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Neural substrates of data-driven scientific discovery: An fMRI study during performance of number series completion task

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Although much has been known about how humans psychologically perform data-driven scientific discovery, less has been known about its brain mechanism. The number series completion is a typical data-driven scientific discovery task, and has been demonstrated to possess the priming effect, which is attributed to the regularity identification and its subsequent extrapolation. In order to reduce the heterogeneities and make the experimental task proper for a brain imaging study, the number magnitude and arithmetic operation involved in number series completion tasks are further restricted. Behavioral performance in Experiment 1 shows the reliable priming effect for targets as expected. Then, a factorial design (the priming effect: prime vs. target; the period length: simple vs. complex) of event-related functional magnetic resonance imaging (fMRI) is used in Experiment 2 to examine the neural basis of data-driven scientific discovery. The fMRI results reveal a double dissociation of the left DLPFC (dorsolateral prefrontal cortex) and the left APFC (anterior prefrontal cortex) between the simple (period length=1) and the complex (period length=2) number series completion task. The priming effect in the left DLPFC is more significant for the simple task than for the complex task, while the priming effect in the left APFC is more significant for the simple task. The reliable double dissociation may suggest the different roles of the left DLPFC and left APFC in data-driven scientific discovery. The left DLPFC is more significant for the complex task than for the simple task. The reliable double dissociation may suggest the different roles of the left DLPFC and left APFC in data-driven scientific discovery. The left DLPFC (BA 46) may play a crucial role in rule identification, while the left APFC (BA 10) may be related to mental set maintenance needed during rule identification and extrapolation.

dorsolateral prefrontal cortex (DLPFC), functional MRI, data-driven scientific discovery, number series completion

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Scientific experiments yield data which are usually represented as numbers, and the rules underlying the data are required to be exploited. For the knowledge-rich scientific domains, some prior knowledge is available to help people to analyze the experimental data and model-based methods are often used. For the knowledge-lean scientific domains,

†Contributed equally to this work *Corresponding author (email: zhong@maebashi-it.ac.jp; ppliang1979@gmail.com) however, the data-driven method is needed. Data-driven scientific discovery [1] can be depicted as a process of rule induction directly from collected experimental data. As a topic of intense scrutiny and speculation for hundreds of years, data-driven scientific discovery has been extensively studied in multiple disciplines, such as artificial intelligence (AI) and cognitive psychology [1–7].

The cognitive processes underlying data-driven scientific discovery have been actively investigated using behavioural

experiments, verbal protocols analysis, computer simulation, and analysis of particular scientific discovery cases [2-5]. For example, Wason et al. [2] treated a key component of scientific discovery as the test of hypotheses using a "2-4-6" task. Simon et al. [3-6] conceived scientific discovery as a form of problem solving. They provided participants (and computer programs), the data to which a scientist had accessed, and asked them to rediscover scientific laws. Along this line, Haverty et al. [7] identified three fundamental stages of data-driven scientific discovery in quadratic-function-finding tasks based on concurrent verbal protocols: data gathering, pattern finding, and hypothesis generation. Overall, these studies have provided detailed psychological analyses of different aspects of data-driven scientific discovery; however, its neural mechanism has been less investigated and understood.

Number series completion, e.g., predicting the next number in the sequence $\{2, 4, 6, 8, 10\}$, is a classical task which has been widely used in data-driven scientific discovery. Studies indicate that four basic cognitive components are involved in solving number series completion problems [8,9]. The first component is the encoding of number series. The second component, identification, contains three sub-components: (i) Relation detection that requires scanning the series and generating a hypothesis with respect to the relation among adjacent elements. Relations among elements may be simple or complex, which is determined by the type of arithmetic operation (e.g., addition/subtraction and multiplication/division) and the magnitude of the numbers that the operation works on. (ii) Discovery of periodicity that involves the detection of period boundary and structure. A simple series has the period length of one (such as {1, 3, 5, 7, 9}, period length=1, rule +2), while a complex series has longer period length (such as $\{2, 4, 3, 5, 4, 6\}$, period length=2, rule +2, -1). (iii) Completion of the pattern description that involves identifying the relations among the elements composing a cycle, and then formulating a rule that accounts for the sequence. The third component, extrapolation, consists of three sub-components: (i) detection of the answer position; (ii) isolation of the related part of the rule; and (iii) application of this part of the rule in computing the answer. The last component is answer production. The period length is critical in determining the processing requirements to solve a number series. A simple number series (period length=1) is solved with a lower working load when performing the sub-component of discovery of periodicity in the second component, and the sub-components of detection of the answer position and isolation of the related part of the rule in the third component are not needed.

Delazer *et al.* [10–12] have validated the reliable priming effect in number series completion tasks in their serial behavioural and neuropsychological studies. The priming effect generally refers to the facilitation of a piece of information such as a word/object/concept (prime) to its subsequent proc-

essing (target) [13]. The priming effect existing among number series completion tasks opens a window to explore the neural mechanism of data-driven scientific discovery. However, there are also some insufficiencies in previous studies. Firstly, some results are not convergent. For example, two behavioural studies in Girelli *et al.* [10] show no identical effect of priming for the error rates: The priming effect in their Experiment 1 is significant while is not significant in their Experiment 2. Secondly, previous studies adopt four kinds of arithmetic operations (addition, subtraction, multiplication and division) in their design. Multiplication and division may cause different priming effects than addition and subtraction. Thirdly, the number magnitude is not explicitly considered. These problems may introduce heterogeneities.

In order to overcome these insufficiencies, some constraints have been set in this study, including the range of number magnitude (0-99) and arithmetic operations (only addition and subtraction are used). These constraints also make the task proper for a functional magnetic resonance imaging (fMRI) experiment. Experiment 1, a behaviour study, is designed to observe if the effects in previous studies will be kept. Our hypothesis for Experiment 1 is that significant effects of the period length and the priming effect may be shown as measured by the reaction time (RT) and percent of correctness. We have no assumption with respect to the interaction effect between the period length and the priming effect. Experiment 2, an fMRI experiment, is designed to explore the neural mechanism of data-driven scientific discovery in human brain using the number series completion task. The same priming effect paradigm is used to functionally segregate the related brain areas involved. Based on previous studies [14-18], we hypothesize that the left dorsolateral prefrontal cortex (DLPFC) and the left anterior prefrontal cortex (APFC) may be both recruited in the priming effect of number series completion tasks, i.e., they may show a more significantly reduced activation for the target task than for the prime task, and they may play different roles.

1 Experiment 1

1.1 Subjects

Thirty paid healthy students (15 males and 15 females, aged 23.9 ± 2.4 , right-handed, normal or corrected-to-normal vision) from Beijing University of Technology participated in the experiment. The Institutional Review Board of the Beijing University of Technology approved all experimental procedures, and written informed consent was obtained from each participant.

1.2 Tasks

This study adopted a 2×2 factorial design (the priming effect: prime vs. target; the period length: 1 vs. 2). The prime

task and the corresponding target task were designed to share the same underlying regularity to be discovered by the participants, while differing in both constituent elements and correct answers. All numbers including answers ranged from 0 to 99, and only addition and subtraction were used in the design of number series completion tasks. Numbers used in a target number series task were different from that in the corresponding prime task. The answer for the target task was also different from that for the prime task. For example, the prime and target had different magnitudes of numbers (e.g., {27, 30, 33, 36, 39} vs. {8, 11, 14, 17, 20}), and required different operands for extrapolation (prime, 39+3; target, 20+3) and different answers (prime, 42; target, 23).

The period length was used to define the simple (*L*=1, e.g., {1, 4, 7, 10, 13} with rule +3) and the complex (*L*=2, e.g., {1, 3, 6, 8, 11} with rule +2, +3) number series tasks. For the simple task, the common difference values were set to 3, 4, 6, 7, 8, 9, 12, and 13 (they were chosen as the result of a trade-off between the number of tasks and the experimental time). For the complex task (e.g., rule $\pm a$, $\pm b$), we had 0<*a*<10 and 0<*b*<10. Totally 72 tasks (16 simple prime tasks, 16 simple tasks, and eight interferential tasks (e.g., {1, 3, 22, 17, 9})) were tested.

Data-driven scientific discovery was mainly a process of inductive reasoning. For simplicity, the experimental tasks (as shown in Table 1) were named SIP (simple induction prime), SIT (simple induction target), CIP (complex induction prime), and CIT (complex induction target), respectively.

Table 1 Experimental tasks

Task	Prime	Target
Simple induction	1, 4, 7, 10, 13	22, 25, 28, 31, 34
Complex induction	2, 3, 6, 7, 10	14, 15, 18, 19, 22

1.3 Stimulus presentation

A number series was presented on the computer screen in white digits in 36 size font against the black background. As shown in Figure 1, stimuli were preceded by a cue for the task type, and followed by a blank. The five numbers in a number series were shown one by one, and the number series would be kept on the screen until a button-pressing response was made. Participants were instructed to press a button as quickly as possible after attaining the value following. A fixation of "+" and a blank were followed. An option of answers (e.g., "A. 16 B. 17") was then presented. Participants were required to make the choice between "A" and "B" by pressing buttons as exactly as possible. Then a random inter-trial interval (ITI) of 2–4 s was followed. It would move to the next trial if the stimuli of the next trial advanced before the participants could respond.

The filler between the prime task and the target task was one. The number series with different rules acted as fillers for each other, or some interferential tasks were used as fillers. Participants reviewed example stimuli from each condition prior to being tested to ensure that they understood the task. All tasks were pseudo-randomly presented in two sessions. Button-pressing responses were balanced among participants.

1.4 Results

Both the mean RT for the correct trials and the percent of correctness are shown in Figure 2. Failure to answer a prime determined the elimination of the corresponding target and *vice versa*. One participant was eliminated for the low correctness (<50% for all kinds of tasks). A repeated measure was performed on the RT and correctness respectively, with the priming effect (prime vs. target) and the period length (simple vs. complex) as within-subject factors. The *P*-value



Figure 2 The mean RT (A) and percent of correctness (B). SIP, simple induction prime; SIT, simple induction target; CIP, complex induction prime; CIT, complex induction target.

was corrected using the Greenhouse-Geisser method.

For the RT, the main effect of the period length (F(1, 28) = 44.718, P < 0.001) and the priming effect (F(1, 28) = 22.173, P < 0.001) were highly significant. As expected, for the mean RT, the target was significantly faster (3962.45 ms) than the prime (4450.05 ms), and the simple task was evidently faster (3721.64 ms) than the complex task (4690.86 ms). The interaction effect was also significant (F(1, 28) = 4.974, P < 0.05), and pair-wise comparisons revealed that the facilitation in the simple task (717.43 ms) was much stronger than that in the complex task (257.77 ms).

For the correctness, the main effect of the period length (F(1, 28)=7.410, P<0.05) and the priming effect (F(1, 28)=11.118, P<0.05) were significant. It was not surprising that more errors would be made for the complex task (15%) than the simple task (10%) and for the prime (15%) than the target (10%). The interaction effect was not significant.

1.5 Discussion

This experiment was performed with relatively low heterogeneities, for the number magnitude (0-99) and arithmetic operations (addition and subtraction) were constrained. Our experimental results show reliable main effects of the priming effect and the period length in number series completion tasks: The target was answered faster and more accurately than the prime; the simple task was solved more quickly and relatively correctly than the complex task. These results which were congruent with Girelli *et al.* [10] supported our assumptions.

The interaction effect between the priming effect and the period length in this study was different from the previous studies [10]. The interaction effect for the RT was significant in this study while not significant in Girelli *et al.*'s study [10]. Additionally, the interaction effect for the correctness in this experiment was not significant while significant or near to be significant in Girelli *et al.*'s study [10]. These differences might be explained by the following two reasons. First, this study made some restrictions as contrast to previous studies. Second, the ceiling effect in the simple task would confound the interaction effect.

The priming effect in number series completion tasks opens a new window for us to observe the neural mechanism of data-driven scientific discovery. At the same time, the inclusion of the simple task (period length=1) and the complex task (period length=2) allows us to further differentiate among processing stages potentially contributing to the priming effect. Thus, a functional MRI experiment would be performed.

2 Experiment 2

2.1 Subjects

Fourteen paid healthy students (male, aged 22.9±2.1,

right-handed, normal or corrected-to-normal vision) from Beijing University of Technology participated in the experiment. The Institutional Review Board of the Beijing University of Technology approved all experimental procedures, and written informed consent was obtained from each participant.

2.2 Tasks

The experimental tasks used in the fMRI experiment were the same as those in Experiment 1.

2.3 Stimulus presentation

The stimulus presentation paradigm was identical to Experiment 1, except the constant 6 s ITI and 11 s duration after the presentation of the fifth number. Additionally, all tasks were evenly and pseudo-randomly distributed in six sessions, which was also different from Experiment 1.

2.4 fMRI recording

Scanning was performed on a Siemens Magnetom Trio Tim 3.0 T system using a standard whole-head coil. Functional data were acquired using a gradient echo planar pulse sequence (TR=2 s, TE=31 ms, 30 axial slices, $3.75 \text{ mm} \times 3.75 \text{ mm} \times 4 \text{ mm}$ voxels, 0.8 mm inter-slice gap, 90° flip angle, 64×64 matrix size in 240 mm ×240 mm field of view). The imaging sequence was optimized for the detection of the blood oxygen level dependent (BOLD) effect including local shimming and 10 s of scanning prior to data collection to allow the MR signal to reach equilibrium. To minimize head motion, bi-temporal pressure pads were employed. The scanner was synchronized with the stimulus presentation of every trial in each session.

2.5 Data processing of fMRI

fMRI data were analyzed using SPM2 (http://www.fil.ion. ucl.ac.uk/spm). The first two images were discarded. Images were corrected for differences in timing of slice acquisition, followed by rigid body motion correction to the median image. The data were realigned and normalized to the standard SPM2 EPI template. The registration of the EPI data to the template was checked for each individual subject. Head movement was less than 2 mm in all cases. The fMRI data were then smoothed with an 8 mm FWHM isotropic Gaussian kernel.

The hemodynamic response was modeled with the canonical hemodynamic response function and its time derivative employed in SPM2. No scaling was implemented for global effects. The resulting time series across each voxel was high-pass filtered with a cut-off of 1/128 Hz to remove section-specific low frequency drifts in the BOLD signal. An auto-regression AR(1) was used to exclude the variance explained by the previous scan. The contrast images for each subject were then used in a random effect analysis to determine what regions were the most consistently activated across subjects using a one-sample *t*-test. The activations reported survived an uncorrected voxel-level intensity threshold of P<0.01 with a minimum cluster size of 10 contiguous voxels.

The functional ROI (spheres with a radius of 12 mm) was defined to best capture the peaks of activation in the group activation map. For each participant, a mean time-course, which represents the average intensity of the ROI, was computed across activated voxels in each ROI. The BOLD response intensity for each scan in each trial was the percent change of the recorded BOLD effect value for this scan relative to the baseline which was the mean value of the recorded BOLD effects of the first two scans and the last two scans of the current trial.

2.6 Results

The mean RT for correct trials and percent of correctness are shown in Figure 3. A two-factor ANOVA (the period length: simple vs. complex; the priming effect: prime vs. target) was also conducted on the behavior data. For RT, the main effects of the period length (F(1, 13)=20.534, P<0.05) and the priming effect (F(1, 13)=31.180, P<0.05) were significant, while the interaction effect between the period length and the priming effect was not significant. For the correctness, the main effect of the period length (F(1,13)=5.029, P < 0.05) and the interaction effect between the period length and the priming effect (F(1, 13)=4.882,P < 0.05) were significant, and the main effect of the priming effect (F(1, 13)=3.460, P=0.086) seemed marginally significant. Pair-wise comparisons revealed that the accuracy gain for the target applied to the complex task only (95.5%) vs. 97.8% for the complex trial, and 98.2% vs. 98.2% for the simple trial). It might be attributed to the ceiling effect of the simple task.

The exploratory analysis of the fMRI BOLD effect mainly shows the activation of the left DLPFC (BA 46) and the left APFC (BA 10) for IP (induction prime) vs. IT (induction target), as shown in Figure 4A. The contrast of SIP vs. SIT activated an extensive neural network, including the left DLPFC, the left APFC, the right prefrontal cortex (PFC), the left parietal cortex and the bilateral occipital cortex, as shown in Figure 4B. The contrast of CIP vs. CIT only shows the activation of the left APFC as shown in Figure 4C.

The functional ROIs of the left DLPFC and the left APFC were defined based on the group activation map. Figure 5 shows the percent change measures for the two functional ROIs: the left DLPFC and the left APFC. For each participant, the values of percent change in BOLD response of each ROI used in statistical analysis were averaged from three scans around the peak, respectively. The mean values of BOLD signal change of the ROI were then used in a two-factor ANOVA. For the left DLPFC, the main effect of the period length (F(1, 13)=9.936, P<0.05), the priming effect (F(1, 13)=5.363, P<0.05), and the interaction effect between the period length and the priming effect (F(1,13)=5.409, P<0.05) were all significant. Pair-wise comparisons reveal that the facilitation for the simple task is larger than that for the complex task. For the left APFC, the main effect of the priming effect (F(1, 13)=31.254, P<0.05) was significant. Although the main effect of the period length and the interaction between the period length and the priming effect did not attain significance, 10 of 14 participants showed more intense facilitation of the priming effect for the complex task than that for the simple task. This effect is reliable, for we observed the same effect when we extended the values of percent change in BOLD response used in ROI statistical analysis from the averaged data of three scans around the peak to five, seven, and nine scans around the peak. Furthermore, binomial test (non-parameter test) showed that the gain for the complex task was larger than that for the simple task, with the probability of 80%. Together, the double dissociation between the left DLPFC and the left APFC can be observed from Figure 6.

3 Discussion

The behavioral performances have revealed the evident priming effect for the number series completion task. fMRI exploratory analyses indicate that the left DLPFC and the left APFC show a reduced activation in IP vs. IT. All of



Figure 3 Behavioral data during the fMRI experiment, including the RT (A) and percent of correctness (B).



Figure 4 Brain localization of the priming effect of the number series completion task. A, Reduced activation for IP vs. IT. The maximum of BOLD response is as follows: MNI coordinate, -48, 30, 26; BA 46. B, Reduced activation for SIP vs. SIT. C, Reduced activation for CIP vs. CIT. The maximum of BOLD response is as follows: MNI coordinate, -40, 40, -6; BA 10. All results survive the thresholds with uncorrected P<0.01 and a minimum cluster size of 10 contiguous voxels. IP, induction prime; IT, induction target.

these facts are consistent with our hypothesis. The experimental design in this study allows us to exclude the facilitation of perceptual processes, arithmetic fact retrieval, and verbal output as sources of potential facilitation in answering the target. Thus, the priming effect in this study, observed from both behavioral performance and BOLD signal, may be attributed to the identification of the underlying regularity and its subsequent extrapolation, the core components of data-driven scientific discovery. Furthermore, the double dissociation found in the priming effect allows us to functionally segregate the roles of the left DLPFC and the left APFC in data-driven scientific discovery.

We observe that the left DLPFC is with more significant priming effect for the simple task, while the left APFC is with more significant priming effect for the complex task, as shown in Figure 4, although we do not find the significant interaction effect between the period length and the priming effect for the RT. ROI analysis as shown in Figure 6 demonstrates this effect. This double dissociation of the left DLPFC and the left APFC in the priming effect may suggest the different neural substrates for the simple and complex task. This is congruent with the different cognitive components involved in the simple and the complex task as aforementioned.

The first question is how to understand the more significant priming effect in the left DLPFC for the simple task than for the complex task, and what the functional role of the left DLPFC is. The percent change of BOLD response in the left DLPFC for the simple and the complex task are both intense, which may suggest the important role of the left DLPFC in data-driven scientific discovery. Compared with the complex task, the simple task does not contain the following components: discovery of periodicity, detection of answer position, and isolation of part of the rule. These components in the complex task may overlap and interact with the other components [10]. The experimental design in this study allows us to exclude the facilitation of perceptual processes, arithmetic fact retrieval, and verbal output as sources of potential facilitation in answering the target. Thus, the role of the left DLPFC in data-driven scientific discovery may be further focused on rule identification, for the simple arithmetic involved in the application of the simple rule in computing the answer (such as 39+3) will not make contributions to the prime effect. This inference is also consistent with many previous studies which have reported the critical role of the left DLPFC in human inductive reasoning, such as monitoring of each processing steps and answer generation [17], recollection of rule knowledge [19], access of world knowledge in the process of hypothesis formation and validation [15,20], and the implementation of control [16].

The second question is how to explain the more significant priming effect in the left APFC for the complex task than the simple task, and what the functional role of the left



Figure 5 BOLD signal change of the left DLPFC (A) is centered at (MNI coordinate: -48, 30, 26; BA 46) and the left APFC (B) is centered at (MNI coordinate: -40, 40, -6; BA 10). The two figures have revealed the double dissociation from the percent change of BOLD responses between the left DLPFC and the left APFC on number series completion tasks.



Figure 6 ROI analysis of the BOLD signal change in the left DLPFC (A) and the left APFC (B), and the facilitation from the percent change of BOLD response for the simple (SIP-SIT) and the complex task (CIP-CIT) in the left DLPFC ROI (C) and the left APFC ROI (D). For each participant, the values of percent change in BOLD response of each ROI used in ROI analysis were averaged from three scans around the peak.

APFC is. The reduced activation of the left APFC in the target task cannot be attributed only to discovery of periodicity, detection of answer position, and isolation of part of the rule, for we also observe the significant priming effect in this area for the simple task. Then, the more evident facilitation of the left APFC for the complex task may be ascribed to mental operations underlying the interaction of the components including discovery of periodicity, detection of answer position, and isolation of part of the rule (as contrast to the complex task, these components are not contained in the simple task) with the other components. Further, consistent with Christoff *et al.* [21] and Sakai *et al.*'s studies [22], we consider the role of the left APFC as mental set maintaining underlying rule identification and extrapolation based on our experimental tasks and results.

The reliable double dissociation between the left DLPFC and the left APFC for the priming effect of the number series completion task helps us to disentangle the different functional roles of the left DLPFC and the left APFC in data-driven scientific discovery. The left DLPFC (BA 46) may play a crucial role in data-driven scientific discovery, and its role is further associated to rule identification, while the left APFC may be related to mental set maintaining required in rule identification and extrapolation. Our inference of the roles of the left DLPFC and the left APFC is also consistent with the three-stage model of the anatomical organization of the left PFC [23,24]. The three-stage model postulates a topographical organization of lateral prefrontal regions, including DLPFC and APFC, according to the level of abstraction in representational content. It is postulated that concrete content representations correspond to posterior prefrontal regions, and representations at an increasing level of abstraction are related to progressively anterior regions.

To our knowledge, this is the first study to explore the neural substrates of data-driven scientific discovery using functional MRI. However, data-driven scientific discovery, which needs to observe and detect the relationship among data, may be a dynamic process implemented by a distributed network that involves closely interacting regions. Hence, we also look forward to future studies that further detail the other complementary brain regions and the interaction among the left DLPFC, the left APFC and these related regions, in order to construct the dynamic spatiotemporal process of data-driven scientific discovery in human brain.

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