Metabolic changes in visual cortex of neonatal monocular enucleated rat: a proton magnetic resonance spectroscopy study

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Abstract

Neonatal monocular enucleation (ME) is often employed to study the developmental mechanisms underlying visual perception and the cross-modal changes in the central nervous system caused by early loss of the visual input. However, underlying biochemical or metabolic mechanisms that accompany the morphological, physiological and behavioral changes after ME are not fully understood. Male Sprague-Dawley rats (N = 14) were prepared and divided into 2 groups. The enucleated group (N = 8) underwent right ME (right eye removal) at postnatal day 10, while the normal group (N = 6) was intact and served as a control. Three weeks after ME, single voxel proton magnetic resonance spectroscopy (1H MRS) was performed over the visual cortex of each hemisphere in all animals with a point-resolved spectroscopy (PRESS) sequence at 7 T. The taurine (Tau) and N-acetylaspartate (NAA) levels were found to be significantly lower in the left visual cortex (contralateral to enucleated eye) for enucleated animals. Such metabolic changes measured in vivo likely reflected the cortical degeneration associated with the reduction of neurons, axon terminals and overall neuronal activity. This study also demonstrated that 1H MRS approach has the potential to characterize neonatal ME and other developmental neuropsychology models noninvasively for the biochemical and metabolic processes involved.

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1. Introduction

The neocortex has an enormous capacity to functionally adapt in response to external perturbations and compensate functional loss after injury (Feldman, 2009; Lewis and Gonzalez-Burgos, 2008). Morphological, functional, behavioral and biochemical changes following injuries have been used to understand the cellular and synaptic plasticity mechanisms that uphold adaptive behavior in brain (Bavelier and Neville, 2002; Rauschecker, 1995; Schroeder et al., 2003; Stein and Stanford, 2008). Neonatal monocular enucleation (ME) has been often utilized to study developmental mechanisms underlying visual perception and neuroplasticity of the brain because of the extensive changes and reorganization in various regions of the visual system following the complete loss of one eye (Toldi et al., 1996). Previous studies suggested that ME during early postnatal period initiates not only neurodegeneration in both dorsal lateral geniculate nucleus (DLGN) and superior colliculus (SC) in the enucleated side, but also a series of adaptive reactions in the visual and other sensory systems at a later stage (Karlen et al., 2006; Toldi et al., 1994; Yagi et al., 2001).

Upon neonatal ME, anatomical structures in projection targets of the visual system are largely affected (Toldi et al., 1996). Physiological changes including enlarged ipsilateral visual field and receptive field in the visual system were observed at 3 months after ME (Fukuda et al., 1983; Jeffery and Thompson, 1986). Plasticity resulted from recruitment of resources to the remaining left eye for adaptation and cross-modal effects were also observed at 3 months to 1 year after ME (Karlen et al., 2006; Toldi et al., 1994; Yagi et al., 2001). However, underlying biochemical or metabolic mechanisms that accompany the morphological, physiological and behavioral changes after ME are not fully understood (Steeves et al., 2008; Toldi et al., 1988, 1994; Yaka et al., 2000). Decreased local cerebral glucose utilization in both DLGN and SC was found in rats within hours to days after ME (Grunwald et al., 1993; Zilles et al., 0736-5748/$36.00 © 2010 ISDN. Published by Elsevier Ltd. All rights reserved.
Proton magnetic resonance spectroscopy (1H MRS) can provide metabolite distribution in selected volume in brain in vivo, revealing the roles of major neurochemicals as markers for neurodegeneration and neuroprotection upon degenerative illness (Choi et al., 2007). This technique has been utilized to investigate in vivo information on neurochemistry of various neurodegenerative diseases noninvasively, including Huntington’s disease, Parkinson’s disease and Alzheimer’s disease (Brownell et al., 1998; Ferrante et al., 2000; Marjanska et al., 2005). A recent study investigated the repair processes and plasticity of stem cell transplantation into rat brain with photochemical lesion (Hrynek et al., 2009); suggesting that 1H MRS may be capable to provide insights into metabolic activity, neurogenesis and plasticity changes. Regarding the visual system, reduction of choline (Cho) in the visual cortex of glaucomatous rat possibly due to dysfunction of the cholinergic system in the visual pathway was reported by our group with 1H MRS (Chan et al., 2009b). Such MRS technique has also been recently applied on blind subjects to reveal elevation of myo-inositol (m-Ins) in the visual cortex, probably due to the participation of glial cells in the reorganization of the brain upon visual deprivation in adult human subjects (Bernabeu et al., 2009).

Measurements of metabolites in brain may provide valuable biochemical information to study neurophysiological changes. Upon neonatal ME, characteristic structural and physiological changes in the visual system are induced. We hypothesized that neonatal ME would lead to metabolite changes in visual cortex. In this study, we aimed to detect and characterize the metabolic changes in ME rat neonates in vivo with 1H MRS at 7T. Such information can be valuable to the future investigation of cortical reorganization and changes associated with the adaptive reactions in the visual and other sensory systems in neonatal ME and other neuropsychiatric models.

2. Materials and methods

All MRI measurements were acquired on a 7T MRI scanner with a maximum gradient of 360 mT/m (70/16 PharmaScan, Bruker Biospin GmbH, Germany). A 72-mm birdcage transmit-only radiofrequency (RF) coil with an actively decoupled receive-only quadrature surface coil was used. All animal experiments were approved by the local institutional animal ethics committee.

2.1. Animal preparation

Male Sprague-Dawley neonatal rats (20–22 g, N = 14) were prepared and were divided into 2 groups. The enucleated group (N = 8) underwent right ME at postnatal day 10 under inhaled isoflurane anaesthesia through an incision in the conjunctiva followed by sectioning of the extraocular muscles and the optic nerve. The right day 10 under inhaled isoflurane anaesthesia through an incision in the conjunctiva (Wu et al., 2004; Yang and Wu, 2008). Body temperature was maintained at about 37°C by circulating warm water in a heating pad. Scout images were first acquired in three planes with a fast spin-echo (FSE) sequence to position the subseveral voxel for 1H MRS along standard anatomical orientations in a reproducible manner. High resolution anatomical images were acquired with two-dimensional (2D) FSE sequence using repetition time (TR) = 4200 ms, echo time (TE) = 17.8 ms, field of view (FOV) = 32 mm × 32 mm, acquisition matrix = 256 × 256, spatial resolution = 0.125 mm × 0.125 mm × 0.8 mm, echo train length = 8 and number of excitations (NEX) = 2. 1H MRS data was acquired using a protocol previously described (Chan et al., 2009a,b, 2010b). In brief, a 0.8 mm × 2.8 mm × 2.8 mm voxel was placed over each side of the visual cortex. The volume of interest was maximized to cover both the enucleated signal-to-noise and the gray matter in the visual cortex, while avoiding the margins of the white matter structures, which were clearly distinguishable in the FSE images underneath the cortex (Chan et al., 2009a,b). After automatically adjusting of first- and second-order shim terms for localized voxel using the field map based shimming technique (Webb and Macovski, 1991), a full-width half-maximum linewidth of water signal of ≤20 Hz would be achieved. The water signal was suppressed by variable power RF pulses with optimized relaxation delays (VAPOR). Outer volume suppression (OVS) combined with point-resolved spectroscopy (PRESS) sequence was used for signal acquisition using TR = 2500 ms, TE = 20 ms, spectral bandwidth = 3 kHz, 2048 data points and 512 averages.

2.2. MR spectroscopy

During MRI, the animals were anesthetized with isoflurane/air at 3% for induction and 1.5% for maintenance via a nose cone with respiratory monitoring (Wu et al., 2004; Yang and Wu, 2008). Body temperature was maintained at about 37°C by circulating warm water in a heating pad. Scout images were first acquired in three planes with a fast spin-echo (FSE) sequence to position the next voxel for 1H MRS along standard anatomical orientations in a reproducible manner. High resolution anatomical images were acquired with two-dimensional (2D) FSE sequence using repetition time (TR) = 4200 ms, echo time (TE) = 17.8 ms, field of view (FOV) = 32 mm × 32 mm, acquisition matrix = 256 × 256, spatial resolution = 0.125 mm × 0.125 mm × 0.8 mm, echo train length = 8 and number of excitations (NEX) = 2. 1H MRS data was acquired using a protocol previously described (Chan et al., 2009a,b, 2010b). In brief, a 0.8 mm × 2.8 mm × 2.8 mm voxel was placed over each side of the visual cortex. The volume of interest was maximized to cover both the enucleated signal-to-noise and the gray matter in the visual cortex, while avoiding the margins of the white matter structures, which were clearly distinguishable in the FSE images underneath the cortex (Chan et al., 2009a,b). After automatically adjusting of first- and second-order shim terms for localized voxel using the field map based shimming technique (Webb and Macovski, 1991), a full-width half-maximum linewidth of water signal of ≤20 Hz would be achieved. The water signal was suppressed by variable power RF pulses with optimized relaxation delays (VAPOR). Outer volume suppression (OVS) combined with point-resolved spectroscopy (PRESS) sequence was used for signal acquisition using TR = 2500 ms, TE = 20 ms, spectral bandwidth = 3 kHz, 2048 data points and 512 averages.

2.3. Data and statistical analysis

In the in vivo MRI spectra were processed as previously described using the MRUI software (version 4.0, http://www.mrui.uab.edu/mrui/)(Chan et al., 2009a,b, 2010b; Ratiney et al., 2005). The raw data were apodized with a 15-Hz Gaussian filter. In addition, the signal of residual water was filtered with Hankel-Lanczos Singular Value Decomposition (HLSVD) algorithm processing with 25 spectral components for modeling. Spectral peaks were assigned in the references to the singlet peak of CHO-group of N-acetylaspartate (NAA). Metabolite areas were estimated using the quantitation based on quantum estimation (QUEST) method combined with subtraction approach for background modeling (Cudalbu et al., 2008). Note that this subtraction approach was performed with both mean of the spectral width of 1.33 ppm and the three principal resonances of macromolecules (at around 2 ppm, 3 ppm and 3.9 ppm) being well identified under this quantitation scheme (Cudalbu et al., 2008). To reduce the systematic variations among the animals studied to extract the dominating metabolite changes, a relative quantification method using creatine (Cr) peak as the internal spectral reference was applied given that concentration of Cr was observed to be relatively constant in vivo (Malisza et al., 1998). The numerical time-domain modal functions of 10 metabolites, including acetate (Ace), alanine (Ala), aspartate (Asp), NAA, Cho, Cr, taurine (Tau), glutamate (Glu), lactate (Lac) and m-Ins, were used as prior knowledge in QUEST for quantitation of the numerical time-domain modal functions of 10 metabolites, including acetate (Ace), alanine (Ala), aspartate (Asp), NAA, Cho, Cr, taurine (Tau), glutamate (Glu), lactate (Lac) and m-Ins, were used as prior knowledge in QUEST for quantitation of these metabolite model signals were quantified using a Gaussian approach to obtain high signal-to-noise ratios and to cover the gray matter in the visual cortex for enucleated animals as contrasted to the right visual cortex for enucleated animals. Enucleated animals showed a decreased Tau signal (with respect to Cr signal) in the left visual cortex (contralateral to enucleated eye) and the right visual cortex. Spectra similar to that in the right visual cortex were observed for normal animals.

Table 1 shows the estimated metabolite ratios and the respective CRLBs at each side of the visual cortex for the enucleated animals and major peaks were labeled correspondingly. All enucleated animals consistently showed a marked difference in Tau signal with respect to Cr signal between the left visual cortex (contralateral to enucleated eye) and the right visual cortex. Spectra similar to that in the right visual cortex were observed for normal animals.

Table 1. The estimated metabolite ratios and the respective CRLBs at each side of the visual cortex for the enucleated animals and normal controls. All enucleated animals consistently showed a marked difference in Tau signal with respect to Cr signal between the left visual cortex (contralateral to enucleated eye) and the right visual cortex. Spectra similar to that in the right visual cortex were observed for normal animals.
Fig. 1. Illustration of the voxel placement over the left and right visual cortex for \(^1\)H MRS in a Sprague-Dawley rat 3 weeks after the right monocular enucleation (ME) (right eye removal) at postnatal day 10. Abbreviations: L, left; R, right; A, anterior; P, posterior.

well as between same sides of the visual cortex of enucleated and normal animals.

4. Discussions

Tau is a sulphur \(\beta\)-amino acid and elevated in many tissues including the retina, brain, skeletal and cardiac muscles in excited state (Chen et al., 2009). Physiological roles of Tau include membrane stabilization, osmoregulation, neuromodulation, regulation of calcium homeostasis, and antioxidation (Boukennooghe et al., 2006). Previous study also showed that Tau might act on various cellular processes such as proliferation, differentiation and inhibition of apoptosis (Park et al., 2006). Reduced Tau signal in degenerating rat brain with Alzheimer’s disease was also reported recently using \(^1\)H MRS (Labak et al., 2010). In the current study, decreased Tau signal in the left visual cortex (contralateral to enucleated eye) likely resulted from the left visual cortex degeneration in response to the right eye enucleation. Note that Tau regulates the calcium fluxes in nerve brain terminals and it may play a role in dendritic and synaptic processes (Magnusson, 1996). This finding is in agreement with a previous study showing a 20% reduction of axon terminals in the visual cortex contralateral to the enucleated eye in neonatal rats at age of 18–90 days (Ribak and Robertson, 1986).

NAA is an amino acid which is found exclusively in neurons but not in glial cells; hence it is regarded as a specific marker for neurons (Sappey-Marinier et al., 1992; Simmons et al., 1991; Urenjak et al., 1992). In general, NAA is reduced or absent in injured or diseased brain tissue due to neuronal loss and/or axonal damage in most pathologies (Choi et al., 2007; Higuchi et al., 1996; Howe et al., 1993). In the current study, the reduced NAA:Cr ratio observed in the left visual cortex likely arose from the reduction of axons at about 3 weeks in consequence of right eye enucleation, which is consistent with an earlier immunocytochemical study (Ribak and Robertson, 1986). Note that the primary visual cortex consists of binocular and monocular areas (Zilles et al., 1984). The binocular area receives prominent input from contralateral eye and a small input from the ipsilateral eye, whereas the monocular area receives input only from the contralateral eye (Zilles et al., 1984). The marginal significance between the left visual cortex (contralateral to enucleated eye) and right visual cortex in enucleated animals \((p = 0.1)\) likely resulted from the reduced inputs in binocular area of the right visual cortex due to ipsilateral eye removal.

In contrast to NAA, m-Ins is a simple sugar-like molecule which can be found at high concentration in astrocytes, thus it is considered as a marker for astrogliosis (Brand et al., 1993; Choi et al., 2007; Hattingen et al., 2008). m-Ins is also involved in osmoregulation as an important organic osmolyte (Thurston et al., 1989) and cell membrane metabolism as a precursor of membrane phosphoinositides and phospholipids (Toker and Cantley, 1997). Previous study of human blind subjects reveals elevation of m-Ins in the visual cortex (Bernabeu et al., 2009), suggesting its active role in astrocytes in the reorganization of the brain in response to visual development. However, no significant change of m-Ins was observed in the current study of neonatal monocular enucleation. Note that the human subjects in the previous study were largely blind with only half of them capable of perceiving light or gross movements. The blindness in these human subjects may lead to a larger extent of adaptive and compensatory changes in brain upon full visual deprivation.

Cho signal reflects cytosolic choline-containing compounds, 98% of which are phosphocholine and glycerophosphocholine (Dowling

Fig. 2. Typical \(^1\)H MR spectra obtained on each side of the visual cortex in rats at 3 weeks after right ME. Note the lower Tau signal in the left visual cortex (contralateral to enucleated eye). Spectra similar to that shown for the right visual cortex were observed for normal intact animals. Abbreviations: Lac, lactate; NAA, N-acetylaspartate; Glu, glutamate; Cr, creatine; Cho, choline; Tau, taurine; m-Ins, myo-inositol.
et al., 2001). They provide free Cho for the synthesis of neurotransmitter acetylcholine (ACh) by choline acetyltransferase (ChAT), and for the storage in membranous phosphatidylcholine (PtdCho) in cholinergic neurons (Boulanger et al., 2000; Kantarci et al., 2007; Michel et al., 2006; Schmidt and Rylett, 1993). ACh plays a crucial role in synaptic transmission. In addition, release of ACh is a marker of activation of the primary visual cortex during visual stimulation (Fournier et al., 2004; Laplante et al., 2005). ChAT is the biosynthesis enzyme of ACh, and its concentration reflects the level of cholinergic activity (Wessler et al., 2003). ChAT is shown to undergo anterograde axonal transport along the rat visual pathway (Yasuhara et al., 2003). In the current study, it is likely that the unchanged Cho:Cr in ME was a result of unaltered ChAT in the hemisphere contralateral to the enucleated eye (Robertson et al., 2005). Recent studies demonstrated the potential of 2D spectroscopic imaging to quantify metabolite concentrations in mammalian brains at micrometer resolution at high magnetic field strengths (Braakman et al., 2008; Juchem et al., 2005; Mlynarik et al., 2008). Given the fact that SC receives visual information via two major afferent projections from the retina and the visual cortex (Baba et al., 2007; Sakakibara et al., 2003), future experiments using 2D spectroscopic imaging to cover the whole brain may provide a better characterization and possibly enable the differentiation of effects on metabolite concentrations in different regions of the visual system upon neonatal ME.

Table 1

| Metabolite ratios and the respective Cramer-Rao lower bounds (CRLBs) in visual cortex in the ME rats with right eye removal (N = 8) and normal intact rats (N = 6). All data were presented as mean ± standard deviation (SD). Two-tailed paired Student’s t tests were performed between contralateral sides for enucleated and normal groups respectively, while two-tailed unpaired Student’s t tests were performed between enucleated and normal groups on the same hemispheres. n.s. for insignificance. |
|---|---|---|---|
| | Left visual cortex | Right visual cortex | p-Value |
| | Ratio | CRLB (%) | Ratio | CRLB (%) |
| Tau:Cr | ME rats | 1.29 ± 0.18 | 4.60 ± 1.22 | ME rats | 1.59 ± 0.29 | 4.42 ± 1.21 | <0.01 |
| Normal intact rats | 1.70 ± 0.38 | 4.81 ± 0.54 | n.s. | Normal intact rats | 1.59 ± 0.45 | 5.59 ± 1.41 | n.s. |
| p-Value | <0.05 | n.s. | n.s. | n.s. | n.s. | n.s. | n.s. |
| NAA:Cr | ME rats | 1.11 ± 0.28 | 4.79 ± 2.40 | ME rats | 1.30 ± 0.34 | 4.37 ± 1.51 | n.s. (<0.10) |
| Normal intact rats | 1.53 ± 0.38 | 4.65 ± 0.61 | n.s. | Normal intact rats | 1.40 ± 0.16 | 5.61 ± 1.54 | n.s. |
| p-Value | <0.05 | n.s. | n.s. | n.s. | n.s. | n.s. | n.s. |
| Glu:Cr | ME rats | 1.04 ± 0.27 | 5.77 ± 2.66 | ME rats | 0.95 ± 0.38 | 7.00 ± 3.94 | n.s. |
| Normal intact rats | 1.01 ± 0.31 | 7.05 ± 1.73 | n.s. | Normal intact rats | 1.25 ± 0.84 | 7.75 ± 3.08 | n.s. |
| p-Value | n.s. | n.s. | n.s. | n.s. | n.s. | n.s. | n.s. |
| Cho:Cr | ME rats | 0.12 ± 0.04 | 13.46 ± 8.36 | ME rats | 0.11 ± 0.05 | 13.49 ± 5.33 | n.s. |
| Normal intact rats | 0.14 ± 0.09 | 13.84 ± 3.35 | n.s. | Normal intact rats | 0.12 ± 0.05 | 14.83 ± 7.30 | n.s. |
| p-Value | n.s. | n.s. | n.s. | n.s. | n.s. | n.s. | n.s. |
| m-Ins:Cr | ME rats | 0.61 ± 0.24 | 7.36 ± 2.99 | ME rats | 0.77 ± 0.33 | 7.30 ± 4.50 | n.s. |
| Normal intact rats | 0.91 ± 0.33 | 6.78 ± 1.76 | n.s. | Normal intact rats | 1.11 ± 0.30 | 6.38 ± 1.10 | n.s. |
| p-Value | n.s. | n.s. | n.s. | n.s. | n.s. | n.s. | n.s. |

Considering the developmental changes in the neurochemical profile of the rat brain (Tkac et al., 2003), the metabolite ratios of normal rat cortices in this study were comparable to that reported previously (Chan et al., 2009b). In the current study, ratio of peak area measurements was used for metabolite level quantitation. As most 1H MRS studies indicate that total Cr content is constant under a variety of conditions (Choi et al., 2007; Malisza et al., 1998), Cr peak is often used as the internal reference. To verify this assumption of constant Cr in neonatal ME, Cr-to-noise ratio was assessed by dividing peak area of Cr by spectral noise, which was calculated from the standard deviation of the residue of QUEST quantitation. Given the fact that noise level was similar among spectra due to identical voxel size and nearly identical hardware setting in different measurements, such Cr-to-noise ratios reasonably reflect the Cr levels. In the current study, no statistically significant difference was observed in Cr-to-noise ratio between contralateral sides of the visual cortex for enucleated animals as well as between same sides of the visual cortex of enucleated and normal animals, thus supporting the use of Cr as an internal reference in analysis of other various metabolites. Moreover, statistical analysis was also performed by using the spectral noise as an internal reference for Tau and NAA signals quantitation. The statistical outcomes were similar to those in Table 1. The unsuppressed water signal at 4.7 ppm (Soher et al., 1996) was not chosen as internal reference in the current study because atrophy might occur in neurodegenerative diseases including ME, and contamination of cerebrospinal fluid was highly possible (Choi et al., 2007). Finally, the findings from the current study were preliminary given the limited sample sizes (N = 8 for ME group and N = 6 for control group). Larger sample sizes would further increase the statistical power in future studies.

Single voxel was used in this study to cover predominately the primary visual cortex as the volume of interest based on the high resolution FSE images and standard neuroanatomy (Paxinos and Watson, 2005). Recent studies demonstrated the potential of 2D spectroscopic imaging to quantify metabolite concentrations in mammalian brains at micrometer resolution at high magnetic field strengths (Braakman et al., 2008; Juchem et al., 2005; Mlynarik et al., 2008). Given the fact that SC receives visual information via two major afferent projections from the retina and the visual cortex (Baba et al., 2007; Sakakibara et al., 2003), future experiments using 2D spectroscopic imaging to cover the whole brain may provide a better characterization and possibly enable the differentiation of effects on metabolite concentrations in different regions of the visual system upon neonatal ME.

1H MRS has been widely used to investigate developmental neurobiology in mammalian brains (Larvaron et al., 2006; Tkac et al., 2003; Weiss et al., 2009). Recently, 1H MRS technique has been employed to study the metabolite profiles for measuring neuropasticity in response to environmental stimuli or injury (Bernabeu et al., 2009; Pajonk et al., 2010; Roche et al., 2008; Singh et al., 2009). In the present study, 1H MRS at 7T has been shown to reveal early biochemical or metabolic changes in visual cortex in neonatal ME model. As the plasticity on cross-modal changes is expected to...
occur at later time point, longitudinal study of neonatal ME model may provide more insights into such developmental neuroplasticity in future studies. It is worth noting that a number of other complementary MR techniques are potentially applicable to investigating the biochemical and functional aspects of the developmental neuroplasticity in various experimental models, including manganese-enhanced MRI (MEMRI), functional MRI, and cell tracking using iron oxide particles (Chan et al., 2008, 2010a; Yang et al., 2009; Yang and Wu, 2008; Zhou et al., 2010). These are presently under investigation at our laboratory. Note that manganese ion (Mn2+) can be uptaken by biological cells via voltage gated calcium channels. It has been shown as a valuable cellular contrast agent for tracing neuronal pathways, enhancing neural architecture and probing brain functions (Aoki et al., 2004). We have recently performed a preliminary MEMRI study in the enucleated group (N = 4) (Zhou et al., 2010). With Mn2+ enhancement, left SC structure could be delineated. It exhibited apparent volume reduction (p < 0.05) and lower manganese uptake (p < 0.05) when compared to right SC. Diminished Mn2+ uptake was also observed in left visual cortex, indicating reduced level of cellular activities or density. However, no apparent volume reduction was observed in visual cortex of ME rats. These morphological and cellular changes in left visual system were likely due to the neurodegeneration associated with right eye enucleation.

5. Conclusions

The current experimental results showed that neonatal monocular enucleation is accompanied by metabolic alterations in visual cortex. The decreased Tau and NAA levels in the left visual cortex are associated with excitatory neurotransmitter-related neuronal cell death. The decreased Tau and NAA levels in the left visual cortex are associated with right eye enucleation. The current study also demonstrated that in vivo 1H MRS approach could characterize the developmental neuroplasticity models for the biochemical and metabolic processes involved. Such information may be valuable in investigating the profound morphological, physiological and behavioral changes in neonatal monocular enucleation and other neuroplasticity models.

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