Revista Argentina de Clínica Psicológica
2020, Vol. XXIX, N°4, 190-195
DOI: 10.24205/03276716.2020.820

Short-latency somatosensory-evoked potentials have prognostic value in patients with acute cerebral infarction

Yixin Zhu[a], Xiaoli Li[b], Chen Li[c], Jinhua Zhang[d], Fuling Yan[e*]

Abstract

Background Cerebral infarction (CI), especially acute severe cerebral infarction, has high disability and fatality rates. Thus, efficient methods for evaluating brain function, implementing medical measures, distributing medical resources and selecting the treatment regimens are of great importance. Short-latency somatosensory-evoked potential (SLSEP), which can be assessed beside the bed, is an ideal tool for assessing brain function because it is unaffected by sedative drugs and state of consciousness. As one of its main parameters, N20 amplitude can directly reflect the number of reservations in medial lemniscus, whose relative integrity is an important influencing factor for CI. Therefore, it has become the focus of studies on the prognosis of brain injury.

Aims The aims of this study are as follows: to evaluate the Judson grading standard of SLSEP and the predictive value of affected side N20 amplitude in the prognosis of patients with acute cerebral infarction and establish the ROC curve of the N20 amplitude of the affected side and Judson grading standard in assessment of CI.

Methods A total of 50 patients with acute cerebral infraction who are admitted to the intensive care unit of the neurology department of Zhongda Hospital affiliated to Southeastern China University from January 2017 to September 2018 were included in the study. All of them were tested using SLSEP in one week. The NIHSS score and Rankin score (Modified Rankin Scale) were recorded on the first day and after 3 months, respectively. SPSS22.0 and MedCalc15.1 software were adopted for statistical analysis.

Results 1) A significant negative correlation between SLSEP N20 amplitude in the affected side and NIHSS score ($p<0.05$) and a significant positive correlation between Judson grading standard and NIHSS score are observed ($p<0.05$). 2) The sensitivity, specificity and accuracy of the N20 amplitude in the affected side predicting the prognosis of patients with acute cerebral infarction are 95.7%, 73.2% and 84%, respectively. Its forecast cutoff is 1.08 uV. The sensitivity, specificity and accuracy of Judson grading predicting the CI patients' prognosis are 95.7%, 74.1% and 82%, respectively. 3) The prognostic values of N20 amplitude and Judson grading standard have no significant differences ($p=0.9324$).

Conclusion 1) The SLSEP N20 amplitude in the affected side and the Judson grading standard may be used for assessing prognosis in patients with acute cerebral infarction after 3 months. No significant differences between the two methods in predicting prognosis. 2) The cutoff value of N20 amplitude of the affected side in predicting the prognosis of patients with CI is 1.085uV after 3 months.

Keywords: short-latency somatosensory-evoked potentials, N20 amplitude, Judson grading standard, cerebral infarction, prognosis.

a,b,c,d,e Department of Neurology, Affiliated ZhongDa Hospital, School of Medicine, Southeast University, Nanjing, Jiangsu 210009, China
**Corresponding Author: Fuling Yan, Email:* yanfuling@hotmail.com

1. Introduction

Cerebral infarction (CI), especially acute severe cerebral infarction, has high morbidity, disability and fatality rates. Apart from imaging tests, some techniques for evaluating brain function after CI are available. Efficient ways for evaluating brain function in the early stage of CI is essential to the implementation of medical measures, distribution of medical resources and selection of treatment regimens. The short-latency somatosensory-evoked potential (SLSEP) can be performed bedside and is an advanced tool that reflects the sensory pathway function of the cerebral cortex, subcortex and spinal cord. SLSEP is unaffected by sedatives and conscious state. Thus, it may be a good option for evaluating brain function after CI.

SLSEP is of subcortical origin and contains several parameters, namely, N9, N13, N18, N20, N25 and central conduction time (CCT). Only N20 originates from the posterior central gyrus sensory cortex. The CCT is the conduction time from the cervical spinal cord to the sensory cortex of the posterior central gyrus. Classification based on these indexes has become the focus of studies evaluating the prognosis of brain injury in recent years. However, studies about the value of N20 amplitude after stroke are rare. In this study, we report the results of SLSEP testing in 50 patients after stroke and evaluate the predictive value of N20 amplitude and the Judson grading standard in the assessment of CI after 3 months.

2. Materials and methods

2.1 Demographic information and baseline data collection

A total of 50 patients with CI who were admitte d to our intensive care unit of neurology (Ethical co de: 2018ZDSYLL146-P01) from January 2017 to Sept ember 2018 were included in the study. The averag e age of the patients were 64.72±11.35 years and c omprised 29 males and 21 females. All the patients underwent CT or MRI scan within 72 hours after str oke. The inclusion criteria and exclusion criteria are listed in Table 1. The severity of CI was evaluated us ing the NIHSS scale immediately on the day of admi ssion.

Demographic baseline data were collected fro m the patients, including sex, age, hypertension, dia betes and previous history of cerebral infarction.

Table 1 : Patient inclusion criteria and exclusion criteria

Inclusion criteria	Exclusion criteria
1) Admission within 72 hours of onset. 2) Skull CT or MRI scan excluded cerebral hemorrhage, In line with the diagnostic criteria of 2010 Chinese Guidelines for the Diagnosis and Treatment of acute ischemic stroke, NIHSS score ≥3. All patients had varying degrees of physical activity disorder at admission, and the NIHSS score was ≥2 for physical activity or ≥2 for consciousness level. 3) Patients or family members require conservative medical treatment. Patients with malignant cerebral infarction still refused surgical treatment after communicating with their families, and signed informed consent to be admitted to the neurology ward for conservative treatment, with an estimated length of stay exceeding 72 hours.	1) Patients whose family members give up treatment within three days after admission or die within 72 hours of illness course. 2) Obvious edema of both hands and wrists or previous median neuropathy. 3) Patients with a definite history of peripheral nerves. 4) Death is caused by factors other than the nervous system. 5) Exclude other serious diseases such as heart, lung, liver and kidney.

2.2 Test and data recording of the SLSEP of the median nerve

For the prevention of ac interference, a regulated or independent power source was used. SLSEP was recorded from the median nerve of the wrist of the upper limbs (Nicolet, USA). Before a disk-shaped electrode was placed, the scrub cream was used for degreasing. Then, an appropriate amount of

conductive paste was applied to minimize impedance (<5 Ω). The international electroencephalogram recording 10-20 system was used in placing the recording and reference electrodes. The stimulation electrode was placed on the midpoint of the wrist transverse stripes 2 cm from the middle of the nerve course. The stimulation current was set at 5–20 mA. Threshold stimulation intensity should cause slight thumb twitching (1 cm).

The stimulus and filter frequencies were 2.7 and 10–2000 Hz, respectively. Three channels, namely, Channel 1: C4'-Fz with a sensitivity of 1 uV/d, Channel 2: C7-R with a sensitivity of 2 uV/d and Channel 3: L.Erb-R with a sensitivity of 2 uV/d. The sensitivity of latency was 5 ms/d. The average stack was over 200 times until the waves were smooth and stable. The process was repeated at least twice in order that the test curve was well repeated.

The N20 waves, all the latency of each wave, the amplitude of N20 and CCT were recorded. The Judson grading for a single mode evoked potential was employed: Level 1: normal and symmetry of bilateral CCT; Level 2: prolonged unilateral or bilateral CCT, or unsymmetrical of bilateral CCT; and Level 3: unilateral or bilateral disappearance of N20 wave.

(EEG and SSEPs were routinely performed in our center. For the purpose of this study, a neurophysiologist expert (O.E.) retrospectively reviewed all the EEG results to ensure similar definitions and increase the homogeneity of the material. He was blinded to the clinical features at the time of the recordings and to the outcomes. EEG was recorded on a system with at least 10 channels and needle electrodes using 10–20 international system (Fp1, Fp2, C3, C4, T5, T6, O1 and O2). The EEG patterns were classified at days one and three according to the classification system of Synek et al. [20,21] [see Additional file 1]. The EEG results were dichotomized as malignant and non-malignant and included benign and uncertain patterns. SSEP were systematically obtained 3 days after cardiac resuscitation. However, when SSEP recording was due on a weekend day, the recording was postponed to Monday. SSEPs were recorded on a Nicolet Viking IV using six channels: erb'point; C6sp; C'3 or C'4 controlateral to the stimulated hand and Fpz (ipsilateral ear was used as reference). The two remaining channels served as channel control: C'3 – C'4 (or C'3–C'4) on which N20 amplitude was measured and Fpz-C'3 (or Fpz-C'4) for the checking of long-latency component, and a large time window was used. The absence of early cortical responses to somatosensory evoked potentials were asserted only if the three following conditions were present: (i) correct peripheral (N10) and medullar (N13) component, (ii) no deflexion higher than 0.5 μV on C3–C'4 (or C'3–C'4) (iii) no late component on Fpz-C'3 (or Fpz-C'4). Two groups of patients were defined for statistical analysis according to SSEP results: Group 1, patients with bilateral absence of early cortical responses (unfavorable result of SSEPs) and Group 2, patients with uni- or bilateral presence of early cortical responses (favorable result of SSEPs).

2.3 Prognostic evaluation

All enrolled patients were followed up 3 months later and evaluated using Modified Rankin Scale (mRS). The patients were divided into three groups according to the mRS scores: 0-3 group with good prognosis and 4-6 group with poor prognosis.

2.4 Statistical method

Statistical analyses were carried out using the SPSS 22.0 and MedCalc15.1. Data were reported as means ± SD. A p value of <0.05 was considered significant in each test. The data in line with the qualitative indicators were expressed as frequency and percentage. A Pearson correlation analysis was performed for the estimation of the relationship between indicators. Multivariate logistic regression was used in analysing the predictors for poor prognosis. The regression prediction model was established, and the relative risk was calculate. ROC curve was drawn for the determination of sensitivity, specificity and cutoff value.

3. Results

On the basis of the neuro-imaging test and the standards of inclusion and exclusion criteria, 50 patients, 29 males and 21 females, were selected in this study. The youngest one was 42 years old, and the oldest was 88 years old. The average age was 66.06±10.78 years. Thirty-six patients had hypertension, eighteen had diabetes, and twenty-four had stroke history.

3.1 NIHSS scale scores, SLSEP and follow-up results

The NIHSS scale scores of the patients ranged from 3 to 40, with an average score 14.52±9.23. Four patients had NIHSS scores of above 30, were previously intubated with trachea cannula and had a score of 9 in the dysarthria scaling.

The average N20 wave amplitude of the affected sides was 1.24±1.10 uV (Fig. 1). According to the Judson grading standard, 20 patients were Grade I in SLSEP (40%, 20/50), 22 were Grade II (44%, 22/50), and 8 were Grade III (16%, 8/50).

Follow-up studies were performed 3 months after stroke. The patients were scaled using the mRS score. Patients with a score of 0–3 were included in the group with good prognosis, and those with a score of 4–6 in the group with poor prognosis. In this study, 27 patients were included in the group with good prognosis, and 23 in the group with poor prognosis.

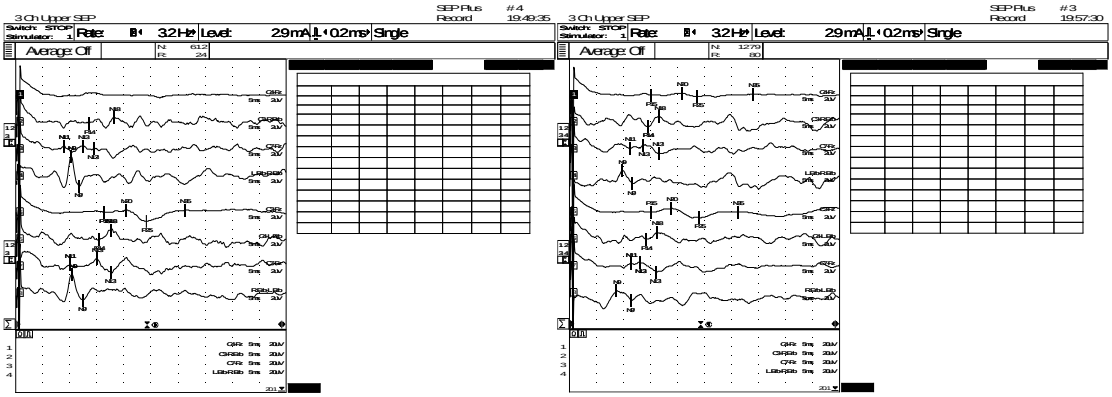

Figure 1*. The SLSEP results of the two patients: At the left is a case of massive cerebral infarction in the right cerebral hemisphere. Left limbs strength level 0, the second day of admission line SLSEP detection, results show that the left side of the N20 wave disappeared, Judson standard class Ⅲ. The mRS score was 4 points (severely disabled) during the 3-month follow-up. At the right is a case of massive cerebral infarction in the right cerebral hemisphere. On the left side of the limb muscle strength level 0, the second day of admission line SLSEP examination, the results showed the left N20 waveform differentiation, slightly lower amplitude, the incubation period is normal, Judson standard class Ⅱ. MRS score was 1 point in the follow-up after 3 months.*

3.2 Correlation analysis of NIHSS scale scores and SLSEP

The Pearson correlation analysis results suggest a negative correlation between N20 amplitude on the affected side and NIHSS score. The higher the amplitude of N20 on the affected side was, the lower the NIHSS score was. According to the Judson classification standard, the grading correlation coefficient was 0.713 (Table 2). Meanwhile, a positive correlation between the Judson standard and NIHSS score was found. The NIHSS score increased with the Judson standard grade.

Table 2 *Correlation analysis between SLSEP N20 amplitude and NIHSS score*

	N20 amplitude on the affected side	Judson standard grading system	NIHSS Score
N20 amplitude on the affected side	1	-0.726**	-0.638**
Judson standard grading system	-0.726**	1	0.713**
NIHSS Score	-0.638**	0.713**	1

**p<0.01

3.3 Prognostic analysis of affected N20 amplitude and Judson standard grade

The predictors included in this study were the affected N20 amplitude, Judson standard grade, hypertension, diabetes, previous cerebral infarction, age and gender. Multivariate logistic regression analysis was used in processing the above indexes. After analysis by forward conditional method and logistic regression equation, only the N20 wave amplitude in the affected side and Judson standard grade exerted effects on the prognosis. The regression coefficient of the affected side N20 amplitude was 4.478, and the relative risk was 88.092 (3.845, 2018.196). With the decrease of N20 amplitude on the affected side, the possibility of poor prognosis increased. Retrospective verification was performed on 50 subjects. A total of 42 cases were correctly predicted by the computational model, and the prediction accuracy was 84%.

The regression coefficient of the Judson standard grade was 3.67, and the relative risk was

39.245 (4.782, 322.087). The possibility of poor outcomes increased with the Judson grade. This regression equation was used for retrospective verification of 50 subjects. A total of 41 cases were correctly predicted by the computational model, and the prediction accuracy was 82%.

3.4 Comparison of the N20 amplitude of the affected side and the Judson classification standard ROC curves

The analysis showed that the area under ROC curve (AUC1) of the N20 amplitude of the affected side was 0.897, the prediction sensitivity was 95.7% and specificity was 73.2%. The best cutoff value was 1.085 μV. When the N20 amplitude of the affected side was ≤1.085 μV, the prognosis of the patients tended to be poor. Meanwhile, when the N20 amplitude of the affected side was >1.085 μV, the patient showed high possibility of good prognosis. The area under the curve (AUC2) based on the Judson standard grade was 0.894, prediction sensitivity was 95.7% and specificity was 74.1%. The ROC curves of the N20 amplitude of the affected side and the Judson standard grade were compared, and the results showed the two curves had no significant differences in the prediction of the prognosis of patients.

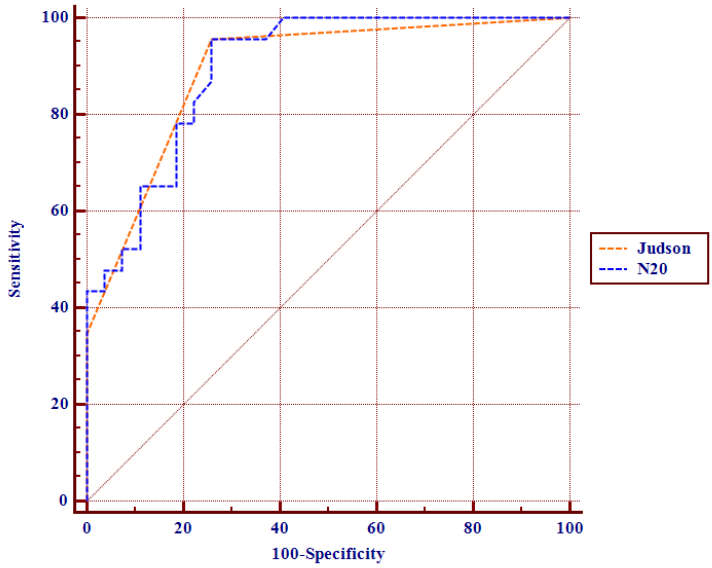

Figure 2. ROC curve of N20 amplitude and Judson grading standard for prognosis prediction on the affected side

4. Discussion

Acute severe cerebral stroke is often accompanied by disturbance in consciousness, intracranial hypertension, persistent high fever and serious medical complications. It is of great significance for the treatment, rehabilitation and prognosis of patients with severe cerebrovascular disease for the evaluation of damages in brain tissues and nerve pathways timely and accurately.

The extent of brain tissue damage after stroke is the decisive factor affecting the prognosis of patients. SLSEP is obtained from patients with sensory nerve stimulation. It originated from the subcortical areas and includes several negative phase waves, for example, the N9, N13, N18 and N20. N20, a negative phase wave originating from the stimulation of the primary sensory cortex in the posterior central gyrus of the contralateral brain, can be clearly recorded in healthy people. When the incoming sensory conduction pathway or the corresponding part of the cerebral hemisphere changes and affects the sensory conduction pathway, SLSEP shows abnormalities. Previous studies focused on whether the N20 waveform of SLSEP appears or whether CCT prolongs and prognosis [6-7]. In recent years, many studies have shown that the prolonged latency of the N20 wave, the decrease in or even the disappearance of N20 wave amplitude, especially in the bilateral cortex, is a good indicator of poor prognosis in coma patients [8].

In the present study, the N20 amplitude was used in evaluating the prognosis of patients. The results indicated that N20 amplitude on the affected

side has a significantly negative effect on poor prognosis. The higher the N20 amplitude on the affected side was, the lower the NIHSS score was. The possibility of poor prognosis increased as the N20 amplitude on the affected side decreased. Zandbergen et al. [9] found that the absence of the bilateral N20 wave within the first week of stroke onset is strongly correlated with poor prognosis owing to severe brain injury. Patients with this condition usually die or are in a persistent vegetative state. This study showed a false-negative rate of less than 2% in patients with ischemic hypoxic brain injury. Different from previous studies, the results of this study intuitively suggest the relationship between amplitude and prognosis, indicating that the N20 amplitude can be used as an indicator for predicting the prognosis of patients with acute cerebral infarction at 3 months.

The results of the present study showed a positive correlation between the Judson standard grading level and NIHSS scores. The Judson standard grade had a significant positive effect on poor outcomes, and the probability of poor outcomes increased with the Judson standard grade. The results indicated that Judson grades can be used as indicators for predicting the prognosis of patients at 3 months. In this study, the prediction accuracy of the Judson grading standard was 82% in 50 patients, which is higher than the values reported in previous studies, which may be related to the exclusion of haemorrhagic stroke due to ischemic stroke in all patients enrolled in this study.

In the present study, all the patients included had acute cerebral infarction, rather than divided in to anterior circulation or posterior circulation infarction according to the infarction site detailed groups. In clinical cases, NIHSS scale scores are suitable for evaluating the anterior circulation infarction, and the Glasgow Coma Scale scores is suitable for patients with posterior circulation infarction. No specific differentiation of the infarction sites was observed, which may have a certain impact on the results. In further studies, variables, such as infarct location and infarct volume, in combination with imaging examination can be considered for the accurate prediction of the prognosis of patients.

Funding: The work was supported by Nanjing Medical Science and Technology Development Project（YKK17274）.

References

Gobert F, Baars JH, Ritzenthaler T, et al. Diagnosing Kernohan-Woltman notch phenomenon by somatosensory evoked potentials in intensive care unit [J]. Clin Neurophysiol, 2018, 129(1): 254-257.

Zhang Y, Su YY, Haupt WF, et al. Application of electrophysiologic techniques in poor outcome prediction among patients with severe focal and diffuse ischemic brain injury [J]. J Clin Neurophysiol, 2011, 28(5): 497-503.

Morgalla MH, Tatagiba M. Long-term outcome prediction after a traumatic brain injury using early somatosensory and acoustic evoked potentials: analysis of the predictive value of the different single components of the potentials [J]. Neurodiagn J, 2014, 54(4): 338-352.

Kang D, Yao P, Wu Z, et al. Ischemia changes and tolerance ratio of evoked potential monitoring in intracranial aneurysm surgery [J]. Clin Neurol Neurosurg, 2013, 115(5): 552-556.

Koohi N, Vickers DA, Lakshmanan R, et al. Hearing Characteristics of Stroke Patients: Prevalence and Characteristics of Hearing Impairment and Auditory Processing Disorders in Stroke Patients [J]. J Am Acad Audiol, 2017, 28(6): 491-505.

Vanhaudenhuyse A, Laureys S, Perrin F. Cognitive event-related potentials in comatose and post-comatose states [J]. Neurocrit Care, 2008, 8(2): 262–270.

Suppiej A, Cappellari A, Franzoi M, et al. Bilateral loss of cortical somatosensory evoked potential at birth predicts cerebral palsy in term and near-term newborns [J]. Early Hum Dev, 2010, 86(2):93–98.

Jennett B, Bond M. Assessment of outcome after severe brain damage [J]. Lancet, 1975, 1 (7905): 480–484.

Zandbergen EG, de Haan RJ, Stoutenbeek CP, et al. Systematic review of early prediction of poor outcome in anoxic ischaemic coma [J]. Lancet, 1998, 352 (9143):1808–1812.