Clinical Neurology and Neurosurgery 187 (2019) 105555

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

journal homepage: www.elsevier.com/locate/clineuro

Inter-rater reliability of primitive signs in dementia

Andrea Plutino*, Sara Baldinelli, Chiara Fiori, Valentina Ranaldi, Mauro Silvestrini, Simona Luzzi

Department of Experimental and Clinical Medicine, Università, Politecnica delle Marche, Via Conca 71, Ancona, 60126, Italy

ARTICLE INFO

Keywords:
Dementia
Primitive signs

ABSTRACT

Objectives: The aim of the present study is to explore inter-rater reliability of primitive signs in a group of patients assessed for dementia.

Patients and methods: 97 patients admitted to our University Hospital for cognitive impairment were enrolled in the study. The mean age was 73.04 ± 8.68 (53 females and 44 males). All patients were examined by two cognitive neurologists in a blind fashion. The grasp reflex, the snout reflex, the glabella tap reflex and the palmomental reflex were elicited according to the current literature. Moreover, we add a stretch reflexes (the masseter reflex) to our battery.

Results: The most frequent primitive reflex was the palmomental reflex followed by the glabella tap, snout, and grasp. The inter-rater reliability was measured for each primitive reflex: grasp reflex (0.884) have a strong correspondence; the glabella tap (0.556), the palmomental (0.516) and the snout reflex (0.445) have otherwise a weak correspondence. The masseter reflex reaches a moderate agreement (0.662). All the measurements reached statistical significance ($p < 0.005$).

Conclusion: The results of the study show weak to substantial agreement for primitive signs and the masseter reflex as expressed by the low-to-high kappa values.

1. Introduction

Primitive signs are physiologically present during infancy and disappear after the maturation of the central nervous system; their reappearance in adult patients is due to a loss of cortical control over brainstem activity, mainly because of dementia or frontal lesions but also as a result of normal ageing [1–4].

However, as shown in the literature, the prevalence of primitive signs is more common in demented patients than in healthy controls; in a large Canadian cohort, 16% of healthy, 32% of mild cognitive impaired and 58% of demented subjects had at least one primitive reflex [4].

The neuroanatomic networks involved in primitive sign generation are currently unknown except for the grasp reflex. When positive, the grasp reflex has a sensitivity of 13%–50%, a specificity of 99% and a positive likelihood ratio of 19.1 in predicting focal lesions of the frontal lobe or deep nuclei [5]. On the other hand, in a study of 39 patients, the unilateral palmomental reflex is correlated in 44% of the subjects with an ipsilateral cerebral lesion, in 36% with a contralateral lesion, in 10% with bilateral lesions and in 10% with no lesions [6].

A previous study, that examined 30 subjects affected by a heterogeneous group of neurological diseases (stroke, vascular dementia, spine disease and other less represented disorders), found modest to good agreement among raters expressed as kappa values: 0.85 for glabellar reflex, 0.67 for snout reflex, 0.52 for grasp reflex and 0.38-0.44 for palmomental reflex. The authors used a quantitative scoring system that evaluated not only the amplitude of the signs but also their persistence [3].

An extensive search in the literature for studies exploring inter-rater reliability produced very few results. One of these was based on a complex protocol that is poorly reproducible in a clinical setting. Furthermore, the small sample assessed could not be considered as reaching statistical significance [3].

The aim of the present study is to explore the inter-rater reliability of primitive signs in a group of patients assessed for dementia. We decided to add a stretch reflex (the masseter reflex) to our battery of tests because of the high prevalence of upper motor neuron lesions especially in vascular dementia and in frontotemporal dementia but also in other neurodegenerative diseases [5,7].

* Corresponding author.
E-mail address: andrea.plutino@outlook.com (A. Plutino).

https://doi.org/10.1016/j.clineuro.2019.105555
Received 15 March 2019; Received in revised form 31 July 2019; Accepted 6 October 2019
Available online 11 October 2019
0303-8467/

2. Materials and methods

2.1. Population study

Ninety-seven subjects were enrolled in the study. All participants gave their informed consent and all procedures performed were in accordance with the ethical standards of the institution and with the 1964 Helsinki declaration. The mean age was 73.04 ± 8.68 (minimum 44, maximum 86) years. 53 were female and 44 male. The mean years of education were 8.11 ± 4.42 (minimum 2, maximum 18). 97 consecutive patients admitted to our University Hospital for cognitive impairment were included: 48 patients with Alzheimer's Disease, 12 patients with amnestic MCI (mild cognitive impairment), 17 patients with vascular cognitive impairment, 10 patients with a behavioural variant of frontotemporal dementia and 10 with subjective cognitive complaints.

Diagnoses were performed in accordance with international criteria and were based on neuropsychological and instrumental examinations including fluoro-deoxy-glucose positron emission tomography (PET) and amyloid PET [8–11].

2.2. Study design

All patients were examined by two cognitive neurologists in a blind fashion. Both of them work as physician in our University Hospital and they have at least two years of expertise in assessing demented patients. The reflexes were elicited in the same order by the same two neurologists within 1 h. The primitive signs and the myotatic reflex were elicited in the following manner, based on the current literature [2,5,13]:

- *Grasp reflex*. The patients were advised that their hands would be touched and they were asked not to grasp the examiner's finger. A moving pressure was then performed on the palmar surface of both hands sequentially. The grasp reflex was considered positive if there was at least one progressive closure of one hand.
- *Snout reflex*. The examiner exerted a gentle pressure over the nasal philtrum. The sign was positive if the lips wrinkled
- *Glabella tap reflex*. Multiple light tapping over the glabella was performed. The glabella tap reflex was considered positive if the reflex blinking of both eyes was still present after five seconds.
- *Palmomental reflex*. The examiner stimulated the thenar eminence of both hands sequentially with a bevel-edged needle. The reflex was positive if there was at least one involuntary contraction of the mentalis muscle of the chin on one side.
- *Masseter reflex*. The reflex was evoked by tapping the patient's chin with a tendon hammer while the mouth was held slightly open. The sign was positive if the masseter muscles jerked the mandible upwards in a qualitatively abnormal fashion or if clonus was present.

2.3. Data analysis

The Statistical Package for Social Science (IBM) was used for the analysis.

In order to measure inter-rater reliability we performed kappa statistics with grading based on the McHugh's paper: values equal to or less than 0.2 were considered as poor agreement, values between 0.21–0.39 were considered as minimal agreement, values between 0.40–0.59 were considered as weak agreement, values between 0.60–0.79 were considered as moderate agreement, values between 0.8–0.9 were considered as strong agreement and values more than 0.9 were considered as almost perfect agreement [12].

3. Results

The most frequent primitive reflex was the palmomental reflex followed by the glabella tap, snout, and grasp reflex. The inter-rater reliability was measured for each primitive reflex and for the stretch reflex as depicted in the Table 1. The masseter and grasp reflex have a good correspondence, whereas the glabella tap, the palmomental and the snout reflex have weak correspondence [Table 1]. All the measurements reached statistical significance. In Table 2, a recording of the assessment of the reflexes, divided for each observer, was provided.

Table 1
The inter-rater reliability of primitive and stretch reflexes expressed as Kappa value.

Reflex	Kappa
Grasp reflex	0.884 ($p < .0005$)
Snout reflex	0.445 ($p < .0005$)
Glabella tap reflex	0.556 ($p < .0005$)
Palmomental reflex	0.516 ($p < .0005$)
Masseter reflex	0.662 ($p < .0005$)

Table 2
The scores of each primitive and stretch reflexes by the two raters.

Reflex	Rater 1		Rater 2	
	Present	Absent	Present	Absent
Grasp reflex	5	92	4	93
Snout reflex	12	85	8	89
Glabella tap reflex	28	69	35	62
Palmomental reflex	42	55	41	56
Masseter reflex	1	96	2	95

4. Discussion and conclusions

Primitive signs are usually part of the canonical neurological examination similar to other signs, such as the well-known Babinski sign. However, although they are commonly checked in clinical practice, data on their utility and reliability are modest [2,13,14]. Even if in the modern era, where imaging and laboratory exams are readily available, it may be considered anachronistic to focus on these signs, renewed interest in the literature is justified by the need to acquire information quickly during the examination in order to decide the best diagnostic tests. These signs acquire particular value in cognitively impaired patients in which they could represent a sort of "red flag" of incipient cognitive impairment.

The results of the study show weak to substantial agreement for primitive signs as expressed by the low-to-high kappa values. The findings of weak agreement for the glabella tap reflex and the substantial agreement for the grasp reflex conflict with previous studies [3,7]. This discrepancy could be partly explained by the different protocols used; for instance, the difference might be due to alternative ways of positioning the patients and eliciting the stimulus. Another explanation might be the different scoring system because of a lack of standardization in the literature. These findings may also be due to the difference between the populations studied: in fact, as shown by the Canadian study, primitive signs are more common in older population, above all in demented people; therefore, a high pre-test probability or a difference in the power needed to elicit the reflex could account for the discrepancy [4]. The low agreement for glabella tap, snout and palmomental reflex, although a precise and clear protocol was applied, could be caused by a slight difference in the amount of the force used to elicit the reflex that might lead to score a reflex as absent even if it was present.

The main strength of our study derives from the large size of our sample, when compared to similar studies in the literature. Furthermore, the study was designed so as to evaluate the inter-rater reliability of two expert raters, using a protocol based on previous literature, but adopting a dichotomic approach in order to simplify the

procedure; a rater could score a sign as present or absent [2,5,13].

A limitation of our study is the lack of intra-observer reliability or test-retest; however, as shown in the literature, there is a very good agreement between two observations [3]. Another pitfall was the fact that both raters work at the same institution.

In conclusion, the evaluation of primitive signs is a quick, and inexpensive bedside test. It is also at least sufficiently reliable, and we think it could be of significant value in the diagnostic work-up, in agreement with previous studies [13,15]. In particular, the presence of more than one primitive reflex is highly suggestive of an organic disease [2,15].

References

[1] G. Paulson, G. Gottlieb, Development reflexes: the reappearance of foetal and neonatal reflexes in aged patients, Brain 91 (1968) 37–52, https://doi.org/10.1093/brain/91.1.37.

[2] J.M. Schott, M.N. Rossor, The grasp and other primitive reflexes, J. Neurol. Neurosurg. Psychiatry 74 (2003) 558–560, https://doi.org/10.1136/jnnp.74.5.558.

[3] F.W. Vreeling, J. Jolles, F.R. Verhey, et al., Primitive reflexes in healthy, adult volunteers and neurological patients: methodological issues, J. Neurol. 240 (1993) 495–504, https://doi.org/10.1007/BF00874119.

[4] D.B. Hogan, E.M. Ebly, Primitive reflexes and dementia: results from the Canadian Study of Health and Aging, Age Ageing 24 (1995) 375–381, https://doi.org/10.1093/ageing/24.5.375.

[5] S.M.C. Gee, Evidence-Based Physical Diagnosis, fourth edition, Elsevier, 2018.

[6] M. Gotkine, S. Haggiag, O. Abramsky, et al., Lack of hemispheric localizing value of the palmomental reflex, J. Neurol. 240 (1993) 495–504, https://doi.org/10.1212/01.WNL.0000160525.50482.C7.

[7] L. Tremolizzo, E. Susani, C. Lunetta, et al., Primitive reflexes in amyotrophic lateral sclerosis: prevalence and correlates, J. Neurol. 261 (2014) 1196–1202, https://doi.org/10.1007/s00415-014-7342-7.

[8] E. Magni, G. Binetti, A. Bianchetti, et al., Mini-mental state examination: a normative study in Italian elderly population, Eur. J. Neurol. 3 (1996) 198–202, https://doi.org/10.1111/j.1468-1331.1996.tb00423.x.

[9] G.M. McKhann, D.S. Knopman, H. Chertkow, et al., The diagnosis of dementia due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease, Alzheimers Dement. 7 (2011) 263–269, https://doi.org/10.1016/j.jalz.2011.03.005.

[10] K. Rascovsky, J.R. Hodges, D. Knopman, et al., Sensitivity of revised diagnostic criteria for the behavioural variant of frontotemporal dementia, Brain 134 (2011) 2456–2477, https://doi.org/10.1093/brain/awr179.

[11] P. Sachdev, R. Kalaria, J. O'Brien, et al., Diagnostic criteria for vascular cognitive disorders: a VASCOG statement, Alzheimer Dis. Assoc. Disord. 28 (2014) 206–218, https://doi.org/10.1097/WAD.0000000000000034.

[12] M.L. MCHugh, Interrater reliability, Biochem. Med. 22 (3) (2012) 276–282, https://doi.org/10.11613/BM.2012.031.

[13] G. Owen, G.P. Mulley, The palmomental reflex: a useful clinical sign? J. Neurol. Neurosurg. Psychiatry 73 (2002) 113–115, https://doi.org/10.1136/jnnp.73.2.113.

[14] C. Dafkin, A. Green, S. Kerr, et al., The interrater reliability of subjective assessments of the Babinski reflex, J. Mot. Behav. 48 (2016) 116–121, https://doi.org/10.1080/00222895.2015.1047486.

[15] A. Damasceno, A.M. Delicio, D.F.C. Mazo, et al., Primitive reflexes and cognitive function, Arq. Neuropsiquiatr. 63 (2005) 577–582, https://doi.org/10.1590/S0004-282X2005000400004.