

CLINICAL ELECTROPHYSIOLOGIC TESTING IN THE AGING NEUROMUSCULAR SYSTEM

Combined Sections Meeting

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Course Description

It is well known that aging affects peripheral nerve function.¹ These changes are not linear with age² and it is often difficult to distinguish changes due to aging vs. a patient's co-morbidities. Thus performing and interpreting clinical electrophysiologic tests on older patients can be a challenge. The clinician often must determine if electrophysiologic findings are "normal" for the individuals' age or indicates pathology. Changes in the peripheral neuromuscular system due to aging will be discussed along with the effects these changes have on the clinical electrophysiological exam. The evidence regarding how to adjust or modify the electrophysiologic exam and how to use normal values for older patients will be presented.

1. Jeronimo A, et al. A morphometric study on the longitudinal and lateral symmetry in the sural nerve in mature and aging female rats. *Brain Research* 1222:51-60, 2008

2. Verdú, E., et al. Influence of aging on peripheral nerve function and regeneration. *J. Peripheral Nerv. Syst.* 5:191-208, 2000

Objectives

1. Discuss the effects of aging on the neuromuscular system
2. Discuss how aging affects data obtained from the electrophysiologic exam
3. Discuss the effects co-morbidities associated with aging have on the neuromuscular system
4. Employ appropriate evidence-based strategies to modify techniques and normal values when performing a clinical electrophysiologic exam on the elderly

Background

- The older population (65+) numbered 37.3 million in 2006, an increase of 3.4 million or 10.0% since 1996.
- About one in every eight of the population is an older American.
- The population 65 and over will increase from 35 million in 2000 to 40 million in 2010 (a 15% increase) and then to 55 million in 2020 (a 36% increase for that decade).

- The 85+ population is projected to increase from 4.2 million in 2000 to 6.1 million in 2010 (a 40% increase) and then to 7.3 million in 2020 (a 44% increase for that decade).

In 1999-2000, 28% of adults aged 70-79 years and 35% of adults aged ≥ 80 years had peripheral neuropathy based on a simple screen for reduced sensation at the foot (Gregg et al, 2004)

Age-related Neuromuscular Changes

Physical exam changes

Decreased strength

Gait: slower, reduced arm swing, flexion posture

Distal DTR changes

Sensory: vibratory loss most marked

Autonomic changes

Orthostatic hypotension

Temperature control

Electrophysiologic Testing in the elderly is a challenge

Are findings “normal” for the age?

Are findings related to co-morbidities often associated with age?

Are findings related to neuromuscular pathology?

Age-related Neuromuscular Changes

Motor and sensory axons: decreased #

Vascular: thickening of walls of small blood vessels

Neurotransmitters: decline in the concentration of acetylcholine, norepinephrine, and dopamine

Muscle: atrophy

Myelin changes – schwann cell death and thinning of myelin sheaths

Age-related Neuromuscular Changes

With the decline of motor neurons (and thus motor units); comes reorganization of motor units

Larger motor units through collateral sprouting

- Little change in the number of muscle fibers
- Little change in tension development of individual motor units, but change in overall muscle tension

More variable firing
Deficits in strength and motor control
Changes are not linear but accelerate with advancing age

Tomlinson & Irving, 1977; study of 13-90+ year old subjects
No motor neuron loss up to age 60
After age 60, 50%+ motor neuron loss

Losses of motor units are greatest in the largest and fastest motor units (Doherty et al, 1993)

Histologic changes

Density of large myelinated fibers of the sural nerve progressively decline after the second decade of life (Jacob & Love, 1985)

After the sixth decade:

Internodal length shortens
Diameter of myelinated fibers thins
Lascelles & Thomas, 1966)

Morphologic changes

Aging sural nerves of rats (Jeronimo et al, 2008)
No change in number of axons
Reduction of fiber diameter,
Large axons affected more than small axons
Demyelination

NMJ changes

Postsynaptic membrane becomes longer
Wokk et al, 1990

Firing rates are slower in the elderly and twitch times are longer
Central and peripheral reasons
Decreased excitability in the corticospinal tract
Preferential loss of large axons
Longer twitch time = slower recovery
Connelly et al, 1999

Degeneration – Regeneration

Clinical electrophysiologic testing in the aging neuromuscular system. CSM Feb 09. Greg Ernst, PT, PhD,
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Both slower in the aged NM system
Terminal sprouting to target organs few in number
End result: higher connective tissue to axonal tissue ration in the age

Challenge: Normal Aging or Co-morbidities?

Systemic Conditions in the Aged

Osteoarthritis

- Radiculopathy
- Spinal stenosis
 - Multiple level involvement
- Cervical Myelopathy
 - Pain not a predominant feature
 - UMN signs below level of injury
 - Unsteady, wide-base gait

Osteoporosis

- Bone tissue is innervated and neurotransmitters affect bone remodeling
- Study of 2000+ men/women 70-79 years:
 - BMD was significantly related to peripheral nerve function (peroneal NCV and CMAP and detection of 10g monofilament)
 - Strength, physical ability, co-morbidities, physical function controlled for
 - Strotmeyer et al, 2006

Alcohol related neuropathy

- 62% of persons b/w 60 – 94 regularly use alcohol
 - 13% of men and 2% of women = heavy drinkers
 - (Mirand and Welte, 1996)
- Axonal, sensorimotor distal polyneuropathy (+/- secondary demyelination)
 - Direct neurotoxic effect (Narita et al, 2007)
 - Nutritional deficiency

EPT findings:

- Primarily reduced sensory/motor amplitudes or absent responses
- Distal involvement > proximal
- Kimura, 2001

Alcohol related myopathy

Chronic

Shoulder and pelvic girdle

72% have a associated neuropathy (Martin et al 1985)

Heavy lifetime use of alcohol (Urbano-Marquez et al, 1989)

Recovery takes weeks to months

46% have muscle biopsy evidence of myopathy (Urbano-Marquez et al, 1989)

Critical Illness Myopathy

Associated with (Biglan, 2002)

- Sepsis
- Multiorgan failure
- Corticosteroids
- NMJ blocking agents

Vit B-12 deficiency from mal-absorption due to GI changes with aging

Occurs in 30% of people > 60 years old (Krasinski, 1986)

Hypothyroidism

Incidence of up to 18% in the elderly (Griffin, 1990)

Symptoms

- Depression
- Weight gain
- Hair loss
- Dry skin
- Cold intolerance
- Constipation
- Muscle cramps

Diabetes

28% - 66% of patients with diabetes have a neuropathy (Young 1993; Dyck 1993)

- 20% have symptoms (Dyck, 1993)

Factors that increase risk of neuropathy in the patient with DM (Young 1993) :

- Extended disease (> 12years)
- Age > 50 years
- Longstanding hyperglycemia due to poor control

typical symptoms (symmetrical)

- Distal paresthesias
- Vibratory loss
- Peripheral weakness
- Potential foot/hand deformity

Distal sensory > motor neuropathy
Axonal with secondary demyelination

— Kimura, 2001

Diabetes – other neuropathic disorders

Mononeuropathy multiplex

Diabetic amyotrophy (proximal asymmetric painful motor neuropathy)

- Unilateral femoral neuropathy
- Thigh pain precedes muscle wasting
- Weight loss
- Older men with poor control
(Kimura, 2001)

Diabetic thoracic neuropathy

- +/- radicular pain along course of intercostal nerve
- Abdominal or chest pain
- Weight loss

EPT findings

- Ventral and/or dorsal rami involvement
- May or may not accompanying distal findings

Renal Failure

- Uremic neuropathy
 - 70% of patients with chronic renal failure
 - Distal, symmetric axonal polyneuropathy with secondary demyelination
 - May resolve or improve with dialysis or kidney transplant
 - EPT findings
 - May affect all limbs
 - Median and peroneal nerves more commonly affected (Nielsen, 1973)
 - Acute – Guillain-Barre type findings reported (Ropper, 1993)

Myopathy

- Proximal

Cancer

Pancoast tumor - brachial plexus
Pelvic tumors – lumbosacral plexus
Nasopharynx tumors – cranial nerves

Chemotherapy

Typically distal, symmetric, sensory > motor polyneuropathy

- Motor recovers; sensory symptoms often do not

Radiation

Neuropathy
Plexopathy
Motor neuron syndrome

Translating neuromuscular changes to findings in the clinical electrophysiology lab

Nerve Conduction Changes

Infants:

NCVs are approximately 50% of adults reaching 75% of adult speed by one year of age and 100% of adult at 4 years of age (Oh, 1984)

Often see double peaks in infants and small children due to two groups of fibers with different levels of maturation

Nerve Conduction Changes Sensory

Adults

Sensory NCV: Consistent decline of 1-2 M/sec for each decade after the second decade (Dumitru, 2002)

- 1.2 m/sec per decade from 20-54 years
- 3.3 M/sec per decade after 54 years

(Ulnar nerve, needle technique Buchthal & Rosenfalck, 1975)

Sensory nerve amplitude can decrease as much as 36% by 60 years of age (Lafratta, 1966)

Median Sensory NCS 14 & 7 cm antidromic study - Buschbacher, 1999

- Increasing BMI and decreasing age lead to decreased amplitudes and area Amplitudes 14cm segment – index finger

Age 19-49	<u>Mean (SD)</u>	<u>Mean (-2SD)</u>
BMI		
<24	49(19)	17
>24	41(19)	11
Age 50-79		
BMI		
<24	28(11)	9
>24	24(11)	7

Nerve Conduction Changes Motor

Norris et al, 1953

Median nerve: Non-linear changes; slowing most pronounced after age 60 Range: 0.6 – 2.3 M/sec

Braddom and Johnson, 1974

Tibial NCV (M/sec):

Age:	<u>20s</u>	<u>30s</u>	<u>40s</u>	<u>50s</u>	<u>60-80</u>
NCV (M/sec)	52.1	48.0	49.0	48.4	44.0

Peroneal Motor NCS - Buschbacher, R M, 1999

Amplitude

6.8 < 40 years

5.1 > 40 years

Retrospectively studied 3969 normal studies in the upper and lower extremities

Age inversely correlated with amplitudes

Height inversely correlated with NCV

Combination of age + height explained more variance

Percentage of absent responses increased with aging

Age N	% absent responses of clinically "normal" subjects			
	Sural	Per M	Ulnar M	Ulnar S
20-29 239	<1	0	0	0
30-39 598	<1	<1	0	<1
40-49 592	<1	<1	<1	<1
50-59 386	3.4	2.5	0	3.0
60-69 194	4.6	1.2	0	4.8
70-79 46	23.9	6.7	0	7.0
80-89 5	40.0	25	<1	50

Gender differences: Study of 2000+ men/women aged 70-79 years (Strotmeyer et al, 2006)

Men were:

Less likely to detect 10g monofilament (11.8% vs. 5.8%)

Higher vibration threshold

Peroneal CMAP of 2.9 vs 3.6mV

Peroneal NCV 41.6M/sec vs. 44.7 M/sec

H reflex Latency in the Healthy Elderly - Falco et al, 1994

103 healthy subjects 60-88 years old

H reflex latency associated with leg length ($r = .55$)

No association between H reflex latency and age

More variability between sides in the elderly

Recommend 1.8msec side to side difference as threshold for normal in patients > 60 years

NORMAL RANGE FOR H-REFLEX RECORDING FROM THE CALF MUSCLES Buschbacher, R M, 1999

251 subjects;

22 absent responses

Avg age of patients with absent responses: 49 years;
with responses: 42 years

Age and height associated with H reflex latency; no association with BMI, race, or gender

No differences in side to side variability in young vs. old

— See table....

EMG in healthy subjects 20-80 years old

Amplitudes, durations, and number of turns all increased with age

Men tended to have larger amplitudes, rise rates and number of turns

Thought to be due to larger muscle fibers

Howard et al, 1988

N = 65; 21-88 years old

41% had PSW or fibs at L4 and/or S1 (> 0.5sec)

7% at L4; 7% at S1; 85% at both levels

>50% of subjects 50-88 years old

r value of .83 when correlating findings with age

Conclusion: PSM findings meaningful in young; insignificant as an isolated finding in the aged

Paraspinal EMG

● Date et al, 1996:

14.5% asymptomatic younger subjects with PSW/fibs (> 1 second duration)

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Dumitru et al, 2001:

AH, EDB, and LS paraspinals of 10 subjects per decade, 20-80 years old
2% had fibs/psws in the foot mm (21 year old)
4% had fibs/psw in PSM (50 and 52 year old)
Many fasciculation potentials in the feet (60-94%)
6% fasciculation potentials in the PSM
Criticized earlier studies – in accurate identification of PSWs/fibs

N = 100; fibs and PSW > .5sec; MUAP

20-40 years: no spontaneous activity
40-60 years: 8% spontaneous activity
> 60 years: 92% spontaneous activity

With age, amplitude and duration of MUAP increased

Carpal Tunnel Syndrome

Increased incidence of CTS (Gelfmen et al, 2009)

Large majority of this increased due to increase in the elderly
Findings are more severe in the elderly
Elderly more likely to have a CTR

Vessey et al:

— CTS rate doubles in females > 55 years (Vessey et al, 1990)

Median Motor NCS

Electrode placement for median motor NCS

Traditional placement of the active recording electrode results in highest amplitude in the Young

In elderly with CMC OA (25 patients, 73 years):

- The amplitudes routinely lower and latencies longer
- Much more variation with small changes in placement of active recording electrode
- Recommendation: in the elderly, try several placements of the active recording electrode and use best responses.

Double Crush Syndrome (DCS)

- Average age of pure CTS = 38 years

- Average age of DCS = 49 years
- The prevalence of CTS was 24% in myelopathic patients
Previous studies ~10%

Increasing *age* of a *male* adult from 50–60 may increase the risk for DCS more than 11 times.

Recommendation: EMG of cervical paraspinals in all elderly men with CTS.

Prevention of Neuromuscular Changes

- Aerobic exercise group had a greater number of schwann cells and a thicker myelin sheath compared to an untrained group (sciatic nerves of rats after one year of training 60min/day, 6 days per week; Shokouhi et al, 2008)
- Neural adaptations are likely to occur with training in the elderly (Williams et al, 2002)
- Exercise prevented the age-related loss of neurons in exercising rats (Gagliardo et al, 2008)

Summary

- No absolute guidelines
- Little concern for those under 60
- Consider co-morbidities
- Amplitudes much more affected than NCV