# Meta-analyses of Mathematical Calculation and Default-Mode Networks: impact on BOLD-based fMRI

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#### Introduction

The consistent and characteristic central correlates of mathematical calculation showed the tripartite system involving bilateral lateral parietal lobes (intraparietal sulci, angular gyri and posterior superior parietal systems) by BOLD-based fMRI (Piazza et al, 2007). Self-construction spatial template of the default-mode network (DMN) included extensive medial and lateral parietal lobes using informax independent component analysis (Yeh et al, 2002 and 2006, Lin et al, 2008). Interaction of calculation-relevant and DMN-modulated regions was proposed for type I error in the fMRI paradigm design and analysis. In this study, meta-analyses using activation likelihood estimation (ALE) were obtained by the activation coordinates and provided statistics of 12 published references for mathematical calculation. The parametric fMRI studies of digit naming, one-digit addition and two-digit addition at a 3T MRI system was applied to examine the conjunction results. Lateral parietal regions showed overlapping among meta-analysis of DMN, meta-analysis of fMRI studies for mental calculation and parametric results of mental addition. Involvement of posterior lateral parietal region was potentially considered as the false positive result by task modulation in DMN.

## **Subjects and Methods**

#### (1) Meta-analyses of FMRI Literatures

Acctication likelihood estimation (GingerALE Version 1.1, Research Imaging Center, University of Texas Health Science Center at San Antonio) was applied with 12 selected references using fMRI methods to study the central correlates of mental calculation. Applied statistical parameters included FWHM=10mm, Gaussian distribution, Permutation steps = 5000, FDR with p<0.05 and volume >100 mm<sup>3</sup>.

## (2) Resting fMRI and Parametric FMRI of Mental Addition

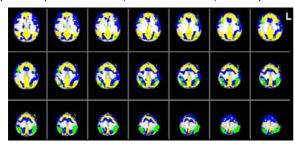
An fMRI database of fifty-five right-handed subjects (gender- and age-matched, age: 27 +/- 6 years old) was constructed for mapping the spatial template of DMN. After 5-minute sensory deprivation by auditory protection and dimmed room light, imaging studies of resting state were obtained with eye fixation on a dimmed red cross which was viewed through a mirror projection. Images were acquired using a 3T Medspec S300 system (Bruker GmbH, Ettlingen, Germany) equipped with an actively shielded gradient coil and a quadrature transceiver of head. Single-shot echo planar images (64x64 matrix, slice thickness/ gap = 5/1 mm, 20 slices) covering whole brain were acquired with a flip angle = 90 degree, echo time (TE) = 50 ms, repetition time (TR) = 2000 ms, dummy scan (DS) = 5 for reaching stable magnetization and repetition number (NR) = 200. And two subjects received parametric fMRI study of mental addition, using three conditions of number naming (NN), one-digit addition (1D) and two-digit addition (2D). For each session of NR=140, one condition with NR of 10 was applied with control of visual fixation as a block-designed paradigm. Six sessions were delivered in counter-balanced design with response time recorded by a button pad.

#### (3) Data Analyses

On-line analysis using modified AFNI (Analysis of Functional NeuroImages, NIMH, USA) ensured the head motion with head translation < 2 mm and head rotation < 1 degree. Off-line processing of DMN template included (1) preprocessing of Individual data sets using SPM2 (Functional Imaging Laboratory, Wellcome Department of Imaging Neuroscience, UK) was applied for spatial normalization; (2) Group ICA was applied to construct the spatial template of DMN using GIFT (Calhoun et al, 2001) of informax ICA (Computational Neurobiology Laboratory, The Salk Institute for Biological Studies, USA) with averaged component number of 27 by MLD (minimal length discrimination); (3) temporal course of DMN was derived for each individual from GIFT, and the temporal course was applied as the regressor for GLM estimation after co-registration/normalization to MNI T1 template and smoothing of 8x8x8 mm in SPM2. Group analyses using two-level statistical evaluation of random-effect analysis was performed for DMN template of 55 subjects (DMN-55) with statistical criteria of p<0.001/voxel extension>0 for the first level and p<0.05/voxel extension>0 for the second level with correction of false discovery rate (FDR), respectively. For fMRI of mental calculation, parametric fMRI analysis using SPM2 was obtained with response time as reference (p<0.01/voxel extension>0, uncorrected).

### Results

In parametric fMRI of mental addition, region defined by DMN-55 showed decreased BOLD activity (de-activation pattern) during task performance. Conjunction maps (**Figure 1**) of ALE-based meta-analysis of mental calculation, DMN-55 and parametric fMRI results of mental addition included bilateral posterior parietal cortices (Brodmann area 31) and left prefrontal cortices (BA 9).



**Figure 1**: Conjunction mapping of ALE-based meta-analysis of mental calculation, DMN-55 and parametric fMRI of mental addition; (1) ALE meta-analysis of mental calculation (from 12 ref., FWHM=10mm, gaussian distribution , permutation steps = 5000, FDR with p<0.05, volume >100 mm3, labeled as green color); (2) spatial template of DMN (N=55, FDR, p<0.001, v>0, in yellow color); (3) parametric fMRI of NN vs.1D vs. 2D (based on response time, p<0.01, v>0, uncorrected, labeled as blue color); and (4) conjunction of three spatial maps described previously (labeled as red color)

### **Discussion**

Correlates of posterior lateral parietal have been extensively reported as central correlates of mental calculation and multi-modal integration. With conjunction analysis with mental addition in parametric design, part of bilateral posterior lateral parietal region was considered as false positive in fMRI parametric analysis due to the deactivation change during task performance within DMN.

### Acknowledgement

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#### References

Piazza et al 2007, Neuron 53, 293; Yeh et al 2002 8th Annual Meeting, Human Brain Map, p431; Yeh et al 2006, 12th Annual Meeting, Human Brain Map, TH 403; Lin et al 2008, 14<sup>th</sup> Annual Meeting, Human Brain Map, 325 M-AM; Calhoun et al 2001, Hum. Brain Map, 14, 140