

## Supplementary Methods

### Study design, settings, and participants

We enrolled patients who met the following criteria: successful pupil evaluation, diagnosis of ischemic stroke or intracerebral hemorrhage, and admission to the SCU of the National Cerebral and Cardiovascular Center (NCVC), Suita, Japan.

Clinical information, including age, sex, blood pressure, heart rate, medical history (hypertension, diabetes mellitus, dyslipidemia, and dementia), stroke subtypes, Glasgow Coma Scale (GCS) score, National Institutes of Health Stroke Scale score, and Intensive Care Delirium Screening Checklist (ICDSC) score, upon admission, was obtained from medical records and the NCVC Stroke Registry (ClinicalTrials.gov identifier: NCT02251665). Diagnoses were performed by board-certified neurologists, based on neurological examinations and computed tomographic and magnetic resonance imaging findings. Patients with insufficient medical records or severe optical diseases as well as those without proper NPi®-200 pupillometer evaluations in the emergency department were excluded.

In the context of the study, "successful pupil evaluation" refers to accurate and complete assessment of the pupils using an NPi®-200 pupillometer. This evaluation aimed to obtain reliable measurements of the pupillary light reflex and related parameters, such as the neurological pupil index (NPI), pupil size before and during constriction, constriction velocity (CV), dilation velocity (DV), and other relevant metrics.

### Evaluation using NPi®-200

We measured the parameters of the pupils using an NPi®-200 pupillometer during treatment in the emergency department while maintaining a consistent level of brightness throughout the day. To ensure accuracy and minimize testing errors, the pupillometry was performed at least three times for each eye, and the median value of each result was analyzed. During the evaluation, an NPi®-200 pupillometer captured and analyzed the changes in pupil size and CV in response to light stimuli, thereby providing objective data on the pupillary light reflex. The parameters measured included NPI, pupil size before constriction, DV, maximum CV, latency of constriction, CV, percent change in pupil size, and pupil size at peak constriction. NPI values range from 0 to 5, and NPI values below 3 indicate an abnormal pupillary light reflex in the ipsilateral eye.<sup>1</sup>

To compare the bilateral pupils, we designated the largest value of each parameter as the "maximum" and the smallest value of each parameter as the "minimum." The differential of each parameter was then calculated by subtracting the minimum value from the maximum. In addition, we computed the average val-

ues of the right and left pupillary findings for each parameter.

### Assessment of delirium

During their stay in the SCU, we performed daily evaluations of each patient's mental status using the ICDSC, which comprises eight items. The ICDSC is widely used with critically ill patients and those with acute stroke,<sup>2,3</sup> and a comprehensive explanation of this evaluation tool has been provided previously.<sup>4</sup> Delirium was diagnosed retrospectively by a certified neurologist when the ICDSC score equaled or exceeded 4 points.<sup>4</sup> However, although patients in a comatose state due to severe brain injury can score 0 points on the ICDSC, they are not classified as having delirium because they do not exhibit any manifestations of delirium.<sup>4</sup>

### Data analysis

The data are presented as means±standard deviations or medians (interquartile range) for continuous variables and as percentages for categorical variables organized into groups of patients with and without delirium. We performed Fisher's exact or the Mann-Whitney U test to evaluate differences in the categorical or continuous variables. For continuous variables, the Mann-Whitney U test or Student's t-test was used, as appropriate. To identify the significant predictors of delirium, we constructed both univariable and multivariable logistic regression models. The multivariable model was adjusted for potential confounding factors, including age, sex, GCS score, and presence of dementia. Odds ratios with 95% confidence intervals were calculated to measure the effect size. All reported *P*-values were two-tailed, and statistical significance was defined as *P*<0.05. All statistical analyses were performed using Stata 18.0 software (StataCorp, College Station, TX, USA).

## Supplementary References

1. Kim TJ, Park SH, Jeong HB, Ha EJ, Cho WS, Kang HS, et al. Neurological pupil index as an indicator of neurological worsening in large hemispheric strokes. *Neurocrit Care* 2020;33: 575-581.
2. BoBelmann C, Zurloh J, Stefanou MI, Stadler V, Weber Y, Le-rche H, et al. Delirium screening in aphasic patients with the Intensive Care Delirium Screening Checklist (ICDSC): a prospective cohort study. *Front Neurol* 2019;10:1198.
3. Krewulak KD, Rosgen BK, Ely EW, Stelfox HT, Fiest KM. The CAM-ICU-7 and ICDSC as measures of delirium severity in critically ill adult patients. *PLoS One* 2020;15:e0242378.
4. Bergeron N, Dubois MJ, Dumont M, Dial S, Skrobik Y. Intensive Care Delirium Screening Checklist: evaluation of a new screening tool. *Intensive Care Med* 2001;27:859-864.