

# Weakness of Eye Closure with Central Facial Paralysis after Unilateral Hemispheric Stroke Predicts a Worse Outcome

Jianwen Lin, MD, PhD,\* Yicong Chen, MD,\* Hongmei Wen, MD, PhD,†  
Zhiyun Yang, MD, PhD,‡ and Jinsheng Zeng, MD, PhD\*

**Background:** Upper facial dysfunction is not generally considered a feature of central facial paralysis after unilateral hemispheric stroke; however, weakness of eye closure (WEC) has been observed in some cases. We aimed to investigate the frequency and characteristics of WEC in unilateral stroke and its association with stroke prognosis. **Methods:** Patients with unilateral stroke and central facial paralysis were prospectively recruited within 7 days of onset. Facial paralysis was evaluated via the fourth item in the National Institute of Health Stroke Scale (NIHSS-4) and the Japan Facial Score (JFS) on admission, and at days 7, 14, 21, and 30 after stroke. Eye closure strength was measured daily using an ergometer for 30 days after stroke. Primary outcome was assessed using the modified Rankin Scale (mRS) at 90 and 180 days. Univariate and multivariate analyses were performed to investigate risk factors of WEC. **Results:** WEC was identified in 16 of 242 patients (6.6%). Baseline characteristics, stroke risk factors, and lesion volume were not significantly different between patients with and patients without WEC. Patients with WEC featured higher NIHSS-4 scores and lower JFS between admission and at 21 days after stroke. Severe central facial paralysis (odds ratio [OR] = 8.1, 95% confidence interval [CI] = 2.3-28.6,  $P = .001$ ) and right hemispheric stroke (OR = 13.7, 95% CI = 3.7-51.2,  $P < .001$ ) were potential predictors of WEC. At 180 days after stroke, patients with WEC demonstrated a lower rate of functional independence (mRS = 0-2: 37.5% versus 72.1%,  $P < .001$ ). **Conclusions:** WEC, which predicts a worse functional outcome at 180 days after unilateral stroke, demonstrates an association with severe central facial paralysis and right hemispheric stroke. **Key Words:** Stroke—central facial paralysis—weakness of eye closure—risk—factor—outcome.

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From the \*Department of Neurology and Stroke Center, The First Affiliated Hospital, Sun Yat-sen University, Guangzhou 510080, China; †Department of Rehabilitation Medicine, The Third Affiliated Hospital, Sun Yat-sen University, Guangzhou 510630, China; and ‡Department of Radiology, The First Affiliated Hospital, Sun Yat-sen University, Guangzhou 510080, China.

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J.L. and Y.C. contributed equally to the study and are joint first authors.

Address correspondence to Jinsheng Zeng, MD, PhD, Department of Neurology and Stroke Center, The First Affiliated Hospital, Sun Yat-sen University, No. 58 Zhongshan Road 2, Guangzhou 510080, China. E-mail: [zengjs@pub.guangzhou.gd.cn](mailto:zengjs@pub.guangzhou.gd.cn).

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## Introduction

The classical perception that describes bilateral corticobulbar innervation of the upper facial nerve nucleus indicates that unilateral hemispheric stroke would not induce upper facial motor dysfunction.<sup>1,3</sup> However, several studies have demonstrated evidence of impaired upper facial motility in unilateral stroke, with patients presenting with weakness of eye closure (WEC) or forehead wrinkling on the contralateral side.<sup>4,6</sup> Two Japanese cases with unilateral cerebral stroke were reported to have decreased contraction of orbicularis oculi muscles in the contralateral face during tight eye closure (with or without wrinkle disturbance), and were further identified to have WEC by electromyographic examination of the orbicularis oculi muscles (spontaneous discharge and right-left difference).<sup>4</sup> Moreover, Willoughby and Anderson<sup>5</sup> found that up to 25 of 100 patients with unilateral hemisphere vascular lesions had WEC or weakness of forehead wrinkling, although such weakness were less severe than that in the lower face. Subclinical upper facial motor dysfunction was also indicated in stroke patients with dysphagia using a facial activity test, in addition to the presence of classical central facial paralysis.<sup>6</sup> However, in these studies, upper facial paralysis was assessed through clinical observation, rather than through quantitative measurement.

Swallowing disorders, which have been similarly linked to bilateral cortical dysfunction, are reported to occur in almost one third of patients with unilateral hemispheric stroke.<sup>7-12</sup> Neuroimaging studies using transcranial magnetic stimulation (TMS),<sup>9,10</sup> functional magnetic resonance imaging (MRI),<sup>11</sup> or positron emission tomography<sup>13</sup> have confirmed that the pharyngeal motor cortex displays interhemispheric asymmetry with unilateral functional dominance, usually in the right hemisphere.<sup>11,12,14-16</sup> However, it remains unclear whether control of the upper facial musculature is represented by bilateral asymmetry in the cerebral cortex. Therefore, further research is required to determine the prevalence of WEC in unilateral hemispheric stroke.

The present study aimed to evaluate the frequency and characteristics of WEC following unilateral hemispheric stroke using quantitative techniques, and to investigate the correlation between WEC and functional prognosis in patients with stroke.

## Materials and Methods

### Participants

For a period of 1 year, we prospectively and continuously enrolled adult patients with stroke admitted to our stroke center within 7 days of stroke onset. Of the 914 patients with stroke who were admitted, 242 (median age = 65.5 years; age range = 26-84 years; men = 158) with central facial paralysis and restricted unilateral hemispheric stroke were included. Stroke was diagnosed according to the definition provided by the World Health

Organization.<sup>17</sup> Eligible patients were required to meet several criteria, including (1) first unilateral hemispheric stroke confirmed by computed tomography (CT) and MRI, or recurrent stroke with lesions restricted to the same hemisphere as the current; (2) evidence of central facial paralysis; (3) being cooperative to eye closure strength measurement; and (4) modified Rankin scale (mRS) score  $\leq 2$  before onset of recurrent stroke. Exclusion criteria included (1) previous diagnosis of Bell's palsy; (2) facial paralysis due to previous stroke; (3) any lesion in the brainstem or bilateral hemispheres; and (4) ineligibility for MRI examination (for patient enrollment, see Supplementary Figure S1). The study protocol was approved by the local Clinical Research Ethics Committee, and all patients provided written informed consent before enrollment.

### Measurement of Eye Closure Strength

Eye closure strength was quantitatively measured using an ergometer (ALGOL NK-10, Japan Instrumentation System Co., Ltd.; rated capacity = 1 kg-f, precision = .01 kg-f; 1 kg-f = 9.8 N). The test point of the ergometer was applied to the patient's upper eyelid with a T-shape slice. Patients were directed to close their eyes gently, and the ergometer reading was adjusted to zero. Next, patients were directed to close their eyes continuously with maximal strength, and the ergometer was moved in the opposite direction to apply pressure to their eyelids (Supplementary Figure S2). The strength required to separate the upper and the lower eyelids and expose the sclera was recorded. The measurement was repeated thrice over a 5-minute period for each eye, and the average was recorded as the eye closure strength. Difference in eye closure strength was defined as the strength of the stronger eye after subtracting the weaker one.

Healthy controls ( $n = 87$ ; median age = 65 years; age range = 20-75 years; men = 44) without history of stroke or Bell's palsy were recruited to establish the reference range for eye closure strength difference following the above method.

### Clinical Data and Brain Imaging

Information regarding patient demographics, medical history, neurological deficit, and current treatment was recorded. Neurological deficit was assessed with the National Institutes of Health Stroke Scale (NIHSS) on admission, and at days 7, 14, 21, and 30 after stroke onset.

All eligible patients underwent both brain CT and MRI examination (Magnetom Trio Tim 1.5T, Siemens (Munich, Germany)); T1-weighted imaging, T2-weighted imaging, fluid-attenuated inversion recovery, diffusion-weighted imaging). Stroke type (cerebral infarction and intracranial hemorrhage) and the Alberta Stroke Program Early CT Score<sup>18,19</sup> were determined by baseline CT, whereas lesion location and lesion volume were determined by diffusion-weighted imaging or T2-weighted MRI. The volume of infarction or hemorrhage was assessed using

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