Overlapping functional networks subserving single-digit multiplication

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INTRODUCTION: Modern neuroimaging techniques, especially fMRI, have advanced our understanding of the neuroanatomical basis of cognitive processes such as mental arithmetic. Most studies so far only attempted to relate individual activated regions with specific processes [1,2]. However, the neural activation within a given region may reflect the summation of multiple distinct networks that carry different functional purposes [3]. By combining general linear model (GLM) and independent components analysis (ICA) into contributive source analysis (CSA) [4], this study aimed to test the hypothesis that multiple functional networks engage in simple mental task of single-digit multiplication and contribute collectively to the activations in prefrontal and parietal cortices.

METHODS: Participants: Five healthy right-handed subjects (F/M=2/3) were scanned in a 3T scanner three times on different dates. **Task:** The fMRI experiment was an event-related design consisting of 30 trials. In each trial, a single-digit multiplication expression (e.g., 2x7) was presented followed by four control expressions (e.g., 5#9) with 2 digits separated by a symbol (#, $, & or %) matching for visual complexity. Each expression lasted for 2s, same as fMRI temporal resolution. Subjects fixated at the expressions and pressed the button upon completing the calculations. The fMRI experiments were repeated four times during each session. **Data analysis:** GLM analysis (SPM8) was first used to generate the statistical maps of activated regions. ICA (GIFT toolbox) was then performed to provide ICs as contributive sources (No. of ICs = 40). Finally, to measure the contributions of these ICs to a region, contributive source values were obtained by multiplying weights from ICs spatial maps in that region by parameter estimates from ICs time-courses using the same design matrix in earlier GLM, following equation $\beta_{GLM} = \sum_{i=1}^{nr\ of\ IC} \beta_{ICi} \cdot S_i$ [4].

RESULTS AND DISCUSSIONS: Prefrontal and parietal regions are highly implicated in mental arithmetic [2]. Fig. 1A shows that GLM revealed robust activations in the bilateral prefrontal and parietal cortices. Moreover, at these activated regions 6 ICs or networks were found to be overlapped (See Fig. 1C for spatial temporal details of the networks). Contributive source analysis (CSA) results in Fig. 2 further clarified the contributions of above networks. The DAN, LFPN, RFPN and ECN have been repeatedly reported in general cognitive and resting-state studies [5,6], yet their functional roles in arithmetic have not been attended. In present study their low CS values suggest that they exerted cognitive control functions during the single-digit multiplication, which is known to have low level cognitive demand [7]. Furthermore, the AGP and FTS contributed to bilateral parietal activations and the FTS exerted a dominant contribution to the prefrontal activations. Previous studies have implicated left AG and left supramarginal gyri (SMG) activations in the process of automatic fact retrieval, and prefrontal activations in phonological manipulation of working memory [8,9]. In contrast, current results suggested that these regions cooperated with distant regions as networks to fulfill the processes including but not exclusive to those mentioned above. Future studies incorporating different arithmetic tasks and resting state will shed more light upon how brain accomplishes arithmetic and more complex tasks in general. In conclusion, current study demonstrated that distinct networks overlapped at parietal and prefrontal cortices with different functional contributions to single-digit multiplication.

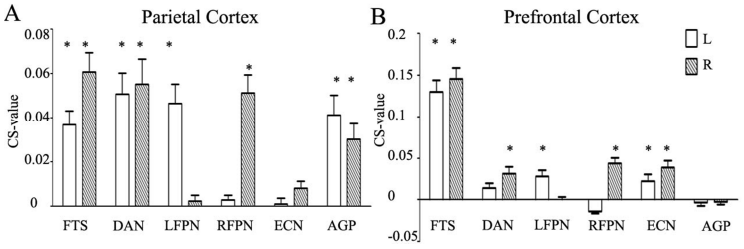

Fig. 2 Contributive sources analysis (CSA) results within activated regions at left and right parietal (**A**) and prefrontal cortices (**B**). CS-values of 6 ICs are presented as mean + SEM. One-sample t-test across different subjects on different dates was performed with *for p<0.05. Bonferroni corrected for 40 ICs. Significant CS-value indicates the IC is indeed contribution.

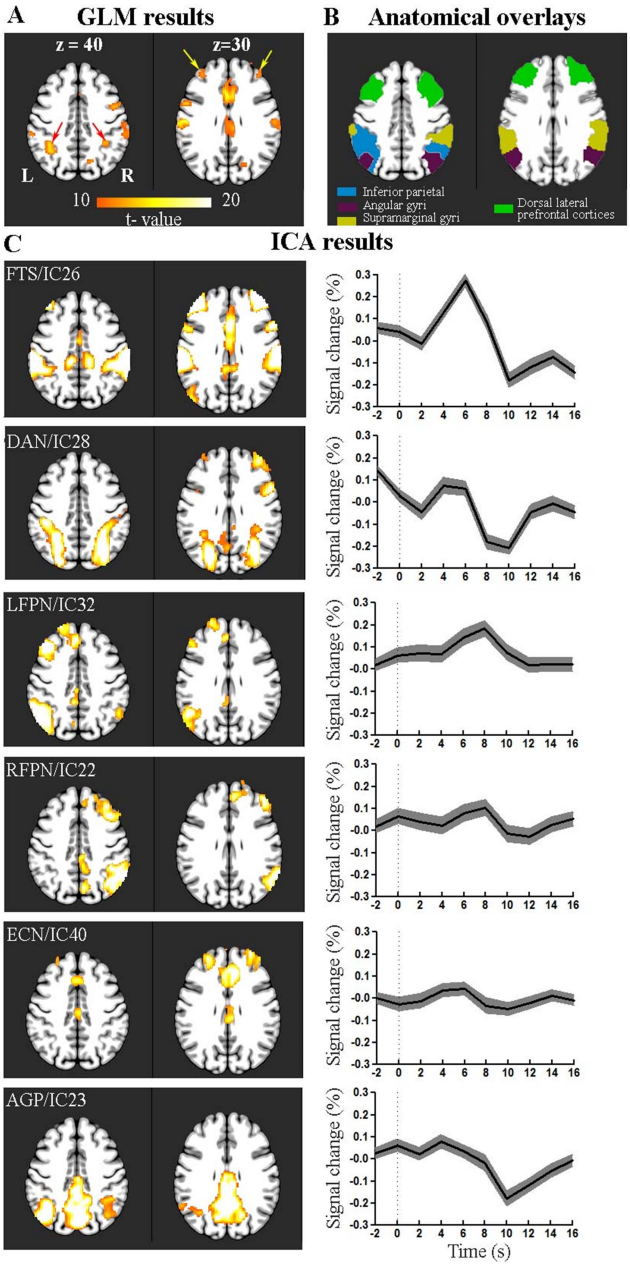

Fig. 1 A GLM results: activated regions (p<0.0005, FDR corrected, cluster >30) overlaid on the MNI152 standard brain. Arrows point to the activated regions within parietal (red) and prefrontal (yellow) cortices. **B**. Anatomical overlays according to Automated Anatomical Labeling. **C.** ICA results: spatial distributions and event-related responses (mean ± STD) of the 6 ICs overlapping at parietal or prefrontal cortices. FTS, fronto-temporal-supramarginal gyri; DAN, dorsal attention network; LFPN, left fronto-parietal network; RFPN, right fronto-parietal network; ECN, executive control network; AGP, angular gyri-precuneus. Dash line indicates the presence of single-digit multiplication expression (e.g., 2x7).

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