The Neurological Examination in Aging, Dementia and Cerebrovascular Disease

Part 4: Reflexes and Sensory Examination

David J. Gladstone, BSc, MD, Fellow, Cognitive Neurology and Stroke Research Unit, Sunnybrook and Women's College Health Sciences Centre, Division of Neurology, University of Toronto, Toronto, ON.

Sandra E. Black, MD, FRCPC, Professor of Medicine (Neurology), University of Toronto; Head, Division of Neurology and Director, Cognitive Neurology Unit, Sunnybrook and Women's College Health Sciences Centre, Toronto, ON.

Abstract

This four-part series of articles provides an overview of the neurological examination of the elderly patient, particularly as it applies to patients with cognitive impairment, dementia or cerebrovascular disease. The focus is on the method and interpretation of the bedside physical examination; the mental state and cognitive examinations are not covered in this review. Part 1 (featured in the September issue) began with an approach to the neurological examination in normal aging and in disease, and reviewed components of the general physical, head and neck, neurovascular and cranial nerve examinations relevant to aging and dementia. Part 2 (featured in the October issue) covered the motor examination with an emphasis on upper motor neuron signs and movement disorders. Part 3(featured in the November issue) reviewed the assessment of coordination, balance and gait, and Part 4, featured here, discusses the muscle stretch reflexes, pathological and primitive reflexes, and sensory examination, and offers concluding remarks. Throughout this series, special emphasis is placed on the evaluation and interpretation of neurological signs in light of findings considered normal in the elderly.

Reflexes

Muscle Stretch Reflexes

Muscle stretch reflexes (also called myotatic reflexes or deep tendon reflexes) are routinely tested for their presence or absence, their degree of hyperactivity or hypoactivity, and their symmetry or asymmetry. Examination of reflexes provides a fairly objective assessment of neurological function that requires little patient cooperation. Although there is a wide range of responses in normal individuals, reflexes that are significantly diminished or absent suggest disease of the peripheral nervous system (peripheral neuropathy), whereas pathologically brisk reflexes usually point to a central nervous system cause (pyramidal tract lesion). The NINDS Myotatic Reflex Scale grades reflexes as follows:

0 = absent
1 = less than normal, trace response or reinforcement required
2 = reflex in lower half of normal range
3 = reflex in upper half of normal range
4 = reflex greater than normal, including clonus if present.[1]

Muscle stretch reflexes tend to diminish with aging. It is often necessary to use reinforcement techniques to bring out reflexes that otherwise appear sluggish or absent. These include teeth clenching, making a fist with the opposite hand, or Jendrassik's maneuver, in which the patient interlocks flexed fingers of each hand and tries to pull them apart. Many studies have reported loss of ankle jerks to be a common finding in the elderly, occurring in up to 20% of healthy community-living elderly over age 65 and, depending on the study, up to 78% of persons over age 85.[2-4] However, recent studies cast doubt on the widely-held notion that ankle jerks are lost as part of normal aging. In one study of 200 consecutive patients (mean age 80) admitted to a geriatric unit at Hammersmith Hospital, UK, ankle jerks were present in 80% of subjects; with reinforcement (Jendrassik's maneuver) ankle jerks were elicited in 94%.[5] In this study, ankle jerks were elicited using the plantar strike technique, which is reported to have greater reliability in the elderly than the traditional tendon strike technique.[6] Of the 6% with absent ankle reflexes, most had an underlying cause for neuropathy; only three individuals had loss of ankle jerks as an isolated finding. Similarly, in a community sample of 398 people over age 65, absent ankle jerks were found in only 7%.[7] Absence of knee jerks or upper extremity reflexes should not normally be attributed to aging alone and suggests disease of the peripheral nervous system.

Hyperreflexia is an uncommon finding in the elderly and should suggest central nervous system disease, especially if accompanied by other features of the upper motor neuron syndrome such as an extensor plantar response, spasticity or pyramidal weakness. Other manifestations of hyperreflexia include clonus (which can be elicited at the ankle, knee or wrist), or a brisk Hoffmann's or Tromner's reflex (variants of the finger-flexor reflex in which there is flexion of thumb and fingers in response to sudden stretch of the distal phalanx of the middle finger). Unilateral hyperreflexia is a common residual finding from hemiparesis due to stroke. In the elderly patient with bilateral hyperreflexia, one should consider cervical spondylitic myelopathy;[8] in

this condition, a normal jaw jerk in the setting of brisk bilateral limb reflexes helps localize the site of pathology to the cervical spinal cord. Diffuse hyperreflexia may also be a sign of hyperthyroidism, whereas severe hypothyroidism can produce "hung-up" reflexes with delayed relaxation.

Multi-infarct vascular dementia often produces asymmetrical brisk reflexes as a sign of focal corticospinal tract dysfunction. Diffuse cerebral hemispheric vascular disease with bilateral corticospinal involvement can produce generalized hyperreflexia, including a brisk jaw jerk and pseudobulbar palsy. Abnormal reflexes are not usually seen in Alzheimer disease (AD),[9,10] although hyperreflexia has been reported (10% of patients in one study).[11] Franssen *et al.* found a correlation between hyperreflexia and increasing severity of dementia in AD.[12,13]

Babinski Sign

The extensor plantar response, described as a neurological sign in 1896 by the French physician Joseph Babinski, is always pathological in adults.[14-16] It signifies interruption of the corticospinal tract (upper motor neuron lesion) anywhere along its pathway from the contralateral motor cortex to the lumbosacral spinal cord. The Babinski sign is not seen as a part of normal aging and can be a helpful clue to the presence of silent stroke, cerebral mass lesion or spinal cord compression. It should not ordinarily be present in AD and is more commonly associated with vascular dementia (VaD).[9,11] The extensor plantar response has been reported in advanced AD,[10,17] but one wonders whether some of these responses may be withdrawal responses.

To elicit the reflex, one gently strokes along the lateral aspect of the sole of the foot toward the base of the toes and across the ball of the foot using a key, thumbnail, edge of a broken tongue blade or a thin stick (for an excellent review of the technique and interpretation, see van Gijn[14,16]). The patient should be relaxed in the supine position and told to expect a light pressure on the foot. One should take care to avoid producing pain or tickle, deep scratches or cuts.[16,18] The usual normal response to plantar stimulation is downward flexion of toes (no response of the toes may also be normal, unless asymmetric). The abnormal response is an upgoing great toe that is best appreciated by watching for tightening of the extensor hallucis longus tendon on the dorsum of the great toe. As the Babinski sign is part of a flexion withdrawal reflex, one should also watch the rest of the leg for signs of the full triple flexion response (upgoing great toe, knee flexion and hip flexion). Sometimes extension of the great toe is preceded by a brief flexion of the great toe. A true Babinski sign is usually associated with some degree of pyramidal motor dysfunction in the foot.[19] Many patients display a withdrawal reaction that can be easily confused with a true extensor plantar response, but withdrawal of the foot and leg is semivoluntary and nonstereotypic. To avoid withdrawal, minimize the stimulus intensity and stroke only a few centimeters on the lateral foot, not the sole. Interpretation of the plantar response is often heavily dependent on the clinical context (i.e., what the examiner expects to find),[20] and interrater reliability is poor (only 17% agreement greater than chance alone).[21] Many alternate methods for eliciting the extensor toe sign have been described, including those of Chaddock (stroking the lateral aspect of the foot), Opphenheim (applying pressure down the shin), Gordon (squeezing the calf), Stransky (abduction and release of the little toe) and Gonda (traction, flexion and release of the third or fourth toe).[14,22]

Primitive Reflexes

Much has been written about the primitive reflexes (also called frontal release signs, cortical disinhibition signs or developmental reflexes) as possible indicators of dementia (Table 1). However, their clinical significance remains controversial and their uselessness as part of routine neurological examination has been emphasized by some authors.[23] Primitive reflexes are present in infancy and disappear with development of the central nervous system. Reappearance of these reflexes has been considered a release of subcortical and brainstem activity due to loss of cortical—particularly frontal—inhibition.[24] Standardized testing protocols have been described.[13,25-27]

Primitive Reflexes in the General Population

Often thought to signify disease, primitive reflexes are relatively common in the general population. In a survey of 240 young, healthy university students (average age 20 years), primitive reflexes could be elicited in one-quarter (23% had one primitive reflex; only 2% of subjects had two primitive reflexes, and 0.4% had three primitive reflexes).[28] Thus, it may be inferred that healthy, young individuals are "allowed" to have one primitive reflex, but multiple primitive reflexes are infrequent. The most common reflex was the palmomental reflex (24%); glabellar, suck or grasp responses occurred in less than 3% of subjects, and none had a snout reflex. Of those with a palmomental reflex, the vast majority had unilateral responses only. In a study comparing normal subjects, patients with hemiplegic stroke and patients with traumatic brain injury, only a combination of several primitive reflexes distinguished between those with and without neurological disease (i.e., none of the control subjects had three primitive reflexes).[29] These findings support the concept that a single isolated primitive reflex is of no consequence, but multiple primitive reflexes may correlate with brain pathology. The prevalence of primitive reflexes increases with age, rising to approximately 50% in normal elderly individuals, although individual studies vary in terms of study population, reflexes tested and methodology.[30,31] A correlation with incidental cerebral lesions on MRI has been reported.[32]

A distinction has been made between the "nociceptive reflexes" (palmomental, glabellar and snout) and the "prehensile reflexes"(grasp, traction and suck). The nociceptive reflexes, particularly the palmomental and snout, are common findings; the palmomental

Table 1

Primitive Reflexes: Definitions and Examination Techniques[13,25-27]

Palmomental reflex	Scratching briskly along the thenar eminence of the patient's hand with a key, tongue depressor blade or thumbnail elicits contraction of the ipsilateral chin (mentalis muscle). The pollicomental reflex is a variation in which the examiner scratches briskly from the thenar eminence towards the tip of the thumb.
Snout reflex	Tapping over the patient's lips or philtrum with a finger or reflex hammer on the finger elicits puckering or protrusion of the lips.
Head retraction reflex	Tapping the upper lip with a reflex hammer elicits a brisk backward jerk of the head.
Glabellar reflex (Meyerson's sign)	Tapping between the patient's eyebrows with a finger at one tap per second elicits eye blinking with no habituation after several repetitions (examiner instructs patient not to blink and must approach from behind patient to avoid a visual threat response).
Sucking reflex	Stroking the lips with a tongue depressor blade elicits sucking movements of the mouth.
Rooting reflex	Stroking the corner of the mouth or cheek with a tongue blade elicits a head turn or movement of the mouth towards the stimulus.
Traction reflex	Extending the patient's flexed fingers elicits hooking of the examiner's fingers.
Nuchocephalic reflex[63]	Turning the patient's shoulders briskly to the right and left with eyes closed elicits no reflexive head turn in the direction of the shoulders.
Corneomandibular reflex (winking jaw)	Corneal stimulation elicits closure of the mouth or deviation of the jaw away from the side of stimulation.
Grasp reflex	Stroking the palm of the patient's hand from proximal to distal while the patient is distracted elicits a grasp response. The patient may be unable to release the examiner's hand. A foot grasp reflex (plantar-flexion of the toes) may be elicited by stimulation on the plantar surface of the foot.

reflex is the most common primitive reflex elicited at all ages in many studies and often appears earliest with advancing age.[33-35] Therefore, the presence of these reflexes alone has neither diagnostic nor prognostic value. In contrast, the grasp, snout and corneomandibular reflexes usually appear at later ages and are elicited less frequently. In a summary of 15 published studies, the grasp and suck reflexes were not seen in the healthy young population (20–60 years old) and were present in only 0–10% of the healthy old population (> 60 years).[35] The grasp reflex is rarely observed in normal individuals[3] and is felt to be the most reliable sign of cortical disinhibition, which is not normal for age.

Primitive Reflexes in Dementia and Cerebrovascular Disease

The prevalence and utility of primitive reflexes in dementia have been investigated in several studies.[9,11,12,24,33,35-37] The prevalence of primitive reflexes is higher among patients with dementia compared to normal elderly and increases with dementia severity. In particular, a greater number of primitive reflexes in the same subject and a prominent and persistent response to the stimulus best distinguishes demented subjects from normal aging.[29]

In the Canadian Study of Health and Aging, the prevalence of six primitive reflexes was determined in 2,914 seniors 65 years and older (palmomental, glabellar, snout, suck, grasp and traction reflexes).[35] At least one primitive reflex was present in 16% of cognitively normal subjects. Primitive reflexes were twice as common in cognitively impaired (but not demented) individuals (32%), and even more common among subjects with dementia (58%). Increasing numbers of primitive reflexes raised the likelihood ratio for a diagnosis of dementia from 0.55 if none was present to 56 if six were present. Of the six reflexes tested, the most significant predictor of a diagnosis of dementia was the presence of a glabellar reflex, followed by the grasp reflex. A strong correlation with dementia severity, disinhibition and psychotic symptoms was found for the prehensile reflexes but not for the nociceptive primitive reflexes.

Similarly, a community survey of 398 elderly people assessed the prevalence of six primitive reflexes (palmomental, snout, glabellar, suck, grasp and corneomandibular). The majority of individuals with dementia had multiple primitive reflexes.[7] Primitive reflexes were a common finding among subjects without central nervous system disease, but were characterized by a short-lasting, non-prominent response; at most, a combination of four primitive reflexes was found in one individual. However, primitive reflexes with a prominent and persistent response and a combination of four or more signs in the same subject were the common findings among those with dementia. The grasp and suck reflexes were elicited only among demented subjects. The combination of five primitive reflexes, or more than two primitive reflexes with a severely abnormal response, was never found in normal people free of central nervous system disease (100% specificity). Thus, primitive reflexes may have value in supporting a clinical diagnosis of dementia when they are numerous and pronounced. An unanswered question is whether they add value to the diagnostic evaluation in patients with mild cognitive impairment but not dementia. As most studies have been cross-sectional, rather than longitudinal, the predictive value of primitive reflexes is not known.

Primitive reflexes have been found to serve as markers of dementia severity.[38] Franssen *et al.* studied AD patients at all stages of clinical severity and employed a standardized examination technique and rating scale to score the reflexes.[12] The frequency and intensity of primitive reflexes increased as a function of increasing dementia severity based on the Global Deterioration Scale (GDS). Prehensile release signs (sucking, grasping, rooting) appeared with high frequency only in advanced stages of AD (GDS stages 6 or 7). In contrast, nociceptive primitive reflexes were commonly present throughout the entire course of AD. Based on these findings, Franssen *et al.* suggest that reflex abnormalities can be useful in the staging of AD, and advocate assessment of primitive reflexes as non-cognitive and education- and culture-independent markers of disease severity and progression in AD.[12,13,39] Several other studies also have found that primitive reflexes correlate significantly with the degree of cognitive impairment in patients with dementia (particularly the prehensile reflexes, and most consistently the grasp reflex).[9,10,25,37,40] In patients with AD, the development of primitive reflexes also coincides with the development of incontinence of cortical origin,[41] and primitive reflexes correlate with functional impairment, behavioural abnormalities, extrapyramidal signs, rigidity and abnormal gait.[42,43]

Primitive reflexes are also more prevalent in individuals with cerebrovascular disease than in normal subjects.[35,44] VaD patients are more likely to have unilateral grasp and traction reflexes than dementia patients with AD or Parkinson's disease (PD).[35] In frontotemporal dementia, primitive reflexes are a supportive feature according to clinical diagnostic criteria.[45] In HIV-positive patients, primitive reflexes have been shown to be a marker for cerebral involvement in neurologically asymptomatic patients.[46-48] In PD, primitive reflexes are also common and correlate with severity of disease and dementia.[34,35,49-51] The glabellar response is common in PD and has been suggested to have more specificity for PD than for other conditions. In the Canadian Study of Health and Aging, patients with PD plus dementia or dementia with parkinsonism were more likely to have glabellar and traction reflexes compared to those with AD or VaD.[52] One paper suggested a more specific sign for PD is Wartenberg's "head retraction reflex", a brisk involuntary backward jerk of the head in response to the tap of a reflex hammer on the upper lip.[52] This reflex was present in 17% of patients with (mostly severe) PD, compared to 8% of patients with dementia without PD and 5% of control subjects.[52] Table 2 presents some generalizations on the utility of primitive reflexes.

Sensory Examination

Primary Sensory Modalities

With normal aging there is a decline in vibration sensation in the distal lower limbs, usually up to the ankles, occurring in up to half of patients over age 75 years.[2-4,53-55] Odenheimer *et al.* found decreased vibration sense in 47% of the total sample of subjects 85+, but in only 21% was this sensory reduction not attributable to medical disease.[30] Kaye *et al.* found absent vibration sense at the toes in 68% of the healthiest oldest old (85+) vs. 12% of those aged 64–75 years.[3] Proprioceptive loss, tested by having the patient identify small upward and downward movements of the joints with eyes closed (usually tested at the great toe and fingertips), is less frequent in the elderly and should be considered a possible indicator of disease. Only 2% of patients in the series of Benassi *et al.* had impaired proprioception and this was of a mild degree.[7] Other reports show higher figures, up to 29%,[4,56] especially in old age.[3]

Studies show age-related increases in sensory thresholds for other modalities but these changes are not clinically apparent on bedside testing. Normal aging should not produce positive sensory symptoms of paresthesias / dysesthesias or significant negative sensory symptoms. In patients with dementia, sensory examination may be difficult and unreliable.

Romberg's Sign

Romberg's sign is tested by having the patient stand with feet together and maintain balance with eyes closed. Historically, it was one of the earliest signs to be described in the neurological examination. Writing in 1853, the German physician Romberg observed: "If (the patient) is ordered to close his eyes while in the erect posture, he at once commences to totter and swing from side to side".[57,58] Romberg considered this to be a sign of tabes dorsalis (a form of neurosyphilis).[59] Today, Romberg's sign remains a useful test of sensory (proprioceptive) function of the feet, indicating peripheral neuropathy or myelopathy affecting the dorsal columns of the spinal cord (e.g., subacute combined degeneration due to vitamin B12 deficiency). Such patients may also have an abnormal gait due to sensory ataxia. Romberg's sign is often misinterpreted as a test of cerebellar function, but patients with cerebellar ataxia should have difficulty standing with feet together with eyes open or closed.[60] Healthy subjects should be able to stand with feet together and eyes closed for 30 seconds up to age 79.[61] According to Kaye *et al.*, a positive Romberg's sign was present in 47% of healthy individuals 85+.[3]

Cortical Sensation

Cortical sensation is important to test for integrity of parietal function. Tactile extinction—an inability to feel a light tap on the back of the hand with bilateral simultaneous stimulation even though unilateral taps can be felt—suggests contralateral parietal dysfunction. This can be a sign of ischemic stroke,[62] especially if accompanied by difficulty identifying numbers written on the palm of one hand (agraphesthesia), or failure to identify small objects placed into the hand by touch, e.g., a quarter vs. a dime (astereognosis). Cortical sensory loss is also an important sign in corticobasal degeneration in which there is often asymmetric parietal involvement. Cortical sensation should remain intact with normal aging, although stereognosis has been found to become impaired in the oldest old.[3] Other cortical sensory tests include texture recognition, two-point discrimination, position sense and baresthesia (the sense of weight).

Summary

The neurological examination begins at first contact with the patient and is direct-

Table 2

Primitive Reflexes (PR): Some Generalizations

– A single PR is common in the general population (1 / 4 of young healthy adults)
– PRs are more common with advancing age (approximately 1 / 2 of normal elderly)
– PRs are even more common in dementia, and should be considered a usual and expected finding in patients with dementia
– PRs are commonly found in patients with cerebrovascular disease
– The palmomental reflex is probably the most common primitive reflex at all ages and does not distinguish between normal and disease states
– The grasp and suck reflexes are the least frequent and correlate more with disease
– A single primitive reflex is usually of no clinical significance; multiple PRs (three or more prominent responses) correlate better with disease
– Multiple PRs are a marker of dementia severity (especially the prehensile reflexes with prominent and sustained responses)
– PRs are not specific for certain disorders and do not predict dementia type
– PRs are not sensitive enough to be an early diagnostic marker for dementia

ed by diagnostic hypotheses generated from the history. Essential elements of the physical examination in aging and dementia include the identification of focal neurological signs that suggest stroke or other structural brain pathology, detection of extrapyramidal features and other movement disorder symptomatology, recognition of gait and balance problems, and uncovering signs that suggest a secondary or reversible cause of the dementia. At the same time, the examiner aims to optimize function by screening for potentially treatable conditions such as impaired vision, hearing loss and poor mobility. At the end of the examination, the clinician must conclude whether the patient's neurological functioning is within normal limits or whether there are abnormalities suggesting disease in the central or peripheral nervous system.

In dementia due to AD, the general neurological examination is usually normal in the initial stages; with advancing disease, patients may develop parkinsonism, myoclonus, gait disorder and immobility. In contrast, in the patient with suspected VaD, the neurological examination aims to identify the presence of lateralized or focal findings indicative of prior stroke (e.g., contralateral upper motor neuron signs, hemisensory loss, homonymous visual field defect) or the early presence of a gait disturbance. The examiner should be familiar with the major arterial stroke syndromes as well as the clinical features associated with diffuse small-vessel cerebrovascular disease. The clinician should screen for the presence of vascular risk factors that may mandate further investigation or treatment, such as atrial fibrillation, hypertension and symptomatic carotid atherosclerotic disease. Other causes of dementia may be suggested by the presence of parkinsonism or other movement disorders.

One of the great challenges in geriatric medicine is distinguishing the clinical signs of disease from those due to normal aging. Although the literature on the clinical neurology of aging is often conflicting, the main age-related changes include alterations in olfaction, vision, upward gaze, hearing, gait, balance, vibration sense and the appearance of bradykinesia and primitive reflexes. Most other neurological findings represent pathology rather than normal aging *per se*. Primitive reflexes are common and therefore have very limited utility, unless multiple and pronounced. This series has hopefully provided a useful resource on the method and interpretation of the neurological examination in the elderly to assist clinicians in the diagnosis and care of patients with dementia. ◆

Reprinted with permission, with modifications, from Gladstone DJ and Black SE. Clinical Neurological Examination. In: Erkinjuntti T, Gauthier S, editors. Vascular Cognitive Impairment. London: Martin Dunitz, 2001.

References

1. Litvan I, Mangone CA, Werden W, et al. Reliability of the NINDS Myotatic Reflex Scale. Neurology 1996;47:969-72.
2. Wolfson L. The neurologic consultation at age 80. In: Katzman R, Rowe JW, eds. Principles of geriatric neurology. Philadelphia: F.A. Davis Co.,1992:75-88.
3. Kaye JA, Oken BS, Howieson DB, et al. Neurologic evaluation of the optimally healthy oldest old. Arch Neurol 1994;51:1205-11.
4. Klawans HL, Tufo HM, Ostfeld A, et al. Neurologic examination in an elderly population. Dis Nerv Syst 1971;32:274-9.
5. Impallomeni M, Kenny RA, Flynn MD, et al. The elderly and their ankle jerks. Lancet 1984;1:670-2.
6. O'Keeffe ST, Smith T, Valacio R, et al. A comparison of two techniques for ankle jerk assessment in elderly subjects. Lancet 1994;344:1619-20.
7. Benassi G, D'Alessandro R, Gallassi R, et al. Neurological examination in subjects over 65 years: an epidemiological survey. Neuroepidemiology 1990;9:27-38.
8. Ferguson RJ, Caplan LR. Cervical spondylitic myelopathy. Neurol Clin 1985;3:373-82.
9. Burns A, Jacoby R, Levy R. Neurological signs in Alzheimer's disease. Age Ageing 1991;20:45-51.
10. Galasko D, Kwo-on-Yuen PE, Klauber MR, et al. Neurological findings in Alzheimer's disease and normal aging. Arch Neurol 1990;47:625-7.
11. Huff FJ, Boller F, Lucchelli F, et al. The neurologic examination in patients with probable Alzheimer's disease. Arch Neurol 1987;44:929-32.
12. Franssen EH, Reisberg B, Kluger A, et al. Cognition-independent neurologic symptoms in normal aging and probable Alzheimer's disease. Arch Neurol 1991;48:148-54.
13. Franssen EH. Neurologic signs in ageing and dementia. In: Burns A, ed. Ageing and dementia: A methodological approach. London, Boston: E. Arnold, 1993.
14. van Gijn J. The Babinski sign: a centenary. Utrecht, The Netherlands: Universiteit Utrecht, 1996.
15. van Gijn J. The Babinski sign: the first hundred years. J Neurol 1996;243:675-83.
16. van Gijn J. The Babinski reflex. Postgraduate Medical Journal 1995;71:645-8.
17. Franssen EH, Kluger A, Torossian CL, et al. The neurologic syndrome of severe Alzheimer's disease. Relationship to functional decline. Arch Neurol 1993;50:1029-39.
18. Rayner PH. The Babinski sign. Eliciting the sign brings out doctors' masochistic tendencies. BMJ 1997;314:374.
19. van Gijn J. The Babinski sign and the pyramidal syndrome. J Neurol Neurosurg Psychiatry 1978;41:865-73.
20. van Gijn J, Bonke B. Interpretation of plantar reflexes: biasing effect of other signs and symptoms. J Neurol Neurosurg Psychiatry 1977;40:787-9.
21. Maher J, Reilly M, Daly L, et al. Plantar power: reproducibility of the plantar response. BMJ 1992;304:482.
22. Wiebers DO, Dale AJD, Kokmen E, et al., eds. Mayo Clinic Examinations in Neurology. 7th ed. St. Louis: Mosby, 1998.
23. Landau WM. Clinical Neuromythology IV. Reflex dementia: disinhibited primitive thinking. Neurology 1989;39:133-7.
24. Paulson G, Gottlieb G. Developmental reflexes: the reappearance of foetal and neonatal reflexes in aged patients. Brain 1968;91:37-52.
25. Tweedy J, Reding M, Garcia C, et al. Significance of cortical disinhibition signs. Neurology 1982;32:169-73.
26. Vreeling FW, Jolles J, Verhey FR, et al. Primitive reflexes in healthy, adult volunteers and neurological patients: methodological issues. J Neurol 1993;240:495-504.
27. Thomas RJ. Blinking and the release reflexes: Are they clinically useful? J Amer Geriat Society 1994;42:609-13.
28. Brown DL, Smith TL, Knepper LE. Evaluation of five primitive reflexes in 240 young adults. Neurology 1998;51:322.
29. Isakov E, Sazbon L, Costeff H, et al. The diagnostic value of three common primitive reflexes. Eur Neurol 1984;23:17-21.
30. Odenheimer G, Funkenstein HH, Beckett L, et al. Comparison of neurologic changes in "successfully aging" persons vs the total aging population. Arch Neurol 1994;51:573-80.
31. Jenkyn LR, Reeves AG, Warren T, et al. Neurologic signs in senescence. Arch Neurol 1985;42:1154-7.
32. Kobayashi S, Yamaguchi S, Okada K, et al. Primitive reflexes and MRI findings, cerebral blood flow in normal elderly. Gerontology 1990;36:199-205.
33. Koller WC, Glatt S, Wilson RS, et al. Primitive reflexes and cognitive function in the elderly. Ann Neurol 1982;12:302-4.

34. Jacobs L, Gossman MD. Three primitive reflexes in normal adults. Neurology 1980;30:184-8.
35. Hogan DB, Ebly EM. Primitive reflexes and dementia: results from the Canadian Study of Health and Aging. Age Ageing 1995;24:375-81.
36. Jenkyn LR, Walsh DB, Culver CM, et al. Clinical signs in diffuse cerebral dysfunction. J Neurol Neurosurg Psychiatry 1977;40:956-66.
37. Huff FJ, Growdon JH. Neurological abnormalities associated with severity of dementia in Alzheimer's disease. Can J Neurol Sci 1986;13:403-5.
38. Vreeling FW, Verhey FR, Houx PJ, et al. Primitive reflexes in Parkinson's disease. J Neurol Neurosurg Psychiatry 1993;56:1323-6.
39. Franssen EH, Reisberg B. Neurologic markers of the progression of Alzheimer's disease. Int Psychogeriatr 1997;9:297S-306S.
40. Bakchine S, Lacomblez L, Palisson E, et al. Relationship between primitive reflexes, extra-pyramidal signs, reflective apraxia and severity of cognitive impairment in dementia of the Alzheimer type. Acta Neurol Scand 1989;79:38-46.
41. Franssen EH, Souren LE, Torossian CL, et al. Utility of developmental reflexes in the differential diagnosis and prognosis of incontinence in Alzheimer's disease. J Geriatric Psychiatry Neurol 1997;10:22-8.
42. Girling DM, Berrios GE. Extrapyramidal signs, primitive reflexes and frontal lobe function in senile dementia of the Alzheimer type. Br J Psychiatry 1990;157:888-93.
43. Molloy DW, Clarnette RM, McIlroy WE, et al. Clinical significance of primitive reflexes in Alzheimer's disease. J Am Geriatr Soc 1991;39:1160-3.
44. Rao R, Jackson S, Howard R. Primitive reflexes in cerebrovascular disease: a community study of older people with stroke and carotid stenosis. Int J Geriatr Psychiatry 1999;14:964-72.
45. Neary D, Snowden JS, Gustafson L, et al. Frontotemporal lobar degeneration: A consensus on clinical diagnostic criteria. Neurology 1998;51:1546-54.
46. Orefice G, Carrieri PB, Troisi E, et al. Three primitive reflexes in HIV-1-infected individuals: a possible clinical marker of early central nervous system involvement. Acta Neurol (Napoli) 1993;15:409-15.
47. Tremont-Lukats IW, Teixeira GM, Hernandez DE. Primitive reflexes in a case-control study of patients with advanced human immunodeficiency virus type 1. J Neurol 1999;246:540-3.
48. Tremont-Lukats IW, Serbanescu R, Teixeira GM, et al. Multivariate analysis of primitive reflexes in patients with human immunodeficiency virus type-1 infection and neurocognitive dysfunction. Ital J Neurol Sci 1999;20:17-22.
49. Huber SJ, Paulson GW. Relationship between primitive reflexes and severity in Parkinson's disease. J Neurol Neurosurg Psychiatry 1986;49:1298-300.
50. Grossman MD, Jacobs L. Three primitive reflexes in parkinsonism patients. Neurology 1980;30(2):189-92.
51. Pearce J, Aziz GH, Gallagher JC. Primitive reflex activity in primary and symptomatic Parkinsonism. J Neurol Neurosurg Psychiatry 1968;31:501-8.
52. Sandyk R, Fleming J, Brennan MJ. The head retraction reflex—its specificity in Parkinson's disease. Clinical Neurol Neurosurg 1982;84:159-62.
53. Critchley M. The neurology of old age: clinical manifestations in old age. Lancet 1931;1:1221-30.
54. Waite LM, Broe GA, Creasey H, et al. Neurological signs, aging, and the neurodegenerative syndromes. Arch Neurol 1996;53:498-502.
55. Smith BH, Sethi PK. Aging and the nervous system. Geriatrics 1975;30:109-15.
56. Skinner HB, Barrack RL, Cook SD. Age-related decline in proprioception. Clin Orthop 1984;184: 208-11.
57. Keppel-Hesselink JM, Koehler PJ. Romberg's Sign. In: Koehler PJ, Bruyn GW, Pearce JMS, eds. Neurological Eponyms. New York: Oxford University Press, 2000:166-71.
58. Schiller F. Staggering gait in medical history. Ann Neurol 1995;37:127-35.
59. Nitrini R. The history of tabes dorsalis and the impact of observational studies in neurology. Arch Neurol 2000;57:605-6.
60. Meyer MA. Romberg sign: sensory dysfunction, not cerebellar disease. Geriatrics 1998;53:10.
61. Bohannon RW, Larkin PA, Cook AC, et al. Decrease in timed balance test scores with aging. Physical Therapy 1984;64:1067-70.
62. Bassetti C, Bogousslavsky J, Regli F. Sensory syndromes in parietal stroke. Neurology 1993;43:1942-9.
63. Jenkyn LR, Walsh DB, Walsh BT, et al. The nuchocephalic reflex. J Neurol Neurosurg Psychiatry 1975;38:561-6.