Use of Magnetic Resonance Spectroscopy to Explore Metacognitive Ability and Academic Performance

Xueyan Zhang  
Binzhou Medical University - Yantai Campus

Jun Li  
Binzhou Medical University - Yantai Campus

Duolao Wang  
Liverpool School of Tropical Medicine

Xiaomei Li (✉️ roselee8825@126.com)  
Xi’an Jiaotong University  🌐 https://orcid.org/0000-0002-4449-9611

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Abstract

Previous studies have reported the importance of the precuneus in mediating metacognition and the prefrontal cortex in decision-making tasks. However, the mechanisms underlying metacognition remain to be fully elucidated. Long echo time proton magnetic resonance spectroscopy (MRS) was used to further explore the neurocognitive correlates of metacognition. Metacognition was based on a self-reported questionnaire of nursing students. MR spectra of the bilateral precuneus and medial prefrontal cortex were recorded. Significant positive correlation was discovered between the total metacognitive score and academic performance (p = 0.007). The precuneus N-acetyl aspartate/creatine + phosphocreatine (NAA/Cr + PCr) ratios corresponded to metacognitive ability. Moreover, the correlation between precuneus NAA/Cr + PCr ratios and metacognitive ability was established for the right and not for the left precuneus. Linear regression suggested that for every increase in the right precuneus NAA/Cr + PCr ratio, there is a predicted decrease in the total metacognitive score (p = 0.020). These findings further indicated that the right precuneal region plays an important role in metacognition and learning.

Introduction

Metacognitive ability is the capacity to introspectively monitor and control one's own cognitive processes; this ability is useful in the improvement of learning efficiency, social communication, and mental health (Frith 2012; Teasdale et al. 2002; Schneider 2008). Researchers have speculated that the deficits in empathic skills in patients with schizophrenia are related to disturbances in metacognition (Bonfils et al. 2019). Previous findings have supported dysfunctional metacognition as a common process across psychopathologies, with certain dimensions being more prevalent in particular disorders (Sun et al. 2017). Metacognitive impairments are considered important characteristics of dementia, particularly in Alzheimer's disease (Bertrand et al. 2016). Understanding the neural bases of metacognition in relation to evidence-based treatment approaches is important for treating cognitive impairments among patients with these neurological and psychiatric conditions. For example, interventions targeted to improve metacognition may be useful in enhancing empathic skills in patients with schizophrenia (Bonfils et al. 2019). Studying the relationship between metacognition and perspective-taking may be useful to improve the quality of life of patients with Alzheimer's disease (Bertrand et al. 2016).

Using repetitive transcranial magnetic stimulation, previous studies have confirmed the role of the precuneus in mediating metacognition (Ye et al. 2018, 2019). Moreover, the prefrontal cortex is essentially involved in metacognition through decision-making tasks (Qiu et al. 2018). Lesions on the anterior prefrontal cortex impair perceptual metacognitive accuracy while sparing memory metacognitive accuracy (Fleming et al. 2010, 2014). The metacognitive capability of Macaque monkeys in introspecting their own memory success is causally dependent on intact superior dorsolateral prefrontal cortices but not orbitofrontal cortices (Kwok et al. 2019). Previous studies have indicated that variation in memory metacognitive efficiency is correlated with the precuneus volume (McCurdy et al. 2013).
Despite recent studies indicating the neural architecture of metacognition in various cognitive domains (Fleming et al. 2010, 2014; Yokoyama et al. 2010; Baird et al. 2013; McCurdy et al. 2013; Rahnev et al. 2016), the complex relationships associated with metacognition are still not fully understood. Magnetic resonance spectroscopy (MRS) is an increasingly used noninvasive technique in recent times; MRS can provide information regarding the chemical or metabolic composition of the brain (Manganas et al. 2007). Some metabolite changes have been identified in patients with mild cognitive impairment as well as Alzheimer's disease, particularly the latter (Gao and Barker 2014; Graff-Radford and Kantarci 2013; Kantarci et al. 2008). We hypothesized that metabolite levels in the associated brain regions might be related to metacognitive ability. In contrast to earlier studies, MRS was used to further explore the complex neurocognitive correlates of metacognition.

Materials And Methods

Participants

A total of 117 nursing students (90 females; age range, 18–21 years) from the Binzhou Medical University voluntarily participated in this study. All participants were healthy. The exclusion criteria were brain injury, encephalitis, and psychiatric disorders. The aims and objectives of the study were explained to each participant, and their written consents were obtained prior to the test. The study was approved by the Ethics Committee of the Binzhou Medical University.

Survey tools

A 24-item metacognitive ability scale developed by Kang and Zhang was used (Kang and Zhang 2005), which involved four factors: metacognitive planning (seven items; 7, 9, 16, 17, 18, 21, and 24), metacognitive monitoring (six items; 8, 10, 12, 13, 22, 23), metacognitive regulating (six items; 1–4, 19, 20), and metacognitive evaluating (five items; 5, 6, 11, 14, 15). The response alternatives were on a five-point Likert scale (1, never; 2, seldom; 3, sometimes; 4, often; and 5, always). The total score range was 24–120, with a higher score indicating better metacognitive ability. Cronbach's alpha for the total score was reported at 0.93/0.87 for metacognitive planning, 0.83 for metacognitive monitoring, 0.85 for metacognitive regulating, and 0.79 for metacognitive evaluating. The results of the confirmation factor analysis were as followed: χ²/df = 2.08; GFI = 0.89; RMSEA = 0.054; CFI = 0.88; and IFI = 0.88. The correlation coefficient between each factor and the total score (r = 0.79–0.86, P < 0.01). The four factors explained 66.9% of the variance (Kang and Zhang, 2005; Zhang and Fan, 2012).

All participants were trained to fully understand the survey process and the meaning of the scale items. All questionnaires were issued and taken back immediately, and each class was considered as a single unit. A total of 117 completed questionnaires were returned.

Academic performance was defined as the sum of the test scores for all subjects of the current semester. These subjects included pathology and pathophysiology, pathogenic biology, mental health of college students, English, nursing etiquette and interpersonal communication, fundamentals of computer, health
assessment, ideology and politics, human morphology, physiology, biochemistry, ideological and moral cultivation and legal basis, pharmacology, medical immunology, and medical statistics.

**Magnetic resonance imaging**

MR examinations were performed using a SIEMENS Skyra 3.0 T MR scanner with a standard quadrature head coil. A standard two-dimensional chemical-shift imaging point-resolved spectroscopy was used with the following parameters: TR, 1700 ms; TE, 135 ms; thickness, 15 mm; matrix, 160 mm × 160 mm; bandwidth, 1200 Hz; flip angle, 90; and average, 3. Axial, sagittal, and coronal T2 weighted imaging scans were acquired for locating the region of interest (ROI). A rectangular volume of interest (A >> P 120 mm; R >> L, 150 mm; F >> H 15 mm) was placed to cover the precuneus and medial prefrontal lobe. MR spectra were observed from the bilateral precuneus and medial prefrontal cortex (Fig. 1), with a voxel size of 10 mm × 10 mm × 15 mm. The voxel in the precuneus was selected from the front side of the parietooccipital sulcus at the roof of the lateral ventricle level. The voxel in the prefrontal lobe was selected from the medial prefrontal cortex. Metabolite ratios, including N-acetyl aspartate/creatine + phosphocreatine (NAA/Cr + PCr), phosphocholine + glycerophosphocholine/creatine + phosphocreatine (PC + GPC/Cr + PCr), and myo-inositol/creatine + phosphocreatine (mI/Cr + PCr), were calculated (Fig. 2). The analyses of the 1H MR spectra were fully automated and did not require manual intervention.

**Statistical methods**

Statistical analysis was conducted using the Statistical Package for the Social Sciences (version 21.0). One-way ANOVA was used to test the difference between males and females in terms of metacognitive scores. The Pearson correlation analysis with adjusted Bonferroni correction was conducted to define the relationships between metacognitive and academic scores. Cross-correlation coefficients between the metacognitive and academic scores and metabolites ratios were calculated. Multiple linear regressions, with metacognitive scores as dependent variables, were analyzed.

**Results**

Most students in the study population were female (n = 90; 76.9%). The students' average age was 19.6 (standard deviation [SD], 0.71; range, 18–21) years. The total score of the metacognitive ability of 117 nursing students was 81.45 ± 11.91, and the scores of the four factors were as follows: 22.96 ± 3.91 for metacognitive planning, 20.90 ± 2.99 for metacognitive monitoring, 19.68 ± 3.81 for metacognitive regulating, and 17.91 ± 2.92 for metacognitive evaluating. Although the majority of the participants in this study were females, no statistical difference was observed between males and females in terms of metacognitive scores, including the four factors (p > 0.05).

The Pearson correlation analysis with adjusted Bonferroni correction demonstrated a significant positive correlation between the total metacognitive score and academic performance (p = 0.007; Table 1). A positive correlation was also observed between the metacognitive evaluating score and academic performance (Table 1).
Table 1
Associations between metacognitive scores and total academic performance for 117 students

| Metacognitive scores                      | Total academic performance |
|-------------------------------------------|---------------------------|
|                                           | r value       | p value     |
| Metacognitive planning score              | 0.203*        | 0.028       |
| Metacognitive monitoring score            | 0.191*        | 0.040       |
| Metacognitive regulating score            | 0.193*        | 0.038       |
| Metacognitive evaluating score            | 0.299**Δ      | 0.001       |
| Total metacognitive score                 | 0.250**Δ      | 0.007       |

Note: Pearson correlation analysis. **Correlation is significant at the 0.01 level (2-tailed). *Correlation is significant at the 0.05 level (2-tailed). Δ = Adjusted Bonferroni correction: Correlation is significant at the 0.05/5 level (2-tailed).

Precuneus NAA/Cr + PCr ratios were found to be correlated to metacognitive monitoring score (p = 0.014, Fig. 3a), metacognitive evaluating score (p = 0.013, Fig. 3b), and total metacognitive score (p = 0.014, Fig. 3c).

Moreover, the correlation between precuneus NAA/Cr + PCr ratios and metacognitive ability was observed for the right precuneus but not for the left precuneus. Right precuneus NAA/Cr + PCr ratios were correlated to metacognitive monitoring score (p = 0.013, Fig. 4a), metacognitive regulating score (p = 0.034, Fig. 4b), and total metacognitive score (p = 0.020, Fig. 4c).

Furthermore, linear regression suggested that for every increase in the right precuneus NAA/Cr + PCr ratio, there is a predicted decrease in the total metacognitive score. Total metacognitive score = 94.493 – 6.819 right precuneus NAA/Cr + PCr ratios (t = -2.365; p = 0.020).

Discussion
Metacognitive ability is a powerful predictor of academic achievement (Schneider 2008; Wang et al. 1990; Winne 1996). The results of this study are in agreement with those of previous studies. A significant positive correlation was found between metacognitive ability and academic performance.

Self-monitoring of memory is necessary for successful learning and retention. Metacognitive monitoring can reportedly be captured through judgments of learning (JOLs) (Koriat 1997). Event-related potentials were used to compare neural correlates of JOLs and successful memory encoding. Therefore, ERP data indicate that JOLs do not reduce the encoding processes that predict the accuracy of memory judgments (Skavhaugh et al 2010). Previous findings reported that JOLs made during studying correlate with memory retrieval during a test; however, this correlation is specific to recollection (Skavhaugh et al 2013). Another previous study revealed that JOLs were accompanied by a positive slow wave over the medial frontal areas and a bilateral negative slow wave over occipital areas (Müller et al. 2016).
A neuropsychological study determined that there are different processes for metacognitive and cognitive judgments in children by providing direct electrophysiological evidence of a more negative slow wave over the centroparietal areas (Tsalas et al. 2018). The significant roles of the anterior prefrontal cortex in perceptual metacognition (Fleming et al. 2014) and the precuneus in memory metacognition (Fleming et al. 2010; McCurdy et al. 2013; Fleck et al. 2006; Morales et al. 2018) have been elucidated. The link between memory metacognitive efficiency and the precuneal gray-matter density has also been identified (McCurdy et al. 2013). A similar relationship was discovered between mnemonic metacognitive efficiency and resting-state functional connectivity between the precuneus and medial anterior prefrontal cortex (Baird et al. 2013).

In this study, MRS measurement of the medial prefrontal cortex was not found to be related to metacognitive ability; this is inconsistent with previous research. The suggested explanation for this phenomenon is that MR measurements of the medial prefrontal cortex were prone to artifact interference due to the anterior skull base and sinus. However, some meaningful discoveries have been made in the precuneus. The precuneus NAA/Cr + PCr ratios were correlated to metacognitive ability. Moreover, the correlation between precuneus NAA/Cr + PCr ratios and metacognitive ability was noted for the right precuneus but not for the left precuneus. Further linear regression suggested that for every increase in the right precuneus NAA/Cr + PCr ratio, there is a predicted decrease in the total metacognitive score. With regard to the relationship between the precuneus and metacognition, a possible circuit encompassing the precuneus and its mnemonic midbrain neighbor, the hippocampus, at the service of realizing meta-awareness during memory recollection of episodic details has been presented (Ye et al. 2019). NAA is commonly referred to as a neuronal marker and is predominantly present in the neurons (Simmons et al. 1991). NAA is a reasonably good surrogate marker of neuronal health in several neurologic and psychiatric disorders. Reduced NAA/Cr + PCr ratios have been identified in Alzheimer’s disease (Graff-Radford and Kantarci 2013; Kantarci et al. 2008), which might reflect neuronal component loss and neuronal function disruption, or both (Kantarci et al. 2008). However, this study reported negative correlations between the right precuneus NAA/Cr + PCr ratios and metacognitive ability. The suggested explanation for this negative correlation is that metacognitive activities lead to increased oxygen consumption in the right precuneus, which then affects neuronal function. Considering that low oxygen consumption may be seen in inattentive students, our findings might help identify individuals who are likely to respond to metacognitive training approaches.

There are several limitations to this study. Participants in this study were mostly females and within a narrow age range. In addition, the MR spectra in this study were only recorded from the precuneus and medial prefrontal cortex. Further studies focusing on other regions, such as the anterior cingulate, are warranted.

Declarations

**Ethical Approval** The study was approved by the Ethics Committee of Binzhou Medical University. All procedures performed in studies involving human participants were in accordance with the ethical
standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

**Consent to Participate** Informed consent was obtained from all participants included in the study.

**Consent to Publish** Informed consent was obtained from all participants included in the study.

**Authors Contributions** Conception and study design (XZ and XL), data collection or acquisition (XZ and JL), statistical analysis (XZ and DW), interpretation of results (XZ, DW and XL), drafting the manuscript work or revising it critically for important intellectual content (XZ, DW and XL) and approval of final version to be published and agreement to be accountable for the integrity and accuracy of all aspects of the work (All authors).

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**Competing Interests** The authors declare that they have no conflict of interest.

**Availability of data and materials** The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

**References**

1. Baird, B., Smallwood, J., Gorgolewski, K. J., & Margulies, D. S. (2013). Medial and lateral networks in anterior prefrontal cortex support metacognitive ability for memory and perception. *J Neurosci, 33,* 16657-16665.

2. Bertrand, E., Landeira-Fernandez, J., & Mograbi, D. C. (2016). Metacognition and Perspective-Taking in Alzheimer’s Disease: A Mini-Review. *Frontiers in psychology,* 7, 1812.

3. Bonfils, K. A., Lysaker, P. H., Minor, K. S., & Salyers, M. P. (2019). Metacognition, Personal Distress, and Performance-Based Empathy in Schizophrenia. *Schizophrenia bulletin,* 45, 19-26.

4. Fleck, M. S., Daselaar, S. M., Dobbins, I. G., & Cabeza, R. (2006). Role of prefrontal and anterior cingulate regions in decision-making processes shared by memory and nonmemory tasks. *Cereb Cortex,* 16, 1623-1630.

5. Fleming, S. M., Ryu, J., Golfinos, J. G., & Blackmon, K. E. (2014). Domain-specific impairment in metacognitive accuracy following anterior prefrontal lesions. *Brain,* 137, 2811-2822.

6. Fleming, S. M., Weil, R. S., Nagy, Z., Dolan, R. J., & Rees, G. (2010). Relating introspective accuracy to individual differences in brain structure. *Science.* 2010; 329: 1541-1543.

7. Frith, C.D. (2012). The role of metacognition in human social interactions. *Philos Trans R Soc Lond B Biol Sci,* 367, 2213-2223.

8. Gao, F., & Barker, P. B. (2014). Various MRS application tools for Alzheimer disease and mild cognitive impairment. *AJNR. American journal of neuroradiology,* 35, S4-S11.
9. Graff-Radford, J., & Kantarci, K. (2013). Magnetic resonance spectroscopy in Alzheimer’s disease. *Neuropsychiatr Dis Treat*, 9, 687-696.

10. Kang, Z. H., & Zhang, J. S. (2005). The Preliminary Construction of the Scale for College Student’s Metacognitive Ability. *Shan Xi University*, Shan Xi, China.

11. Kantarci, K., Knopman, D. S., Dickson, D. W., Parisi, J. E., Whitwell, J. L., Weigand, S. D., et al. (2008). Alzheimer disease: postmortem neuropathologic correlates of antemortem 1H MR spectroscopy metabolite measurements. *Radiology*, 248, 210-220.

12. Koriat, A. (1997). Monitoring one’s own knowledge during study: a cue-utilization approach to judgments of learning. *J Exp Psychol: Gen*, 126, 349–370.

13. Kwok, S. C., Cai, Y., & Buckley, M. J. (2019). Mnemonic Introspection in Macaques Is Dependent on Superior Dorsolateral Prefrontal Cortex But Not Orbitofrontal Cortex. *The Journal of Neuroscience*, 39, 5922-5934.

14. Manganas, L. N., Zhang, X., Li, Y., Hazel, R. D., Smith, S. D., Wagshul, M. E., et al. (2007). Magnetic resonance spectroscopy identifies neural progenitor cells in the live human brain. *Science*, 318, 980-985.

15. McCurdy, L. Y., Maniscalco, B., Metcalfe, J., Liu, K. Y., de Lange, F. P., & Lau, H. (2013). Anatomical coupling between distinct metacognitive systems for memory and visual perception. *J Neurosci*, 33, 1897-1906.

16. Morales, J., Lau, H., & Fleming, S. M. (2018). Domain-general and domain-specific patterns of activity supporting metacognition in human prefrontal cortex. *J Neurosci*, 38, 3534-3546.

17. Müller, B. C. N., Tsalas, N. R. H., van Schie, H. T., Meinhardt, J., Proust, J., Sodian, B., et al. (2016). Neural correlates of judgments of learning - An ERP study on metacognition. *Brain Res*, 1652, 170-177.

18. Qiu, L., Su, J., Ni, Y., Bai, Y., Zhang, X., Li, X., et al. (2018). The neural system of metacognition accompanying decision-making in the prefrontal cortex. *PLoS Biol*, 16(4), e2004037.

19. Rahnev, D., Nee, D. E., Riddle, J., Larson, A. S., & D’Esposito, M.. (2016). Causal evidence for frontal cortex organization for perceptual decision making. *Proc Natl Acad Sci USA*, 113, 6059-6064.

20. Schneider, W. (2008). The development of metacognitive knowledge in children and adolescents: major trends and implications for education. *Mind Brain Educ*, 2, 114-121.

21. Skavhaug I. M., Wilding E. L., Donaldson D. I. (2010). Judgments of learning do not reduce to memory encoding operations: event-related potential evidence for distinct metacognitive processes. *Brain Res*. 1318, 87-95.

22. Skavhaug I. M., Wilding E. L., Donaldson D. I. (2013). Immediate judgments of learning predict subsequent recollection: evidence from event-related potentials. *J Exp Psychol Learn Mem Cogn*. 39(1), 159-166.

23. Simmons, M. L., Frondoza, C. G., & Coyle, J. T. (1991). Immunocytochemical localization of N-acetyl-aspartate with monoclonal antibodies. *Neuroscience*, 45, 37-45.
24. Sun, X., Zhu, C., & So, S. (2017). Dysfunctional metacognition across psychopathologies: A meta-analytic review. *European psychiatry: the journal of the Association of European Psychiatrists, 45*, 139-153.

25. Teasdale, J. D., Moore, R. G., Hayhurst, H., Pope, M., Williams, S., & Segal, Z. V. (2002). Metacognitive awareness and prevention of relapse in depression: empirical evidence. *J Consult Clin Psychol, 70*, 275-287.

26. Tsalas N. R. H., Müller B. C. N., Meinhardt J., Proust J., Paulus M., Sodian B. (2018). An ERP study on metacognitive monitoring processes in children. *Brain Res.* 1695, 84-90.

27. Wang, M. C., Haertel, G. D., & Walberg, H. J. (1990). What influences learning? A content analysis of review literature. *J Educ Res, 84*, 30-43.

28. Winne, P. H. (1996). A metacognitive view of individual differences in self-regulated learning. *Learn Individ Differ, 8*, 327-353.

29. Ye, Q., Zou, F., Dayan, M., Lau, H., Hu, Y., & Kwok, S. C. (2019). Individual susceptibility to TMS affirms the precuneal role in meta-memory upon recollection. *Brain Structure and Function, 224*, 2407-2419.

30. Ye, Q., Zou, F., Lau, H., Hu, Y., & Kwok, S. C. (2018). Causal Evidence for Mnemonic Metacognition in Human Precuneus. *J Neurosci, 38*(28), 6379-6387.

31. Yokoyama, O., Miura, N., Watanabe, J., Takemoto, A., Uchida, S., Sugiura, M., et al. (2010). Right frontopolar cortex activity correlates with reliability of retrospective rating of confidence in short-term recognition memory performance. *Neurosci Res, 68*, 199-206.

32. Zhang, X. Y., Fan, X. Z. (2012). The Relationship among Meta-Cognition, Self-efficacy and Perceived Critical Thinking in Nursing Students. *Shan Dong University, Shan Dong, China.*

**Figures**
Figure 1

MRS location images Axial ROIs of the right precuneus (a) and left medial prefrontal cortex (b).

Figure 2

MR spectra Metabolites, including NAA, PC+GPC, Cr+PCr, and mI of the right precuneus (a) and left medial prefrontal cortex (b).
Relationship between precuneus NAA/Cr+PCr ratios and metacognitive ability Negative correlation were reported between precuneus NAA/Cr+PCr ratios and metacognitive monitoring score (a; r = −0.238, p = 0.014), metacognitive evaluating score (b; r = −0.240, p = 0.013), and total metacognitive score (c; r = −0.237, p = 0.014).

Relationship between right precuneus NAA/Cr+PCr ratios and metacognitive ability Negative correlations were reported between the right precuneus NAA/Cr+PCr ratios and metacognitive monitoring score (a; r = −0.241, p = 0.013), metacognitive regulating score (b; r = −0.206, p = 0.034), and total metacognitive score (c; r = −0.226, p = 0.020).

Supplementary Files

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