CENTRAL ASIAN JOURNAL of MEDICAL SCIENCES
CAJMS
Brief Communication
Cent Asian J Med Sci. 2018 March;4(1):85-91. https://doi.org/10.24079/CAJMS.2018.03.011

A Study of Relationship between Post Stroke Epilepsy and Solar Activity

Tungalagtamir Shagjaa[1,2], **Efremov Valery Vilyamovich**[2], **Otgonbayar Luvsannorov**[1]

[1]Department of Neurology, School of Medicine, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia; [2]Department of Neurology and Neurosurgery, Faculty of Medicine, Rostov State Medical University, Rostov-on-Don, Russia

Submitted: December 11, 2017
Revised: March 14, 2018
Accepted: March 21, 2018

Corresponding Author
Tungalagtamir Shagjaa, MD
Department of Neurology, School of Medicine, Mongolian National University of Medical Sciences,
Ulaanbaatar 14210, Mongolia
Tel: +976-9999-6305
Fax: +11-318-410
E-mail:
tungalagtamir.sh@mnums.edu.mn

Objective: Symptomatic seizure or post-stroke seizure are the most common seizure subtypes among the elderly. The purpose of our study was to better understand post-stroke epilepsy in relation to their cerebral location, and to find a possible link between epileptic seizure after stroke debut and the differences in solar activity. **Methods:** This retrospective chart review of patients who died from hemorrhagic stroke in Ulaanbaatar, Mongolia. Only patients with a hemorrhagic stroke from periods with relatively high solar activity (2000-2002 and 2013-2015) and relatively low solar activity (2008-2010) were considered. **Results:** Hemorrhagic stroke affected mainly patients between 45-59 years of age. Post-stroke epilepsy was less prevalent less during decreased solar activity years. Post-stroke epilepsy was more prevalent in patients with subarachnoid hemorrhage and brainstem hematoma and even more prevalent in patients with diabetes ($p<0.01$). **Conclusion:** Post-stroke epilepsy was less frequent during low solar activity years. Post-stroke epilepsy with concomitant brainstem hematoma resulted in poor outcomes following stroke.

Keywords: Solar Activity, Intracranial Hemorrhage, Epilepsy, Mongolia, Mortality

Introduction

Stroke often leaves its survivors with severe disabilities that cause emotional and economic hardships for both patients and their families. It also poses enormous costs to health care system [1]. Stroke kills about 140,000 Americans each year and is the 3rd leading cause of death in the US causing 1 out of every 20 deaths [2]. In the USA, every 40 seconds someone is affects by a stroke, and every 4 minutes someone dies because of stroke [3]. Cerebrovascular mortality in Mongolia is 3rd highest in world at 240 per 100,000 persons per year [4]. In 2015, Mongolia had the highest the age-standardized global mortality rate following hemorrhagic stroke per at 230 per 100000 people [4].

The regulatory systems of the human body are designed to adapt to daily, seasonal climatic, and geomagnetic variations;

however sharp changes in solar and geomagnetic activity can stress these regulatory systems, resulting in alterations in melatonin/serotonin balance, blood pressure, immune system, reproductive, cardiac and neurological processes [5]. Research linking cardiovascular disorders to geomagnetic activity during the past 40 years is accumulating [6]. Solar activity (SA) and geomagnetic storms influence human behavior and mental changes, hereditary aspects, sudden cardiac death and stroke and attract the attention of researchers worldwide. Some studies have shown that geomagnetic storms account for 2.64% of all strokes on a population level, exposure to geomagnetic storms (with A index <60) on an individual level are found to increase the relative risk of stroke by 19% across all ages [5].

Geomagnetic activity are perturbations of the Earth's magnetic field, associated with changes in the magnetosphere-ionospheric system. Geomagnetic activity is a part of solar-terrestrial physics and its practical part is known as space weather. The main manifestations of geomagnetic activity are strong perturbations that are known as magnetic substorms and magnetic storms, as well as weaker perturbations manifested as various types of magnetic pulsations. A geomagnetic storm is a strong geomagnetic field disturbance lasting from several hours to several days. Along with substorms, geomagnetic storms are a type of geomagnetic activity. The intensity of the geomagnetic storm is usually described by the Kp-index. The A-index provides a daily average level for geomagnetic activity.

Symptomatic seizure after stroke or post-stroke epilepsy (PSE) is a common seizure type among elderly. Acute symptomatic seizures occur at the time of the brain insult and may be a marker of the severity of injury [7]. Patients with hemorrhagic stroke are at significantly greater risk of seizures, with an almost 2-fold increase in the risk of seizures [8]. Seizures occurs in about 10% of stroke patients. Five percent are early-onset seizures (peak onset within the first day after the stroke) and another 5% occur later [9]. Most seizures occur within 24 to 48 hours after stroke [14]. Patients over 60 years of age have a stroke incidence of 2–4% and the majority of strokes occur in the right hemisphere, in the territory of the middle cerebral artery [10]. It is thought that acute damage to the site of the stroke precipitates the seizure.

In a univariate analysis, the risk factors for PSE were subcortical location of hematoma, larger hematoma volume, hematoma evacuation, and lower Glasgow coma scale score on admission, whereas patients with infratentorial hematoma or hypertension were less likely to develop PSE [11]. Also having a high National Institutes of Health Stroke Scale (NIHSS) score was a significant predictor of epilepsy and epilepsy after stroke [15].

Our study differs from other studies by relating PSE with solar activity. The aim of this retrospective study was to better understand PSE in relation to their location, consciousness state after and before seizure and to develop possible link of epileptic seizure debut after stroke with the amount of solar activity in patients from Ulaanbaatar, Mongolia.

Methods

Patients

This study is based on results of 669 autopsies of patients in Ulaanbaatar, Mongolia who died from nontraumatic hemorrhagic stroke during the years of above average solar activity (2000-2002, 2013-2015) and and during the years of below average solar activity (2008-2010). Autopsy cases where the proven cause of death was hemorrhagic stroke were gathered from the archive database of First and Third clinical hospitals of Ulaanbaatar, and from National Pathological Center of Mongolia. All cases of intracranial hemorrhage (ICH) were divided into 14 age groups with 5-year intervals by gender. ICH was classified on epidural, subdural, subarachnoid, parenchymal, intraventricular, cerebellar hemorrhage. Stroke cases subdivided also by general location (right hemisphere, left hemisphere, brain stem), lobe (frontal, temporal, occipital, parietal, frontotemporal, frontoparietal, temporooccipital, temporoparietal, parietooccipital) and hematoma herniated into the ventricles. Stroke cases which were caused by rupture of the intracranial vessels were subdivided by the location of the aneurysm. Most common causes of intracranial bleeding were arterial hypertension, intracranial aneurysm, Moyamoya disease, arteriovenous malformation, cerebral amyloid angiopathy, and hemorrhage per diapedesis. Risk factors including arterial hypertension, diabetes, alcohol abuse, antiplatelet drug intake, obesity, and atherosclerosis were recorded. The seizure history was gathered from the patients' medical records and the personal history of seizures was recorded categorically as positive or negative. Seizures were defined according to the International League Against Epilepsy criteria [28].

External environmental factors: The yearly average of the solar indices A and Kp, Geomagnetic data were extracted from Figure 1 from the International Space Environment Service and Solar Influences Data Analysis Center of the solar physics research department of the Royal Observatory of Belgium [29]. The yearly mean average of Kp index was extracted from the U.S. National Oceanic and Atmospheric Administration's DSCOVR Space Weather Data Portal [30].

Geomagnetic storms were classified into minor or moderate depending on annual mean Kp index. After reviewing Figure 1, we focused our study on 2000-2002 when solar activity was high, on 2008-2010 when solar activity was low and on 2013-2015 when solar activity increased again.

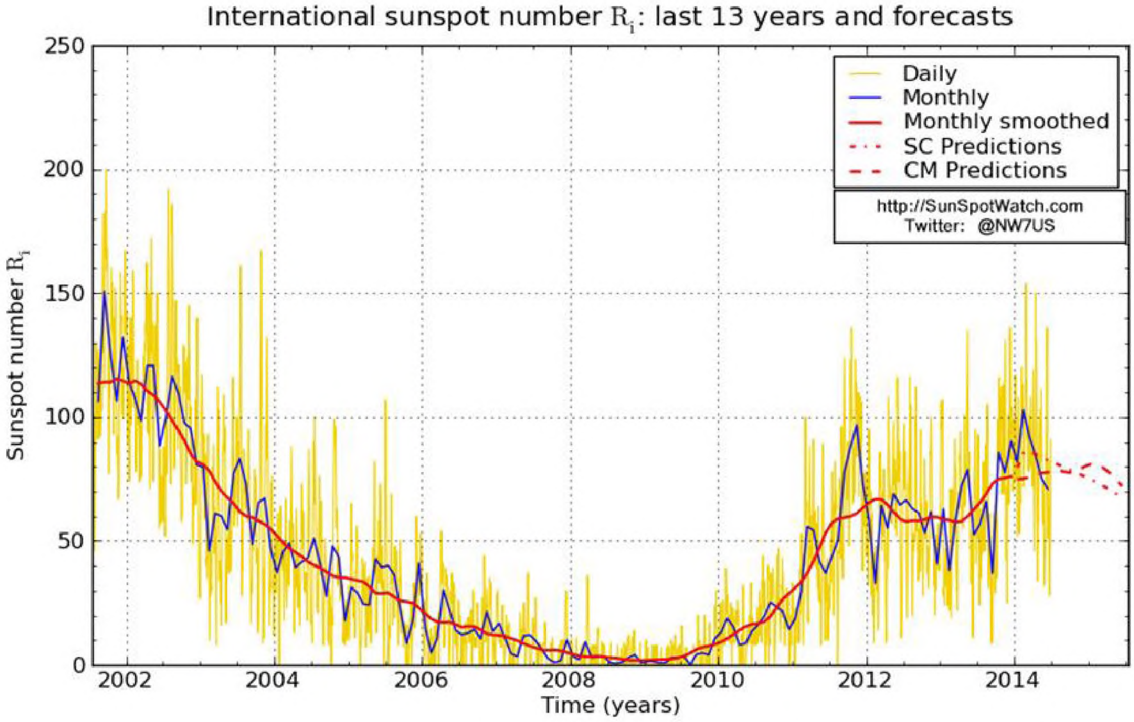
Statistical analysis

The statistical analysis was done using statistic package STATISTICA 10, and SPSS-20. Logistic regression analysis compared quantitative variables patient age, A index, Kp index, and the month of when stroke was noted with categorical variables of brain stem damage, gender, elevated blood pressure upon stroke, debut, time of day when first symptom of stroke was noted, stroke location, gender, post stroke epilepsy, mortality, and herniation of hematoma into the ventricles, and other risk factors such as smoking, alcohol consumption, obesity, arterial hypertension, kidney disease, liver disease, diabetes, season of when stroke was noted. The regression intercept was the expected mean value of independent variable when the dependent variables were all zero.

Results

We identified 669 cases of death from intracranial hemorrhage during high and low phases of solar activity. Fifty six percent were in men with a mean age of 54.4±12.2 years and 44% were women with a mean age of 54.23±12.52. There were 98 cases with an unclear medical history, arriving in a hospital in unconsciousness state.

During low solar activity years intracranial hematoma was more often located in the parietal and frontal lobe in contrast to the period of higher solar activity years, where hematomas more often were located in the frontotemporal



SILSO graphics (http://sidc.be) Royal Observatory of Belgium 01/07/2014

Figure 1. Daily and monthly sunspot number from 2001 to 2014). Daily sunspot number (yellow), monthly mean sunspot number (blue), smoothed monthly sunspot number (red) over a 13 year period.

Table 1. Predictors of Post-stroke epilepsy from logistic regression.

Analysis of Maximum Likelihood Estimates						
Parameter	Odds Ratio	DF	St.Estimate	Walid Error	Chi-Square	p-value
Seizure appearance intercept 1		1	4.9373	1.1478	18.5045	<.0001
Seizure appearance intercept 2		1	7.9189	1.1807	44.9872	<.0001
Patient age	0.982	1	-0.0186	0.00645	8.3152	0.0039
A index (max 24-hour disturbance)	1.063	1	0.0607	0.0177	11.8129	0.0006
Kp index (magnetic field disturbance)	0.329	1	-1.1131	0.2603	18.2911	<.0001
Elevated BP after stroke debut	0692	1	-0.3676	0.1871	3.8583	0.0495
Time of day of stroke debut	0.891	1	-0.1151	0.0541	4.5254	0.0334
Stoke location	1.475		0.3884	0.1311	8.773	0.0031
Brain stem involvement	0.576		-0.5518	0.2357	5.4801	0.0192
Association of Predicted Probabilities and Observed Responses						
Percent Concordant 63.3 Somer's D 0.272						

lobe ($p<0.05$). Larger hematomas, like hematomas herniated into the brain ventricles were found during higher solar activity years ($p<0.05$). Intracranial hemorrhage caused by arterial hypertension prevailed throughout the high solar activity years in comparison with low solar activity years ($p<0.05$).

Using analysis of maximum likelihood estimates of logistic regression with elimination we identified the risk factors most predictive of PSE. Our analysis of Pearsons Chi-Square and Walid Chi-square there the predictive factors are shown in Table 1.

We compared the ICH mortality rates of those which presented epilepsy with those that did not. Of the cases that developed epilepsy, 43% (n=74) survived the first day, 22% (n=39) survived until the third day, 17% (n=29) survived until the seventh day, 7% (n=12) survived until the eleventh day, 4.7% (n=8) until the fourteenth day and 3.5% (n=10) survived more than 14 days after stroke. In comparison with patients who did not develop epilepsy after stroke, 62% (n=152) survived the first day, 21% (n=84) survived until the third day, 21% (n=85) survived until the seventh day, 7.5%% (n=30) survived until the eleventh day, 6.5 (n=26) until the fourteenth day and 5.5% (n=22) survived more than 14 days after stroke.

PSE was observed less during years with decreased solar activity ($p<0.0001$) in comparison with high years with solar activity. The mean age of PSE presented patients was 51.2±11.9. Most of the cases with PSE developed in patients with subarachnoid hemorrhage ($p<0.05$), brainstem hematoma ($p<0.03$) and cases with combined hematoma ($p<0.0001$). PSE appeared more frequently after ICH debut in cases with type 2 diabetes ($p<0.02$). Aneurysms ruptured more frequently when present in the anterior circulation ($p<0.02$). There was no association between pre-stroke hypertension and hypertension at time of hospitalization ($p<0.05$). The debut of PSE shown was associated with elevated arterial blood pressure at the time of arrival at hospital ($p<0.0001$).

Discussion

Solar activity has multiple effects on the human body including effects on heart rate, myocardial infarction mortality, stroke morbidity and epilepsy [15-18]. Previous studies which involved 11453 patients with stroke collected during 16,031,764 person-years of observation concluded that geomagnetic storms can trigger strokes [6]. PSE as a presenting sign of an ICH in 172 of 669 (26%) cases. The main limitation of that study was that the authors were not able to get individual-participant data from studies in Asia, Africa, North and Latin America. They concluded that their findings needed to be confirmed in other regions of the world. One-hundred-seventy-two of 669 cases who had ICH presented PSE.

Our study showed that PSE occur more frequent after subarachnoid hemorrhage and when combined with hematoma. Similar results were found in the study of Burn et al. where the PSE risk was increased in survivors of subarachnoid and intracerebral hemorrhage [20].

We found that PSE was more frequent in patients with brain stem hematoma. In contrast, Lahti et al. reported that patients with infratentorial hematoma developed PSE less frequently [11]. The proposed mechanism for seizure after ICH with brain stem damage is that local hypoxia at respiratory center leads to global hypoxia of the cerebral cortex leading to seizure. There is a similar mechanism of neonatal epilepsy and epilepsy of experimental animals where hypoxic-ischemic encephalopathy plays a key role [22, 23]. Stoupel et al. hypothesized that the suppression of the nocturnal concentrations of the endogenous anticonvulsant melatonin by sudden increases in geomagnetic activity may cause fatal cardiac arrhythmias by uncoupling the insular/amygdaloid-paraventricular hypothalamic-solitary nucleus pathways [20]. Our results were similar in that PSE was less frequent during the years there was lower solar activity. Geomagnetic storms was not identified as a predicting risk factor of PSE in our logistic regression analysis and that result was diverges with results of Stoupel et al.

It has been shown by other investigators that the risk of death is increased in patients with PSE and also the risk of PSE is increased in young patients with hemorrhagic stroke [24]. The mean age of the patients with PSE in our study was 51.2±11.9 and PSE affected more often men in this age.

Other investigators found that loss of consciousness at arrival was associated with increased risk of PSE [26]. We did not observe this in our study.

The increased incidence of PSE after total anterior circulation infarction may reflect the extensive damage frequently sustained to the frontal and temporal cortex, the most epileptogenic areas of the brain [27]. This is comparable to our results where rupture of an intracranial aneurysm located in the area of internal carotid artery more frequently resulted in PSE ($p<0.02$).

Patients with diabetes presented with PSE more often than those with other risk factors ($p<0.02$) but the mechanism of their seizures may need to be differentiated from hypoglycemic seizures which may be partially explained by pathophysiological implications of diabetes, especially in the context of anti-glutamic acid decarboxylase antibodies [27].

Logistic regression analysis identified location of hematoma, complication of hematoma with herniation to ventricles, and age of patients as factors which provoke PSE.

Our study has the limitation of a retrospective review and used records that were not designed specifically designed for our topic and including the possibility of an absence of data on potential confounding factors. Another limitation of this study is that we did not study the impact of solar radiation on PSE after ischemic stroke, cerebral venous thrombosis, and transient ischemic attack. Future prospective studies about PSE after the different types of stroke are needed.

Conclusions

Predicting factors for PSE were the location of hematoma, time of day of stroke debut, and age. The PSE more often affected people between 30-34 and 65-69 years old and there were no gender differences in this age groups. Post-stroke epilepsy was less frequent during low solar activity years. Post-stroke epilepsy was more prevalent in patients with subarachnoid hemorrhage and brainstem hematoma and even more in patients with diabetes. Post-stroke epilepsy with concomitant brainstem hematoma result in poor outcomes following stroke.

Acknowledgements

The authors express their gratitude to the Computer Science Department, Biostatistics center of Tomsk State University Russia, Department of Epidemiology and Biostatistics School of Public health, Mongolian National University of Medical Sciences, Third and First clinical hospital of Mongolia, National Pathological center of Mongolia.

Conflict of interest

None

References

1. Lopez AD, Mathers CD, Ezzati M, Jamison DT, Murray CJ. Global and regional burden of disease and risk factors, 2001: Systematic analysis of population health data. Lancet 2006; 367: 1747-57.
2. Yang Q, Tong X, Schieb L, Vaughan A, Gillespie C, Jennifer L, et al. Vital Signs: Recent Trends in Stroke Death Rates — United States, 2000–2015. Morb Mortal Wkly Rep 2017; 66: 933–9. DOI: http://dx.doi.org/10.15585/mmwr.mm6635e1.
3. Benjamin EJ, Blaha MJ, Chiuve SE, Cushman M, Das SR, Deo R, et al. Heart Disease and Stroke Statistics-2017 Update: A Report from the American Heart Association. Circulation 2017; 135: e146-e603.
4. Global Burden of Disease Study 2015. Global Burden of Disease Study 2015 (GBD 2015) results. Seattle, WA: Institute for Health Metrics and Evaluation (IHME), University of Washington [accessed on 1 Aug 2017]. Available at: http://ghdx.healthdata.org/gbd-results-tool.
5. McCraty R, Atkinson M, Stolc V, Alabdulgader AA, Vainoras A, Ragulskis M. Synchronization of Human Autonomic Nervous System Rhythms with Geomagnetic Activity in Human Subjects. Int J Environ Res Public Health 2017; 14.
6. Feigin VL, Parmar PG, Barker-Collo S, Bennett DA, Anderson CS, Thrift AG, et al. Geomagnetic storms can trigger stroke: evidence from 6 large population-based studies in Europe and Australasia. Stroke 2014; 45: 1639-45.
7. Herman ST. Epilepsy after brain insult: targeting epileptogenesis. Neurology 2002; 59: S21-6.
8. Bladin CF, Alexandrov AV, Bellavance A, Bornstein N, Chambers B, Coté R, et al. Seizures After Stroke: A Prospective Multicenter Study. Arch Neurol 2000; 57: 1617-22.
9. Olsen TS. Post-stroke epilepsy. Curr Atheroscler Rep 2001; 3: 340-4.
10. Benbir G, Ince B, Bozluolcay M. The epidemiology of post-stroke epilepsy according to stroke subtypes. Acta Neurol Scand 2006; 114: 8-12.
11. Lahti AM, Saloheimo P, Huhtakangas J, Salminen H, Juvela S, Bode MK, et al. Poststroke epilepsy in long-term survivors of primary intracerebral hemorrhage. Neurology 2017; 88: 2169-75.
12. Sitajayalakshmi S, Mani J, Borgohain R, Mohandas S. Post Stroke Epilepsy. Neurol India 2002; 50: S78-84.
13. Kilpatrick CJ, Davis SM, Tress BM, Rossiter SC, Hopper JL, Vandendriesen ML. Epileptic Seizures in Acute Stroke. Arch Neurol 1990; 47: 157–160.
14. Arntz R, Rutten-Jacobs L, Maaijwee N, Schoonderwaldt H, Dorresteijn L, van Dijk E, et al. Post-stroke epilepsy in young adults: a long-term follow-up study. PLoS One 2013; 8: e55498.
15. Dimitrovo S, Angelov I, Petrova E. Solar and geomagnetic activity effects on heart rate variability. Natural Hazards 2013; 69. DOI: 10.1007/s11069-013-0686-y.
16. Dimitrovo S, Stoilova I, Georgieva K, Taseva T, Jordanova M, Maslarov D, et al. Solar and Geomagnetic Activity and Acute Myocardial Infarction Morbidity and Mortality. Comptes rendus de l'Académiebulgare des sciences: sciences mathématiques et naturelles 2010; 3: 161-5.
17. Martirosyan V, Krupskaya J. Study of the factors influencing mortality from the cerebral stroke in patients of different ages. Br J Med Med Res 2013; 3: 1530-57. DOI: 10.9734/BJMMR/2013/3991.
18. Persinger MA, Psych C. Sudden unexpected death in epileptics following sudden, intense, increases in geomagnetic activity: prevalence of effect and potential mechanisms. Int J Biometeorol 1995; 38: 180-7.
19. Belov DR, Kanunikov IE, Kiselev BV. Dependence of human EEG spatial synchronization on the geomagnetic activity on the day of experiment. Ross Fiziol Zh Im I M Sechenova 1998; 84: 761-74.
20. Burn J, Dennis M, Bamford J, Sandercock P, Wade D, Warlow C. Epileptic seizures after a first stroke: the Oxfordshire Community Stroke Project. BMJ 1997; 315: 1582-7.
21. Mueller SG, Nei M, Bateman L. Evidence for brainstem network disruption in focal epilepsy and sudden unexplained death in epilepsy: a first validation study. Presented at: 2017 American Epilepsy Society Annual Meeting 2017; Washington DC. Abstract 3.205.
22. Sanchez RM, Koh S, Rio C, Wang C, Lamperti ED, Sharma D, et al. Decreased glutamate receptor 2 expression and enhanced epileptogenesis in immature rat hippocampus after perinatal hypoxia-induced seizures. J Neurosci 2001; 21: 8154-63.
23. Yamada K, Ji JJ, Yuan H, Miki T, Sato S, Horimoto N, et

al. Protective role of ATP-sensitive potassium channels in hypoxia-induced generalized seizure. Science 2001; 292: 1543-6.

24. Stoupel E, Martfel J, Rotenberg Z. Admissions of patients with epileptic seizures (E) and dizziness (D) related to geomagnetic and solar activity levels: differences in female and male patients. Med Hypotheses 1991; 36: 384-8.
25. Zelano J, Redfors P, Asberg S, Kumlien E. Association between poststroke epilepsy and death: A nationwide cohort study. European Stroke Journal 2016; 1: 272–8.
26. French J, Gernandt B, Livingston R. Regional differences in seizure susceptibility in monkey cortex. AMA Arch Neurol Psychiatry 1956; 75: 260-74.
27. Keezer MR, Novy J, Sander JW. Type 1 diabetes mellitus in people with pharmacoresistant epilepsy: Prevalence and clinical characteristics. Epilepsy Res 2015; 115: 55-7.
28. Robert S. Fisher The New Classification of Seizures by the International League Against Epilepsy. Curr Neurol Neurosci Rep 2017; 17: 6-1.
29. International Space Environment Service [accessed on 15 Sep 2017]. Available at: http://www.spaceweather.org, www.sidc.be.
30. National Center for Environmental Information [accessed on 15 Sep 2017]. Available at: https://www.ngdc.noaa.gov/dscovr/portal/#/.