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EXPLORING THE CORELATION BETWEEN ASYMMETRY RATE OF THE CEREBRAL PEDUNCLE AND THE RECOVERY OF POSTSTROKE APHASIA

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ABSTRACT

Objective: To explore the corelation between asymmetry rate of the cerebral peduncle (ARCP) and the recovery of poststroke aphasia (PSA). **Methods:** Thirty-three recurrent stroke participants with PSA completed the retrospective study. They were divided into two groups according to the sides of recurrent stroke, ipsilateral group (dominant side) and contra lateral group. The aphasia quotient (AQ) of post-first time stroke (AQ_{postFS}), pre-recurrent stroke (AQ_{preRS}), and post-recurrent stroke (AQ_{postRS}) were collected, which were based on the Chinese version western aphasia battery. The ARCP was calculated based on the latest magnetic resonance imaging (MRI). Changing of AQ (ΔAQ, ΔAQ1= AQ_{preRS}-AQ_{postFS}; ΔAQ2= AQ_{preRS}-AQ_{postRS}), and the correlation between ΔAQ and ARCP of the two groups were analyzed. **Results:** The AQ_{postRS} of the contralateral group is significantly lower than that of the ipsilateral group (32.42 [18.73] vs. 44.97 [11.65], p=0.029).ΔAQ2 in CG was higher than that in IG (38.54 [17.89] vs. 27.03 [10.76], p=0.034).ΔAQ1 (r = 0.792, p<0.0001) and ΔAQ2 (r = 0.940, p<0.0001) showed a significant correlation with ARCP. Subjects with an ARCP of more than 1.5 presented a higher ΔAQ2 than patients with ARCP less than 1.5 In CG (56.77 [2.98] vs. 25.77 [11.11], p<0.0001), a contrary consequence was observed in IG (19.08 [11.44] vs. 30.64 [8.68], p=0.042). **Conclusion:** Patients with higher ARCP showed a worse prognosis of PSA followed recurrent stroke of the non-dominant hemisphere, The synergistic effect between the two hemispheres is the key mechanism of PSA recovery.

Citation: Xiuyu Du, Xuefei Zhang, Xiaodong Zhai, Hongpeng Hu and Qian Xue. "Exploring the Corelation Between Asymmetry Rate of the Cerebral Peduncle and the Recovery of Poststroke Aphasia*", 2021. International Journal of Current Research, 13, (04), 17044-17050.*

INTRODUCTION

Trial registration clinical trials: Chi CTR 2000031285 Poststroke aphasia (PSA) is a language disorder followed dominant hemisphere stroke which often leave the survivor inconvenient and distressed dailylife[1]. The recovery proceeding of PSA was complex and ambiguous. Despite various therapeutic methods that have been used in the adjuvant treatment of PSA[2-4], the mechanism of PSA recovery was unclear. Take the noninvasive brain stimulation treatment in PSA for example, until now, which hemisphere should be a therapeutic target was still controversial, and it was inconsistent among previous accumulative studies. Winhuisen *et al.*[5]reported that the dominant hemisphere was more effective in the recovery of PSA, due to the restoration of language network.

Abo *et al.* [6]suggested both hemispheres should be considered when noninvasive brain stimulation techniques were used to improve PSA. Stockert, *et al.*[7]noted the dynamics of language reorganization in the recovery of PSA. Raboyeau, *et al.*[8]noted that the right inferior frontal regions play an important role in the recovery of post stroke aphasic patients. Due to the uniqueness of human language, it was impossible to explore language function by animal experiments. The development of functional neuroimaging had promoted the research of PSA to more depth[9, 10]. However, as indirect clinical evidence, functional neuroimaging cannot differentiate primary or compensable brain regions in patients with PSA. Authors[11, 12]suggested it should not be used to determine the functional localization and accurate detection of essential cortical language areas. For patients with PSA, especially, for those patients combine with severe injury in the dominant hemisphere, the non-dominant hemisphere become the best prospect for recovery of PSA.

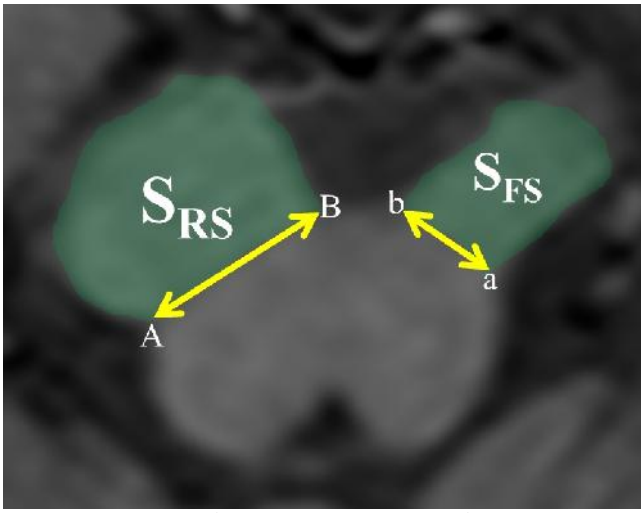
However, it is difficult to evaluate the compensative capacity of the non-dominant hemisphere accurately based on currently available technologies. So, there was an urgent need for more valid and convinced evidence in the research of PSA. In this study, representative clinical records (recurrent stroke in the non-dominant hemisphere for patients with PSA) were collected and analyzed, through which we could confirm whether language function exising in the non-dominant hemisphere. It is hypothesized in this paper that the compensating language function in non-dominant hemisphere for patients with PSA, and the AQ would be decline followed recurrent stroke. We also hypothesized that the compensating capacity of language function in the non-dominant hemisphere correlated with the severity of the first time stroke in the dominant hemisphere, which could be the quantity of morphological change of the cerebral peduncle. Thus, in this study, we'd like to explore the value and mechanism of the non-dominant hemisphere in the recovery of PSA, and which is based on the correlation of the ARCP and the change of AQ.

METHODS

Study population and screening criteria: Patients with recurrent (the second time) stroke were recruited in this study from the First Affiliated Hospital of Hebei North University from January 1, 2016 and October 1, 2020. There were four hundred sixty-nine recurrent stroke patients who were screened based on the following criteria: (1) the first and second time stroke happened in basal ganglia or/and thalamus, (2) the first time stroke occurred in the dominant hemisphere and resulted inanaphasia, (3) no other neurological disorders except for stroke, (4) the native language is Chinese and without communication disorder and recognition disorder before the first time stroke, (5) the AQ within one month and beyond one year after first time stroke can be acquired from clinical record, the AQ within one month after the second time stroke can be obtained also, and (6) MRI data that one year after the first stroke or within one week of the second time stroke can be obtained to calculate ARCP. Forty -three patients met the initial screening criteria. Among them, three patients with a history of an epileptic seizure, three bilingual (Chinese and Mongolian) patients, and four illiterate patients were excluded. Finally, thirty-three patients were analyzed in this study. According to the lateral of the second time stroke, they were divided into an ipsilateral (dominant hemisphere, n=16) group (IG) and contra lateral (non-dominant hemisphere, n=17) group (CG)

Standard protocol approvals, registrations: This study was conducted following the Declaration of Helsinki and approved by the ethics committee of the First Affiliated Hospital of Hebei North University (No. K2020263).As a retrospective study of clinical record, the ethics committee has approved the use of humans for this study, need not a written consent from subjects.

ARCP calculation: The area of the cerebral peduncle was measured (figure 1) by two neuroimagingexperts by the method of Warabi *et al.*[13]at an MRI workstation, and experts were blinded to the information of every enrolled patient.



RS: recurrent stroke. FS: first-time stroke. S_{RS}: area of cerebral peduncle of recurrent side. S_{FS}: area of cerebral peduncle of first-time stroke side. Point A and a represent the side of RS and FS lateral sulcus of the cerebral peduncle, respectively. They are also the lateral start point of measurement of the cerebral peduncle. The medial start points of the cerebral peduncle are point B and b which represent the oculomotor sulcus of the RS side and FS side, respectively. The calculation method of ARCP as below: $A = \frac{S_F}{S_R}$

Figure 1. Measurement of cerebral peduncle and calculation of ARCP

Aphasia quotient: The Chinese version of Western Aphasia Battery (WAB)[14] was used to evaluate the patients' language function. Spontaneous speech, auditory comprehension, repetition, and naming ability were evaluated. The result was shown as an aphasia quotient (AQ). AQ less than 93.8 can be diagnosed as aphasia. AQ was calculated as below:

$$A = 2 \times (s \quad o \quad s \quad n \quad h + \frac{s \quad o \quad a \quad cc \quad he}{20} + \frac{s \quad o \quad r \quad s \quad o \quad nc}{10} + \frac{}{10})$$

The AQ score within one week after the first stroke was used to quantify the affected language function by the first stroke (AQ_{postFS}).The AQ score more than one year after the first stroke (the last one, before the recurrent stroke) was used to quantify the recovery extent of PSA (AQ_{preRS}). The AQ score within one week after the recurrent stroke was used to quantify the affected language function by the recurrent stroke (AQ_{postRS}).ΔAQ represented the changing range of the PSA, ΔAQ1was defined as the improvement of PSA from the first time stroke to the recurrent stroke, $\Delta AQ1 = AQ_{preRS} - AQ_{postFS}$; ΔAQ2 was defined as the deterioration of PSA after recurrent stroke, $\Delta AQ2 = AQ_{preRS} - AQ_{postRS}$.

Statistical analyses: For all of the date, categorical variables are presented as number of subjects (%) and were compared using the Pearson's chi-square test or Fisher's exact method, and Continuous variables were presented as mean [standard deviation] ± and were compared using the independent sample t-test. $P<0.05$ was considered as the result at a significant level. Basedon previous study of our team and relevant study, we have choosed ARCP=1.5 as a cutoff point, the patients in CG and IG were divided into two subgroups respectively by the cutoff point value of ARCP (ARCP≥1.5, and ARCP ＜1.5). Correlation between ARCP and ΔAQ was performed by Pearson correlation analysis method, degree of relevant indicated by correlation coefficient (CC). Weak correlation,

medium correlation, strong correlation defined as CC=0.1~0.3, CC=0.3~0.5, CC>0.5, respectively. IBM SPSS Version 21 (IBM Corp., Armonk, New York, USA) was used for the statistical analysis.

Data availability: The anonymized study data for the present study are available from the corresponding author (dxy8108@163.com) on reasonable request.

RESULTS

General characteristic of the patients

The patients for this study contained: (1) eleven male and six female in CG, (2) elevenmale and five female in IG, there was no significant difference between the two groups. The mean age of subjects as follows: (1) 54.76 [8.03] years for CG, (2) 53.94 [8.58] years for IG, no significant difference between the two groups. The dominant hemisphere of the patients was: (1) all the seventeen patients of CG for the left hemisphere, (2) fifteen patients for the left hemisphere and one for the right hemisphere.

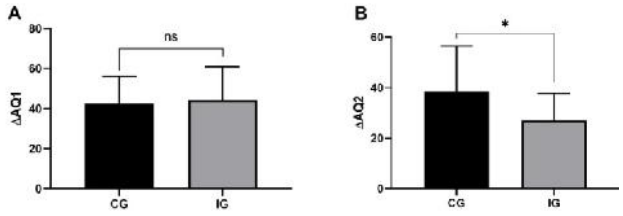
The stroke types of each group was: (1)eight patients with hemorrhagic stroke and nine patients with ischemia stroke in CG when the first time stroke happened, (2)eight patients with hemorrhagic stroke and eight patients with ischemia stroke in IG when the first time stroke happened, (3) thirteen patients with hemorrhagic stroke and four patients with ischemia stroke of CG in recurrent stroke, (4) twelve patients with hemorrhagic stroke and four patients with ischemia stroke of IG in recurrent stroke, with no significant difference between the two groups. The mean duration, AQ_{postFS}, AQ_{preRS} and mean ARCP of CG and IG was compared respectively, there was no significant difference between the two groups. The AQ_{postRS} of IG significant higher than that of CG (Table 1).

Table 1. Demographic and general clinical characteristics of enrolled patients

Characteristic	CG (n=17)	IG (n=16)	*p* Value
Gender, n(%)			0.8055
Female	6(35.29)	5(31.25)	
Male	11(64.71)	11(68.75)	
Age, y			0.7767
Mean (SD)	54.76(8.03)	53.94(8.58)	
Dominant hemisphere, n (%)			0.2952
Right hemisphere	0(0)	1(6.25)	
Left hemisphere	17(100)	15(93.75)	
First stroke type, n (%)			0.8658
Hemorrhagic	8(47.06)	8(50)	
Ischemic	9(52.94)	8(50)	
Recurrent stroke type, n (%)			0.9215
Hemorrhagic	13(76.47)	12(75)	
Ischemic	4(23.53)	4(25)	
Duration			0.6403
Mean (SD)	4.44(2.03)	4.78(2.19)	
ARCP			0.9639
Mean (SD)	1.39(0.15)	1.39(0.14)	
AQ_{postFS} score			0.8523
Mean (SD)	28.59(14.03)	27.63(15.25)	
AQ_{preRS} score			0.3372
Mean (SD)	70.95(2.79)	71.99(3.33)	
AQ_{postRS} score			0.0287*
Mean (SD)	32.42(18.73)	44.97(11.65)	

Abbreviations: CG = contralateral group; IG = ipsilateral group; ARCP = asymmetry rate of cerebral peduncle; AQ_{postFS} = The aphasia quotient after the first time stroke; AQ_{preRS} = The aphasia quotient pre-recurrent stroke; $AQ_{post\text{-}RS}$ = The aphasia quotient post-recurrent stroke;*: $p<0.05$.

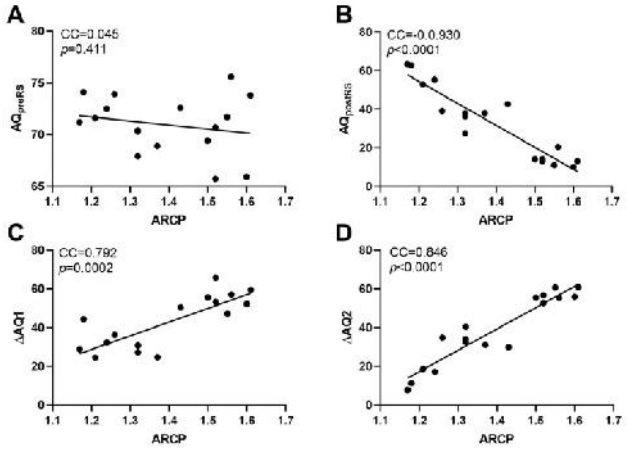
Comparison of ΔAQ1 andΔAQ2 between the two groups: As a quantity index of recovery of PSA before the recurrent stroke, the value of ΔAQ1 between CG and IG were compared by independent sample *t*-test method. It was showed that the ΔAQ1in the CG was 42.36 [13.67], in the IG was 44.36 [16.55], there was no significant difference between the two groups (t=-0.379 p=0.707) (Figure 2A). As a quantity index of deterioration of PSA after the recurrent stroke, the same method was conducted to make a distinction between ΔAQ2 in CG and in IG, a significant difference was found between the two groups (Figure 2B), the value of ΔAQ2 in CG was higher than that in IG (38.54 [17.89] vs. 27.03 [10.76], t=2.255, p=0.034).



The characteristics of changing of aphasia quotient (AQ) in different period and groups were demonstrated. AQ of pre-recurrent stroke (ΔAQ1) and AQ of post-recurrent stroke (ΔAQ2) between the CG and IG were compared respectively in figure1. CG= contralateral group; IG= ipsilateral group. ns: $p>0.05$ by independent sample t-test. *: $p<0.05$ by an approximate independent sample t-test.

Figure 2. Change of AQ before and after recurrent stroke in the two groups

Correlation of AQ_{preRS}, AQ_{postRS}, ΔAQ, and ARCP in CG: To explore the correlation between the AQ of peri-recurrent stroke period (AQ_{preRS}, AQ_{postRS}, ΔAQ1, and ΔAQ2) and asymmetry rate of the cerebral peduncle (ARCP), a Pearson correlation analysis was performed. There were significant correlation between ΔAQ1 and ARCP (r = 0.792, p<0.0001, 95% confidence interval 0.502 to 0.922) and between ΔAQ2 and ARCP(r = 0.940, p<0.0001, 95% confidence interval 0.838 to 0.979) but not between AQ_{preRS} and ARCP (r = 0.213, p=0.411, 95% confidence interval -0.623 to 0.298). When considering the changing of aphasia after the recurrent stroke, we observed a strong and significant correlation between AQ_{postRS} and ARCP (r = -0.930, p<0.0001, 95% confidence interval -0.975 to -0.812). According to the results, ΔAQ1 andΔAQ2 showed a positive correlation with ARCP, and a negative correlation presentedbetween ARCP and AQ_{postRS} (Figure 3).

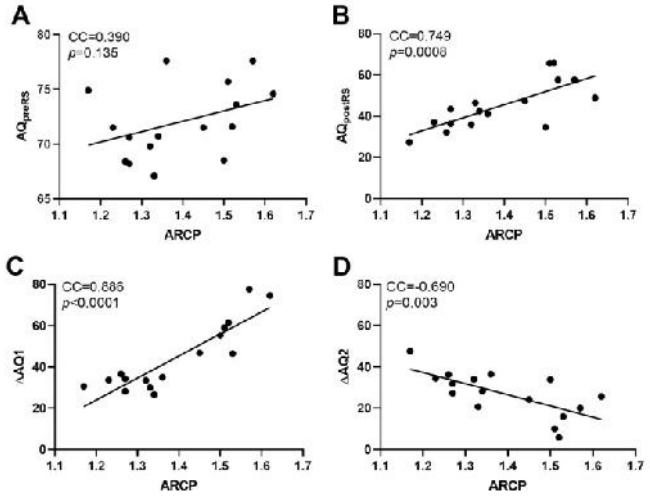


The relationship (A, B)between aphasiac severity scale of pre- and post-recurrent stroke and asymptomatic change of cerebral peduncle is shown as aphasiac quotient [AQ_{preRS} and AQ_{postRS}] and asymmetry rate of the cerebral peduncle (ARCP). There is a significant negative association between AQ_{postRS} and ARCP, but between AQ_{preRS} and ARCP. The association (C, D) between changing range of AQ pre- and post-recurrent stroke and ARCP is described as ΔAQ (ΔAQ1, ΔAQ2) and ARCP. Patients with bigger ARCP value showed a lager fluctuating in ΔAQ1 and ΔAQ2, and presented a positive correlation. CC: correlation coefficient; CG: contralateral group; AQ: aphasiac quotient; ΔAQ represented the changing range of the PSA, ΔAQ1 was defined as the improvement of PSA from the first time stroke to the recurrent stroke, ΔAQ1= AQpreRS- AQpostFS; ΔAQ2 was defined as the deterioration of PSA after recurrent stroke, ΔAQ2= AQpreRS- AQpostRS.

Figure 3. Correlation analysis of AQ and ARCP in CG

Correlation of AQ_{preRS}, AQ_{postRS}, ΔAQ, and ARCP in IG: For the patients who were suffered a recurrent stroke in the ipsilateral hemisphere (dominant hemisphere), a Pearson correlation analysis was employed to evaluate the correlation between the AQ of peri-recurrent stroke period (AQ_{preRS}, AQ_{postRS}, ΔAQ1, and ΔAQ2) and asymmetry rate of the cerebral peduncle (ARCP).

Different from the correlation in contralateral group (CG), there was a significant positive correlation between ARCP and AQ_{postRS}(r = 0.749, p=0.0008, 95% confidence interval 0.440 to 0.908). There was no significant correlation between ARCP and AQ_{preRS}. The change of AQ before recurrent stroke (ΔAQ1) and post recurrent stroke (ΔAQ2) are both shown a correlation with ARCP ([r = 0.886, p<0.0001, 95% confidence interval 0.696 to 0.960] vs.[r = -0.690, p=0.003, 95% confidence interval -0.883 to -0.295]), among them ΔAQ2 present a negative correlation with ARCP (Figure 4).

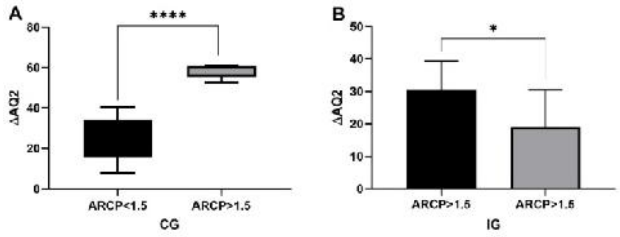


The association (A, B)between aphasiac severity scale of pre- and post-recurrent stroke and asymptomatic change of cerebral peduncle is shown as aphasiac quotient [AQ_{preRS} and AQ_{postRS}] and asymmetry rate of the cerebral peduncle (ARCP). There is no significant correlation between AQ_{preRS} and ARCP (A). Opposite with tht in contralateral group, the value of AQ_{postRS} is showed a positive correlation with ARCP (B). The relationship (C, D) between changing range of AQ pre- and post-recurrent stroke and ARCP is shown as ΔAQ (ΔAQ1, ΔAQ2) and ARCP. A strong significant correlation (C) is observed between ΔAQ1 and ARCP. There is weak correlation between ΔAQ2 and ARCP (D). CC: correlation coefficient; CG: contralateral group; AQ: aphasiac quotient; ΔAQ represented the changing range of the PSA, ΔAQ1 was defined as the improvement of PSA from the first time stroke to the recurrent stroke, ΔAQ1= AQpreRS- AQpostFS; ΔAQ2 was defined as the deterioration of PSA after recurrent stroke, ΔAQ2= AQpreRS- AQpostRS.

Figure 4. Correlation analysis of AQ and ARCP in IG

Comparison of ΔAQ2 in different ARCP subgroups: In the CG and IG, patients were divided into two subgroups by the cutoff point (1.5) of ARCP, respectively. In CG, subjects with an ARCP of more than 1.5 showed an obviously worsened language function followed the recurrent stroke, and presented a higher ΔAQ2 (56.77 [2.98]) than patients with ARCP less than 1.5 (25.77 [11.11]), there was a significant difference between the two subgroups (t=7.142, p<0.0001) (Figure 5A).

Surprisingly, a contrary consequence was observed in IG, patients with ARCP of more than 1.5showed a lowerΔAQ2 (19.08 [11.44]) than the patients with ARCP of less than 1.5 (30.64 [8.68]), with a significant difference (t=2.244, p=0.042) (Figure 5B).



Comparison of ΔAQ2 in different ARCP subgroups (ARCP>1.5 and ARCP<1.5) in CG, a two-sample t-test was performed. ARCP=1.5 as a cutoff point has been widely used previous studies, here, as a boundary of obvious asymmetry and unobvious asymmetry of cerebral peduncle. ****: p<0.0001; *: p<0.05, by independent sample t-test. CG= contralateral group; ΔAQ represented the changing range of the PSA, ΔAQ2 was defined as the deterioration of PSA after recurrent stroke, ΔAQ2= AQ_{preRS}- AQ_{postRS}. ARCP= asymmetry rate of the cerebral peduncle.

Figure 5. Comparison of ΔAQ2 in different ARCP subgroups in CG

Influence factors of the recovery capacity of PSA: In the present study, the quantitative criterion of the recovery capacity of PSA was ΔAQ1. All the enrolled patients had received the same language training guidance from the rehabilitation physician after first-time stroke. The influence factors of this study included: age, gender, duration, and stroke types. In the CG, mean ΔAQ1 for hemorrhagic stroke was 40.79 [12.82], for ischemic stroke was 43.37 [15.01], there was no significant difference between the stroke types (t=0.437, p=0.668); mean ΔAQ1 for male patients was 39.82 [14.15], for female patients was 47.03 [12.54], there was no significant difference between genders (t=-1.0427, p=0.314). We also have not found a significant association between duration (r=-0.072, p=0.785) and ΔAQ1, and between age (r=-0.467, p=0.059) with ΔAQ1. In the IG, mean ΔAQ1 for hemorrhagic stroke was39.31 [12.63], for ischemic stroke was 49.41 [19.22], there was no significant difference between the stroke types (t=1.242, p=0.235); mean ΔAQ1 for male patients was 41.83 [16.24], for female patients was 49.94 [17.57], there was no significant difference between genders (t=-0.903, p=0.382). There was no significant correlation between duration (r=-0.118, p=0.663), age (r=0.434 p=0.093) and ΔAQ1.

AQ, ΔAQ, ARCP in special subjects: In our study, there were six patients (three male and three female, two in CG, four in IG, mean age is 54.33[10.61])suffered a first-time chronic ischemic hemispherical stroke in dominant hemisphere (left), nearly global aphasia was manifested following the stroke. The mean AQ after first-time stroke was significantly lower than that of others (6.75 [7.68] vs. 32.87[10.74],t=5.617, p<0.0001).Through years (3.92 [2.26]) of recovery, the mean AQ increased, until before the recurrent stroke, there was no significant difference between AQ of the special subjects and AQ of others(71.85[5.07] vs. 71.37 [2.56], t=-0.225, p=0.830), besides, the recovery duration between them was not shown a significant difference (4.20 [2.08] vs. 4.69 [2.11], t=-5.19, p=0.608).However, followed the recurrent stroke two of six patients in CG showed an almost global aphasia (AQ_{postRS}=11.50[2.12]), on the contrary, four of six patients in IG presented a mild changing in language function (ΔAQ2=15.38 [9.10]). When the ARCP was concerned, we observed special subjects with a higher ARCP, there was a significant difference between special subjects and others (1.56 [0.05] vs. 1.36 [0.13], t=-6.367, p<0.0001).

The hypothesis process and mechanism of recovery of PSA

Based on the direct and actual clinical evidence, and correlation analysis between aphasia recovery and relevant

factors, we considered the synergistic effect between the dominant hemisphere and the non-dominant hemisphere as the key mechanism in the process of recovery of PSA (figure 6).

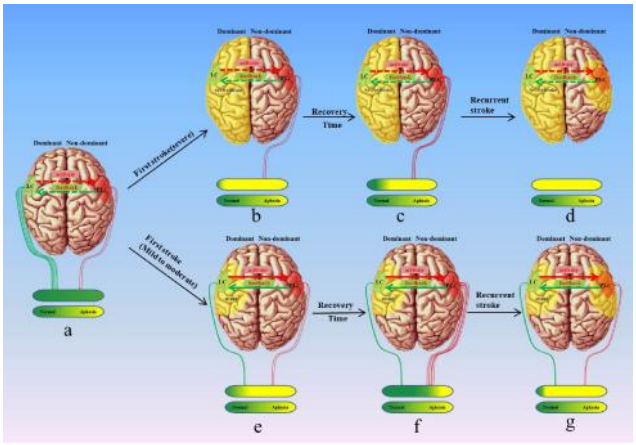


Figure 6. Process and mechanism of recovery of PSA

LC=language cortex, it's in the dominant hemisphere and present as a green area; PLC=potential language cortex, it's in the non-dominant hemisphere, present as a red area (silent state). The red dotted line (unactivated) means a potential network from LC to PLC which can be activated when the dominant hemisphere suffering a stroke. The green descend curve line derived from the dominant hemisphere means the signals from LC to speech organ. The red descend curve line derived from the non-dominant hemisphere means the potential compensative signaling pathway from PLC to speech organ, it can produce compensative language signal in common condition (figure 5a). The green and yellow color bar under every demo picture mean the degree of aphasia, green means normal language, and yellow means aphasia. The green dotted line means potential feedback signals from activated PLC to LC (figure 5a). The dotted line will become a solid line (activated state) when LC starts the activation signal (figure 6e). The activated proceed is a cycled procedure with continuous activating and feed backing.

The upper three demo pictures show the process of post-severe stroke aphasia recovery. From the pictures we can see that there is no signal from LC to PLC (unactivated) which ascribe to extensive severe injury of dominant hemisphere (figure 5b), the speech organ only accepts fewer compensative language signal from PLC and present a poor outcome (figure 5c). When the recurrent stroke happened in PLC the speech organ would lose all of the language signal (figure 5d). The patients would become global aphasia.

The below three demo pictures show the process of post-mild to moderate stroke aphasia recovery. From the pictures, we can see that there is a fewer signals from LC to speech organ followed the first stroke which caused post stroke aphasia (figure 5e). Meanwhile, the PLC is activated by the LC and then feedback to LC, with time going the PLC accept more and more activation and send out more compensative signal to speech organ in the recovery procedure of aphasia and present a better outcome (figure 5f). When the recurrent stroke happened in PLC the speech organ would lose the compensative language signal (figure 5g). The patients' aphasia becomes worsen.

DISCUSSION

This direct clinical evidence-based study stressed the crucial role of the non-dominant hemisphere and the synergistic effect of both hemispheres in the process of recovery of PSA. In the past decades there were a growing number of studies focusing on the recovery of PSA[1-4, 6, 15-17], however, up to now, few studies could explain which hemisphere is responsible for language repair confirmly[5, 7, 818], which ascribe to inadequate of direct clinical evidence. The cerebral spinal tract (CST), as the largest descending motor tract, pass through the cerebral peduncle downward to brain stem and spine. Injury of CST would lead to an atrophic change of cerebral peduncle, which caused asymmetry of cerebral peduncle[19, 20]. So, ARCP has been used to evaluate and predict motor function for single hemispherical diseases. However, Some studies found that patients with PSA recovered combined with limb rehabilitation training after brain stroke[21, 22]. Hertrich *et al.* [23]And Turkeltaub *et al.* [24]indicated that supplementary motor areas and cerebellum participate in language proceeding. Ivanova *et al.* [25]And Sollmann *et al.*[26]had used tractography to access the correlation between language function and CST, and noted that major white matter tracts implicated in language processing in each hemisphere. To our knowledge, this is the first study to analyze the correlation between ARCP and language function for patients with PSA.

Previous studies have demonstrated that PSA recovery was a dynamic and complex process, which involved both hemispheres[10, 18]. Studies about language and comprehension training after PSA showed that both hemispheres were involved in the process of the therapy[27, 28]. Similar to our study, patients obtained a different recovery of PSA after the first time of stroke, the mechanism of recovery was the synergistic effect between dominant hemisphere and non-dominant hemisphere (figure 5). Before the recurrent stroke, some extent of language function compensated or reorganized in the non-dominant hemisphere, the validated clinical evidence was the significant decline of AQ followed the recurrent stroke in CG. Several studies have shown that the value of ARCP could be used as a quantity index of severity of dominant hemisphere[20, 29].

With more Wallerian degeneration happened in the affected hemisphere, the cerebral peduncle became smaller, and which result in a higher ARCP value. In our study, patients with a higher ARCP showed a higher ΔAQ1 in both CG and IG, which means more language function was compensated or reorganized in the non-dominant hemisphere, vice versa. Patients with a higher ARCP showed a higher ΔAQ2 (Figure 2) in CG and a lower ΔAQ2 (Figure 3) in IG, which means more compensative language function was lost and more compensative language function survival, respectively. In the present study, we hypothesized that the potential capacity of language reparation of the non-dominant hemisphere was activated by the dominant hemisphere after the first stroke. For the six patients with severe hemispherical stroke in the dominant hemisphere, reduced the activation signal that transmit to the non-dominant hemisphere, result in a decompensation of PSA of the non-dominant hemisphere, and finally, caused a deterioration of language function. Similar studies [30, 31]shown that the non-dominant hemisphere was difficult to compensate PSA completely.

The recovery of aphasia after stroke will be better if it is mainly compensated by the dominant hemisphere. If a severe stroke or permanent injury happened in the dominant hemisphere extensively, less or no activation and feedback signal would be produced between the two hemispheres, which left an unfavourite recovery of PSA and mainly benefit from the non-dominant hemisphere, moreover, the debilitated speech function would be destroyed thoroughly followed a recurrent stroke in the non-dominant hemisphere (figure 6b-d). Various recent studies have shown that Initial aphasia severity and lesion size could be used to predict the outcome of PSA[32], which was similar to our study. According to our hypotheses, mild or reversible stroke in the dominant hemisphere would transmit less activation signal to the non-dominant hemisphere and received less feedback signal from the non-dominant hemisphere, the reparation of the abnormal language network mainly independently in the dominant hemisphere. Meanwhile, the mild or reversible injury would not contribute to an obvious morphological change of cerebral peduncle, left a lower ARCP. In this study, patients with lower ARCP showed higher AQ_{postRS} and lower ΔAQ2 in CG, which means without significant loss of language function followed the recurrent stroke in the non-dominant hemisphere, the main language function pre-exist in the dominant hemisphere for those subjects.

An obvious atrophic change of the cerebral peduncle is associated with significant damage in the ipsilateral hemisphere[33], which leads to a higher ARCP. ARCP more than 1.5 was considered a significant index correlated with motor function[20, 29, 34]. For the present study, in the CG, patients with an ARCP more than 1.5 present a significant higher ΔAQ2 than patients with ARCP less than 1.5 (figure 5), and in the IG there were six patients with ARCP of more than 1.5, all the six patients have not shown significant change after recurrent stroke, which means most language function in the non-dominant hemisphere of the patients with ARCP of more than 1.5. However, patients with acute severe hemispherical stroke result in a worse outcome than patients with chronic hemispherical diseases[35], which due to the weakened synergistic effect after the sudden attack in dominant hemisphere (figure 6b-d).The early recovery mechanism of PSA may different from those involved in long-term recovery[36].

There were several limitations in our study as follows: as a retrospective study we only can use the clinical data passively, and the small sample made it's impossible to consider more affected factors statistically, such as lesion location, duration, age and adjuvant treatment procedures. However, in our small sample study, the factors: age, gender did not showed a significant correlation with ΔAQ1, the result consistent with Watila[37]. In this study we employed strict inclusion criteria, such as: stroke in basal ganglia or/and thalamus, patients without communication disorder and recognition disorder before the first time stroke, besides, patients with a history of an epileptic seizure, bilingual and illiterate patients were excluded in this study. Nevertheless, the value of non-dominant hemisphere in the recovery of PSA was confirmed by direct clinical evidence, and the correlation between ARCP and AQ. Cognitive impairment after stroke maybe a noteworthy that could retard recovery of PSA[38, 39], it was not analyzed in this study. To make the findings more valid, a prospective study with a large sample and multimode evaluation methods should be conducted in the near future[40, 41].

Conclusion

Above all, our study showed that in the process of recovery of PSA, the non-dominant hemisphere played a very important role in reparation of incomplete language network, and we can also confirm that more compensative language function in the non-dominant hemisphere for patients with a higher ARCP, especially when the patients with an ARCP more than 1.5. The synergistic effect between the two hemispheres is the key mechanism of PSA recovery.

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