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The Brain Metabolites Within Cerebellum of Native Chinese Speakers Who Are Using the Traditional Logographic Reading and Writing Systems – A Magnetic Resonance Spectroscopy Approach to Dyslexia*

Ying-Fang Sun[1], Ralph Kirby[2] and Chun-Wei Li[3]
[1]Department of Biomedical Imaging and Radiological Sciences, National Yang-Ming University No.155, Sec 2, Linong Street, Taipei,
[2]Department of Life Sciences and Institute of Genome Sciences, National Yang-Ming University No.155, Sec 2, Linong Street, Taipei,
[3]Chairman, Department of Medical Imaging and Radiological Sciences, Kaohsiung Medical University No.100, Shih-Chuan 1st Road, Kaohsiung, Taiwan, R.O.C.

1. Introduction

Dyslexia is a term for persons who are suffering from difficulties in learning to read, write and spell, but who have a normal or even higher intelligence quotient (Hsiung, Kaplan, Petryshen, Lu, & Field, 2004). In addition to linguistic difficulties, deficits in non-linguistic domains, such as automatization, time estimation (Nicolson RI, Fawcett AJ, & Dean, P., 1996), and motor skills (Wilsher, et al., 1987) are also documented. However, not a single hypothesis is able to yet account for all the behavioural symptoms of dyslexia (Pernet, Andersson, Paulesu, & Demonet, 2009). The definition used for dyslexia depends on the research teams and varies significantly (Gersons-Wolfensberger & Ruijssenaars, 1997; Habib, 2000; Lyon, Shaywitz, & Shaywitz, 2003 ; Tunmer & Greaney, 2010). The estimates of prevalence for dyslexia in the West have ranged from 5% (Deffenbacher, et al., 2004) to 15% (Stoodley, Fawcett, Nicolson, & Stein, 2006). In addition, the gifted talents associated with dyslexia are usually neglected (Chakravarty, 2009; Everatt, Weeks, & Brooks, 2008; Levy, 1983; von Karolyi, Winner, Gray, & Sherman, 2003). Although linguistic interventions (Breteler, Arns, Peters, Giepmans, & Verhoeven, 2010; Penolazzi, Spironelli, Vio, & Angrilli, 2010) and pharmaceutical drugs (Wilsher, et al., 1987; Zavadenko, Rumiantseva, & Tolstova, 2009) might assist the reading and spelling performance of the dyslexics, some of the disadvantages are persistent, such as the difficulties in reciting multiplication tables (Miles, 1993). Gregorenko claimed that dyslexia is one of the most important public health problems (Grigorenko, et al., 2003) and despite intensive studies for more than a hundred

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years in the Western world, the exact mechanism(s) causing these difficulties is still not yet clear. The World Health Organization (WHO) recognizes dyslexia as a disease and it has ICD-10 code for R48.0, (WHO, July 2011). Many researchers believed that dyslexia has a universal biological basis (Demonet, Taylor, & Chaix, 2004; Schulte-Korne, et al., 2007; Ziegler, Perry, Ma-Wyatt, Ladner, & Schulte-Korne, 2003). In addition to behavioural (Eden, Wood, & Stein, 2003) and cognitive information on dyslexia, post-mortem studies by Galaburda et al. have shown that the dyslexics have unusual brains (Galaburda & Cestnick, 2003). Twin studies have also indicated that genes are very likely to be involved (Olson, 2002). However, the genetic transmission mode is not known. The advent of brain imaging tools permits us to undertake exploration of the brain's structure and function *in vivo*. However, due to the various subtypes of the subjects (Ho, Chan, Chung, Lee, & Tsang, 2007; King, Giess, & Lombardino, 2007; Spinelli, et al., 2010; Tree, 2008) and the different parameters applied in the various studies carried out, no consensus has been reached as yet (Sun, Lee, & Kirby, 2010). *In silico* cloning for gene prediction is still challenging and only ten candidate genes are found up to the present (Sun, Lee, & Kirby, 2009).

There are no standard tests for adult dyslexia (Brachacki, Nicolson, & Fawcett, 1995), not even a formal medical diagnosis (Demonet, et al., 2004). This is particularly true for dyslexics with Chinese ethnicity, specifically the members of communities that use the traditional Chinese logographic reading and writing systems. Therefore, an objective means that assists with diagnosis is needed. Reading performance is related to balance and involves of cerebellum (Lonnemanna, Linkersdörfera, Heselhausa, Hasselhorn & Lindberg S., 2011). Recently, the right cerebellar hemisphere has become a target for study (Pernet, Poline, Demonet, & Rousselet, 2009) and has been pinpointed as a possible biomarker for dyslexics. We have followed this trend and concentrated our efforts on the relationship between dyslexia and cerebellum (Stoodley & Stein, 2011).

2. The MRS studies on dyslexia using Caucasian subjects

The application of magnetic resonance spectroscopy (MRS) on the live human brain chemistry studies has involved Caucasians as research subjects for the most part. Specifically, the available articles on dyslexia include only volunteers that are Westerners, see Table 1. The brain metabolites in these studies could be further grouped into three categories. Firstly, ^{31}P-MRS technology that is used to assess brain metabolite ratios, namely, phosphomonoester, phosphodiester and ßNTP, which are changed in the basal ganglia of the dyslexics compared to the controls (Richardson, Cox, Sargentoni & Puri, 1997). Another study (Rae, et al., 1998) also used ^{31}P-MRS, but did not find any significant differences in the frontal lobe region. Secondly, the study used proton-MRS to detect the lactate during phonologic linguistic tasks that require extra mental efforts, which were compared to lactate levels during the passive listening. Higher levels of lactate were detected during the formal task in right handed male dyslexics but such an increase was not found with the controls (Richards, et al., 1999). Intensive linguistic training for the dyslexics was found to reduce the elevation of the lactate peak (Richards, et al., 2000) in the left anterior quadrant. This was further confirmed by using right handed female subjects and it is the morphological component (Richards, et al., 2002) of the treatments that causes the therapeutic effects, but not the phonological one. Lastly, the measurements of N-acetylaspartate (NAA), choline (Cho) and creatine (Cr) ratio in the cerebellar hemispheres have been examined (Rae, et al., 1998) and the findings suggest that there is a lowered Cho/NAA ratio in the right cerebellum and left temporo-parietal lobe of the dyslexic males.

Authors/ Reference	**Metabolites/ Brain regions**	**Parameters for MRS**	**Subjects**	**Findings**
Richardson et al. NMR in Biomedicine 1997	PME/ ßNTP PME/PDE PDE/ ßNTP **Basal ganglia**	1.5 T, ^{31}P-MRS, 4D CSI TR=5000ms T_1-weighted multi-slice transverse images	**Caucasians** 12 dyslexics (7 male, 5 females) 34.1±9.5 yr 10 controls (5 male, 5 females) 28.3± 7.2 yr No current or previous reading difficulties	The PME peak area was significantly elevated in the dyslexic group, this reflects the reduced incorporation of phospholipids into cell membranes
Rae et al. Lancet 1998	Cho, NAA, Cr **Temporo-parietal Cerebellum** ***Frontal lobe***	^{1}H-MRS T_1-weighted, multi-slice images 5 mm thickness axial view 3x3x3 cm single voxel Birdcage coil STEAM ***^{31}P-MRS***	**Caucasians** 20-41yr male 14 dyslexics 15 controls Discrepancy between reading and spelling achievement	Altered patterns of cell density in the cerebellum of the dyslexic individuals ***No significance was found***
Richards et al. J Neuroradiol. 1999	Lactate **Left anterior quadrant**	1.5T GE ^{1}H- MRS, PEPSI 1 cm^3 voxel 20mm thickness TR=4000ms TE=272ms	**Caucasians** Right handed, age, IQ, head size matched boy 6 dyslexics (124.3±1 1.1 month), 7 controls (127.3 ±10.8 months) Discrepancy in reading skills	The dyslexics have a greater area of lactate elevation in the left anterior quadrant than that of the controls during a phonological task stimulus
Richards et al. J Neuroradiol. 2000	Lactate **Left anterior quadrant**	^{1}H-MRS, PEPSI 1 cm^3 voxel TR=4000ms TE=272ms	**Caucasians** 10-13 yr right handed boy Head size (number of total voxels) matched 8 dyslexics, 7 controls	Reduced elevation of lactate level after reading/science workshop treatment in the left anterior quadrant of the dyslexics
Richards et al. Am J Neuroradiol. 2002	Lactate **Left anterior quadrant**	1.5T GE ^{1}H-MRS, PEPSI 1 cm^3 voxel TR=4000ms TE=144ms	**Caucasians** 9-12 yr 10 dyslexics (6 boys, 4 girls) 8 controls (6 boys, 2 girls)	The morphological component of language treatment reduces activation of lactate in the left frontal region in dyslexics
Rae et al. Neuropsychologia 2002	Cho, NAA, Cr **Cerebellum**	85.2MHz, Bruker ^{1}H-MRS T_1-weighted coronal images TR=803ms TE=13ms	**Caucasians** 20-41yr Handedness controlled 11 male dyslexics 9 similarly-aged controls	There are alterations in the neurological organization of the cerebellum in dyslexics
Laycock et al. Ann.N.Y. Acad.Sci.2008	Cho, NAA, Cr **Cerebellum**	3T Philip Intera ^{1}H-MRS, PRESS 1.5x1.5x1.5 cm single voxel TR=1600ms TE=144ms	**Caucasians** 20-21yrs right handed Male 6 dyslexics 6 controls	A smaller NAA/Cho ratio in right cerebellum, higher Cho/Cr in left cerebellum of the dyslexics Indicative of excessive connectivity and abnormal mylination

Table 1. The Application of Magnetic Resonance Spectroscopy (MRS) to the Study of Dyslexia

By using male subjects with handedness information and proton-MRS, the same team indicated the brain metabolites do not differ between the left and right cerebellar hemispheres of the control subjects (Rae, et al., 2002). In contrast, it is the Cho/NAA ratio in the right cerebellar hemisphere of the dyslexics that differs significantly to the controls (Rae, et al., 1998). However, in 2008, another study (Laycock, et al., 2008) found a lower NAA/Cho in the right cerebellar hemisphere and a higher Cho/Cr in the left cerebellar hemisphere of the dyslexics compared to the controls. This conflicts with the previous results (Rae, et al., 1998). The discrepancy probably comes from the differences of the voxel size, the parameters used for conducting proton-MRS and the age of the subjects, see Table 2.

Author	Brain Metabolite Ratio within Right Cerebellar Hemisphere							
Rae et al. 1998	Control N=15, 20-41 yrs, male			Dyslexic N=14, 20-41 yrs, male			Single voxel volume	Pulse sequence
	Cr/NAA	**Cho/Cr**	**Cho/NAA**	**Cr/NAA**	**Cho/Cr**	**Cho/NAA**		
	0.65±0.16	0.80±0.27	0.52±0.18	0.53±0.15	0.74±0.29	0.37±0.10	27 cm^3	STEAM
Laycock et al. 2008	Control N=6, 20-21 yrs, male			Dyslexic N=6, 20-21yrs, male			Single voxel volume	Pulse sequence
	NAA/Cr	**Cho/Cr**	**NAA/Cho**	**NAA/Cr**	**Cho/Cr**	**NAA/Cho**		
	2.01±0.33	0.9±0.18	2.30±0.50	1.94±0.25	1.10±0.20	1.78±0.12	3.75 cm^3	PRESS

Table 2. The Comparison of Brain Metabolite Ratio within Right Cerebellar Hemisphere of Two Studies Using Caucasian Subjects

3. Aims of the study

An appropriate diagnosis for dyslexic adults is lacking and has been involved to the present using behavioural or cognitive symptoms (Fawcett, 2007). We attempted to identify a more objective means for assisting dyslexic diagnosis and our aim was to test the hypothesis if the NAA/Cho ratio in the right cerebellar hemisphere of the dyslexics is lesser than that of the counterpart. It seems the right cerebellar hemisphere is the target of the dyslexic research because Pernet's group claimed that *"the best biomarker of dyslexia is the right cerebellum"* (Pernet, et al., 2009). Therefore, in this study we recruited Chinese who use the traditional Chinese logographic reading and writing systems and carried out a proton-MRS study. Specifically, we measured the NAA/Cho ratio in the cerebellum and make a comparison of the results with those obtained by other groups using Caucasians. The Institutional Review Board of National Yang-Ming University approved the study (No. 980046).

4. Materials and methods

We used a Trio Tim 3T MRI scanner from German Siemens with 12 channel head coils and Syngo MR B15 software. Water suppression was achieved with a chemically selective saturation (CHESS) pulse. A point-resolved spectroscopy sequence (PRESS) was performed for single voxel data acquisition. The parameters were similar to the ones used in Laycock's experiments, namely, TR= 2000ms, TE=135ms, single voxel size= 15X15X15mm, each voxel takes 4min 24 sec for acquisition (Laycock, et al., 2008). The placement of a single voxel

within the right and left cerebellar hemispheres was achieved by using the T_1 and T_2-weighted structural images in a coronal view as described by Laycock et al.

Participants were 37 native Chinese volunteers who had given written informed consent. The including criteria for controls were healthy subjects, who enjoy reading and writing. They do not have reading or writing problems and have no history of learning disability, claustrophobia, surgical implants, pregnancy, pacemakers, psychiatric disease, neurological disease or any known medical conditions that affected brain morphology and metabolism. These controls consist of 8 right handed males aged 19-89 yrs (49.1± 22.8) and 9 right handed females aged 14-59 yrs (40.3±16.2). The potential dyslexics who joined the MRS study were self-reported from a questionnaire survey (Sun, Ting-Hsiang Lin, & Liao, 2010) conducted in July-December of year 2009.

5. Our findings and discussions

5.1 The single voxel study

5.1.1 The NAA/Cr, Cho/Cr and NAA/Cho within the cerebellar hemispheres of 37 Chinese who are using the traditional Chinese logographic reading and writing systems

Across the 19 males, the NAA/Cr ranged from 0.76-1.23 (mean ± SD 1.03±0.13) and 0.73-1.81 (1.06 ±0.26) within the right and left cerebellar hemispheres, respectively. The Cho/Cr ranged from 0.73-1.05 (0.86 ± 0.09) and 0.65-1.11 (0.91± 0.12) within the right and left cerebellar hemispheres, respectively. The NAA/Cho ranged from 0.96-1.47 (1.21 ± 0.16) and 0.81-1.69 (1.16 ± 0.22) within the right and left cerebellar hemispheres respectively.

Across the 18 females, the NAA/Cr ranged from 0.7-1.65 (mean ± SD 1.10 ± 0.21) and 0.92-1.92 (1.16 ± 0.27) within the right and left cerebellar hemispheres, respectively. The Cho/Cr ranged from 0.56-1.13 (0.91 ± 1.13) and 0.59-1.50 (0.89 ± 0.19) within the right and left cerebellar hemispheres, respectively. The NAA/Cho ranged from 0.91-1.66 (1.22 ± 0.20) and 1.08-1.89 (1.31 ± 0.23) within the right and left cerebellar hemispheres, respectively.

5.1.2 A trend toward biochemical symmetry of the cerebellar hemispheres in 37 Chinese who are using the traditional Chinese logographic reading and writing systems

The differences of the NAA/Cho between the right and left cerebellar hemispheres were determined as follows: if the NAA/Cho in the right hemisphere is greater than that of the left hemisphere, then a "+" was designated, otherwise a "-" was given; if the difference is equal to or lesser than 0.09, a "0" was assigned arbitrarily.

Across the19 males, there are 10 participants whose NAA/Cho ratio within the right cerebellar hemisphere were greater than that of the left hemisphere (designated as "+", 52.6%), 4 were about equal (designated as "0", 21.1%) and 5 had a lesser value than that of the left hemisphere (designated as "-" 26.3%). Conversely, across the 18 female subjects, there are 10 participants whose NAA/Cho ratio in the right cerebellar hemisphere were lesser than that of the left hemisphere (designated as "-", 56%), 4 were about equal (designated as "0", 22.2%) and 4 had a greater value than that of the left hemisphere (designated as "+", 22.2%).

Apparently, the NAA/Cho in the right cerebellar hemisphere of males tends to be greater than that of the left hemisphere, but this trend is absent from the female subjects that we scanned. The lateralization of NAA/Cho within the cerebellar hemispheres seems to be opposite for our Chinese male and female subjects and the percentage of biochemical symmetry is similar, namely, 21.1% and 22.2% for male and female respectively. The NAA/Cho between the right and left cerebellar hemispheres across the male control group follows the similar trend, namely, there is 1 out of 8 being symmetric (12.5%) and 7 out of 8 being rightward (87.5%). Across the female control group, there are 2 out of 9 being symmetric (22.2%), 2 out of 9 being rightward (22.2%) and 5 out of 9 being leftward (55.5%).

We further compared the ratios of NAA/Cr, Cho/Cr and NAA/Cho between the right and left cerebellar hemispheres in the control groups and designed them as NAA/Cr R/L, Cho/Cr R/L and NAA/Cr R/L respectively in Table 3. Across the 8 right handed male controls (19-89yrs), the mean of NAA/Cr R/L ratio is 1.13±0.23, with 1 out of 8 being greater than 1.5 (12.5%), 1 out 8 being lesser than 1 (12.5%), and the rest of them being slightly more than 1 (75%); the mean of Cho/Cr R/L ratio is 0.91±0.12, with 1 out of 8 being equal to 1 (12.5%), 2 out of 8 being greater than 1 (25%), and 5 out of 8 being lesser than 1 (62.5%); the mean of NAA/Cho R/L ratio is 1.25±0.21, with 1 out of 8 being greater than 1.5 (12.5%); 1 out of 8 being lesser than 1 (12.5%) and the rest of them being slightly more than 1 (75%). See Table 3.

Across the 9 right handed female controls (14-59yrs), the mean of NAA/Cr R/L ratio is 0.90±0.19, with 1 out of 9 being equal to 1 (11.1%) , 2 out of 9 being greater than 1 (22.2%) and 6 out of 9 being lesser than 1 (66.6%); the mean of Cho/Cr R/L ratio is 0.96±0.24, with 6 out of 9 being greater than 1 (66.6%), and 3 out of 9 being lesser than 1 (33.3%) ; the mean of NAA/Cho R/L ratio is 0.97± 0.26, with 4 out of 9 being greater than 1 (44.4%) and 5 out of 9 being lesser than 1 (55.5%). See Table 3.

Thus, generally speaking, the NAA/Cho R/L ratios for male controls tend to be greater than 1, while in contrast, the NAA/Cho R/L ratios for our Chinese female controls, show a trend of being lesser than 1. See Table 3.

Male ID	Age	NAA/Cr R/L	Cho /Cr R/L	NAA/Cho R/L	Female ID	Age	NAA/Cr R/L	Cho/Cr R/L	NAA/Cho R/L
1	19	1.15	0.96	1.20	1	14	0.53	0.49	1.08
2	23	1.19	1.01	1.18	2	23	0.88	1.01	0.88
3	43	1.62	1	1.63	3	25	0.91	1.14	0.80
4	45	1.02	0.77	1.32	4	39	1	1.21	0.83
5	52	1.15	1.07	1.08	5	43	0.90	1.21	0.75
6	53	1.05	0.81	1.30	6	51	1.17	0.77	1.52
7	69	0.81	0.86	0.95	7	53	0.75	1.04	0.73
8	89	1.09	0.79	1.38	8	56	1.09	1.03	1.06
-	-	-	-	-	9	59	0.86	0.75	1.14
Mean ±SD	49.1 ±22.8	1.13 ±0.23	0.91 ±0.11	1.25 ±0.21	Mean ±SD	40.3 ±16.2	0.90 ±0.19	0.96 ±0.24	0.97 ±0.26

Table 3. The Metabolite Lateralization in the Cerebellum of Chinese Male and Female Controls Who Are Using the Traditional Chinese Logographic Reading and Writing Systems

By using 28 right handed 20-30 yr old normal male subjects from India, Jayasundar found that there was laterization of various brain metabolites (NAA, Cr and Cho) between the interhemisphere of cerebellar regions with the following parameters: STEAM pulse, TR=6000ms, TE=135 ms, with an 8ml single voxel and a 1.5 T Siemens Helicon scanner (Jayasundar, 2002). Our results seem to agree with these earlier findings.

5.1.3 A comparison of the NAA/Cr, Cho/Cr and NAA/Cho within the cerebellar hemispheres of the controls and the potential dyslexics who are using the traditional Chinese logographic reading and writing systems

Across the 8 right handed male controls, the NAA/Cr ratio within the right and left cerebellum ranged from 0.85-1.23 and 0.76-1.18, respectively. The Cho/Cr ratio within the right and left cerebellar hemisphere ranged from 0.73-0.90 and 0.72-1.03, respectively. The NAA/Cho within the right and left cerebellar hemisphere ranged from 1.12-1.47 and 0.81-1.39, respectively. Across the 9 right handed female controls, the NAA/Cr within right and left cerebellar hemisphere ranged from 0.7-1.65 and 0.93-1.92, respectively. The Cho/Cr within right and left cerebellar hemisphere ranged from 0.56-1.13 and 0.72-1.5, respectively. The NAA/Cho within right and left cerebellar hemisphere ranged from 0.98-1.66 and 1.09-1.89, respectively.

Our results indicated that the potential dyslexics have lesser NAA/Cho within right cerebellum than the mean of 17 controls (1.29±0.19). This agrees with the findings of Laycock (Laycock, et al., 2008). Nonetheless, our sample size is too small to reach any statistical power; yet, it seems fair to suggest that these measurements might be useful for diagnosis.

Safriel et al. found the NAA/Cr, Cho/Cr and NAA/Cho in the cerebellum to be 1.51±0.26, 1.51±0.14 and 1 respectively by using 1.5T, PRESS,TR=2000 ms, TE=135ms, and an 8ml voxel. There were 10 male and 10 female normal Caucasian subjects in the age range of 22-44 years without handedness control. No specific right or left hemisphere was recorded. They concluded that sex does not seem to be a confounding factor, the NAA/Cho ratio is equal to 1 (Safriel, Pol-Rodriguez, Novotny, Rothman, & Fulbright, 2005) and the brain metabolites were equally distributed across their subjects. Rae also indicated that the bran metabolites do not differ between the left and right cerebellar hemispheres of the control subjects (Rae, et al., 2002). For our 8 right handed Chinese male controls (19-89yrs), the NAA/Cho within right cerebellar hemisphere is significantly greater than that of the left hemisphere. However, this phenomenon was not found in our female subjects.

A study by Lei et al. found that the NAA/Cho in the cerebellum to be 1.306 of 27 Chinese subjects (23-49 yrs) who are using the simplified form of Chinese characters daily. They did not specify the sex, handedness and hemispheres (Lei, et al., 2011). The parameters for the experiments are following: svs-se-135 pulse sequence, single voxel size= 15X10X15mm, TR=1500ms, TE= 1500 ms via 1.5 T German Siemens scanner. This figure is similar to the mean of NAA/Cho in the right cerebellar hemisphere of our male control group.

5.2 The chemical shift imaging study (CSI)

The comparison of metabolites in the right and left cerebellar hemispheres could be achieved more precisely by mirroring the voxels simultaneously using the chemical shift

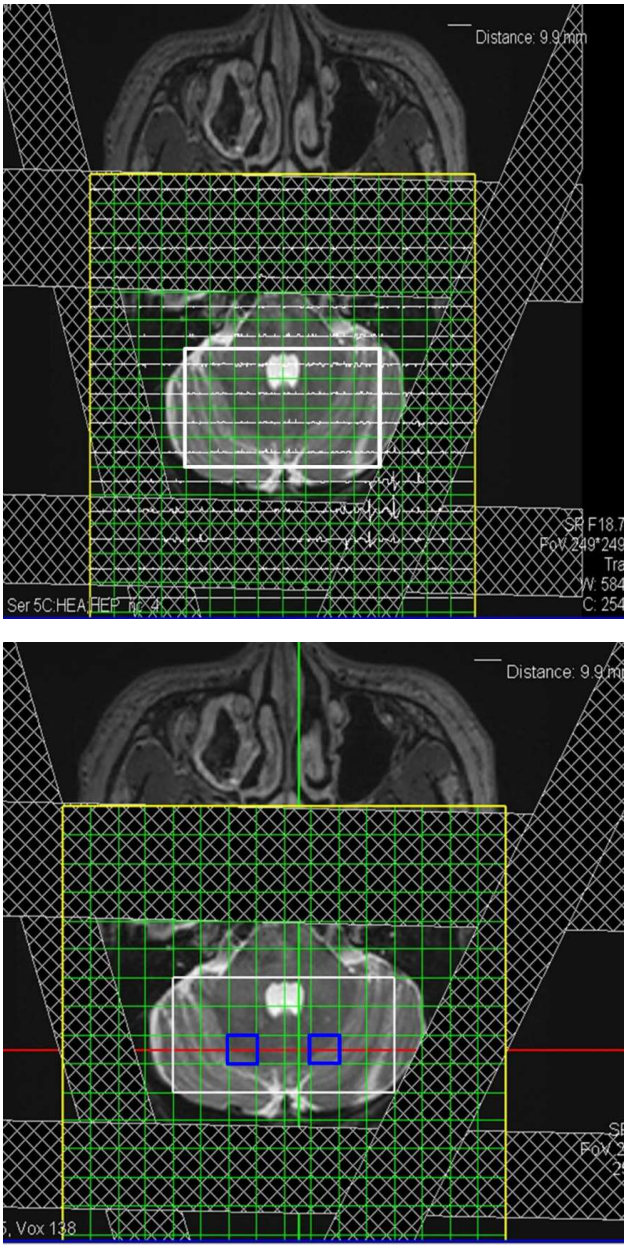

Fig. 1. Chemical shift images of the T_2-weighted axial view from a male control subject. Top: the white rectangle is the area for MRS acquiring and the yellow region with green grids shows the phase encoding steps. Four saturation bands could remove the unwanted signals from scalp and skull. Bottom: the CSI technique allows the mirror placement of a single voxel (blue square) at right and left cerebellar hemispheres simultaneously.

imaging technique with the following parameters: TR=2000ms, TE=135ms, FOV R L 160, VOL AP 160, thickness 15X15X15mm, FOV R L 60, VOL AP 40. The acquisition time is about 8 minutes. Table 4 demonstrates the NAA/Cr, Cho/Cr and NAA/Cho ratios within the right and left cerebellar hemispheres of two Chinese male controls that are using the traditional Chinese logographic reading and writing systems. Figure 1 and 2 indicated the spectra and the metabolite ratios in the specific voxels of a control subject via CSI technology.

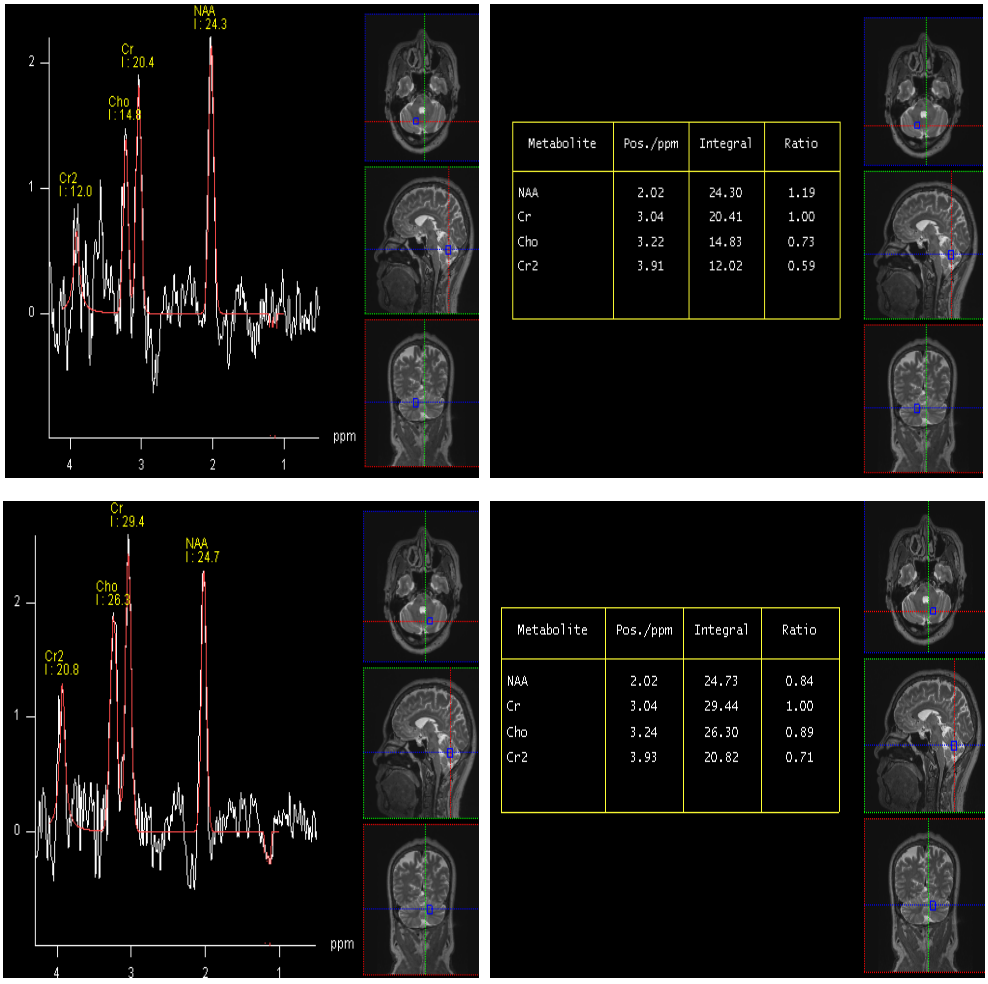

Fig. 2. The spectra and the NAA/Cr, Cho/Cr and NAA/Cho ratio of the right (up panel) and left (bottom panel) voxel in the cerebellar hemispheres corresponding to the bottom panel of Figure 1.

Male	Age	NAA/Cr		Cho/Cr		NAA/Cho	
		Right Hemi-sphere	Left Hemi-sphere	Right Hemi-sphere	Left Hemi-sphere	Right Hemi-sphere	Left Hemi-sphere
ID1	69	1.55	1.40	0.98	0.98	1.58	1.43
ID2	51	1.19	0.84	0.73	0.89	1.63	0.94

Table 4. The NAA/Cr, Cho/Cr and NAA/Cho Ratios within Cerebellum of Two Chinese Male Controls via Chemical Shift Imaging (CSI)

6. Present knowledge and future perspectives

Very few MRS studies using Chinese subjects for the measurement of brain metabolites, specifically, studies on those using traditional Chinese logographic reading and writing systems. We measured the ratios of NAA, Cr, and Cho metabolites within cerebellar cortex with handedness and sex information which offers valuable references for future studies. In addition, the chemical shift imaging technique used in a preliminary investigation here seems to be a good approach to assess the chemical lateralization of cerebellar hemispheres in future. More potential dyslexic subjects with detailed documentation in clinical features are needed for MRS experiments in order to make meaningful statistical inferences on the usefulness of this approach. Nonetheless, MRS measurement seems to be a promising approach that avoids the pitfalls of questionnaires and similar in dyslexic study.

The major limitation of the study is the difficulty in recruiting and identifying sufficient dyslexic probands, since there is no standard test for adult dyslexics. An objective reading test with an appropriate norm in traditional Chinese logographic characters might be used when screening for Chinese with dyslexia, in addition to self-reporting. A second limitation is that we were unable to examine the effect of age on the various parameters measured. To do this, it would require much larger cohorts in various age bands.

7. Summary

In this original article, we reviewed the application of magnetic resonance spectroscopy (MRS) to dyslexia. We used this non-invasive technique to measure the N-acetylaspartate (NAA) and Choline (Cho) ratio within the cerebellum of native Chinese volunteers. The aims of the experiment are, firstly, to compare the data with the results obtained from Western studies. These findings will act as a reference for longitudinal studies in future since most MRS studies have used Caucasian subjects. Secondly, we tested the hypothesis as to whether the NAA/Cho ratio within the right cerebellum is able to discriminate dyslexics from the non-dyslexics as suggested by the previous research in West. However, in contrast to the Western studies, we recruited native Chinese who use traditional Chinese characters (a logographic reading and writing linguistic system) in their daily life as subjects for our studies. Thus, this study is novel in this respect. Finally, we explored the use of the chemical

shift imaging for the acquisition of data since this should yield a more precise sampling of the left and right cerebellar hemisphere simultaneously than the use of a single voxel approach.

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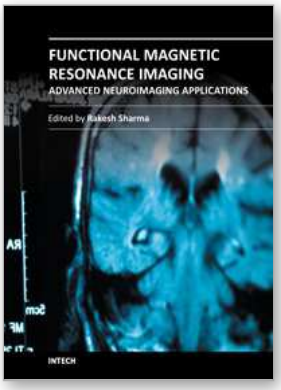

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"Functional Magnetic Resonance Imaging - Advanced Neuroimaging Applications" is a concise book on applied methods of fMRI used in assessment of cognitive functions in brain and neuropsychological evaluation using motor-sensory activities, language, orthographic disabilities in children. The book will serve the purpose of applied neuropsychological evaluation methods in neuropsychological research projects, as well as relatively experienced psychologists and neuroscientists. Chapters are arranged in the order of basic concepts of fMRI and physiological basis of fMRI after event-related stimulus in first two chapters followed by new concepts of fMRI applied in constraint-induced movement therapy; reliability analysis; refractory SMA epilepsy; consciousness states; rule-guided behavioral analysis; orthographic frequency neighbor analysis for phonological activation; and quantitative multimodal spectroscopic fMRI to evaluate different neuropsychological states.

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Phone: +86-21-62489820
Fax: +86-21-62489821