1H-MRS study in investigating the effect of dioscorea modified pill to the cognitive impairment of patients with VCIND

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Introduction: Vascular Cognitive Impairment No Dementia (VCIND) is introduced to identify the earliest stage of cognitive decline associated with vascular disease, which does not meet dementia criteria but with an increased risk of death and institutionalization[1]. Early detection of VCIND has significant clinical implications for a valid prognosis and treatement[2]. Proton magnetic resonance spectroscopy (^{1}H-MRS) has been proved useful in investigating neurodegenerative diseases[3]. In this study, the therapeutic effect of Dioscorea modified pill and Aricept to VCIND patients was evaluated using brain ^{1}H-MRS, mini-mental state examination (MMSE), clinical dementia rating (CDR) and Montreal Cognitive Assessment (MoCA) simultaneously and the relationship of these measurements was investigated as well.

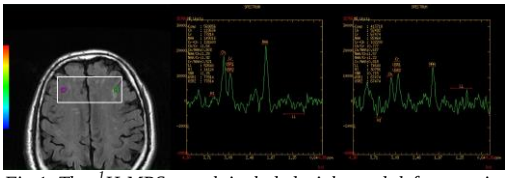

Fig.1 The ^{1}H-MRS voxel included right and left posterior middle frontal gyrus.

Methods: 100 VCIND patients were randomly assigned to the Dioscorea modified pill group (group I, n=50) and the Aricept western medicine group (group Ⅱ, n=50), and 50 healthy volunteers were recruited as the control group. Age, gender and education level were matched for the three groups. Each patient was examined with ^{1}H-MRS and scored with MMSE, CDR and MoCA before and after the treatment. The changes in ratio of middle frontal gyrus(MFG), angular gyrus(AG), posterior cingulate gyrus(PCG), hippocampus(HC) and thalamus(Thala) were detected and the scores of MMSE, CDR and MoCA were recorded. All MR acquisitions was performed on a 3.0T MR scanner (GE Signa HDxt, USA) using an 8-channel head coil. Participants were asked to lie quietly during the scan. The acquisition parameters of ^{1}H-MRS were, TR/TE/NEX=1000ms/144m/1, matrix =18 × 18; FOV = 200mm × 200 mm.

Results: 1. The cognitive assessment scale scores of the MMSE, CDR and MoCA in the VCIND group (Dioscorea modified pill and Aricept) compared with the healthy control group had statistical significance, as shown in Tab. 1.

2. The NAA/Cr ratios in bilateral MFG, AG, PCG, HC and Thala in the VCIND group were lower than those of the control group before therapy, however, no significant differences was observed in the Cho/Cr ratios in the same areas, Tab. 2.

3. After therapy for 16 weeks, the scores of the items of cognitive scale in the Dioscorea modified pill group compared with pre-therapy were significantly different, and still significantly different with that of the control group. The NAA/Cr ratios of the MFG, AG, PCG, HC and Thala in the Dioscorea modified pill group increased, with no statistical significance compared with the control group, Tab. 3. Similarly for the Aricept western medicine group, no apparent change happened, significantly different with the control group. The NAA/Cr ratios of the HC and Thala increased, not statistically significant with the control group. And the NAA/Cr ratios of the MFG, AG and PCG had no obvious increasing, still lower than that of the control group. But the Dioscorea modified pill group had significantly difference with the Aricept western medicine group. Before and after therapy, the scores of CDR had no relationship with MMSE and MoCA, but the latter two scales had apparent positive relationship. The ratios of NAA/Cr in the bilateral MFG, AG, PCG, HC and Thala of the pre- and post- treatment in the three groups had positive relationship with the scores of MMSE and MoCA.

Table 1 Clinical and demographic variables (±s)

Variables	Age(years)	Education (years)	Pretherapy MMSE(score)	Pre-therapy CDR(score)	Pretherapy MoCA(score)	Post-therapy MMSE(score)	Post-therapy CDR(score)	Post-therapy MoCA(score)
Control	61.86±9.10	11.18±3.62	27.64±1.59	0	25.82±1.96	27.64±1.59	0	25.82±1.96
VCIND	63.20±8.24	10.48±3.39	25.17±2.22$^{\triangle}$	0.5$^{\triangle}$	23.19±2.32$^{\triangle}$	—	—	—
Ⅰ	62.76±7.72	10.44±3.08	25.12±2.31$^{\triangle}$	0.5$^{\triangle}$	23.02±2.00$^{\triangle}$	26.48±1.97$^{\triangle\circ\bigstar}$	0.14±0.23$^{\triangle\circ\bigstar}$	24.56±2.17$^{\triangle\circ\bigstar}$
Ⅱ	63.64±8.78	10.52±3.70	25.22±2.15$^{\triangle}$	0.5$^{\triangle}$	23.36±2.61$^{\triangle}$	24.92±2.38$^{\triangle}$	0.47±0.12$^{\triangle}$	23.14±2.44$^{\triangle}$
F	0.43	0.56	18.22	0	18.32	23.14	132.72	18.62

VCIND include group I and Ⅱ. group I= Dioscorea modified pill group. group Ⅱ= Aricept western medicine group. Compared with Normal controls, $^{\triangle}P<0.05$. Compared with Pretherapy, $^{\circ}P<0.05$. Compared with group Ⅱ, $^{\bigstar}P<0.05$. MMSE= Mini-Mental State Examination. CDR=clinical dementia rating. MoCA=Montreal Cognitive Assessment.

Table 2 ^{1}H-MRS metabolite ratios at baseline before treatment (±s)

Variables	MFG		AG		PCG		HC		Thala	
	NAA/Cr	Cho/Cr	NAA/Cr	Cho/Cr	NAA/Cr	Cho/Cr	NAA/Cr	Cho/Cr	NAA/Cr	Cho/Cr
Control	1.65±0.36	0.94±0.28	1.55±0.26	0.87±0.17	1.65±0.40	0.96±0.21	1.72±0.20	1.09±0.18	1.71±0.20	1.09±0.21
Ⅰ	1.53±0.23$^{\blacktriangle}$	0.93±0.20	1.40±0.22$^{\blacktriangle}$	0.86±0.15	1.53±0.29$^{\blacktriangle}$	0.92±0.18	1.59±0.20$^{\blacktriangle}$	1.07±0.19	1.57±0.23$^{\blacktriangle}$	1.11±0.21
Ⅱ	1.53±0.25$^{\blacktriangle}$	0.92±0.20	1.42±0.23$^{\blacktriangle}$	0.86±0.15	1.52±0.26$^{\blacktriangle}$	0.95±0.18	1.59±0.23$^{\blacktriangle}$	1.08±0.19	1.59±0.19$^{\blacktriangle}$	1.09±0.18
F	6.08	0.33	11.34	0.39	5.22	1.14	13.52	0.47	11.38	0.32

MFG=middle frontal gyrus, AG=angular gyrus, PCG=posterior cingulate gyrus, HC=hippocampus, Thala=thalamus. Compared with Normal controls, $^{\blacktriangle}P<0.05$.

Table 3 NAA/Cr ratios after treatment(±s)

NAA/Cr	MFG	AG	PCG	HC	Thala
Controls	1.65±0.36	1.55±0.26	1.65±0.40	1.72±0.20	1.71±0.20
Ⅰ	1.62±0.19	1.53±0.21	1.63±0.21	1.68±0.20	1.68±0.19
Ⅱ	1.57±0.17$^{\blacklozenge}$	1.44±0.18$^{\blacklozenge}$	1.53±0.22$^{\blacklozenge}$	1.68±0.20	1.69±0.19
F	2.68	7.82	5.33	1.42	0.6

Compared with Normal controls, $^{\blacklozenge}P<0.05$.

Discussion & Conclusion: (1) The impaired and lost neurons could be discovered in bilateral MFG, AG, PCG, HC and Thala in the VCIND patients, but without apparent cellular membrane splitting and glial cellular proliferation. (2) The Dioscorea modified pill could repair the damaged neurons in bilateral MFG, AG, PCG, HC and Thala and improve the cognitive dysfunction. But the Aricept could only repair the neurons in HC and Thala while the NAA/Cr without apparent change in bilateral MFG, AG and PCG. It might imply that both the Dioscorea modified pill and Aricept could improve the neurons functional activities and maintain their integrity and improve the neuron function recovery. While the Dioscorea modified pill seems to effect in larger areas. (3) The Dioscorea modified pill could improve the cognitive dysfunction obviously in VCIND patients, but the Aricept showed no obvious improvement. Thus, it might imply that the therapeutic effect of the Dioscorea modified pill surpassed the sole Aricept in treating VCIND patients. (4) The scores of CDR were not perfect enough. But both MMSE and MoCA had satisfactory evaluating effect on the cognitive function while the scores of MoCA was more stable than that of MMSE. (5) The NAA/Cr ratios had good correlationship with the scores of MMSE and MoCA in each of the three subjects groups. Therefore, the stability and exactitude of the ^{1}H-MRS was rather high and it could detect the change of the NAA/Cr in the brain of the VCIND patients. It might imply that 1H-MRS had the potentiality of diagnosing VCIND and quantifying its therapeutic effect.

References: 1. Zhou A, et al. Int J Geriatr Psychiatry 2008, 23: 422-426. 2. Zhou A, Jia J. Int J Geriatr Psychiatry 2009, 24: 1252-1357. 3.Erichsen AK, et al. J Neurol Sci 2009, 277: 124-129.