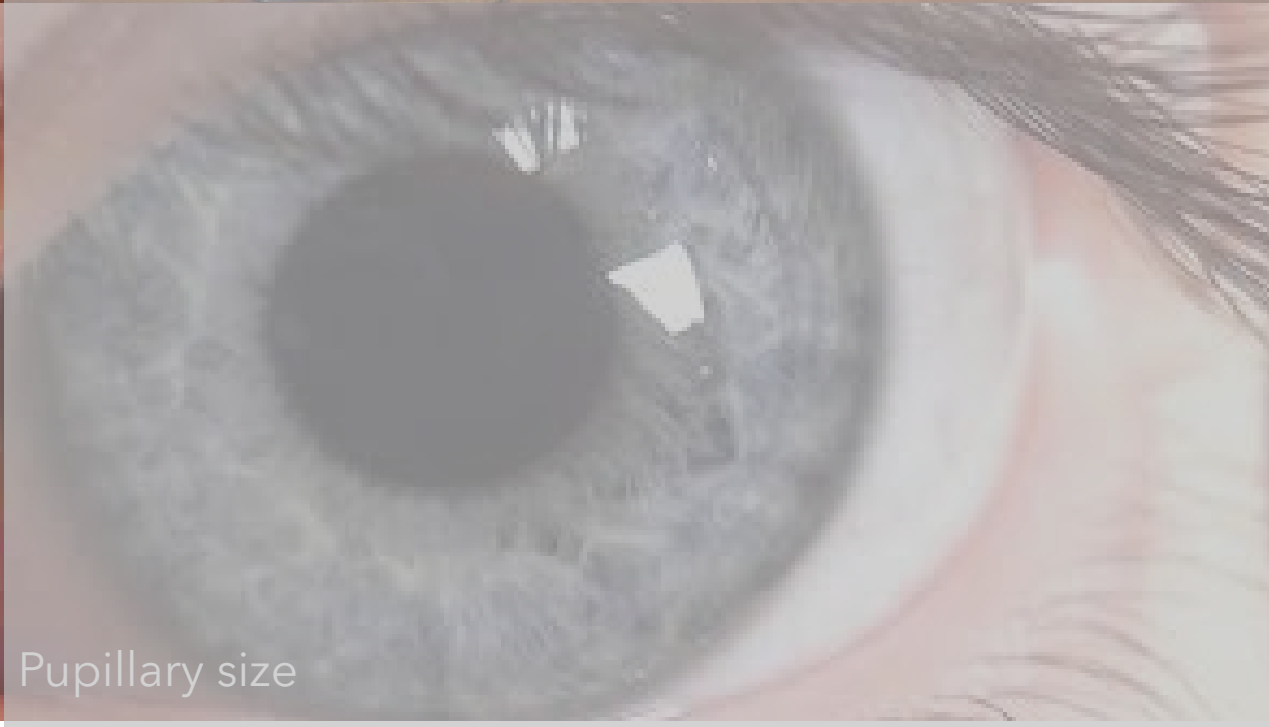
Sleep problems



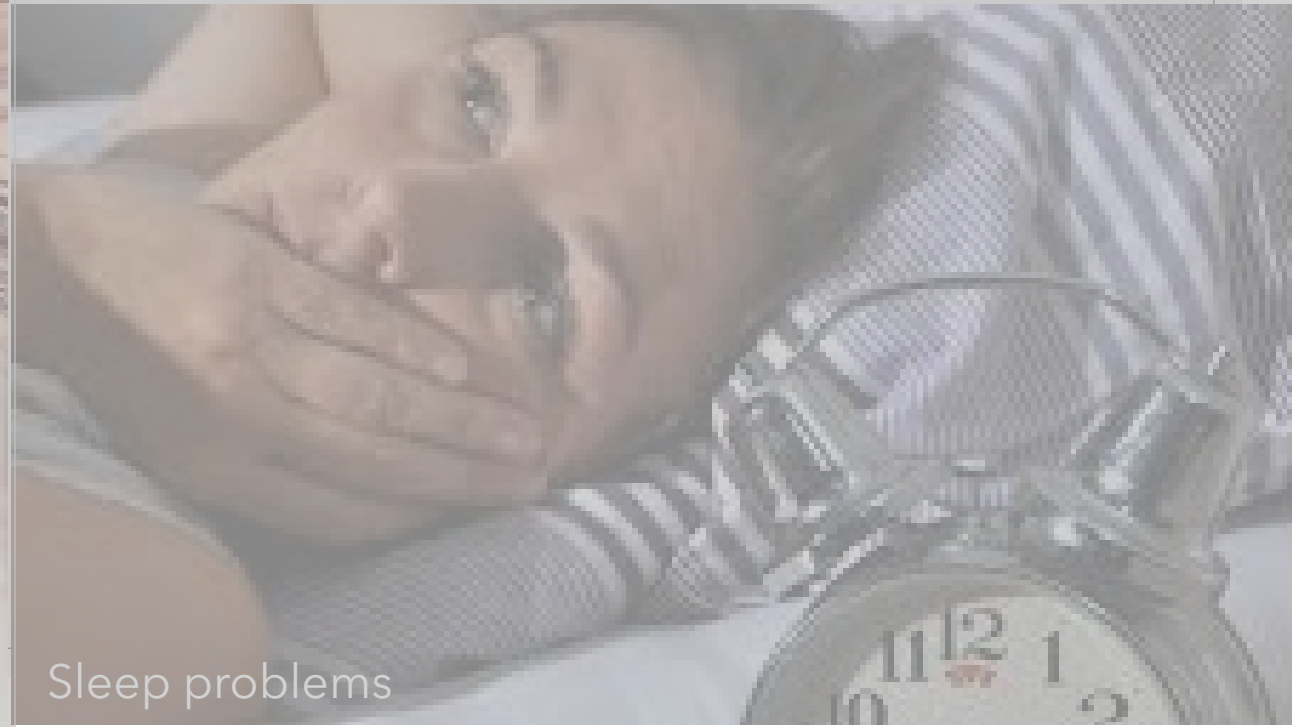
Skin conductance: Electrodermal response



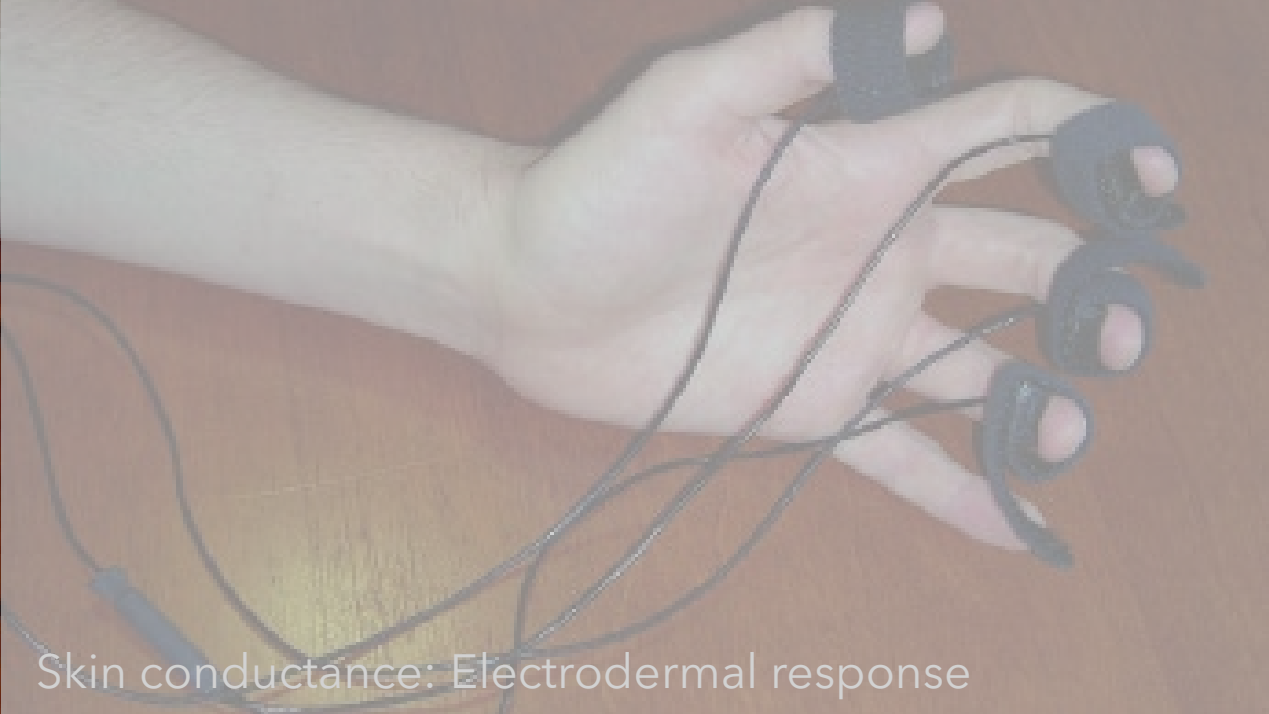
Heart rate regulation



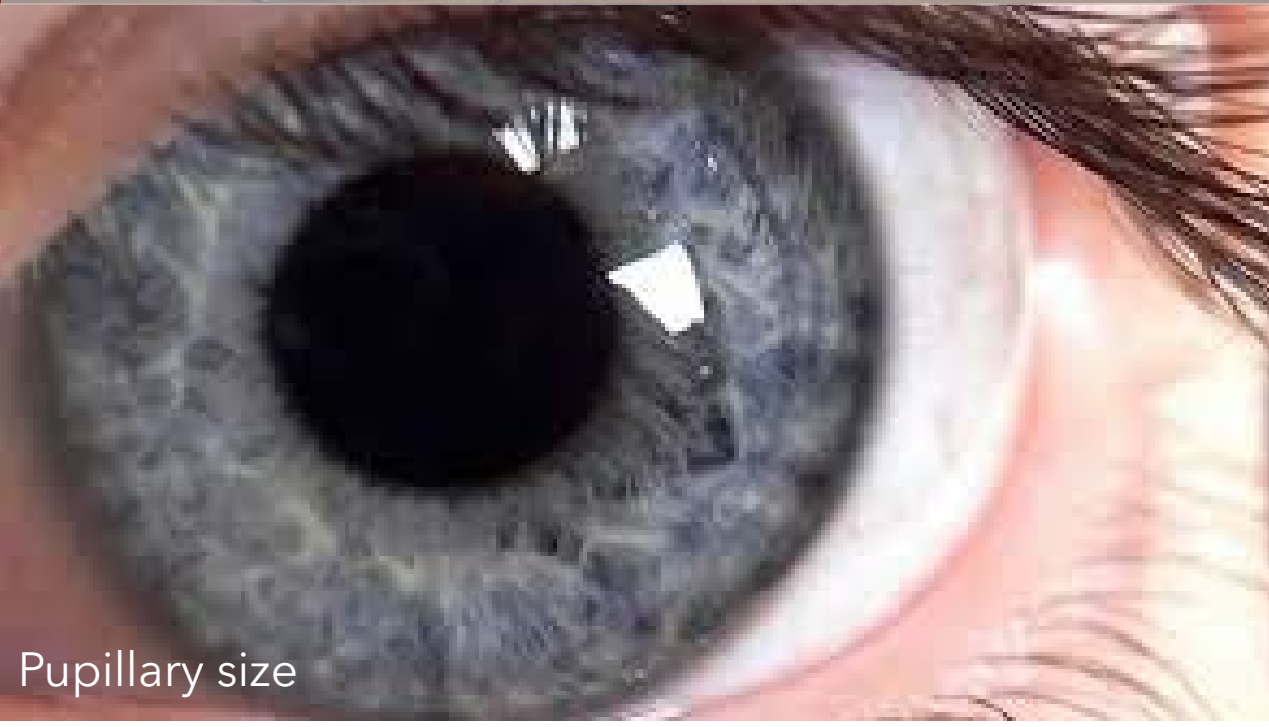
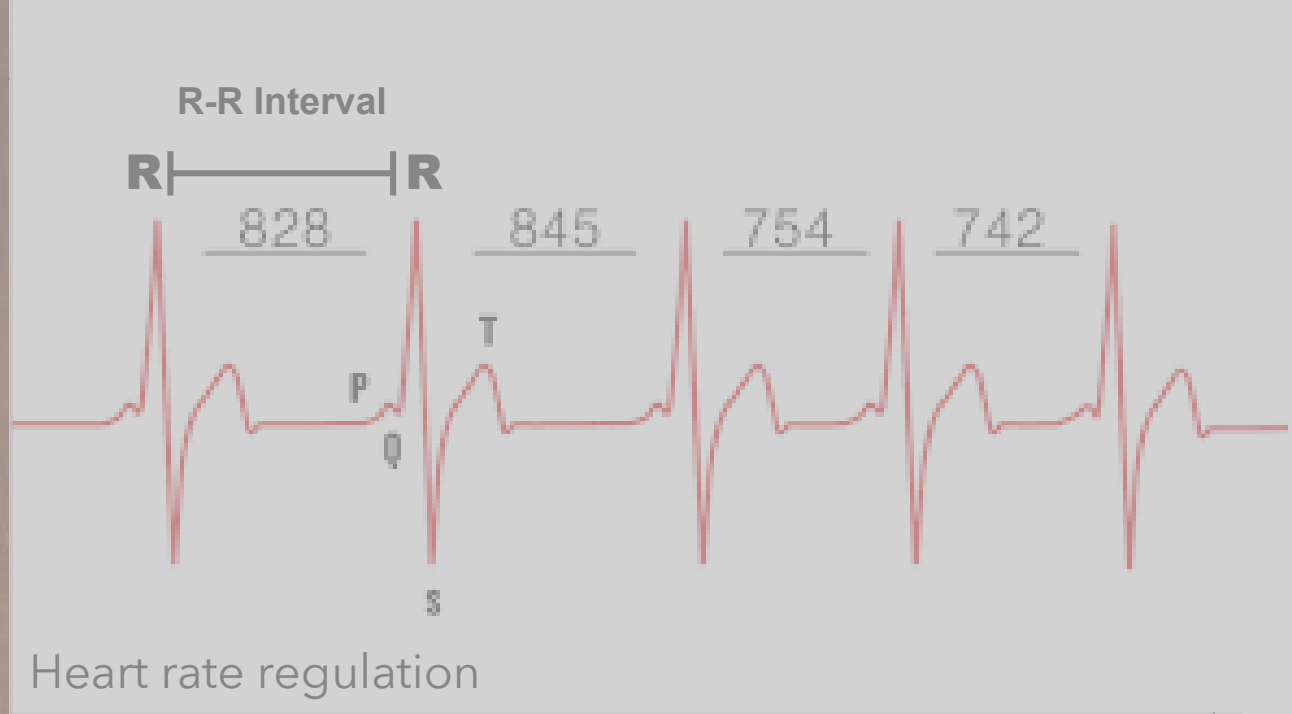
Pupillary size



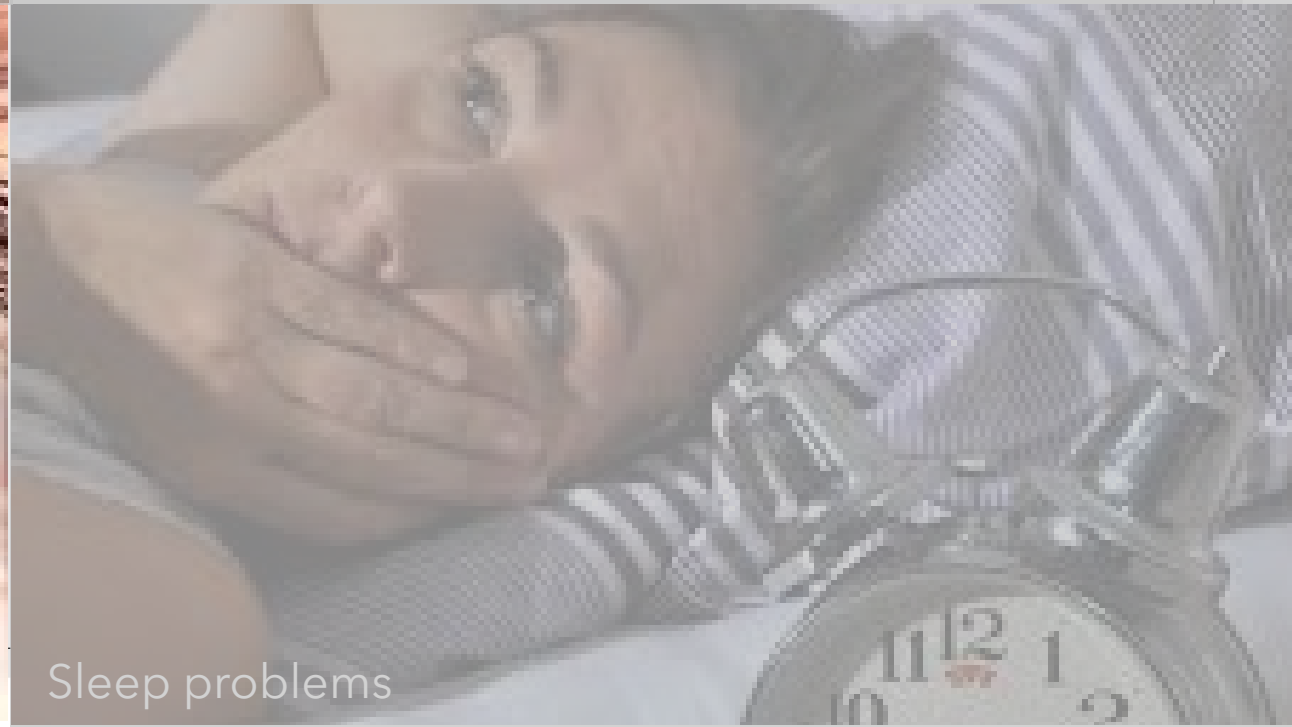
Sleep problems



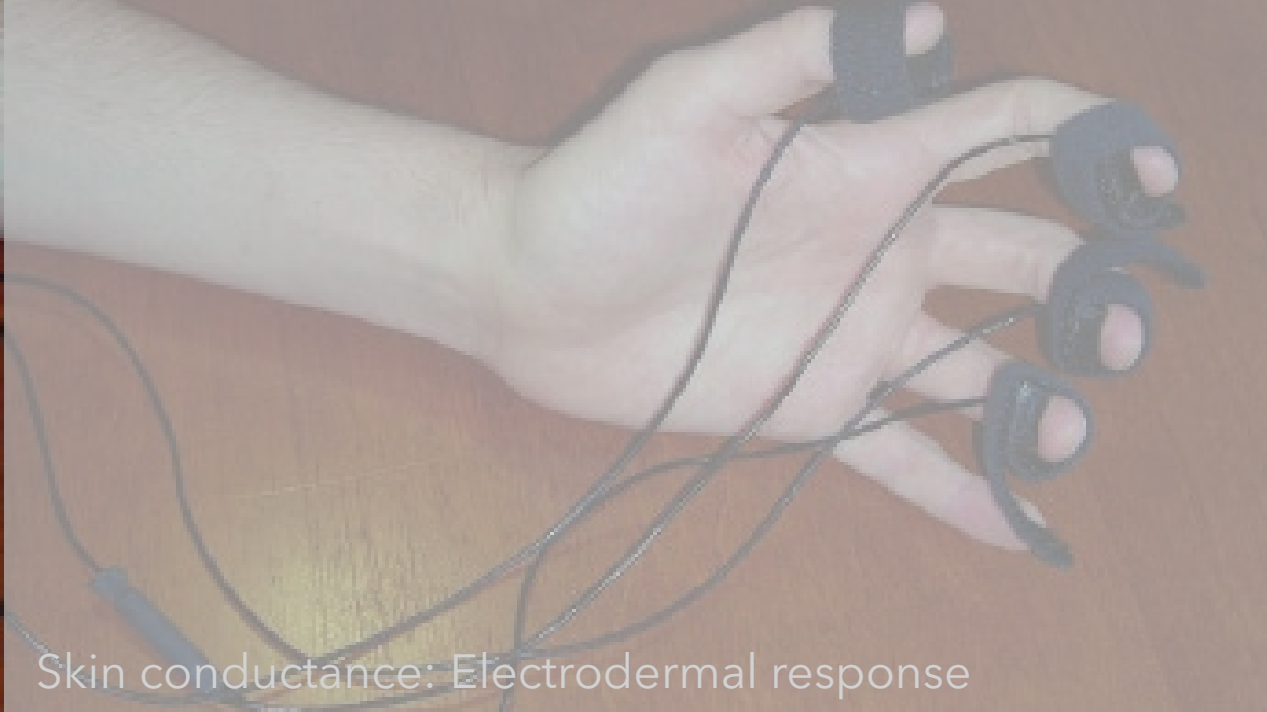
Skin conductance: Electrodermal response



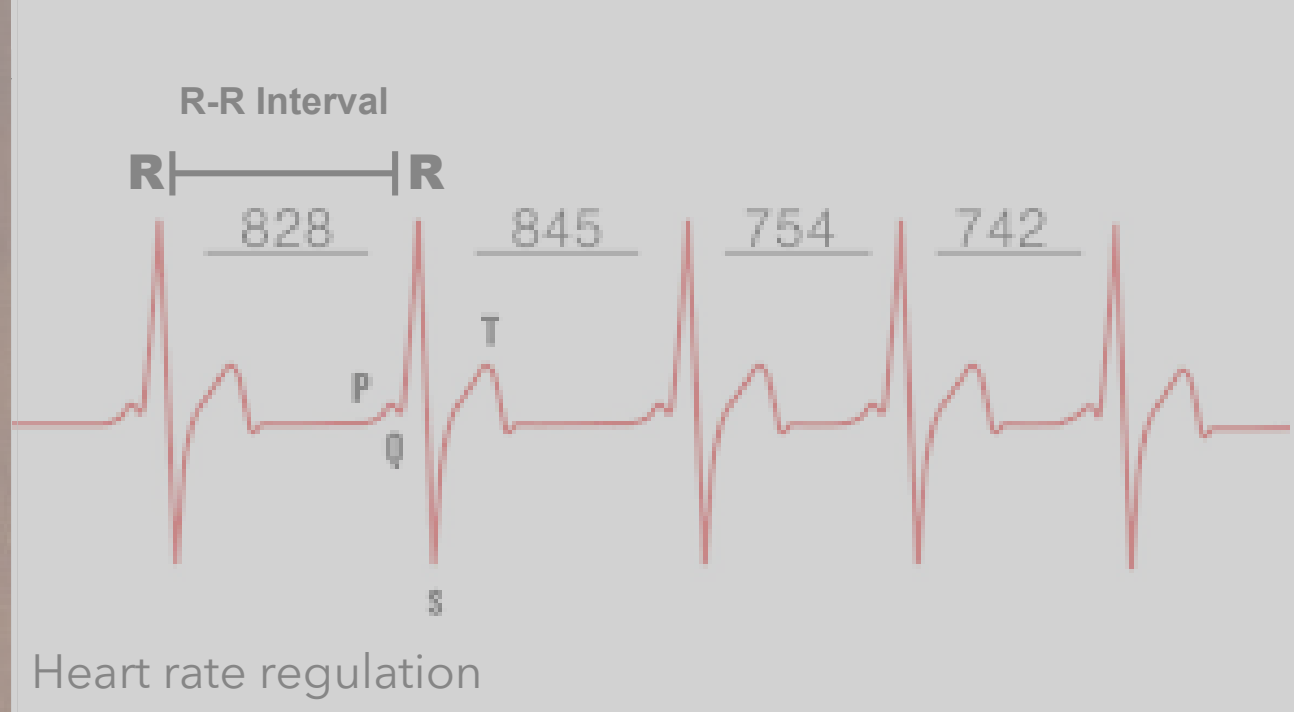
Pupillary size



Sleep problems



Skin conductance: Electrodermal response



Heart rate regulation



Pupillary size



Sleep problems

Anxiety

Subjective experience of fear and its physical manifestations.



Autonomic symptoms

Palpitations
Perspiration
Dizziness
Mydriasis
GI disturbances
Urinary urgency and frequency
Trembling
“Butterflies” in the abdomen
Tingling in the peripheral
extremities
Shortness of breath
Choking sensation



UNDERSTANDING AND TREATING ANXIETY IN AUTISM

A MULTI-DISCIPLINARY PERSPECTIVE

EDITED BY STEPHEN M. EDELSON
AND JANE BOTSFORD JOHNSON

Catatonia: a disturbance that may involve muscle rigidity, stupor or mutism, purposeless movements, negativism, echolalia and inappropriate or unusual movements.

Catatonia and Autism

- Increased recognition of catatonia as a comorbid syndrome of autism
- A limited number of studies suggest catatonia occurs in 12-17% of adolescents and young adults with autism
- An increasing number of cases of catatonia in autism have been reported throughout the world over the last 15 years

(Kakooza-Mwesige, A., Wachtel. L.E., Dhossche, D.M. 2008)

“My son had suffered a terrible breakdown, he was constantly pacing the house with his arms bent at the elbows and his hands pointing downwards with his head flexed back. He was hitting his whole body with great force and extremely distressed. Eating a meal could take a very long time from two to 5 hours. This went on for 3 months, it was soul destroying.”

Straw Breathing for Anxiety

Signs and Symptoms of Stress and Anxiety in Youth

- Recurrent fears and worries
- Difficulty falling asleep or nightmares
- Hard to relax
- Difficulty separating from parents
- Scared about going to school
- Irritability, crying, tantrums
- Uncomfortable in social situations at school, restaurants, parties



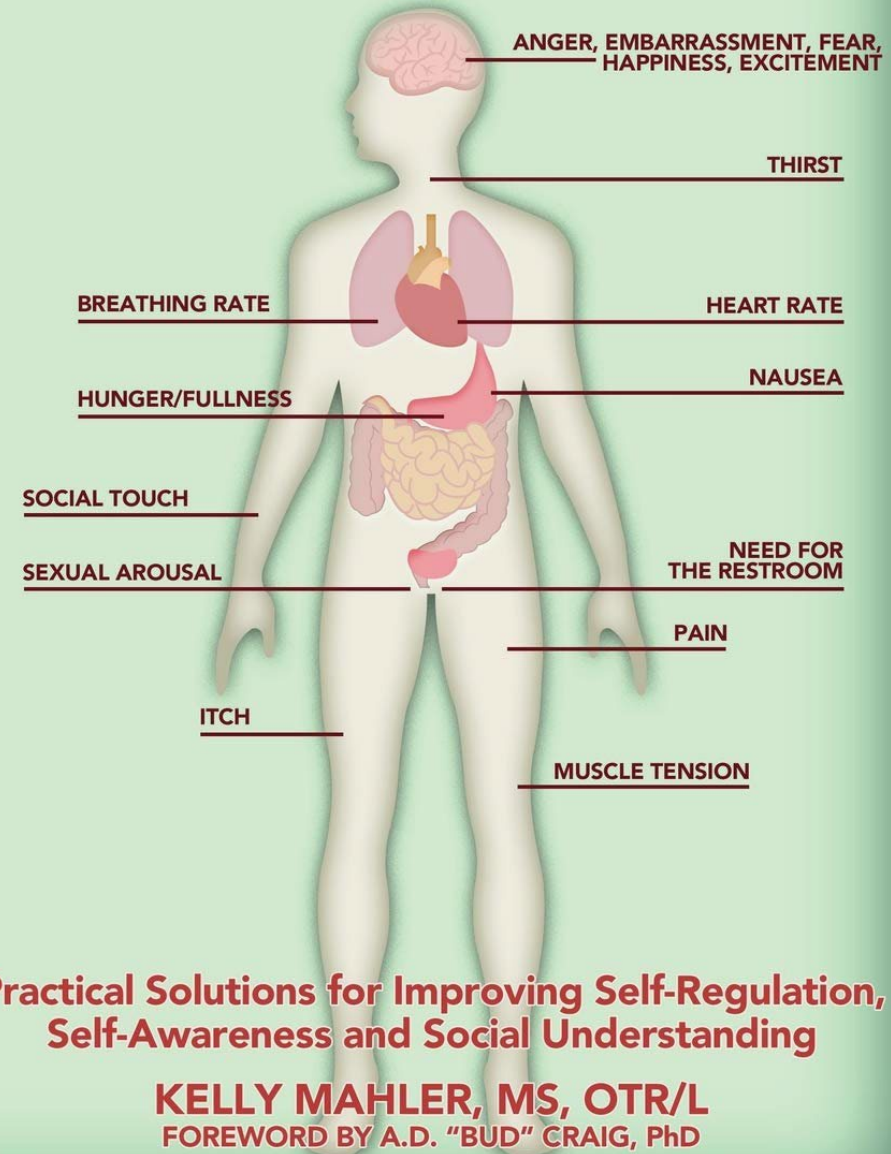
CLINICAL
PEARLS

"I do not realize that I am getting angry until I am exploding with anger. By then it is too late. I can't control it." – Jason, 9-year-old boy with autism.

"A lot of times the inside of my body feels like one of those glitter timers- the ones that you can shake and the glitter goes every which way. I feel so many different things at once and I'm not sure what is important. It is very overwhelming." – Gracies, 13-year-old girl with autism.

INTEROCEPTION

THE EIGHTH SENSORY SYSTEM



INTEROCEPTION

THE EIGHTH SENSE: KNOWING WHAT IS GOING ON INSIDE YOUR BODY

Evidence suggests poor interoception awareness can lead to difficulties with emotional regulation

Overeating or forgetting to eat, not feeling thirsty or feeling thirsty too frequently

Not feeling the urge to urinate or feeling an intense urge to urinate frequently

Inability to recognize signs of getting tired or fatigue

Not noticing increased heart or breathing rate or noticing it to the point it becomes distracting or overwhelming

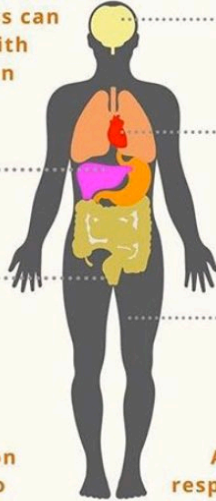
Unusually high tolerance or sensitivity to pain, may not notice if cold or overheated

Disrupted interoception awareness can lead to autistic meltdowns

A person can be over-responsive to one particular internal signal and under-responsive to another



NEUROPOSITIVE LIVING



Interoception

Heart



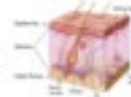
Kidneys



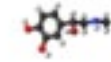
Bladder



Skin



Hormones



Lungs



Stomach



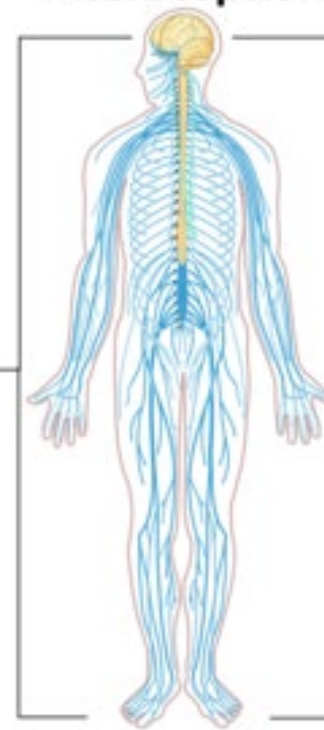
Intestines



Bone

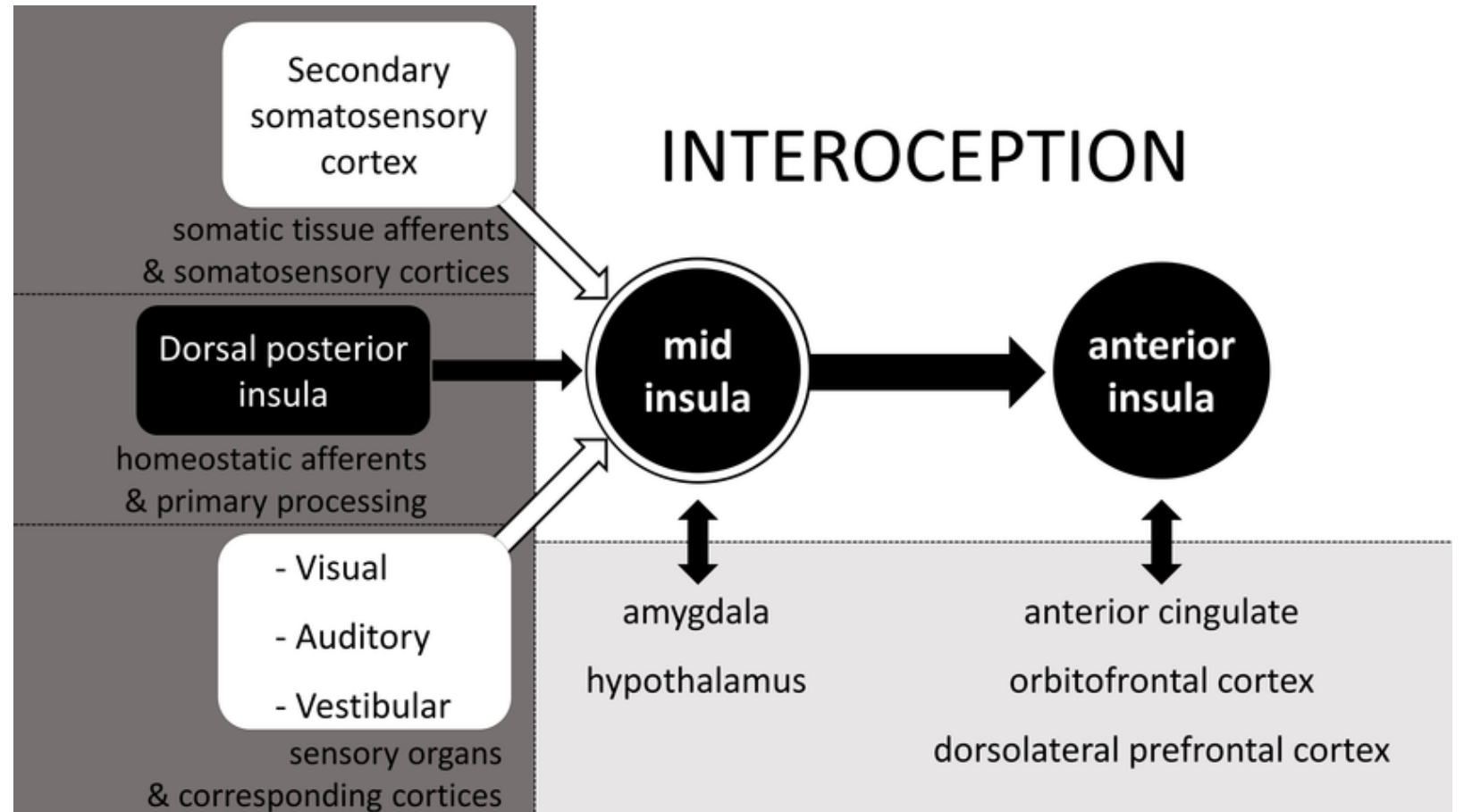


Immune cells



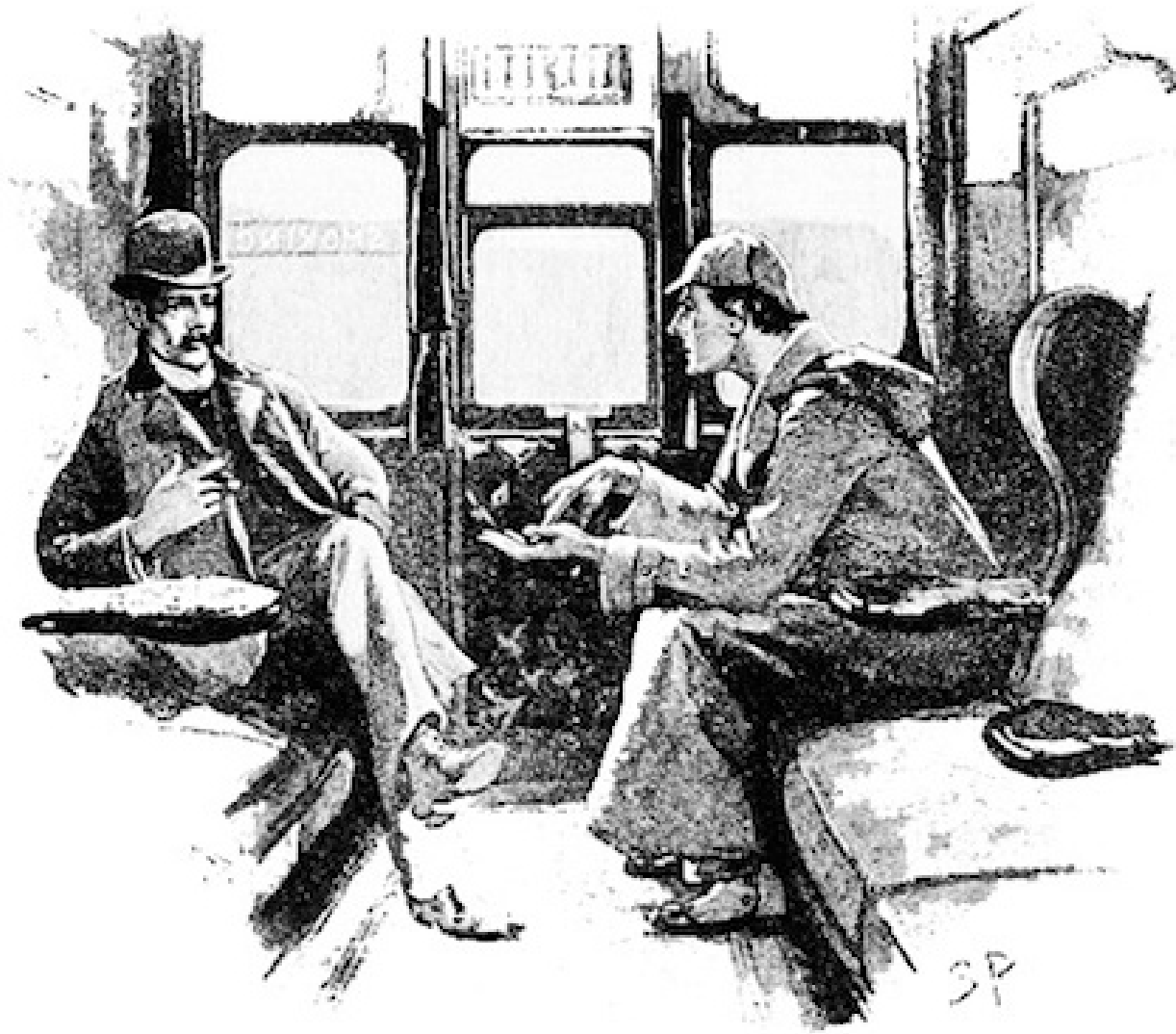
HOW DO I FEEL?

Interoception and the Central Nervous System

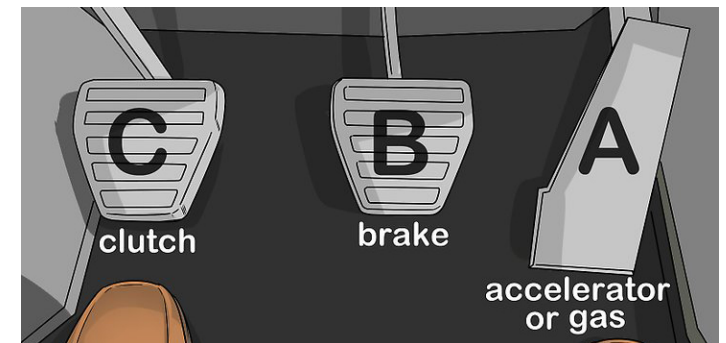
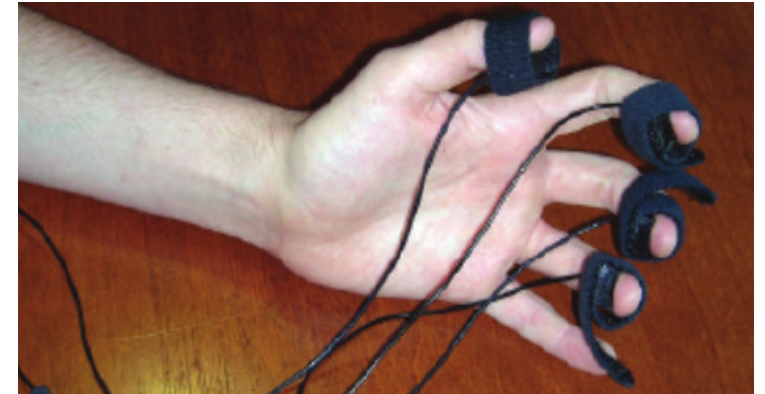


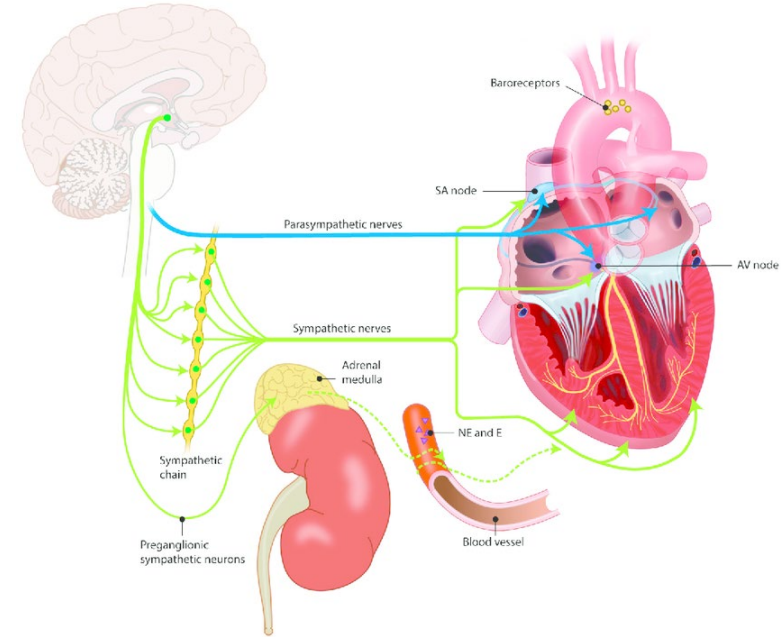
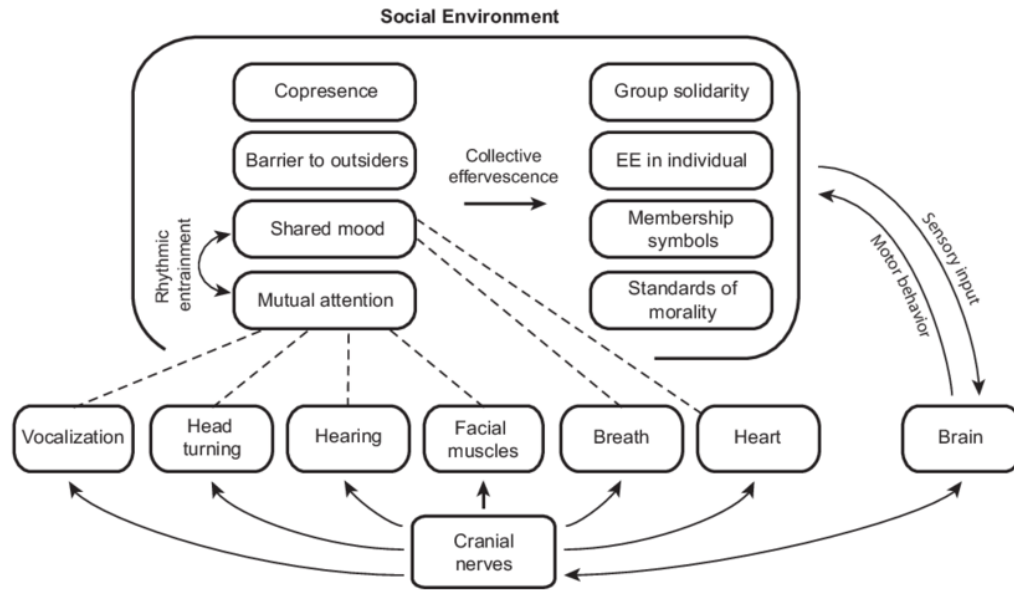
...I would emphasize something that may be somewhat speculative as of present: **That many of the behaviors, emotions, and physiological manifestations that we observe in autism are the result of a dysregulated top down process stemming from cortical influences on the limbic system and brainstem centers.**

Sherlock Holmes & Dr. Watson

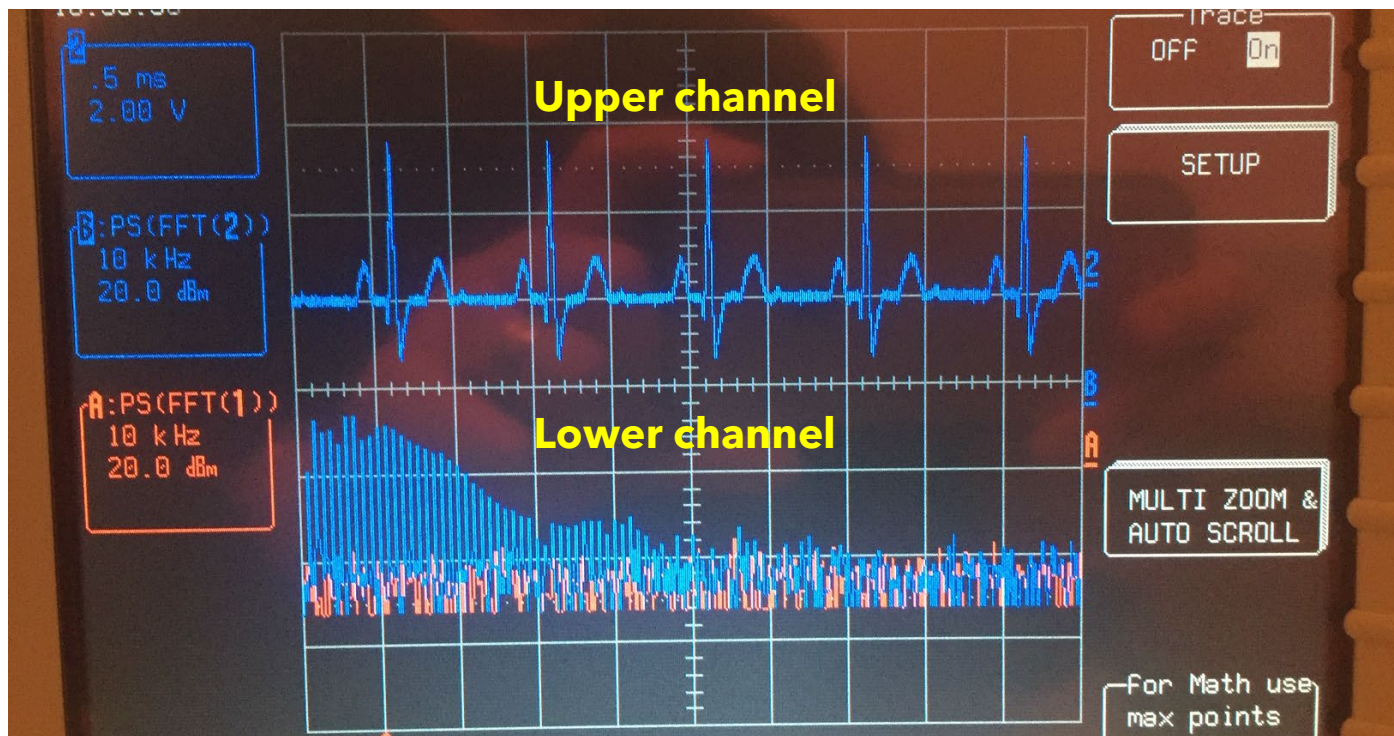


Skin conductance

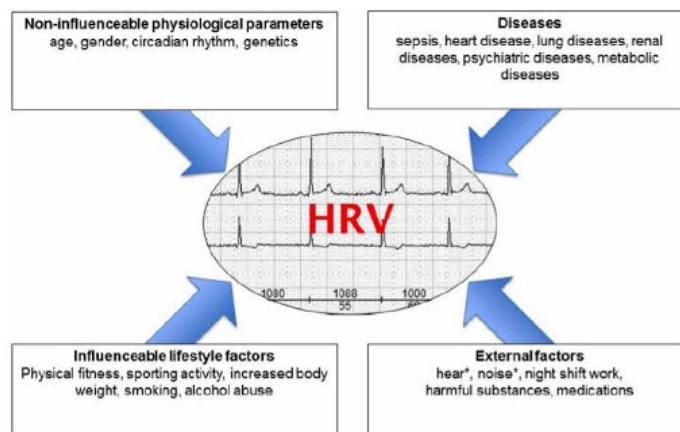
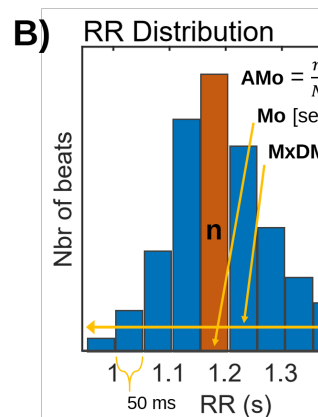
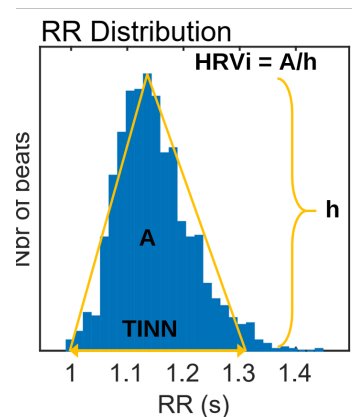




ANS : CNS : SOCIAL ENGAGEMENT



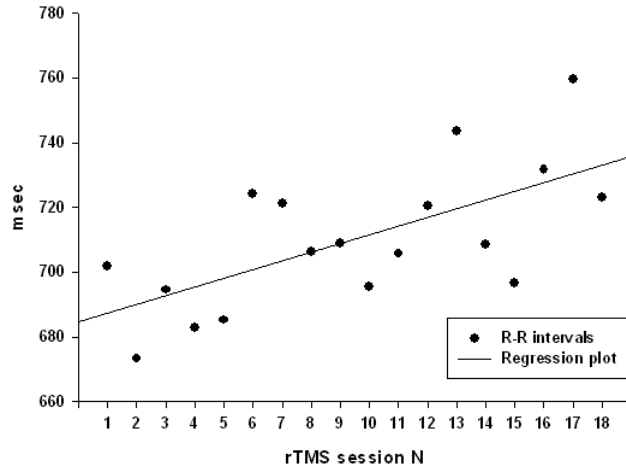
HEART RATE : TIME AND SPECTRAL MEASUREMENTS



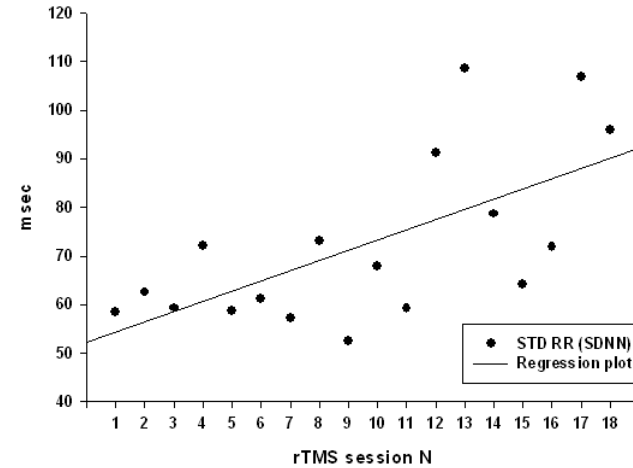
Measure	Units	t	p-value	R	R ²	Regression equation	Power at $\alpha = 0.05$
RR	ms	3.52	0.003	0.661	0.437	$y = 2.696x + 684.57$	0.868
SDNN	ms	3.38	0.004	0.645	0.417	$y = 2.098x + 52.28$	0.844
RMSSD	ms ²	2.15	0.047	0.473	0.224	$y = 1.480x + 52.80$	0.512
LF power	ms ²	-1.02	0.323	0.247	0.061	$y = -15.23x + 1775.4$	0.163
HF power	ms ²	5.12	<0.001	0.788	0.621	$y = 68.65x + 671.9$	0.985
LF/HF ratio	N/A	-3.83	0.001	0.691	0.478	$y = -0.028x + 1.619$	0.913
SCL	μ S	-3.71	0.002	0.681	0.464	$y = -0.17x + 8.65$	0.948

EFFECTS OF 18 SESSIONS OF RTMS ON AUTONOMIC FUNCTIONS IN AUTISM

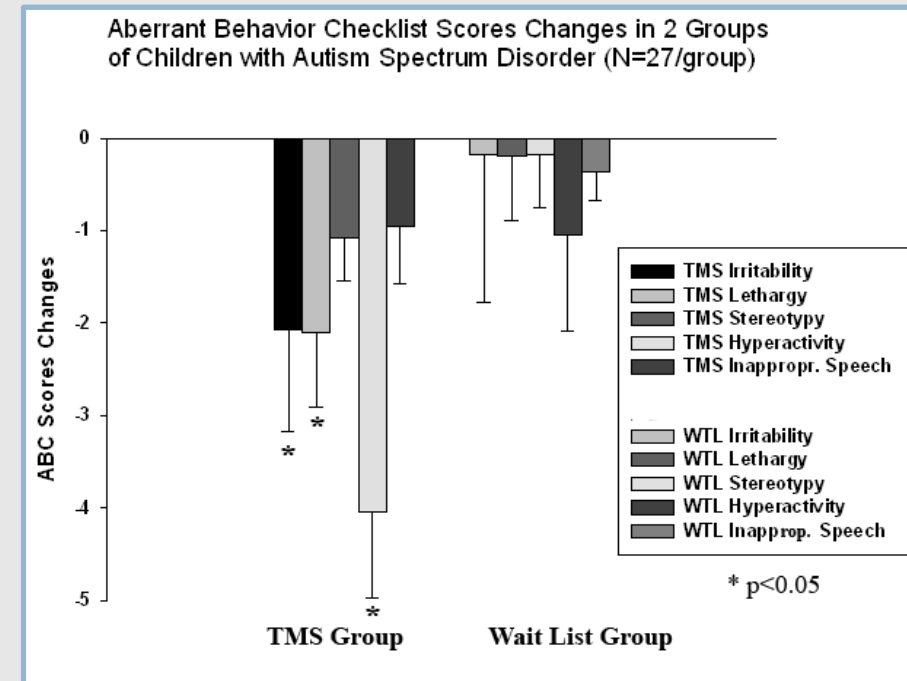
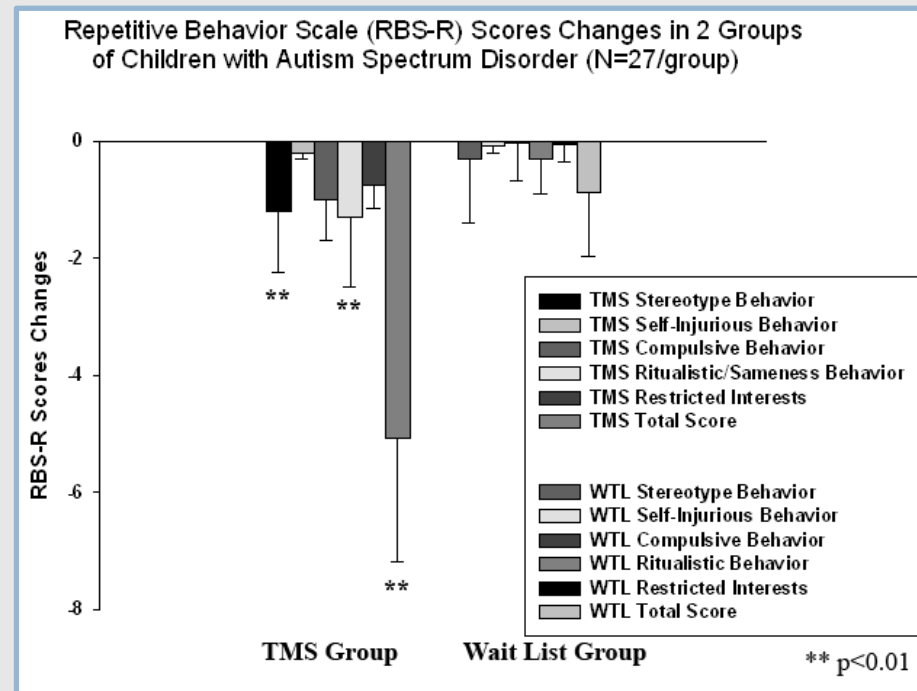
(a) R-R intervals of ECG in 18 sessions of rTMS course



(b) Standard Deviations of R-R intervals in 18 sessions of rTMS



Effects of 18 Sessions of rTMS on Autism



Our results showed a positive correlation of LF of HRV with Stereotyped ratings on ABC and a positive correlation of LF/HF index with Total Repetitive and Stereotyped Behaviors scores on RBS-R.

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about manuel



Dr. Manuel Casanova is a neurologist, with extensive experience



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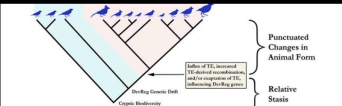


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