

## Hierarchical rule switching in prefrontal cortex

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### ABSTRACT

Most real-world decision-making problems involve consideration of numerous possible actions, and it is often impossible to evaluate all of them before settling on preferred strategy. In such situations, humans might explore actions more efficiently by searching only the most likely subspace of the whole action space. To study how the brain solves such action selection problems, we designed a Multi Feature Sorting Task in which the task rules defining an optimal action have a hierarchical structure and studied concurrent brain activity using it. The task consisted of two kinds of rule switches: a higher-order switch to search for a rule across different subspaces and a lower-order switch to change a rule within the same subspace. The results revealed that the left dorsolateral prefrontal cortex (DLPFC) was more active in the higher-order switching, and the right fronto-polar cortex (FPC) was significantly activated with the lower-order switching. We discuss a possible functional model in the prefrontal cortex where the left DLPFC encodes the hierarchical organization of behaviours and the right FPC maintains and updates multiple behavioural. This interpretation is highly consistent with the previous findings and current theories of hierarchical organization in the prefrontal functional network.

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### Introduction

In the real environment around us, there may be numerous possible behaviours available to us at any point, and it may be impossible to immediately make an appropriate decision by evaluating all of them. To adapt to a dynamic environment, moreover, humans must seek candidate actions efficiently and select the best one within a limited time. Recent studies in the theoretical field suggest that adopting a hierarchical structure of candidate actions seem to exhibit superior performance in action selection and learning (Barto and Mahadevan, 2003; Wiering and Schmidhuber, 1998). In psychology, hierarchy has played a pivotal role in understanding organized, goal-directed behaviour, from early pioneering work (Milner, 1963; Newell and Simon, 1963) through to recent studies (e.g., Botvinick and Plaut, 2004; Schneider and Logan, 2006). From a neuroanatomical point of view, the organization of cortex is strongly hierarchical, and behavioural hierarchies in decision making has been proposed to be implemented within the prefrontal cortex (Badre, 2008; Botvinick, 2008; Koechlin et al., 2003; Wood and Grafman, 2003). Recently, theoretical studies have suggested that a hierarchical method derived from computational theory (i.e., hierarchical reinforcement learning) might be implemented by human prefrontal cortex (Botvinick, 2008; Hazy et al., 2007); however, it remains

unclear whether and how such a hierarchical mechanism might operate in the brain.

Humans often select actions according to some sort of decision rule; he/she should consider switching between rules in response to environmental changes. The Wisconsin Card Sorting Task (WCST) (Grant and Berg, 1948) is one of the best-known tasks for studying such a rule switching process. In the WCST, the subject is required to discover a hidden correct rule from many possible rules using true/false feedback given correspondingly to the selected rule. Since the correct rule often changes without notice, the subject should try a new rule if he/she receives a false feedback. Many imaging and lesion studies have shown that prefrontal cortex is closely involved in solving WCST (Berman et al., 1995; Goldberg et al., 1998; Hampshire and Owen, 2006; Konishi et al., 1998; Konishi et al., 2002; Lie et al., 2006; Monchi et al., 2001; Wang et al., 2001). However, although all of these tasks involved rule switch processes, different regions of the prefrontal cortex were reported as being engaged in rule switch functions and functional segregation of these regions has yet to be clarified.

To identify brain regions involved in a hierarchical rule searching mechanism, in this study, we designed a Multi Feature Sorting Task whereby behavioural decision rules have a hierarchical structure. The rules in our task could be categorized into two levels: high level meta-rules and low level standard rules. Accordingly, this produces two kinds of rule switches: a higher-order meta-rule switch which changes a meta-rule to search for a rule belonging to the other meta-rule class and a lower-order rule switch to change rules within

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the same meta-rule class. Based on neuropsychological and neurophysiological findings, recent studies have suggested that the neural mechanisms underlying the production of hierarchically organized behaviour resides, at least in part, within the prefrontal cortex (Badre, 2008; Botvinick, 2008). Koechlin and Hyafil (2007) showed that the PFC not only represents nested levels of behavioural rules but also allows switching among multiple independent hierarchies. We assume that the dorsolateral prefrontal cortex and the fronto-polar cortex, in which the activations are observed in several decision-making tasks that involve hierarchical switching (Daw et al., 2005; Koechlin and Jubault, 2006; Strange et al., 2001; Thompson-Schill et al., 2005), are involved in levels of switching in hierarchically structured behavioural rules. Using this newly devised task, we conducted an fMRI experiment which showed that the different cortical brain regions were activated during higher- and lower-order rule switching. Our results suggest that different regions in the prefrontal cortex may cooperate to solve complicated decision making in an efficient manner.

**Materials and methods**

*Subjects*

Sixteen healthy subjects (12 males and 4 females) participated, having given written informed consent. The study was approved by the ethical committee of Advanced Telecommunications Research Institute International (ATR-I), Japan. Each subject was paid a fixed monetary reward regardless of task performance. To acquire proficiency in the task, on the day before scanning, all subjects were given verbal and written explanations of the aim and procedures of the behavioural tasks and practiced a training task, which is identical to the scanning task, outside of the MRI scanner.

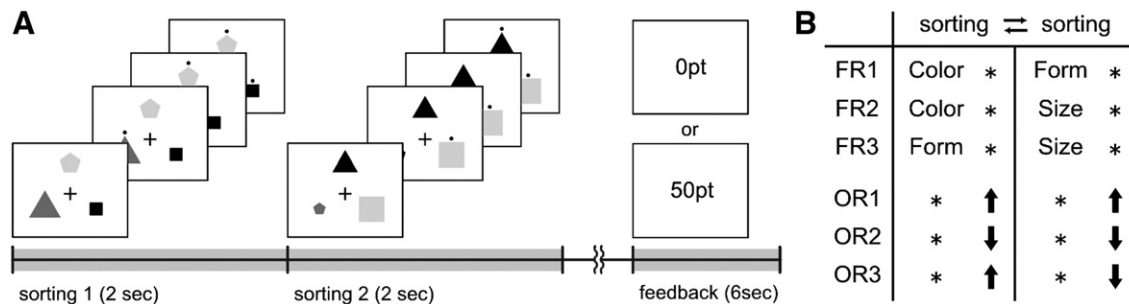
*Experimental task*

We designed a Multi Feature Sorting Task in which the subject was required to sort three figures according to their features, and this was repeated twice in a given trial. The task was displayed on a computer screen, and the sorting was performed by pressing buttons with his/her right hand (Fig. 1A). Each figure had three cardinal features; ‘form (number of vertices: triangle, square, or pentagon)’, ‘size (small, medium, or large)’ and ‘colour/brightness (light, medium, or dark green)’. Thus on each of these features, each figure could be categorized as ‘large’, ‘middle’ or ‘small’. Each figure never shared any feature with either of the other two figures on each presentation;

i.e., for example, there was only ever one triangle, and only ever one large figure. Thus, a set of three figures can be sorted in either two ways, ‘ascending order’ or ‘descending order’, with respect to each of the three features; such that there are six possible sorting ways for each set of three figures. After the first sorting, another set of figures were displayed for the second sorting, and the subjects were required to sort them in the same or different way. Thus, there are 36 possible pairs of options in each trial.

The goal of the task was to correctly sort the figures according to a particular rule among six rules, which are defined based on the combination of the pair of sorting options (see Fig. 1B). Since the abstract rule was defined based not on features, sorting options or orders of two sorting options but only on their combination, the correspondence between rules and pairs of sorting options is not one-to-one but one-to-many. For example, a rule might be ‘sort the figures once according to form, and once according to size’ or, alternatively, ‘sort the figures once in an ascending order of any feature, and once in a descending order of any feature’. The six rules are illustrated in Fig. 1B. The rules were categorized into two meta-rules; in summary, the subject’s behaviour of each trial is one of 36 sorting pairs, which is categorized in one of six rules, which is categorized in one of two meta-rules, so as to give a hierarchical structure for the sorting rules. One meta-rule was a ‘feature meta-rule’ which focuses only on the combination of features in the two sorting options and not on sorting orders. The other meta-rule was an ‘order meta-rule’ which focused only on the combination of orders in the sorting options regardless of features. Thus, each rule never required the combination of a feature sorting and an order sorting within a trial. Each meta-rule has the same number of rules (three rules each), while the numbers of sorting pairs belonging to each rule vary from three to eight. Namely, order meta-rules have three or six sorting pairs; a meta-rule with a pair of ascending and descending orders (OR3 in Fig. 1B) has six sorting pairs because there are three features and two ways of order (sort in ascending order first and then descending order and the opposite way) and the other meta-rules have three sorting pairs (OR1 and OR2). All of feature meta-rules (FR1, 2, and 3) have eight sorting pairs because the feature in the order meta-rule was required to be the same for two sorting options. However, all subjects showed a pronounced tendency to use only 1 or 2 preferred sorting option pair(s) within each rule, and thus the behavioural variation (entropy) of used sorting pairs did not significantly depend on the number of option pairs in each rules.

For each trial, a hidden correct rule was selected by the computer from the six rules, and feedback was displayed after the subject finished a pair of two sorting options. In real life, it is often difficult to



**Fig. 1.** Experimental design. (A) Each single trial contained two sorting behaviours. At the beginning of a trial, three figures and a fixation cross were displayed (2 s), and the subjects sorted the three figures by pushing the corresponding three buttons one by one (sorting 1), after which three figures of the next set were displayed (2 s) to sort once again (sorting 2). With the button pressing, a circle above the corresponding figure was displayed so that the subjects could confirm their sorting actions. After a short delay (0–4 s), a positive (50 pt) or a negative (0 pt) feedback was displayed (6 s) based probabilistically on whether the rule used for sorting the two sets was correct or not. Each figure has three features (form, size and colour), and each feature has three levels. Thus, there are six options for each sorting in total. For example, the option selected by the subject in sorting 1 in panel A could be identified from the subject’s behaviours indicated by circles as ‘descending order of size’, i.e., the sorting order is large, middle and small size figures. (B) For each trial, the sorting rule, which was the criterion of feedback, was defined based on the combination of the used pair of sorting options. There were six abstract rules, and they were categorized into two meta-rules; a ‘feature meta-rule’ (FR) and an ‘order meta-rule’ (OR), each of which includes three sorting rules. Asterisks denote the acceptance of any features or orders (wild cards). For example, FR1 requires that the features used in two sorting behaviours are colour and form, or the opposite but allows either of the descending and ascending orders in each of the two options.

decide optimal action for sure due to the ambiguity and uncertainty inherent in environmental signals. To reflect this environmental realism and focus on self-generated switching by evaluating the value of actions bit-by-bit using past experiences, we use probabilistic reward and rule transitions. For the feedback, when the subject's rule was same as the correct one, the subject received positive feedback (50 points) with 90% probability but negative feedback (0 points) with 10% probability, while if they were incorrect, they received negative feedback with 90% probability but positive feedback with 10% probability. When the used rule agreed with the correct one on three successive trials, even if the positive feedback was not given in those trials, the correct rule was changed to another one, unbeknownst to the subject. The new rule was selected with a higher probability (70%) from the same meta-rule class (called rule change) than from the other meta-rule class (called meta-rule change). Although the subjects did not know the detail of the settings, which are both the probability of feedback and the changing frequency of correct rules, they were informed that the feedback would be probabilistic and the frequencies between rule and meta-rule change would be different. They were trained to perform the task well beforehand, such that they had ample opportunity to learn the hierarchical rule structure.

Each single trial contains two sorting procedures, each of which lasted 2 s. If the subject successfully finished two sortings within this period, a positive or negative feedback was displayed for 6 s after a short delay. The feedback delay was set between 0 and 4 s at random; thus, each trial took between 10 and 14 s. The scanning experiment was composed of three contiguous sessions separated by brief interval. Each session consisted of the first main task (45 trials), a control task (5 trials) and the second main task block (45 trials). Thus, each subject performed six task blocks in total. In the control task, the basic experimental procedure was the same as the main sorting task, but the correct rule was instructed as a visual message at the beginning and fixed during all trials, and the subjects thus did not need to select a rule by themselves.

#### *Behavioural model and simulation procedure*

To investigate whether the subjects performed the task based on a hierarchical searching strategy that incorporated the hidden rules, we proposed a simple behavioural model and assessed its ability to reproduce the behaviour on a subject-by-subject basis.

At the  $t$ th trial in this task, the subject selected a rule  $R_t$  based on the history of rules estimated and used in the past,  $R_{1:t-1}$ , and the corresponding feedback,  $FB_{1:t-1}$ . Since the feedback information was probabilistic, it did not allow the subject to fully identify the correct rule after each trial. Thus, we assumed that the subjects, after having been given a feedback stimulus, evaluated whether their used rule had been correct or not and then predicted the correct rule on the subsequent trial. Corresponding to the ambiguity in the feedback, we assumed that the subjects estimated the correctness of their used rules in a probabilistic manner; this process was modelled as a probabilistic generative model (likelihood). When the used rule agreed with the correct rule, the probability that positive feedback was given was  $\beta$  and negative feedback was  $1 - \beta$ . When the used rule disagreed with the correct rule, on the other hand, the positive feedback probability was  $1 - \beta$  and the negative feedback was  $\beta$ . Based on the estimation of a correct rule and the given feedback, the subjects would predict whether the correct rule should change or not. Since the subjects were instructed that the correct rule was not changed until they had found it successfully, in the case of negative feedback ( $FB_t = 0$ ), they were assumed to predict the correct current rule to remain as previous  $R_{t+1} = R_t$ . In the case of positive feedback  $FB_t = 1$ , in contrast, it was assumed that the subjects expected that the correct rule might be changed probabilistically: meta-rule change with probability  $\alpha_m$ , rule change with  $\alpha_r$  or no rule change with  $(1 - \alpha_m - \alpha_r)$ .

According to the Bayes rule, the probability for selecting each rule  $R$  was calculated as the probability for being a new correct rule at the next trial, i.e., the prediction using the previous information consisting of used rules and given feedback.

$$P(R_{t+1} | FB_{1:t}, R_{1:t}) \propto \sum_{R_t} P(R_{t+1} | R_t, FB_t) P(FB_t | R_t) P(R_t | FB_{1:t-1}, R_{1:t-1})$$

Considering the hierarchical structure of rules, subjects ought to give priority to the rules within the current meta-rule class. When the subject switched to the other meta-rule class, the probabilities of the rules being included in the new meta-rule class were equal because there was no information to prioritize those rules. These factors were modelled as  $P(R_{t+1} | R_t, FB_t)$ . The three parameters of our simulation model,  $\beta$ ,  $\alpha_m$  and  $\alpha_r$ , were determined so as to maximize the 'marginal likelihood' (MacKay, 2003),  $P(R_{1:T}) = \prod_t P(R_t | R_{1:t-1})$ , which represents the reproducibility of the sequence of rules selected by the subject,  $R_{1:T}$ , where  $T$  is the number of trials in the block.

We assumed that the subjects would select the most likely rule in this prediction: the rule whose probability was maximum among all rules would be selected, defined as the rule prediction by the model. At each trial, we examined whether or not the rule selected by the subject agreed with the prediction one and then calculated the action reproduction accuracy of our model as the rate of successful prediction. When there were multiple rules whose probabilities were equally maximal, the prediction was regarded as correct when the selected rule agreed with any of the predicted ones.

#### *Imaging data and analysis*

Functional images were obtained with T2\*-weighted EPIs with BOLD contrast (TE: 48 ms; FA: 80°) using a 1.5-T scanner (Magnetic Eclipse; Shimadzu Marconi, Kyoto, Japan). The volumes were acquired every 2 s (TR) and contained 20 slices each of 5-mm thickness (matrix size: 64 × 64; FOV: 192 × 192 mm), synchronized with stimulus presentation. The first six (12-s) EPIs in each session were removed from scanning data to avoid T1 equilibrium effects. Each scanning run began with a T1-weighted anatomical image acquisition (voxel size: 1 mm<sup>3</sup>).

The imaging data were analyzed with SPM5 (Wellcome Trust Centre for Neuroimaging, UCL, London, UK) in a standard manner. Briefly, all functional images from each subject were realigned to the first image as a reference, coregistered to the individual anatomical image and normalized into a standard template (Montreal Neurological Institute) and spatially smoothed with a Gaussian kernel (FWHM: 10 mm). For each subject, the data were high-pass filtered using a low-frequency cosine function with a cutoff time of 60 s and modelled as the weighted sum of regressors corresponding to the effects of interest. To identify neural activities involved in switching behaviours, we defined three kinds of event at the onset of feedback in the previous trial according to the subject's behaviour in that trial. The first was 'rule switch', in which a subject used a different rule within the same meta-rule class as the previous one. The second was 'meta-rule switch', in which a subject tried a new sorting rule whose meta-rule class was different from the previous one. The third was 'exploitation', in which a subject used the same rule as in the previous trial. In addition, to control for motor-related activity, another event at the onset of sorting (stimulus presentation) was created. For the sorting and control tasks, sustained activity was modelled as an epoch using a boxcar function covering the whole block consisting of 45 and 5 trials, respectively. The events were orthogonalised by the Gram-Schmidt method to remove inter-event correlations: the rule switch event was orthogonalised to the sorting boxcar function first. All events and epochs were convolved with the canonical hemodynamic response function.

Accordingly, we conducted an event-related analysis utilizing the rule switch, meta-rule switch, and exploitation events on the whole

brain. The parameters, the coefficients of the regressors, for the best fitting model were found for each subject and then subjected to a group random effects analysis; for each voxel in the brain, single-sample *t* tests were used to determine whether the contrast of parameter estimates between conditions (e.g., rule and meta-rule switch) was significantly different from zero. For the second analysis, we applied statistical thresholds at the voxel level of  $p < 0.001$  (uncorrected) and at the cluster level of  $p < 0.05$  (corrected). To see how the activation within a particular brain area changed with time, we also conducted a time-course analysis of regions using activations from previous SPM group analyses and an anatomically defined area. The activation level for each region was represented as the percent signal change at the peak voxel within the region.

## Results

### Behavioural results

Performance on the task did not differ among the six sorting blocks: the ratio of missed trials, where the subjects did not finish three button-pressing actions within the allotted time,  $3.36 \pm 1.53\%$ , and the mean reaction time (RTs),  $728.6 \pm 10.9$  ms, did not change across sessions. This lack of a learning effect is in keeping with the fact that subjects were trained to perform the task well before scanning, and subsequent imaging and behavioural analyses considered all blocks together.

Since the rule change in the task was dependent on the subject's performance, the number of rule changes varied among subjects: the mean was  $40 \pm 5$ , in which the meta-rule change ( $13 \pm 2$ ) occurred less frequently than the rule change ( $27 \pm 3$ ). Fig. 2 shows a typical example of a behavioural profile during a block including two meta-rule and five rule changes.

Each trial consisted of a pair of sortings, any of which can be uniquely defined as a rule. Following positive feedback, subjects typically kept choosing the same rule (exploitation), and the probability of such exploitation, averaged over all subjects, was  $95.1 \pm 3.8\%$  (Fig. 3A). In contrast, following negative feedback, the subject typically switched to try another rule. In this situation, as expected, the subject tended to exhaustively explore all rules within the same meta-rule class as the previous rule (rule search) before switching to search the rules of the other meta-rule class. Specifically, most meta-rule switches ( $71.6 \pm 19.6\%$ ) occurred after exploring *all* rules within the previous meta-rule class, and very few ( $3.8 \pm 6.5\%$ ) occurred with none. We also confirmed that the behavioural strategy shifted sequentially from exploration, to rule search, and then to meta-rule

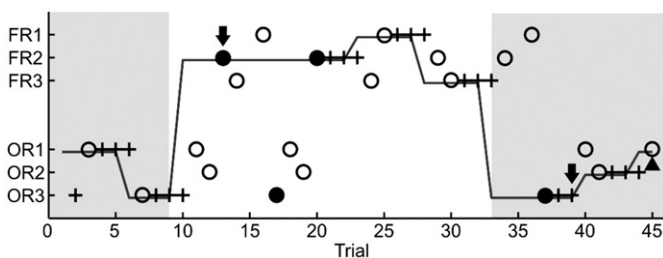
search following successive negative feedback (Fig. 3B). These results support the hypothesis that the subjects employed a hierarchical exploration strategy for the correct rule using two switching behaviours, the rule and meta-rule switches.

For each trial, we analyzed the RTs of the six actions from the two sorting procedures (each of which involved three button-press actions). A statistical *t*-test analyzing the RTs demonstrated that the first action (727.8 and 683.2 ms) took significantly longer time than the second (248.3 and 247.3 ms) and third actions (241.0 and 238.0 ms) in both the first and second sorting decisions ( $p < 10^{-5}$  for all). This suggests that subjects may have decided on their sorting procedure following the first presentation of each set of figures. The RTs of first action did not show any statistically significant difference, however, between the first and second sorting ( $t = 1.554$ ,  $p = 0.131$ ). In addition, in the first sorting, there was no significant evidence that the RT was shorter in the no-switching trials (exploitation) (727.8 ms) than in the switching trials (728.2 ms) ( $t = 0.013$ ,  $p = 0.990$ ), even though the switching operations might require additional neural processing (Wylie and Allport, 2000) in general. Furthermore, there was no significant difference in the RTs between the meta-rule switch (759.4 ms) and rule switch trials (719.4 ms) ( $t = 1.307$ ,  $p = 0.202$ ). These results suggest that the time interval from the feedback in the previous trial to the first stimulus presentation (6 s) was sufficient for the subjects to determine their sorting rule, including both rule and meta-rule switching, and suggests that switching-related brain activity may be observed during this period.

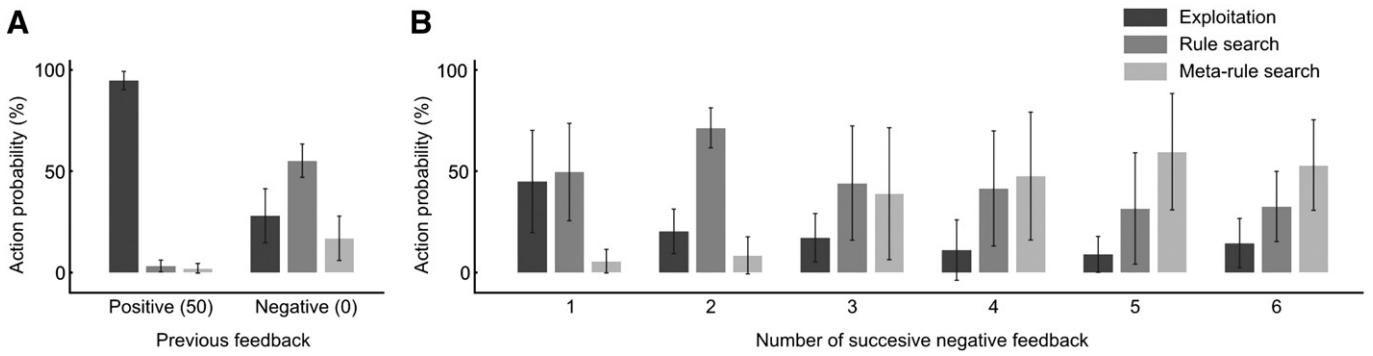
To quantitatively examine the hypothesis that the subjects searched for the correct rule in consideration of the hierarchical structure of rules in the task, we modelled the subjects' behaviours as a probabilistic model and estimated the three model parameters  $\beta$ ,  $\alpha_m$  and  $\alpha_r$ , which correspond to the probabilities that the true feedback was given, meta-rule change occurred after a positive feedback and rule change after a positive feedback, respectively (see Methods). According to the maximum likelihood estimation for each block, the feedback probability ( $\beta$ ) was estimated as  $92.0 \pm 7.2\%$ , which was close to the actual value of 90%. Furthermore, the estimated rule change probability was larger than that of meta-rule change,  $\alpha_r > \alpha_m$  ( $67.8 \pm 16.6\% > 13.6 \pm 9.1\%$ ), for all 96 blocks. These results suggest that the subjects proficiently estimated the detailed but hidden probabilistic structure of the task and efficiently searched for rules in a hierarchical manner. In addition, by inserting the estimated parameters back into the model, we were able to reproduce the subjects' selected rules with  $81.5 \pm 5.6\%$  accuracy. This reproduction accuracy was substantially higher than the chance level, 25%, which corresponds to the case that the subjects randomly selected any one of three rules within the same meta-rule class or any rule within the other meta-rule class at each trial, suggesting that the subject processing model we assumed was substantially reliable, whose parameters estimated by the maximum likelihood criterion on a subject-by-subject basis could incorporate somehow different information processing between the subjects.

### Imaging results

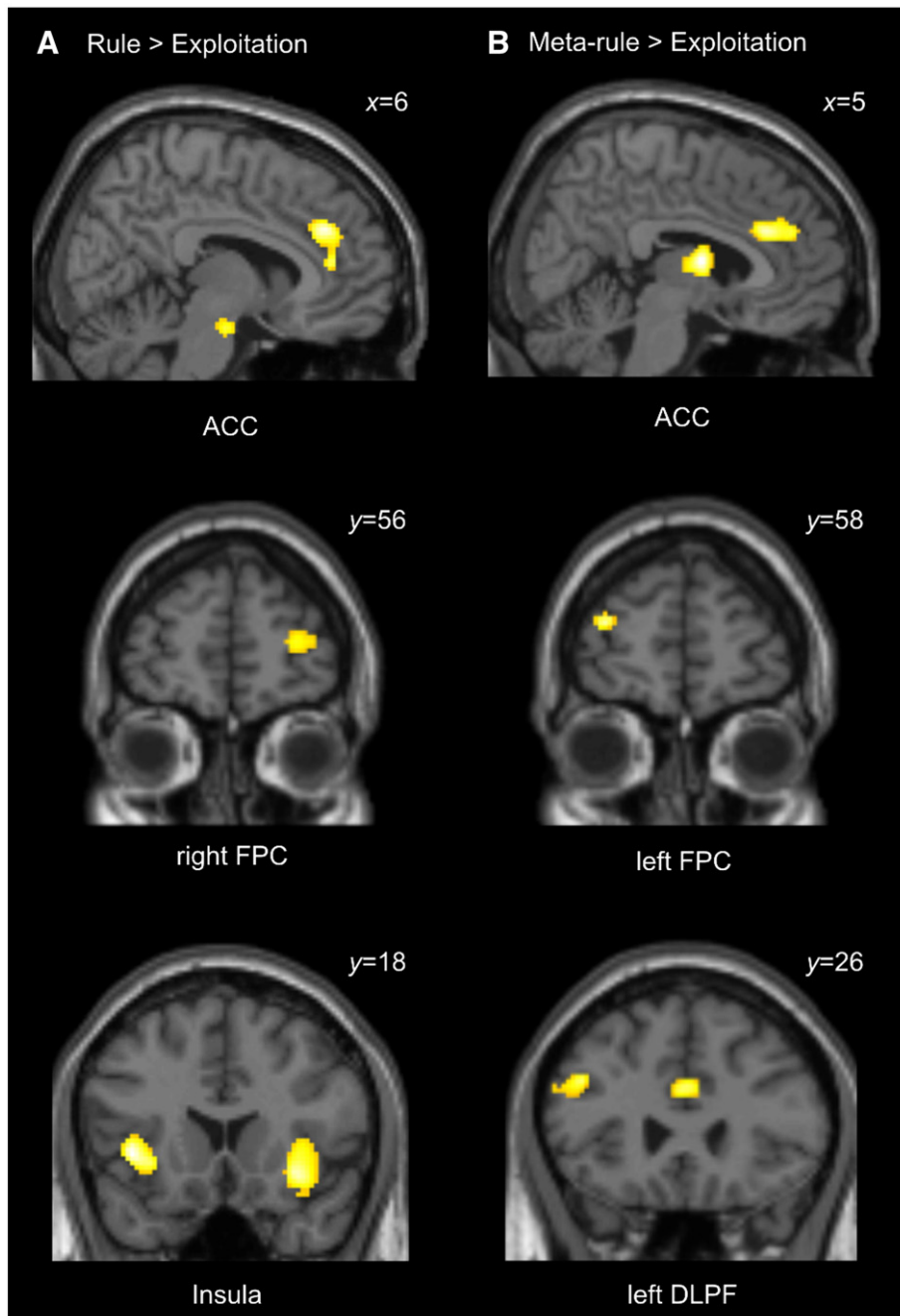
We first investigated areas significantly activated with the two different kinds of rule switch in comparison to the exploitation condition. While the switch trials almost always occurred after negative feedback, the exploitation trials also follow negative feedback sometimes ( $26.6 \pm 15.3\%$ ) because of the probabilistic feedback. To identify brain activity correlate with rule switch which is not affected by feedback type, we compared the switch trials and the exploitation trials only after negative feedback (Fig. 4, and the statistics are also summarized in Table 1). In the rule switch condition, the group analysis showed significant activation in anterior cingulate cortex (ACC), the right fronto-polar cortex (FPC) on the middle frontal gyrus (BA10) and bilateral insula. On the other hand, we observed



**Fig. 2.** An example of a subject's behaviour profile in a sorting task block, where the abscissa denotes the number of trials. The line denotes the transition of correct rules and the cross denotes the subject's used rule in each trial, either of meta-rule switch (MSW, closed circle), rule switch (RSW, open circle) or exploitation (EXP, cross). Triangles indicate the trials in which the subject received feedback stimuli contradictory to the used rule due to the probabilistic nature of feedback stimuli. The gray and white backgrounds show the periods when the correct rule is in order and feature meta-rule classes, respectively. When the meta-rule change occurred at the 10th trial, the subject first explored all rules within order meta-rule class and then switched to feature meta-rule class. Opposite-directional behaviours were also observed after the 33rd trial.



**Fig. 3.** Action selection probabilities of three kinds of behaviors; exploitation, rule search and meta-rule search. The means and standard deviations (error bars) of the subjects after a positive (50 pt) and negative (0 pt) feedback (A) and after one to six negative feedbacks in a row (B).



**Fig. 4.** Significantly activated areas related to rule switch vs. exploitation (A) and meta-rule switch vs. exploitation (B) after negative feedback.

**Table 1**

Maximally activated voxels in areas exhibiting significant activity in rule switch and meta-rule switch than exploitation.

|   | Talairach axis |    |     |     |     |         |     |
|---|----------------|----|-----|-----|-----|---------|-----|
|   | R/L            | BA | x   | y   | z   | Z-value | k   |
| <b>Rule switch&gt;exploitation</b>      |                |    |     |     |     |         |     |
| Insula                                  | L              | 21 | -40 | 16  | -1  | 3.88    | 207 |
| Anterior cingulate                      | R              | 24 | 6   | 38  | 26  | 3.84    | 296 |
| Insula                                  | R              | 21 | 32  | 19  | -8  | 3.65    | 374 |
| Middle frontal gyrus                    | R              | 10 | 30  | 55  | 6   | 3.06    | 332 |
| Mediodorsal thalamic nucleus            | -              | -  | -12 | -14 | -11 | 3.59    | 424 |
| <b>Meta-rule switch&gt;exploitation</b> |                |    |     |     |     |         |     |
| Substantia nigra                        | -              | 7  | 6   | -1  | 9   | 3.88    | 313 |
| Anterior cingulate                      | -              | 24 | 0   | 28  | 24  | 3.73    | 347 |
| Middle frontal gyrus                    | L              | 10 | -32 | 57  | 12  | 3.54    | 147 |
| Inferior frontal gyrus                  | L              | 46 | -53 | 32  | 21  | 3.42    | 141 |

similar activation patterns but on the left cortical hemisphere in the meta-rule switch condition: ACC, the left middle frontal gyrus (FPC, BA10) and the left dorsolateral prefrontal cortex (DLPFC, BA46). We also observed the activations of some nuclei in the basal ganglia and the thalamus for both switch conditions.

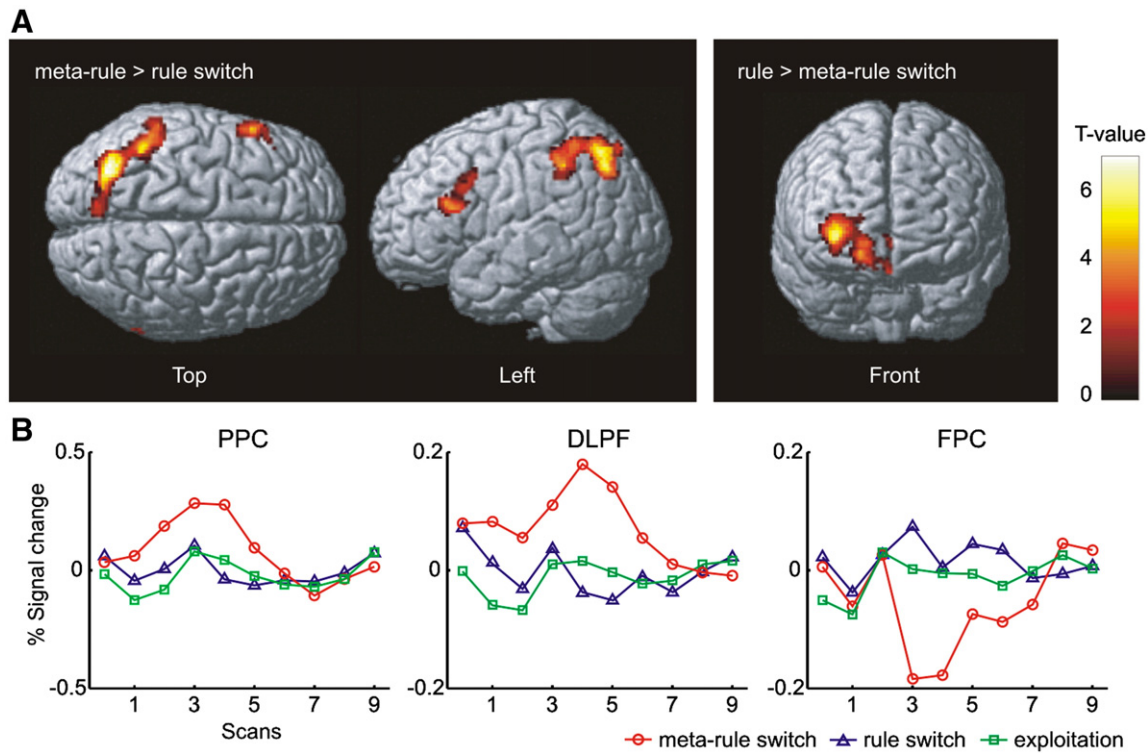
To clarify which of these activated areas is specifically related to each of switching functions, we next compared brain images between the rule and meta-rule switch trials (Fig. 5A with the related statistics summarized in Table 2). In the rule switch condition, we observed correlated activity only in the right middle frontal gyrus in FPC (BA10), while in the meta-rule switch condition, the significant areas were in the left posterior parietal cortex (PPC) on the superior parietal lobe (BA7) and the left dorsolateral prefrontal cortex (DLPFC) on the inferior frontal gyrus (BA45) and middle frontal gyrus (BA46). Here we showed the results of analysis with both positive and negative feedback trials; however, the

**Table 2**

Maximally activated voxels in areas where significant evoked activity was related to two switch events.

|  | Talairach axis |       |     |     |    |         |      |
|--|----------------|-------|-----|-----|----|---------|------|
|  | R/L            | BA    | x   | y   | z  | Z-value | k    |
| <b>Rule switch&gt;meta-rule switch</b> |                |       |     |     |    |         |      |
| Middle frontal gyrus                   | R              | 10    | 34  | 56  | 3  | 3.43    | 241  |
| <b>Meta-rule switch&gt;rule switch</b> |                |       |     |     |    |         |      |
| Superior parietal lobule               | L              | 7/19  | -32 | -64 | 40 | 4.70    | 1306 |
| Posterior cingulate                    | -              | 23/31 | -6  | -32 | -4 | 4.02    | 418  |
| Inferior/middle frontal gyrus          | L              | 45/46 | -54 | 20  | 16 | 3.94    | 307  |

analysis limited to only negative feedback trials did not alter the results significantly. To compare the temporal changes of signal intensities after feedback presentation which is the trigger of the rule switching, we applied a time-course analysis to each of these four areas (Fig. 5B). In the meta-rule switch trials, the left PPC showed a salient activation peak but not in the rule switch and exploitation trials. In the left DLPFC, although the overall activation level was higher in the meta-rule switch trials than in the rule switch and exploitation trials, the time courses resembled each other in all three conditions. The right FPC, the activated area with the rule switch condition, showed significant activations but no distinct peak or rather the activity decreased in the meta-rule switch condition. To test the possibility that this deactivation is mainly comprised by the medial FPC—an area previously shown to active in the ‘default-mode’ processing (or the ‘default-mode’ network) (Gustard and Raichle, 2001), we divided the right FPC into two regions – the lateral and the medial part – and calculated the signal time courses separately. We found the deactivation starts faster and stays longer in the medial part, although there was no overall significant difference ( $p=0.92$ , data not shown).



**Fig. 5.** (A) Significantly activated areas related to meta-rule switch vs. rule switch (left), rule switch vs. meta-rule switch (right). (B) Time courses of BOLD responses in the three activated areas in panel A; the left posterior parietal cortex (PPC) and dorsolateral prefrontal cortex (DLPFC) with the meta-rule switch, and the fronto-polar cortex (FPC) with the rule switch, related to three conditions: the meta-rule switch (red), the rule switch (blue) and the exploitation (green). The ordinate and abscissa denote the BOLD signal changing rate and the scan number (2 s per each scan) elapsed since the feedback presentation in the previous trial, respectively.

## Discussion

The behavioural results show that humans can accurately learn and represent the probabilistic architecture of the environment and use it to guide decisions. The imaging results show that distributed regions of prefrontal cortex could be involved in such processing. Critically, we show that dissociable regions of prefrontal cortex are engaged in decisions at different levels of the decision structure, suggesting that different hierarchical levels of an internal model of the environment are encoded in an anatomically distributed manner.

### Rule switch

In the task, subjects decided whether or not to switch sorting rule based on feedback relating to the previously applied sorting rule. Because there was a hierarchical structure to the rules, an appropriate exploration strategy for a new rule is also hierarchical, consisting of either a switch *within* the same class of rules; a (lower-order) rule switch, or of a switch to a different *class* of rules; and a (higher-order) meta-rule switch. The ACC was the only brain region to be activated for both types of rule switch.

The ACC has been considered to be related to error detection (Braver et al., 2001; Rushworth and Behrens, 2008) and response conflict (Botvinick et al., 1999; Carter et al., 1998) and activated with voluntary switching of behavioural rules based on monitoring of self-generated actions in both human (Bush et al., 2002) and monkey studies (Shima and Tanji, 1998). Although the switch behaviour follows negative feedback in general, the ACC activity has been observed with either negative or positive stimuli (Knutson et al., 2001; Shidara and Richmond, 2002) and it is suggested that this area monitors whether the given information induces immediate behavioural changes regardless of the value (Ullsperger and von Cramon, 2004). In our task, the subjects perceived the feedback with some degree of uncertainty because it was given probabilistically, and thus they sometimes did not switch the rule after a negative feedback. The probabilistic nature of reward allowed us directly to compare brain activation induced by rule switch but not by feedback type unlike previous studies in which the control is non-switch trials after positive feedback. Our results show the ACC activity with two types of rule switch consistently and suggest that this area monitors response conflict to adjust a behavioural rule appropriately both within and over a category.

### Higher-order meta-rule switch

In the higher-order 'meta-rule switch' compared with the lower-order 'rule switch' condition, we observed increased activation in the left DLPFC and the left PPC.

The DLPFC has been shown to be active when negative feedback is given in rule switching tasks (Konishi et al., 2002; Monchi et al., 2001), considered to be related with cognitive functions; for instance, attention allocation (MacDonald and Joordens, 2000), response competition (Bunge et al., 2002; Rowe et al., 2000) and suppression of irrelevant information (Dreher and Berman, 2002; Swainson et al., 2003). Especially this region on the left hemisphere has been also known as a pivotal area in the retrieval process for episodic memory from patient (Burgess and Shallice, 1996; Milner, 1963; Moscovitch and Melo, 1997) and imaging studies (Dobbins et al., 2002; Lepage et al., 2003; Rugg and Wilding, 2000), the left inferior frontal gyrus has been also known as a pivotal area in the retrieval process for episodic memory. Dobbins and his colleagues studied the dissociation of cognitive functions involved in episodic memory and showed that the activated region in our task is also related to the strategic control of source memory when a cue does not directly specify the requisite representation. As the meta-rules in our task can involve intensive representations of lower-order rules, restricting the search space

based on meta-rule switches may exploit the strategic control for episodic memory, i.e., contextual information, and our result is consistent with the theory that this region manipulates aggregated information.

The other activation area, the PPC, has long been studied primarily in relation to attention, and recent imaging studies have revealed that this area is activated during switching tasks (Dove et al., 2000; Kimberg et al., 2000; Sohn et al., 2000). Such activation was also reported during switching between different modalities, namely motion and location, of visual stimuli (Liston et al., 2006), and suggested to be involved in shifting attentional set (Yeung and Cohen, 2006). In our task, only the left PPC activation was stronger in the meta-rule switch than in the rule switch condition.

The left posterior prefrontal region has been known to be associated with human language (Martin, 2003), especially for the processing of sentences requiring a hierarchical reordering of the arguments due to a non-canonical surface structure or due to embedded structure (Kaan and Swaab, 2002; Musso et al., 2003; Roder et al., 2002). Although this area plays a pivotal role in unification within the domain of language, this does not mean that it is a language-specific area and the activity has also been found during action recognition (Decety et al., 1997; Hamzei et al., 2003) and movement preparation (Thoenissen et al., 2002). Recent imaging experiment (Koechlin and Jubault, 2006) have observed the activity increase of this area in hierarchically structured action plan task. In this task, there is 'simple chunks' consisting of pre-learned sequential actions and 'superordinate chunks' composed of simple action chunks. Their results showed a clear posterior–anterior gradient in the left prefrontal cortex; the posterior part activates during boundaries between simple chunks and the anterior part activates between superordinate chunks. This is consistent with a monkey study which showed 'higher-order' category information is encoded in prefrontal neurons (Shima et al., 2007). The meta-rule in our task has a superordinate structure of the abstract rules and our results support the hypothesis that this brain region is involved in a specialized executive system for the hierarchical organization in multiple domains of human cognition (Thompson-Schill et al., 2005) including goal-directed decision making.

Time course analysis of significantly activated regions indicated that the timing of activation was different between the DLPFC and PPC (Fig. 5). The peak activity in the PPC occurred 6 s (3 scans) after the feedback presentation, followed by the DLPFC peak activation with a 2-s delay. These results are consistent with a result of the WCST task in which the DLPFC showed a prominent increase 7 s after the switching cue (Konishi et al., 1998) and with the present knowledge that sensory inputs are integrated in the PPC and then delivered to the DLPFC to allow decisions of appropriate behaviours. As a speculative interpretation, after a negative feedback is given, the subject shifts attentional set in the PPC and then loads superordinate chunks of rule candidates in working memory in the DLPFC.

### Lower-order rule switch

In the rule switch condition, only the right FPC (BA10) was significantly activated. A previous study using a categorization task suggested that the right FPC was involved in seeking of hidden correct rule by trial and error (Strange et al., 2001), while this region was not activated when subjects sought a correct rule in WCST (Konishi et al., 1998; Monchi et al., 2001). Although subjects in both of these tasks had to switch rules after a given unfavourable feedback, the operation required for selecting the next rule was different between these tasks. In the categorization task, since each stimulus could be compatible with multiple rules, the subject could eliminate not only the used rule but also several other rules. In the WCST, in contrast, since the feedback was dependent only on the used rule, the subject removed only that from the candidates. This difference implies that the some

additional operation on possible rule candidates is allowable in the categorization task, but not in the WCST.

While these tasks used deterministic feedback, feedback in our task was given probabilistically. The common feature of the categorization task (Strange et al., 2001) and our task, in both of which BA10 activated, is that two or more rule candidates should be handled in response to a given feedback due to the vague nature of given feedback. In the rule switch trials of our task, likelihoods of rules were updated so that the probability of the attempted rule (which was maximum in the previous trial) was decreased and that of the others within the same meta-rule class was increased. In the meta-rule condition, on the other hand, as feedback for the used rule did not yield any information of rule candidates belonging to the other meta-rule class, the subjects just had to choose one of them arbitrarily. Thus, we suggest that the FPC may be involved in updating the likelihoods of multiple candidates (entropy maintenance) so as to redefine the rules' priorities. This hypothesis is highly consistent with recent imaging studies which showed the FPC is activated when subjects are exploring a hidden optimal option with simultaneous tracking of multiple putative options (Daw et al., 2006; Yoshida and Ishii, 2006).

From the time-course analysis, we found the right FPC deactivation in the meta-rule switch condition (Fig. 5B), while the left lateral FPC showed significant positive activity (Fig. 4B). Recent study showed that the FPC activity is positively correlated with evidence of unchosen actions and negatively correlated with evidence of chosen actions (Boorman et al., 2009). In our task, the subjects were required to track two evidences calculated with different time scale; one for meta-rules and one for rules, and at the time of meta-rule switch, the evidence of unchosen meta-rule was increased and the evidence of unchosen rules in the chosen meta-rule was decreased. The functional laterality of the FPC is currently an area of fervent interest (Braver et al., 2003; Yeung et al., 2006; Konishi et al., 2002), which, however, remains to be fully clarified. Our results suggest that the right and left lateral FPC might encode short-term and long-term evidences of unchosen rules, respectively.

### Concluding remarks

We designed a Multi Feature Sorting Task in which the behavioural rules have a hierarchical structure and conducted an fMRI experiment using this task. Subjects were able to apply two kinds of rule switch which corresponded to the retrieval of different hierarchies. The left DLPFC was specifically activated in the higher-order meta-rule switch condition. It is considered that this region restricts the searching space by handling intensive information, in agreement with previous studies suggesting that the left DLPFC is involved in controlling the hierarchical organization in decision making and recollecting information from episodic memory. The right FPC was specifically activated in the lower-order rule switch condition; this region may thus be involved in prioritizing rules, in agreement with previous work suggesting that the right FPC is involved in exploration with maintaining and switching multiple behavioural options in search of optimal behaviour. Our results suggest that humans can effectively represent information in a hierarchical manner and support current theories of hierarchical organization in the prefrontal functional network (Badre, 2008; Botvinick, 2008).

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