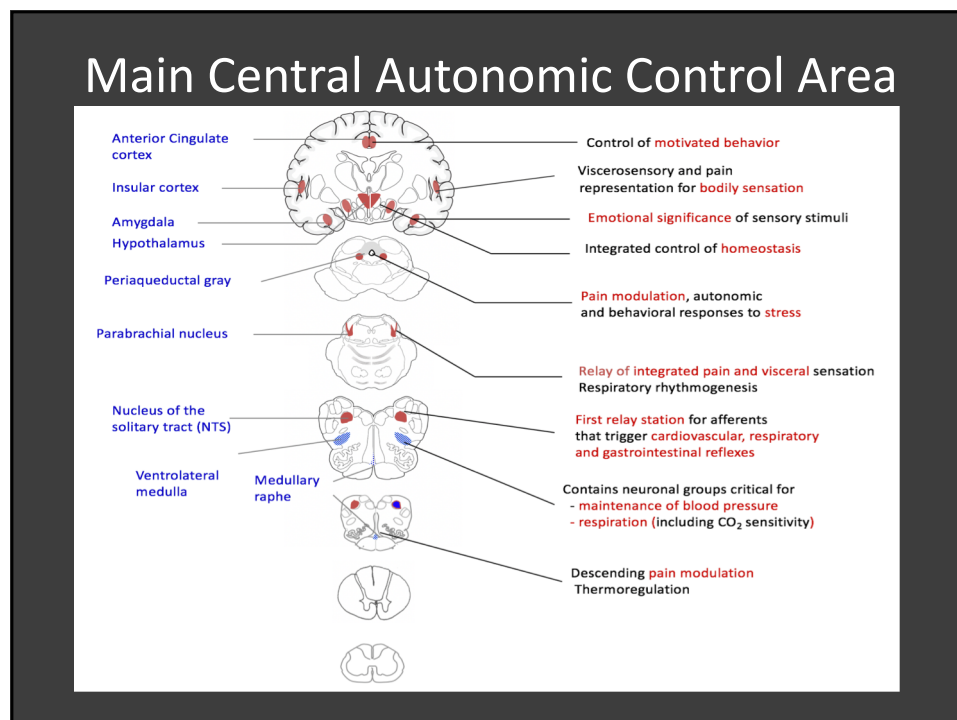
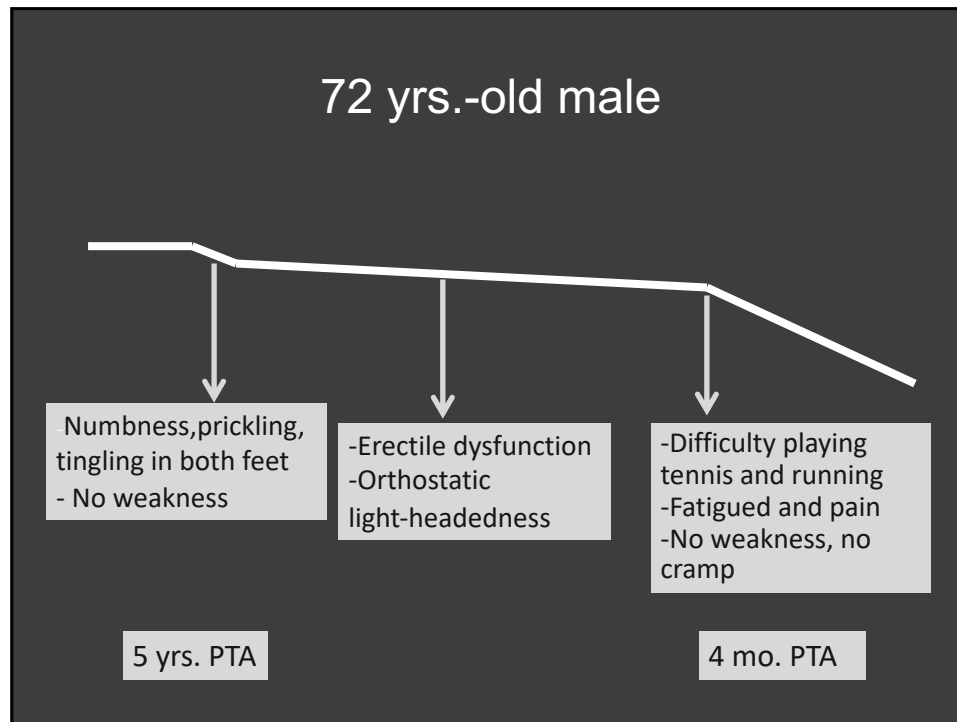


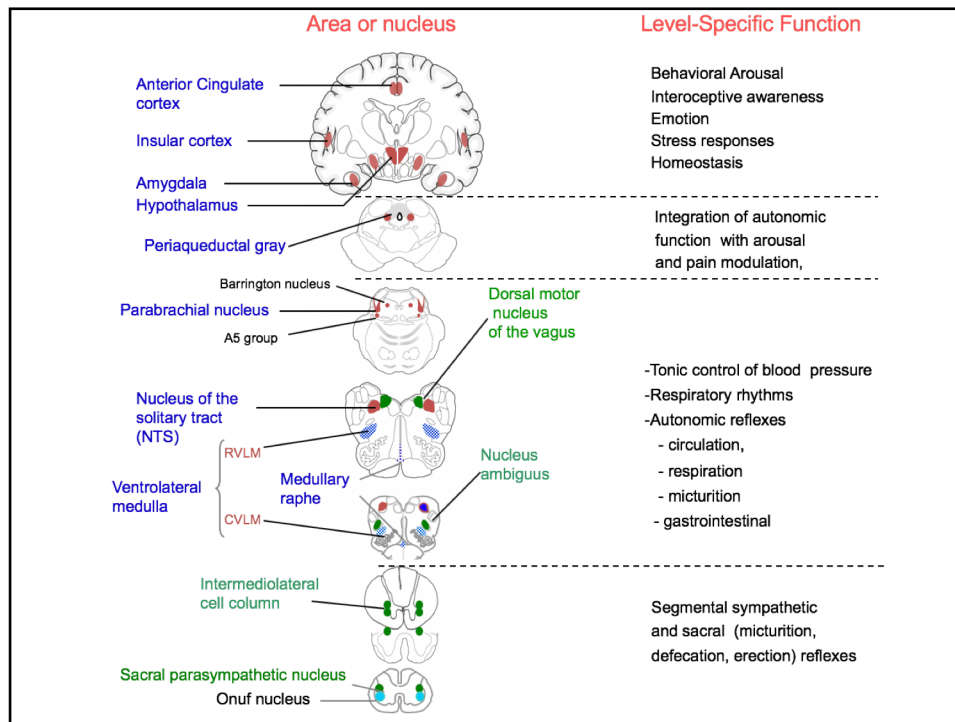
Evaluation of patient with autonomic disorder

Narupat Suanprasert, MD.

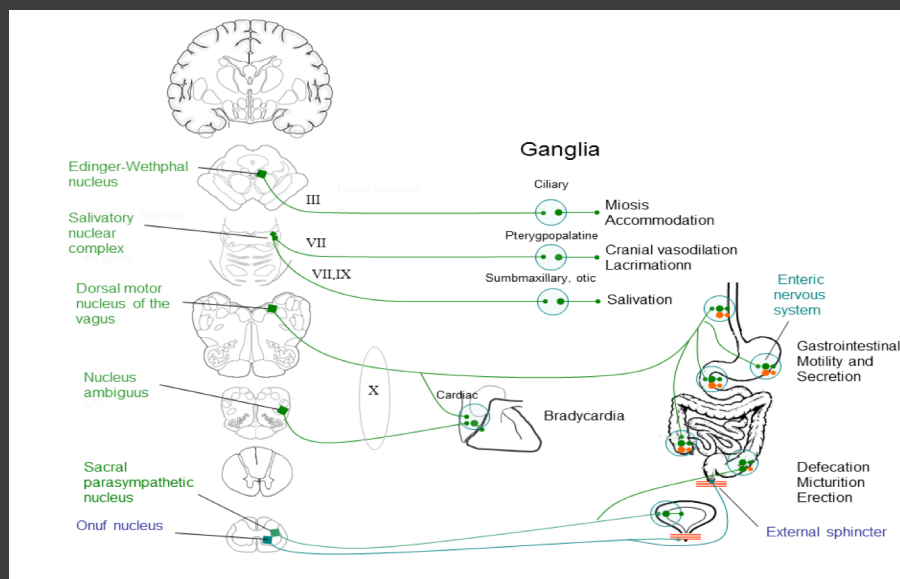
Case

- 72 yrs.-old male
- 5 yrs. prior pt. had numbness, prickling and tingling in both feet up to mid ankles but this has not really been bothering him
- During this period, pt. developed erectile dysfunction and light-headedness if pt. gets up too quickly
- 4 mo. prior pt. could not run as well. He had difficulty playing tennis and running
- His legs feel fatigued and run out when he walks for more than 1-1/2 miles
- No weakness , no cramp, no unusual gait
- Pt. had sharp and stabbing pains in both feet
- At this point, his symptoms are progressing

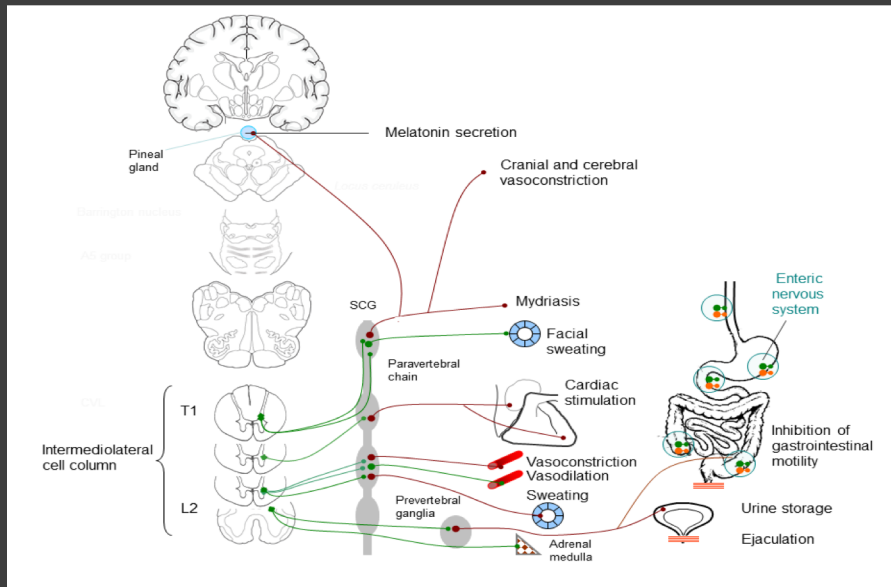




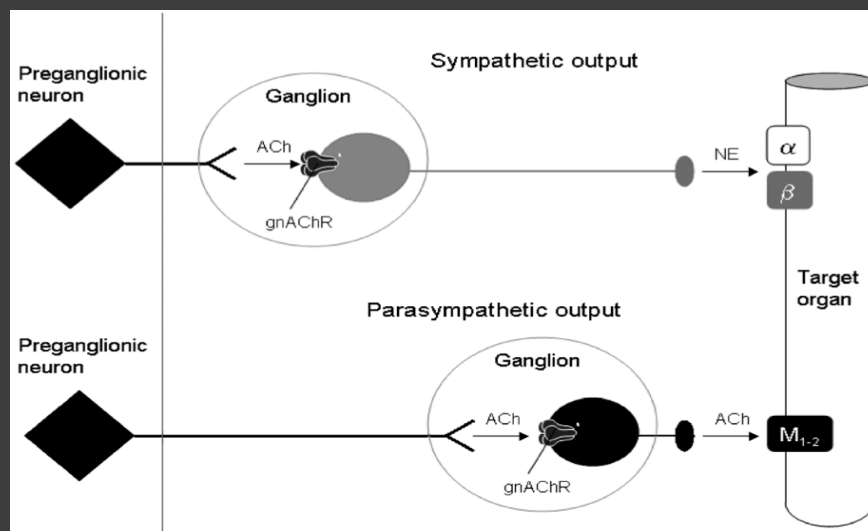
Parasympathetic nervous system



Sympathetic nervous system



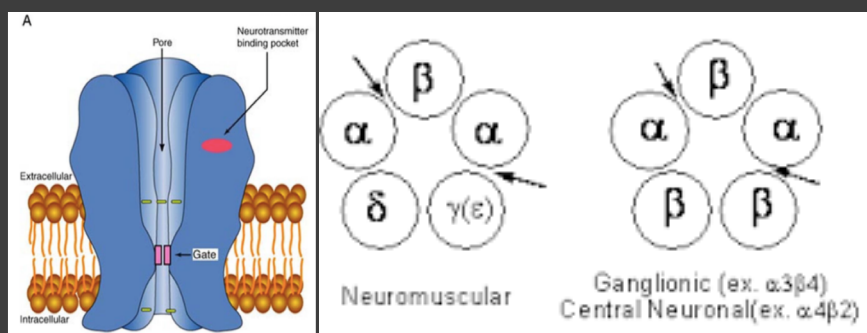
Neurochemical Transmitter



Acetylcholine (ACh)

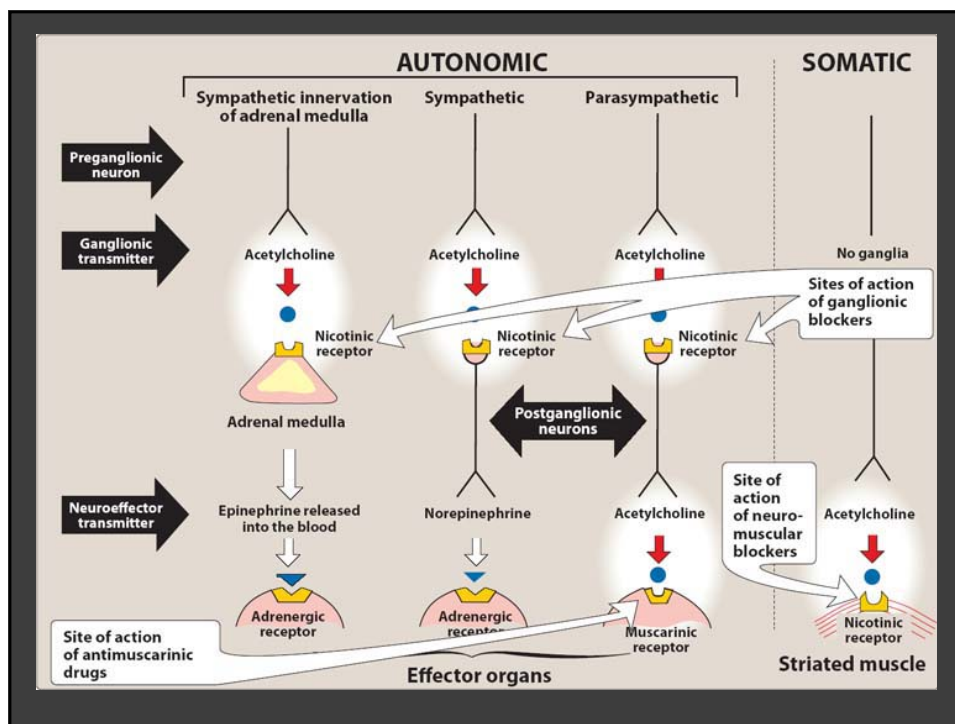
- Ganglion nicotinic ACh receptor
 - autonomic ganglia, adrenal medulla, enteric nervous system
- Muscarinic receptors
 - M1
 - activate secretion from stomach
 - M2
 - inhibitory cardiac automatism
 - contraction of smooth muscle in bladder and gut
 - M3
 - contraction of smooth muscle in visceral organ
 - exocrine glandular secretion, sweat gland
 - Vasodilatation, pupil constriction

ACh receptor



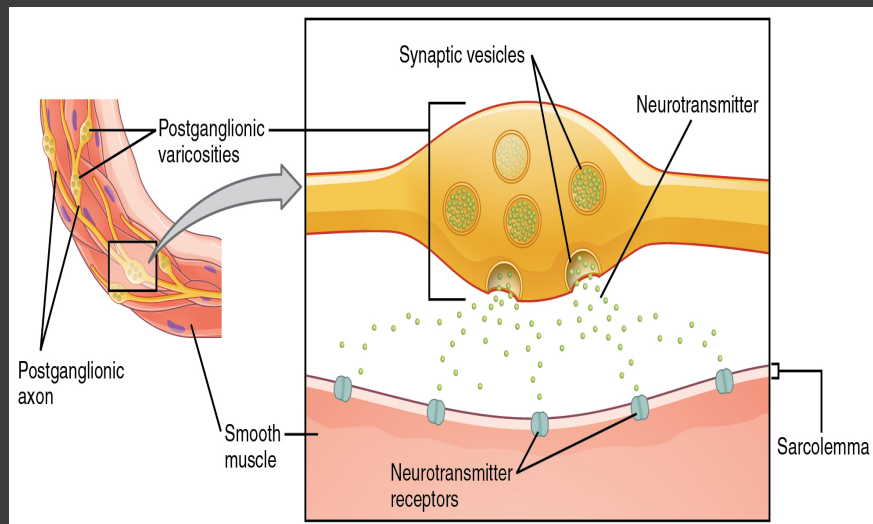
Norepinephrine (NE)

- | | |
|--|--|
| <ul style="list-style-type: none"> • α-1 receptor <ul style="list-style-type: none"> – contraction of smooth muscle in blood vessels, bladder neck, and vas deferens – pupil dilation • α-2 receptor <ul style="list-style-type: none"> – inhibit ACh release from presynaptic parasympathetic terminal | <ul style="list-style-type: none"> • β-1 receptor <ul style="list-style-type: none"> – stimulation of cardiac automatism, excitability and contractility • β-2 receptor <ul style="list-style-type: none"> – relaxation of smooth muscle in blood vessels, bronchi, bladder, gut • β-3 receptors <ul style="list-style-type: none"> – lipolysis in brown fat → thermogenesis |
|--|--|

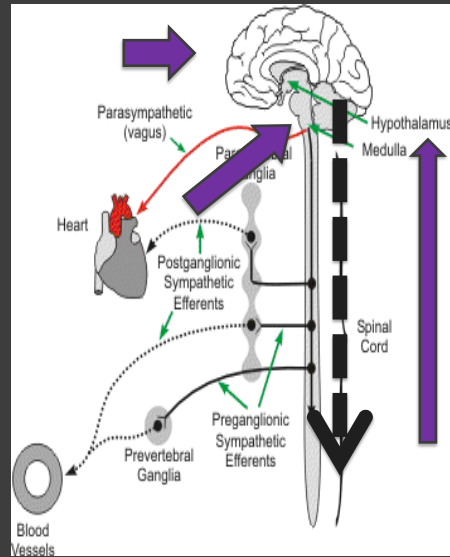
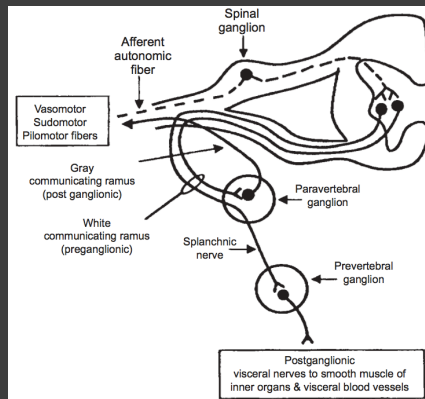


Autonomic neurons	Transmitter characteristics (not all inclusive)
Sympathetic neurons	
Paravertebral ganglia	NE, CCK, somatostatin,
Prevertebral ganglia	SP, Enk, ACh
Terminal ganglia (previsceral ganglia)	VIP, 5-HT, NPY, DYN1-8, DYN1-17
Parasympathetic neurons	
Major parasympathetic ganglia	
Ciliary	
Sphenopalatine	ACh, VIP, SP, CAs-SIF, NPY, NO
Otic	
Submandibular/sublingual	
Pelvic ganglia	
Terminal parasympathetic ganglia (previsceral ganglia)	
Enteric neurons	
Myenteric plexus (Auerbach's)	GABA, ACh, VIP, 5-HT
Submucosal plexus (Meisner's)	SP, Enk, SRIF, motilinlike peptide, bombesinlike peptide
Enteric ganglia	
Chromaffin cells of adrenal medulla	E, NE, Enk, NPY, APUD
Paraganglia-chromaffin SIF cells, ganglia	

Varicosities



Central - peripheral autonomic control



Sympathetic nervous system



Fight and flight

- Maintain blood pressure
- Thermoregulation
- Cardiovascular and metabolic response
 - exercise
 - stress
 - emotion

Parasympathetic nervous system



Rest and digest

- GI motility and digestion
- Lacrimation
- Urination
- Defecation
- Sexual arousal

Target	Sympathetic (Receptor)	Parasympathetic (Receptor)
Pupil	Dilatation (α_1)	Constriction (M_3)
Ciliary muscle	...	Accommodation (M_3)
Salivary and lacrimal glands	Inhibition (presynaptic [α_2 ?])	Stimulation (M_3)
Heart	Stimulation (β_1)	Inhibition (M_2)
Bronchi	Dilatation (β_2)	Constriction (M_3)
Muscle vessels	Constriction (α_1) (α_2) Dilatation (β_2)	...
Skin vessels	Constriction (α_1) Dilatation (NO?)	...
Visceral vessels	Constriction (α_1)	Dilatation (M_3 via NO; VIP)
Sweat glands	Stimulation (M_3)	...
Gastrointestinal motility	Inhibition (β_2)	Contraction (M_3) Relaxation (NO, VIP)
Gastrointestinal secretion	Inhibition (α_2)	Gastric stimulation (M_1) Gut and glands (M_3 , VIP)
Bladder detrusor	Inhibition (β_2)	Stimulation (M_3 , M_2 , ATP)
Bladder neck	Stimulation (α_1)	Inhibition?
Rectal smooth muscle	Inhibition (β_2)	Stimulation (M_3)
Erectile tissue	Constriction (α_1)	Dilatation (NO)
Vas deferens	Contraction (α_1)	...
Endocrine secretion	Stimulation of epinephrine, glucagon, renin, and thyroxine (β_2)	Stimulation of insulin, gastrin, secretin, cholecystokinin, and pancreatic polypeptide (M_3 ?)

Autonomic testing

Autonomic testing

- Sustained handgrip test
- Squat test
- BP response to alternate stressors
- Plasma catecholamine levels (supine/standing)
- Microneurography
- Mental stress tests
- Cold pressor test
- Spectral and transfer function BP analysis
- Vasomotor testing
- Pharmacologic challenges
- Pupillary testing (pharmacologic)
- Pupillometry, pupillography
- Urodynamics/cystometrogram
- GI motility studies
- GI manometry
- Salivary testing/Schirmer test
- Penile plethysmography
- Neuroendocrine tests
- Neurogenic flare test
- Cardiac fluorodopamine PET scanning

Quantitative autonomic testing



Phillip A. Low, M.D.

- Quantitative sudomotor axon reflex test (QSART)
- Thermoregulatory sweat test
- Heart rate variability to deep breathing
- Valsalva maneuver
- Tilt table test

Indications for Autonomic Function Tests

- Suspected
 - autonomic neuropathy
 - distal small fiber neuropathy
 - orthostatic intolerance
 - vasovagal syncope
- Monitor - course of neuropathy
 - autonomic involvement?
 - severity
 - disease progression
 - response to Rx
- Sympathetic dysfunction in sympathetically maintained pain
- In clinical treatment trials

Goals of clinical autonomic testing

- To detect autonomic involvement in peripheral nerve disease
- To quantitate the severity and type of deficits
 - sudomotor
 - adrenergic
 - cardiovagal
- To determine the distribution of autonomic failure
- To determine the site of the autonomic lesion

Patient preparation

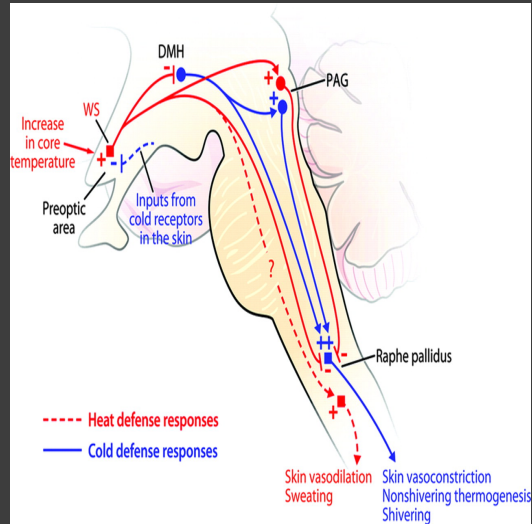
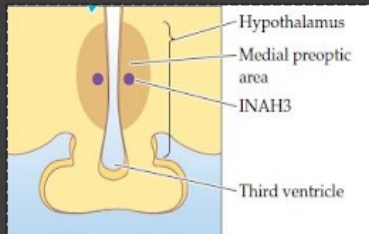
- No food, nicotine – 4 hrs. before study
- No alcohol, caffeine – 12 hrs. before study
- No acute illness in the previous 48 hrs.
- Avoid vigorous exercise - 24 hours.

Patient preparation

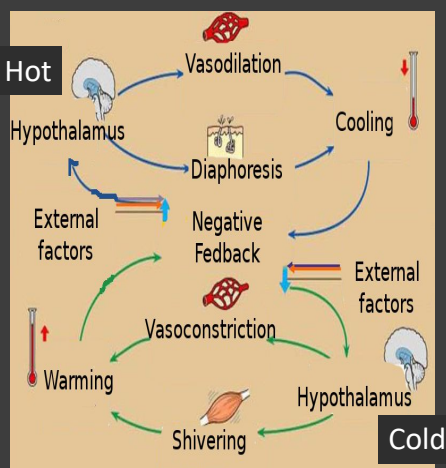
- Stop medication – 48 hrs.
 - anticholinergic - antidepressants, antihistamines, cough suppressant, cold medication, diuretics
 - sympathomimetics agents
 - parasympathomimetic agents
- Short-acting α and β antagonists - 24 hrs.
- Opioid - avoided the day of the test

Quantitative sudomotor axon reflex test (QSART)

Thermoregulation



Thermoregulation

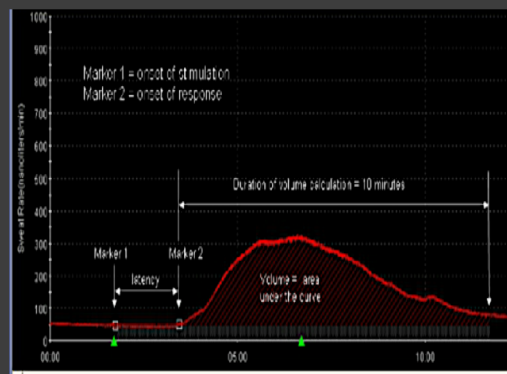
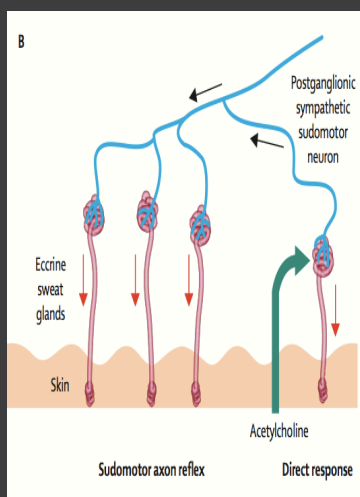


- Exposure to cold
 - α_1 receptors
 - preserve heat
 - skin vasoconstriction
 - piloerection
- Exposure to heat
 - cholinergic M3 receptors
 - liberate heat
 - sweating
 - skin vasodilatation

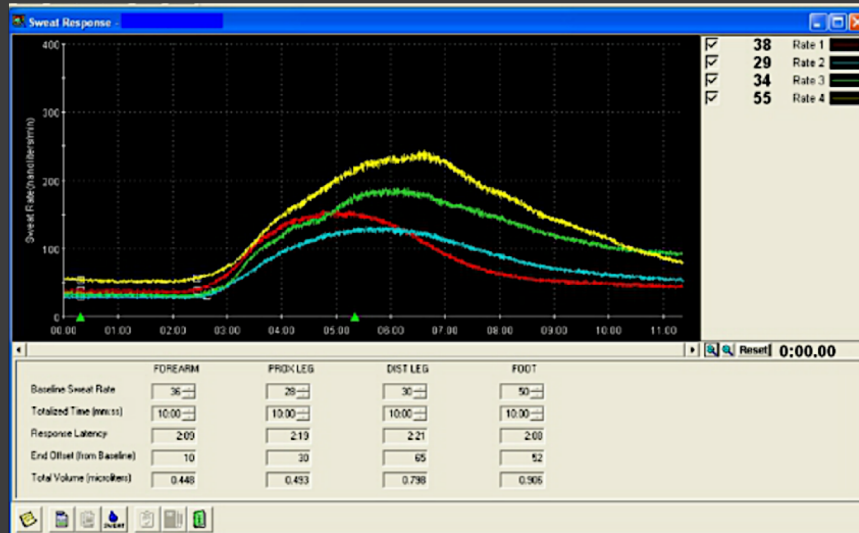
Quantitative sudomotor axon reflex test (QSART)



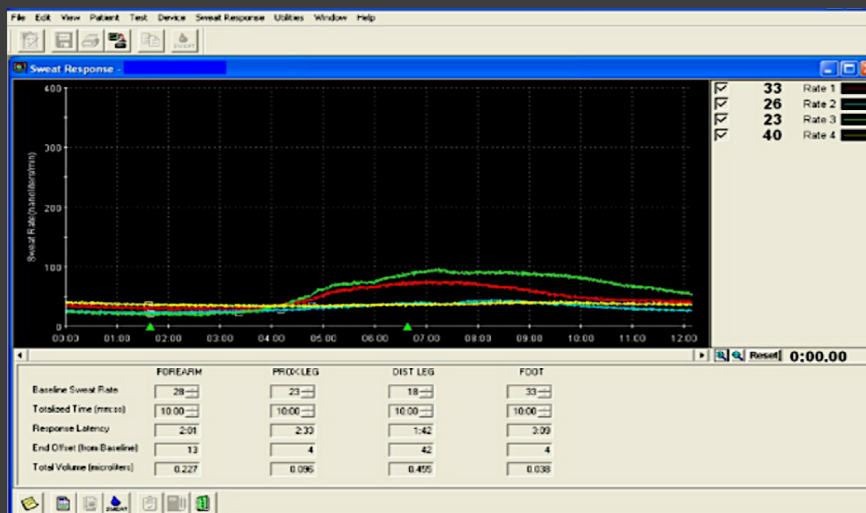
Quantitative sudomotor axon reflex test (QSART)



QSART- normal



QSART- abnormal



Severity of abnormal QSART

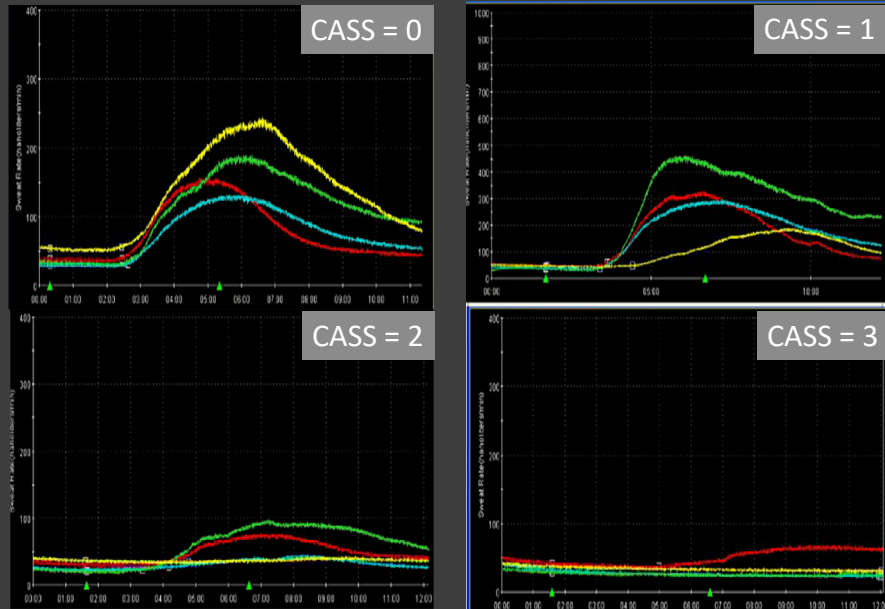


Table 44–10. Male QSART Responses: Mean, 5th, and 95th Percentile Values

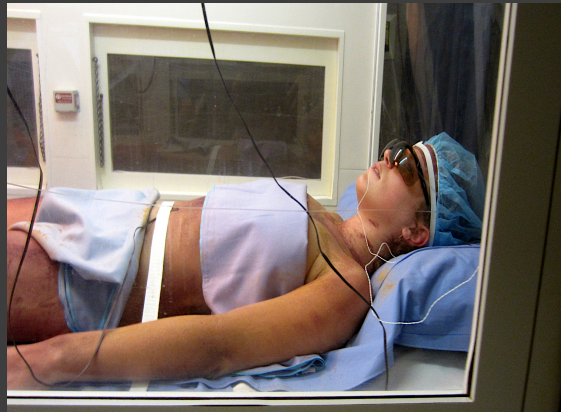
Sites	10–29 yr			30–49 yr			>50 yr		
	Mean	5th	95th	Mean	5th	95th	Mean	5th	95th
Forearm	2.67	0.76	5.06	2.67	0.76	5.06	2.67	0.76	5.06
Proximal leg	2.67	1.27	4.54	2.32	0.93	4.19	1.97	0.58	3.84
Distal leg	3.28	1.37	5.27	2.55	0.98	4.55	1.83	0.59	3.82
Proximal foot	2.58	0.87	4.48	2.17	0.78	4.07	1.75	0.68	3.65

Table 44–11. Female QSART Responses: Mean, 5th, and 95th Percentile Values

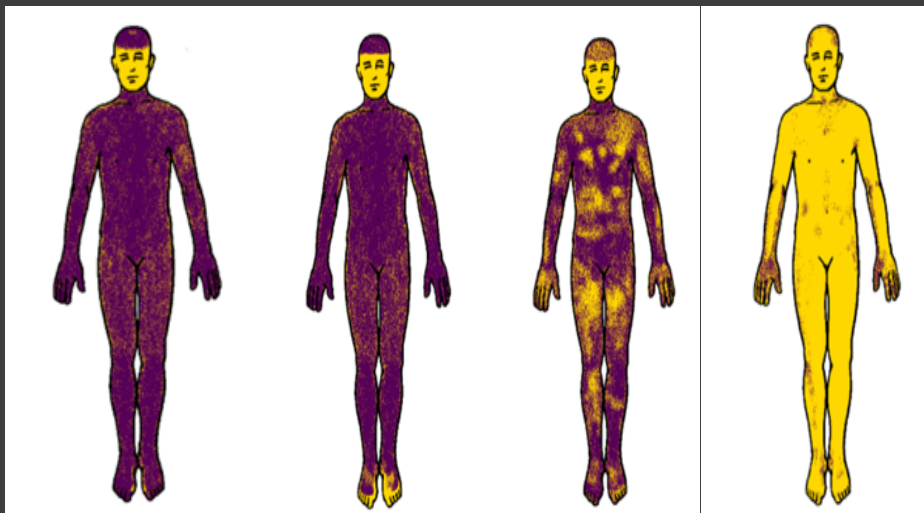
Sites	10–29 yr			30–49 yr			>50 yr		
	Mean	5th	95th	Mean	5th	95th	Mean	5th	95th
Forearm	1.15	0.20	2.78	1.15	0.20	2.78	1.15	0.20	2.78
Proximal leg	1.48	0.36	3.17	1.48	0.36	3.17	1.48	0.36	3.17
Distal leg	1.83	0.61	2.85	1.26	0.39	2.28	0.68	0.18	1.70
Proximal foot	1.27	0.23	3.07	1.05	0.18	2.85	0.84	0.12	2.64

Reference value

Thermoregulatory sweat test



TST



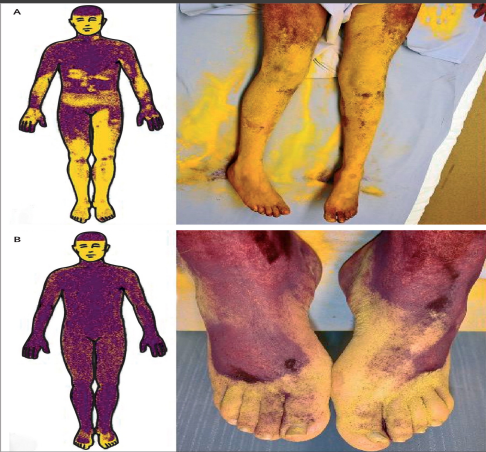
Normal

Distal anhidrosis

Patchy anhidrosis

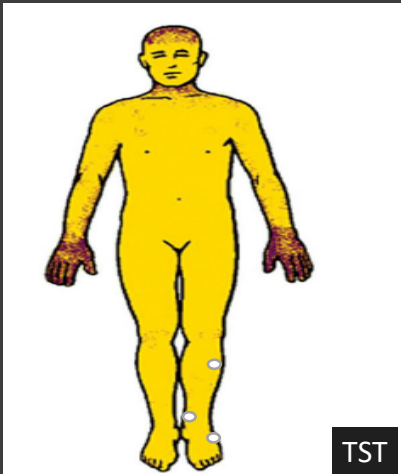
Global anhidrosis

TST

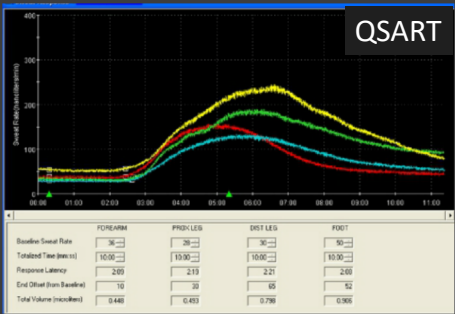


Lancet Neurol. 2010

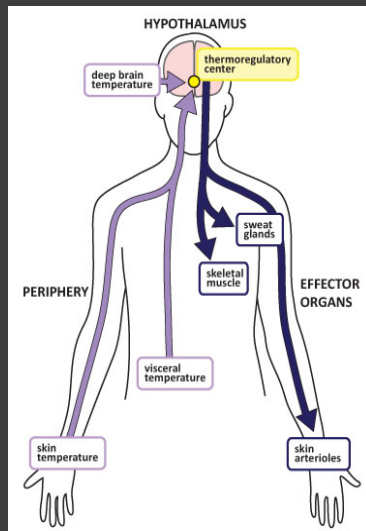
Central or Peripheral autonomic disorder



TST

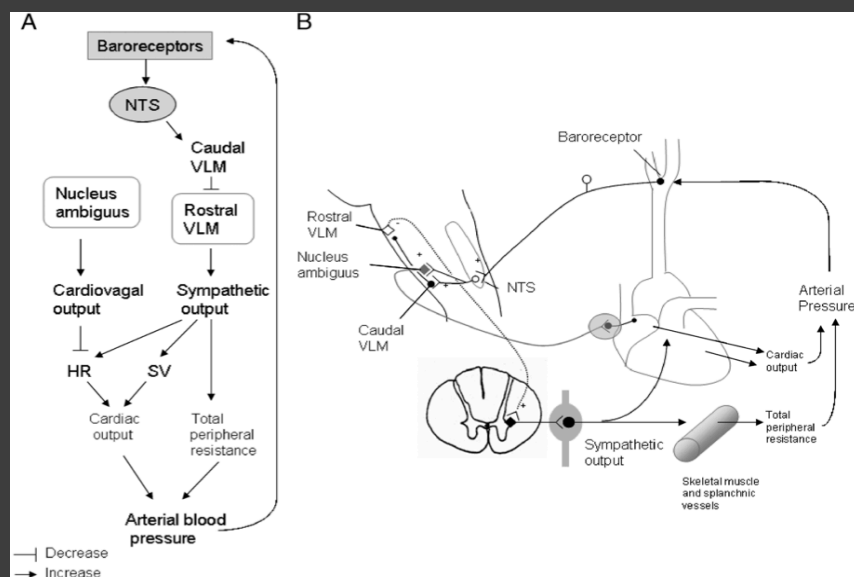


Central- peripheral autonomic disorder

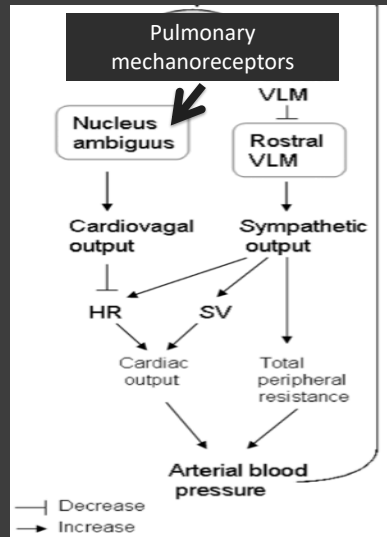


	TST	QSART
Central	Decreased	Normal
Peripheral	Decreased	Decreased

Baroreceptor reflex



Respiratory reflex



- During inspiration
 - Inhibit cardiovagal neuron in nucleus ambiguus
 - tachycardia
- During expiration
 - Withdrawn inhibition of cardiovagal neurons in nucleus ambiguus → bradycardia

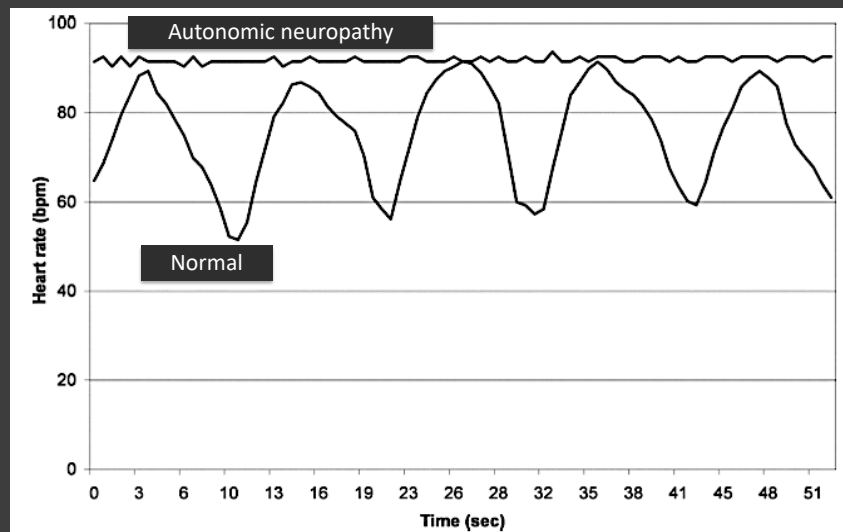
HR variability to deep breathing



HR variability to deep breathing



HR variability to deep breathing



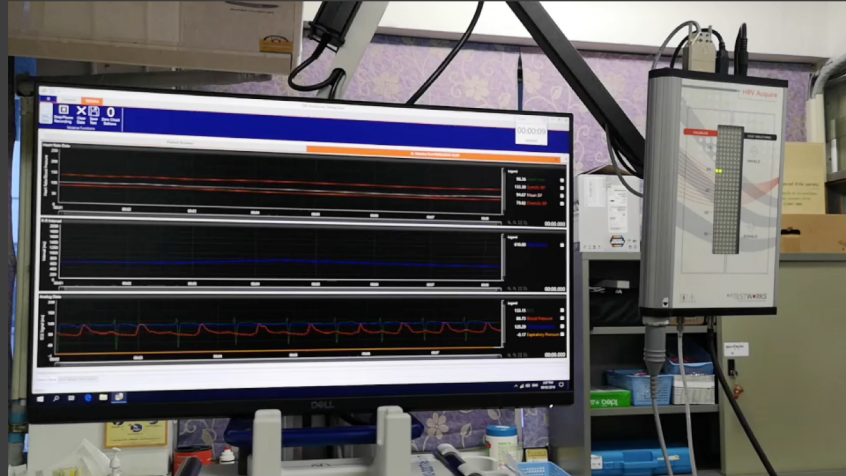
**Table 44-12. Heart Rate Response to Deep Breathing:
2.5th, 5th, 95th, and 97.5th Percentile Values by Age**

Percentile	11-29 yr	30-49 yr	50-69 yr	≥70 yr
2.5; 5.0	13; 14	9; 10	7; 7	7; 7
95; 97.5	41; 43	33; 36	27; 29	27; 29

Valsalva maneuver



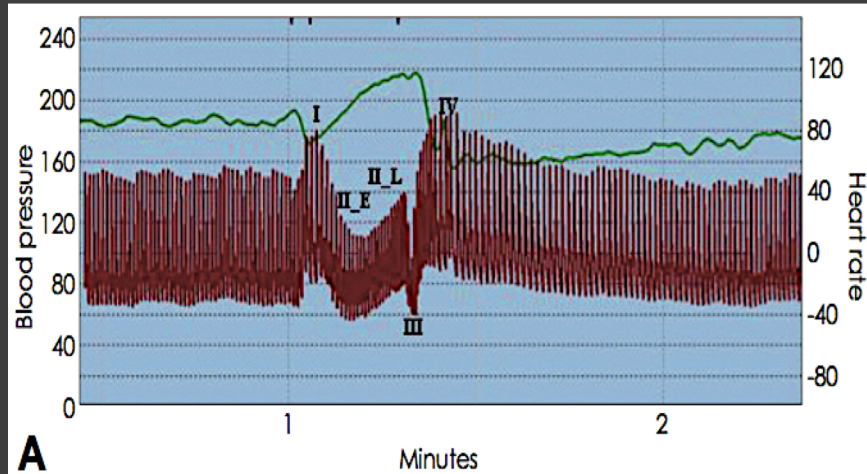
Valsalva maneuver



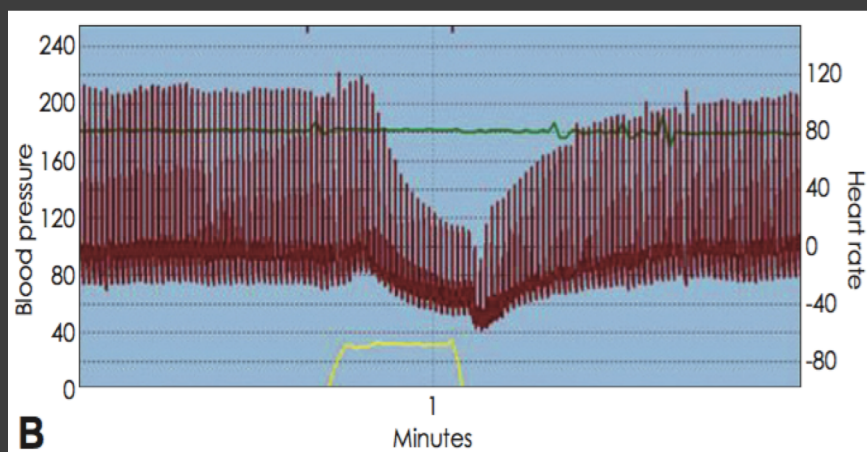
Valsalva maneuver



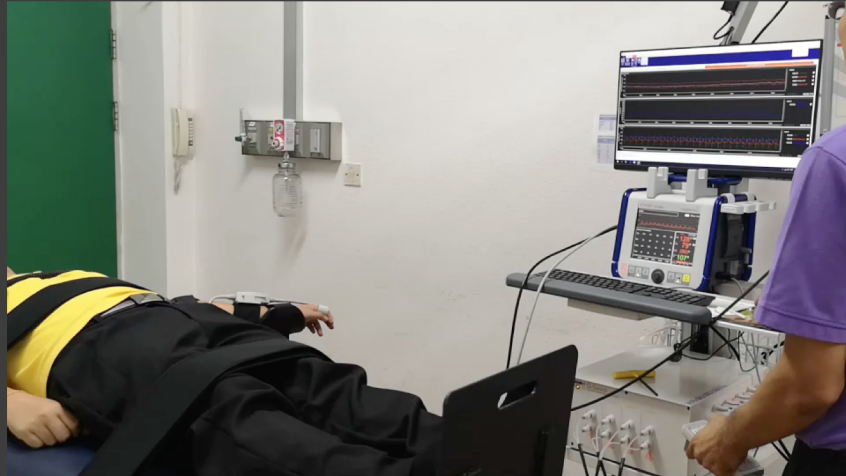
BP response to Valsalva maneuver (Normal)



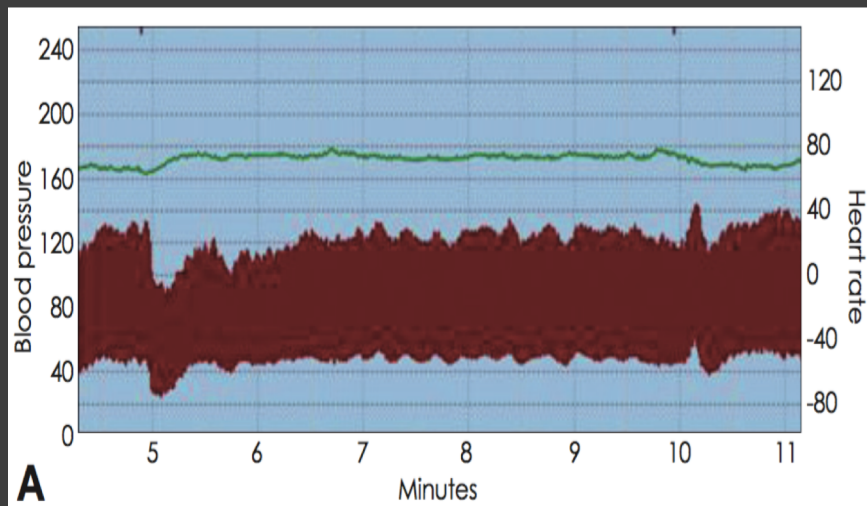
BP response to Valsalva maneuver (Abnormal)



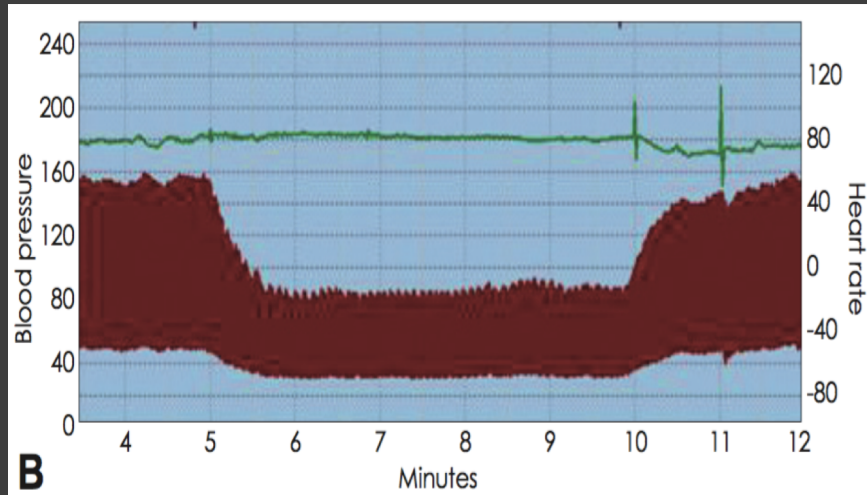
Tilt table test



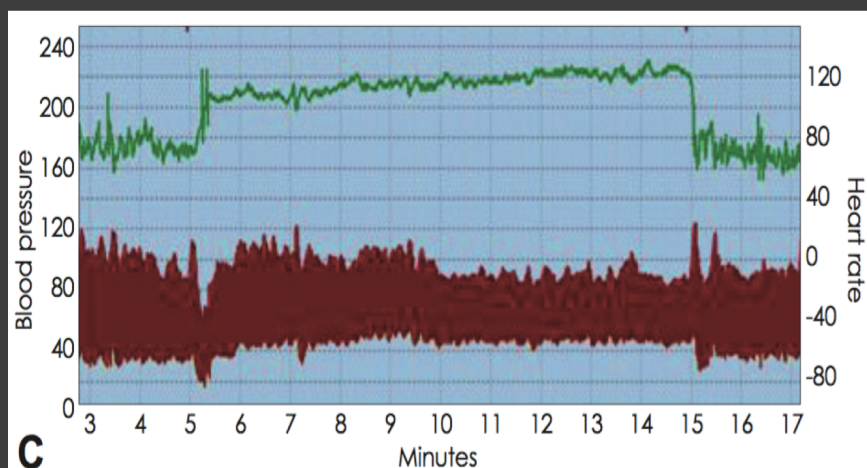
Normal



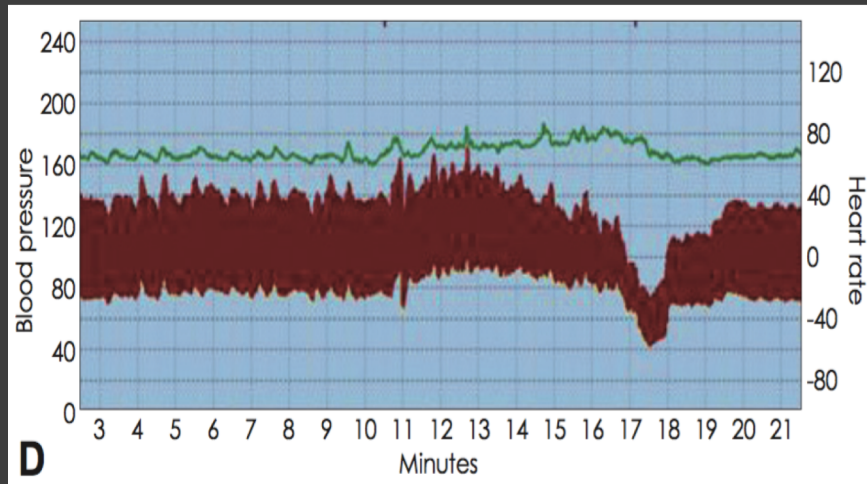
Neurogenic OH



Postural tachycardia syndrome (POTS)



Syncope



Autonomic test

Test	System evaluated	Pathways	Interpretation
QSART	Postganglionic sudomotor	Axon Reflex	Defines distribution of sweat loss
TST	Sudomotor	Central, preganglionic, postganglionic pathways and eccrine sweat gland	Provides accurate patterns of anhidrosis; pattern can suggest site of lesion
HRV	Cardiovascular function	Vagal afferent and efferent pathways	Normal or impaired cardiovascular function
Valsalva ratio	Cardiovascular function	Vagal pathway mediating baroreflex function	Normal or impaired cardiovascular function
BP responses to Valsalva Maneuver	Adrenergic function and baroreflex sensitivity	Baroreflex afferent and efferents	Baroreflex function
HUT	Baroreflex function	Baroreflex afferents and efferents	Detection of OH
Plasma NE supine/standing	Adrenergic terminals and baroreflexes	Baroreflexes and adrenergic terminals	NE response to standing
Cardiac MIBG	Adrenergic function	Postganglionic innervation of the heart	Postganglionic adrenergic denervation

Composite Autonomic Severity Score (CASS)

Sudomotor Subscore

- 0 Normal
- 1 Any of the following alterations:
 - a. Single QSART site reduced but $\geq 50\%$ of lower limit *or*
 - b. Distal sweat volume $< 1/3$ of forearm or proximal leg values *or*
 - c. TST anhidrosis present but $< 25\%$
- 2 Any of the following alterations:
 - a. Single QSART site $\leq 50\%$ of lower limit
 - b. ≥ 2 QSART sites reduced
 - c. TST anhidrosis $25\% - 50\%$
- 3
 - a. 2 or more QSART sites $\leq 50\%$ of lower limit
 - b. TST % anhidrosis $\geq 50\%$

Cardiovagal Subscore

- 0 Normal
- 1 HR_{DB} or VR reduced but $> 50\%$ of the lower limit of normal
- 2 HR_{DB} or VR reduced to $\leq 50\%$ of the lower limit of normal
- 3 Both HR_{DB} and VR reduced to $\leq 50\%$ of the lower limit of normal

Composite Autonomic Severity Score (CASS)

Adrenergic Subscore

The adrenergic subscore is based on alterations in blood pressure in response to the Valsalva maneuver and HUT

- 0 Normal
- 1 The presence of any of the following changes on the Valsalva maneuver:
 - a. Phase II_E reduction ≥ 30 mm Hg MBP *or*
 - b. Phase II_L does not return to baseline *or*
 - c. Pulse pressure reduction to $\leq 50\%$ of baseline
- The presence of any of the following changes occur on HUT:
 - d. Excessive oscillations in MBP (≥ 20 mm Hg occupying at least 50% of HUT)
 - e. Fall in pulse pressure $\geq 50\%$
 - f. Transient fall in SBP ≥ 40 mm Hg with recovery (within 1 min)
 - g. SBP reduction ≥ 20 mm Hg beyond 1 min
 - h. DBP reduction ≥ 10 mm Hg beyond 1 min

Composite Autonomic Severity Score (CASS)

- 2 If a score of 1 is determined from the Valsalva maneuver, it can be increased to 2 if the following changes occur on HUT:
 - a. Transient fall in SBP > 30 mm Hg with recovery within 2 min
 - b. SBP reduction ≥ 20 mm Hg beyond 1 min
 - c. DBP reduction ≥ 10 mm Hg beyond 1 min
- 3 A score of 3 is assigned if the following changes occur on the Valsalva maneuver:
 - a. Phase II_E reduction > 40 mm Hg MBP + absent phases II_L and IV
- 4 An additional point is assigned if a reduction in manual SBP ≥ 30 mm Hg occurs beyond 2 min and is sustained for at least 2 min

Clinical autonomic tests

- Indirect assess the integrity of sympathetic and parasympathetic output in target organ
- Response affected by
 - patient's preparation, effort
 - age
 - underlying disease – heart, lung
 - environment
 - drugs