Autonomic Testing

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Overview

- Review of the Autonomic Nervous System Anatomy
- Essentials of Clinical ANS Testing: Purpose, Indications, What’s involved?
- Clinical Correlation & pearls
- Research ANS Testing
ANS Central Component

- Insula: HTN, tachycardia, piloerection, pupillary dilation, and salivation
  - Left insula lesion: reduced parasympathetic activity
  - Right insular lesion: reduced inhibition of sympathetic tone
- Medial prefrontal cortex: Bradycardia, hypotension, modulates gastric secretion
- Hypothalamus: Relay station
- Amygdala: emotions, modulates autonomic function
- Ventrolateral medulla:
  - Nucleus of the tractus solitarius
  - Periaqueductal gray: integrative relay & pain modulation

Controls most reflex & autonomic cardiorespiratory fx
ANS Peripheral Component

- Sympathetic Nervous System --> Fight or flight
  ↑HR & BP, Pupil dilation & bronchodilation

- Parasympathetic Nervous System --> homeostasis & digestion
  ↓HR, pupil size, perstalsis, ↑bronchoconstriction

- Enteric Autonomic Nervous System
Review of the Autonomic Nervous System

- SNS or PNS activation can cause lacrimal, parotid, and submandibular glands secretion (PNS > SNS)

- Sexual function: PNS (erection) & SNS (ejaculation) have a complementary relationship.

- Organs receiving only sympathetic innervation:
  - Sweat glands
  - Piloerector muscles
  - Most small blood vessels
Review of the Autonomic Nervous System

- Cell bodies in the brain stem or spinal cord
- Efferent axons leave cell bodies and synapse on ganglia
- Axons from these 2nd order neurons synapse on the target organ.
Review of the Autonomic Nervous System

- Sympathetic preganglionic fibers are short; postganglionic fibers are long.
- ACh is the neurotransmitter for all preganglionic fibers in the autonomic nervous system.
- All postganglionic fibers in the PNS and sudomotor fibers in the SNS use Ach.
- Extension of clinical autonomic history & exam
- Tests will not be sufficiently comprehensive to evaluate all autonomic systems
- Efferent postganglionic autonomic fibers are unmyelinated --> cannot be tested directly by conventional neurophysiological methods (EMG/NCS)
ANS Testing

- Assess end organ ANS function by evaluating the response elicited reflexively by stimuli/maneuvers --> Conclusions of the reflexes are largely extrapolative
- Patient selection, adequate preparation
- Adequate panel of autonomic tests
Purpose

- Diagnose autonomic dysfunction
- Quantify the severity and determine the type of deficits
  - Sudomotor vs adrenergic vs cardiovagal
- Define the severity & distribution of autonomic failure
- Define the site of the lesion
  - Preganglionic vs post ganglionic
Indications

- Orthostatic Intolerance
  - POTS, Orthostatic hypotension, Loss of consciousness (Syncope, Seizures)

- Generalized Autonomic Failure
  - Autonomic Neuropathies
  - Multiple System Atrophy
  - Pure Autonomic Failure

- Limited Autonomic Neuropathy
  - Cholinergic, adrenergic, regional, distal
Indications

- Detect neuropathic basis in neurocardiogenic syncope
- Evaluate autonomic involvement in the peripheral neuropathies
- Monitor the course of autonomic neuropathy
- Evaluate therapy response
- Detect sympathetic dysfunction in sympathetically maintained pain
- Pt. w/ autonomic failure show an increase in mortality
Patient Preparation

- No food, coffee, or nicotine 3 hrs before ANS testing
- Medications
  - Anticholinergics:
    - antidepressant, antihistamine, OTC cough & cold meds
  - Sympathomimetics & Parasympathomimetics
  - α- & β- antagonists
  - Analgesics
- No compressive clothing the morning of the test
- No acute illness the previous 48 hours
- Vigorous exercise should be avoided within 24 hrs of the test
### Table 2: Autonomic features of common antiepileptic drugs

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Clinical ANS Testing

- Tests of sudomotor function
  - Quantitative Sudomotor Axon Reflex Test (QSART)
  - Thermoregulatory Sweat Test (TST)
  - Sympathetic Skin Response

- Cardiovagal function
  - Heart Rate Variability
  - Valsalva

- Tests of adrenergic function
  - Tilt Table Test
  - Active Standing
Axon reflex mediated by the postganglionic sympathetic sudomotor axon

Axon terminal activated by ACh

The impulse travels antidromically then orthodromically to release Ach

ACh binds M3 muscarinic receptors on sweat glands --> sweat response

Innervation mostly sympathetic cholinergic
- Post ganglionic sympathetic sudomotor axon
- Reduced, absent, excessive, or persistent sweating
- Abnormal in:
  - Generalized dysautonomias
  - Complex regional pain syndrome
  - Atopic dermatitis
  - Anticholinergic medication use
Sympathetic Skin Response

- Skin potential recording

- Stimulus: inspiratory gasp, cough, loud noise, electric shock
  - Induces changes in resistance of skin to electrical conduction

- Responses tend to habituate

- Significant sensory deficit can lead to absent SSR

- SSR can be present when QSART clearly impaired
Metronomic Breathing

- Heart rate response to deep breathing (metronomic breathing)
  - Affected by age and rate of breathing
  - Maximum variation at a rate of 5-6 breaths/min
Metronomic Breathing

- Max-Min: The difference between the avg maximum and avg. minimum heart rate during deep breathing

- E/I Ratio: Ratio of HR during exhalation to that during inhalation

- Effort dependent, sinus rhythm, obesity, medications, pacer

- High sensitivity for detecting diabetic autonomic neuropathy even before obvious symptoms
Valsalva Maneuver

- 40 mm Hg for 15 seconds x 2
- 40mm Hg yield reproducible results
Valsalva maneuver

P1: ↑ BP due to increased intrathoracic pressure
P2 (early): Steady BP falls as cardiac return falls
P2 (late): Fall in BP opposed via baroreflex mediated increase in HR & peripheral vasomotor tone.
P3: Release of the Valsalva --> transient decrease in BP caused by decreased intrathoracic pressure during inhalation
P4: CO returns to baseline rapidly but peripheral vasomotor tone remains elevated --> transient BP overshoot.

Valsalva Ratio:
The Maximum HR generated by the valsalva maneuver divided by the lowest HR occurring within 30 seconds of the peak heart rate.
Valsalva

- Square-wave curve: non-specific finding seen in hypervolemic state, CHF, mitral stenosis, constrictive pericarditis, and atrial septal defects.
Tilt Table test

- 60 Degree head-up tilt over 10-20 sec.

- Orthostatic BP drop greatest after 20 minutes of supine --> performed at the end of the study.

- Immediate response: Sharp decrease in BP & total systemic resistance followed by a rebound & overshoot.

- Corresponding HR increase follows in 3-5 sec.
Relative Contraindications

- Severe LV outflow obstruction
- Critical mitral stenosis
- Critical proximal coronary artery stenosis
- Critical cerebrovascular stenosis
Orthostatic Hypotension

A decrease in systolic pressure by 20 mm Hg or greater that’s sustained for at least 3 minutes in which the onset occurs after the 1st 3 minutes.

163/89→67/44

cc: Generalized dysfx
HR increase of 30 BPM or greater occurring within the 1st 10 minutes of the tilt and sustained for at least 3 minutes

Associated with a mild or early autonomic neuropathy, neuropathy that involves the distal vasculature sparing the cardiac innervation, cardiovascular deconditioning, cardiac beta adrenoreceptor supersensitivity, mitral valve prolapse, fever, and volume depletion.

The response can also be seen in patients diagnosed with the chronic fatigue syndrome.

A postural tachycardia may be a provocative factor for neurally mediated syncope.
POTS

- Neuropathic:
  - Peripheral adrenergic denervation → impaired sympathetically mediated vasoconstriction in the LE.
  - Blunted late phase II in the Valsava maneuver
  - Modest BP reduction on tilt
  - Abnormal QSART or TST
  - Epidermal nerve fiber pathology

Singer and Benarroch, Autonomic Neurology
POTS

Hyperadrenergic:

- Standing plasma NE $\geq 600$ pg/ml
- Higher HR, fluctuating BP or hypertension during the tilt.
- Symptoms of sympathetic hyperactivity (palpitation, tremulousness)

Singer and Benarroch, Autonomic Neurology
- Autoimmune POTS:
  - Nicotinic AChR Ab positive in ~ 15%

- POTS secondary to deconditioning (most common)
  - Modest HR increase; fall in pulse pressure
Baroreflex mediated HR increase peaks at the 15th beats after standing.

Baroreflex mediated HR suppression max at 30th beats after standing.
NMS (Hypotensive-bradycardic response)

Asystole x 15 sec
NMS (Hypotensive-bradycardic response)

- Periods of electrocerebral silence (flat EEG)
- Associated with shorter duration of prodromes
- Higher incidence of tonic-clonic jerks
- Longer duration of syncope
NMS (paroxysmal vasodepressor response)

Diffuse generalized EEG slowing in NMS with hypotension alone.
TST

- Alizarin red + sodium carbonate + corn starch
- Air temp = 44-50°C; skin temperature 39-50°C; relative humidity 35-45% x 45-65 minutes.
  - Minimize heat injury or direct sweat gland activation
- Oral temp must rise above 38°C or by 1°C above baseline temp
- % anhidrosis calculated by digital image processing
Generalized anhidrosis suggests generalized involvement of adrenergic and cardiovagal function.

- Characteristic of MSA and pure autonomic failure
- Distal small fiber neuropathy
- PD pts invariably have $<40\%$ anhidrosis
- MSA pts almost always have $>40\%$ anhidrosis
Sweat distribution patterns

- Distal anhidrosis: length dependent distribution
- Segmental anhidrosis: Large contiguous zones, maybe b/l
  - PAF, MSA, Ross Syndrome, immune-mediated autosympathectomy, surgical sympathectomy
- Regional anhidrosis
- Focal anhidrosis
- Global anhidrosis
  - MSA & generalized ANS Failure
Acquired Idiopathic anhidrosis

- Ross Syndrome
  - Adie’s pupil, areflexia, segmental anhidrosis
  - Compensatory hyperhydrosis

- Idiopathic Pure Sudomotor Failure
  - Sudden onset sharp pain or cholinergic urticaria over the entire body
  - Generalized anhidrosis but no other dysautonomia
  - Elevated IgE
  - Absence of thermoregulatory sweating but intact emotional sweating
TST in secondary disorders

- Hypothalamic tumors --> global anhidrosis
- Traumatic spinal cord injury
  - global anhidrosis with complete cervical cord lesions
  - segmental anhidrosis below the level of the lesion in T- cord
  - Variable sweat loss with lesion in lumbar cord.
- Pancoast tumor, MS, PD, MSA, LBD
**TST vs QSART**

- **TST**
  - Semi-quantitative topographic measure of pre- & post- ganglionic sudomotor function of the entire body
  - Does not localize pre- vs post ganglionic lesions

- **QSART**
  - Measure post ganglionic axon reflex mediated sudomotor function
  - Provides temporal resolution to data (continuous analysis of sweat response)
- If absent sweating on both --> postganglionic lesion
- If absent on TST but normal QSART --> preganglionic lesion
ANS Testing w/ EEG Monitoring

- Patients w/ recurrent unexplained convulsive syncope
- Ictal syncope
- Psychogenic syncope
- PNES
Research ANS tests

- Skin reflex studies
  - Ionophorese Ach --> releases NO and nitroprusside
  - Laser Doppler flowmeter to measure the ensuing changes in skin blood flow.

- Baroreflex sensitivity estimate
  - IV Na nitroprusside followed by phenylephrine bolus --> HR monitoring

- Microneurography
  - Microelectrode inserted into a peripheral nerve to measure sympathetic neural discharges from unmyelinated axons
Research ANS Tests

- Cardiac autonomic innervation
  - MIBG (I-123 meta-iodobenzylguanidine) cardiac scintigraphy.
  - Isotope that traces postganglionic sympathetic adrenergic neurons.
  - Sensitive tool for detecting cardiac sympathetic denervation
    - Normal uptake in MSA
    - Reduced uptake when dysautonomia present in PD and Diabetic autonomic neuropathy

Research ANS Tests

• Cold Pressor Test
  • Triggers a vascular sympathetic activation and an increase in blood pressure.
  • Immerse a subject’s hand into ice water (1-5 °C) for 1-6 minutes while measuring BP & HR.
  • Increased peripheral resistance and a sustained BP increase.