

Bending the Rules: Strategic Behavioral Differences Are Reflected in the Brain

Uta Wolfensteller^{1,2} and D. Yves von Cramon^{2,3}

Abstract

■ The implementation of higher-order conditional motor behavior was investigated in the present fMRI study with the objective of answering three questions: (a) what happens in situations where one stimulus dimension alone does not sufficiently determine the correct response?; (b) does the implementation of second-order stimulus–response (S–R) rules on the basis of matching (congruent) or nonmatching (incongruent) S–R associations differ from the implementation of congruent and incongruent first-order S–R rules?; and (c) is the cerebral implementation of second-order rules influenced by interindividual behavioral differences arising from the use of different strategies? The findings indicate that several cortical areas were more strongly engaged for second-order rules. More specifically, rule integration based on a rule match led to enhanced activation in posterior parietal cortex, whereas rule integration based on

a rule mismatch was associated with enhanced activation in dorsal premotor cortex and left rostralateral prefrontal cortex. Interindividual strategy differences were revealed by strikingly different behavioral data patterns: One subgroup of participants displayed strong congruency effects for second-order rules, whereas another subgroup displayed nonsignificant or even reversed congruency effects. Importantly, these strategy differences strongly modulated the cerebral implementation of second-order rules based on a rule mismatch. Together, the present findings reveal differential brain activation patterns for higher-order S–R rules depending on rule congruency and interindividual strategy differences. Moreover, they emphasize the necessity of taking interindividual behavioral differences into account when investigating the cerebral implementation of cognitive processes even in rather simple and well-controlled experimental paradigms. ■

INTRODUCTION

Given the impressive number of recreational games that have been invented throughout the centuries, it is apparent that humans enjoy learning, applying, and flexibly combining even the most arbitrary rules. When taking horse betting as one prominent example, it turns out that one rarely relies on only one source of information, such as the horse, the trainer, the jockey, or the most recent rates, but rather on the integration of all the information. What is more, the combined information might actually imply a completely different bet than any piece of information on its own. One can quite easily imagine that, under these circumstances, people will apply different strategies to come up with a good solution.

An elegant way to approach this topic experimentally is to investigate the implementation of arbitrary stimulus–response (S–R) rules. These rules are defined as associations between an antecedent stimulus and a consequential response. Previous research has mainly focused on S–R rules based on one stimulus dimension at a time, which will be referred to as first-order S–R rules in the following. The present fMRI study goes one step further by investigating second-order S–R rules with the objective to answer

three questions. First, what happens in situations that require the combination of rules, namely, situations where one stimulus dimension alone does not sufficiently determine the correct response? Apparently, for any particular situation (i.e., a stimulus), different first-order rules can either imply congruent S–R associations, in which case they would lead to the same response, or incongruent S–R associations, in which case they would lead to different responses. In the same manner, rule integration as required by second-order rules can result in a rule match, when the first-order rules imply congruent S–R associations, or a rule mismatch, when the first-order rules imply incongruent S–R associations (e.g., a bad jockey, but a good horse). The second question is therefore whether second-order rules based on a rule match or mismatch differ from congruent and incongruent first-order rules, respectively. It has to be considered, however, that the consequences of dealing with interfering information might differ depending on the applied strategy (Meiran & Kessler, 2008; Dreisbach, Goschke, & Haider, 2006, 2007). Given that for second-order rules, interference between the S–R associations in the first-order rules has to be used to determine a rule match or mismatch, it can be assumed that they should give rise to different strategies. When applying a rule integration strategy, the participants would compare the responses associated with the two dimensions of a given stimulus in the two first-order rules, which could

¹Technische Universität Dresden, Germany, ²Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, ³Max Planck Institute for Neurological Research, Cologne, Germany

result in either a rule match or mismatch. However, participants might eventually come up with a different strategy, such as, for instance, taking the individual color–shape combinations as exemplars and associating them directly with a given response. Consequently, our third question relates to whether the cerebral implementation of second-order rules is influenced by interindividual behavioral differences arising from different behavioral strategies.

Regarding the first question, previous studies revealed that a number of cortical areas are engaged in the implementation of arbitrary S–R rules (for reviews, see Hadj-Bouziane, Frankowska, Meunier, Coquelin, & Boussaoud, 2006; Bunge et al., 2005; Tanji & Hoshi, 2001; Wise & Murray, 2000). Note that most of these studies used S–R rules, which required attending to one stimulus dimension at a time or comparing the stimulus with a previous one in order to come up with the correct response (for an exception, see Boettiger & D’Esposito, 2005). The areas reported to be engaged in S–R rule implementation comprise posterior parietal cortex (Cavina-Pratesi et al., 2006; Crone, Wendelken, Donohue, & Bunge, 2006; Grol, de Lange, Verstraten, Passingham, & Toni, 2006; Bunge, Kahn, Wallis, Miller, & Wagner, 2003; Toni, Schluter, Josephs, Friston, & Passingham, 1999; Grafton, Fagg, & Arbib, 1998), dorsal premotor cortex (PMd; Cavina-Pratesi et al., 2006; Crone et al., 2006; Grol et al., 2006; Toni et al., 1999; Grafton et al., 1998; Wise, di Pellegrino, & Boussaoud, 1996; Germain & Lamarre, 1993; Mitz, Godschalk, & Wise, 1991), the supplementary and presupplementary motor areas (Cavina-Pratesi et al., 2006; Crone et al., 2006; Genovesio, Brasted, Mitz, & Wise, 2005; Sakai et al., 1999, 2000; Toni et al., 1999), as well as ventrolateral prefrontal cortex (Crone et al., 2006; Donohue, Wendelken, Crone, & Bunge, 2005; Bunge et al., 2003; Hoshi, Shima, & Tanji, 2000) and dorsolateral prefrontal cortex (Crone et al., 2006; Genovesio et al., 2005; Toni, Rushworth, & Passingham, 2001).

In the present experiment, we introduced second-order rules, which created situations where one stimulus dimension (color or shape) alone does not sufficiently determine the correct response. There are mainly three candidate areas for an enhanced or specific engagement during second-order rule application. First, posterior parietal cortex has been suggested to play a role in feature conjunction (Coull, Walsh, Frith, & Nobre, 2003; Donner et al., 2000, 2002), which would be relevant for evaluating the color–shape conjunctions of a stimulus in the present experiment. Second, PMd has been shown to be engaged in mapping complex stimuli to responses, even after an extensive amount of training (Grol et al., 2006), and could therefore be expected to be relevant when considering more than one stimulus dimension at a time in order to come up with a response. Finally, rostral prefrontal cortex (RLPFC) has been discussed in the context of several processes that might be relevant for rule integration as employed in the present experiment (for a review, see Ramnani & Owen, 2004), most prominently in the context of relational integration (Wendelken, Bunge, &

Carter, 2008; Smith, Keramatian, & Christoff, 2007; Bunge et al., 2005; Christoff, Ream, Geddes, & Gabrieli, 2003; Christoff et al., 2001).

Ultimately, these processes should be especially relevant in situations demanding cognitive control¹ such as when the two dimensions of a stimulus are associated with different (incongruent) responses in the first-order rules. To explicitly test this assumption, which corresponds to our second question, congruency between the S–R rules was manipulated within the experimental design. This manipulation should lead to behavioral congruency effects, such that incongruent first- and second-order rules should be associated with prolonged reaction times as compared to congruent first- and second-order rules, respectively. Moreover, because rule integration as employed in the present experiment requires that one compares the congruency between the S–R rules, determining a rule match or mismatch, in order to come up with a correct response, the congruency effect should be enhanced for second-order compared to first-order rules. Given that mismatch has been argued to place higher demands on relational integration (Cho, Holyoak, & Cannon, 2007), RLPFC should be strongly engaged during incongruent rule integration as it is based on a rule mismatch.

The third question, which pertains to interindividual strategy differences when applying second-order rules, and their effect on brain activation patterns, is inspired by the recently growing interest to more explicitly characterize the relationship between brain and behavior (e.g., Forstmann, van den Wildenberg, & Ridderinkhof, 2008). In a recent fMRI study, the comparison of participants who were sensitive or insensitive to S–R congruency during target-based task preparation revealed activation differences in dorsal premotor and posterior parietal cortex, which was taken to reflect strategic differences (Ruge & Braver, 2007). In the present experimental setup, we are interested in strategic differences at the level of combined rules. When applying a rule integration strategy, the participants would compare the responses associated with the two dimensions of a given stimulus in the two first-order rules. This comparison could either result in a response match (congruent second-order rule), prompting the execution of this correct response, or in a response mismatch (incongruent second-order rule). In case of a mismatch, the participants would then have to suppress the two incorrect responses and select the third response option, which would be incorrect in either of the single S–R rules. Consequently, participants adopting the rule integration strategy should display larger behavioral congruency effects for second-order rules than for first-order rules. In contrast, participants not adopting a rule integration strategy should not show larger congruency effects for second-order rules, if such congruency effects were present at all. These potential strategic differences were taken into account in the present study by explicitly testing their effect on the brain activation pattern associated with behavior based on higher-order S–R rules.

METHODS

Participants

Thirty-two participants took part in a training session 1 week prior to scanning. The final sample (25 participants) was chosen based on (a) their behavioral performance (3 participants committed more than 25% errors when applying second-order rules), and (b) the scanning schedule (2 were not included because they could not be fit into the schedule, 2 did not show up for their scheduled appointments). Of the 25 participants who took part in the fMRI experiment, the data of one participant had to be excluded due to technical problems. Hence, the final sample consisted of 24 participants (11 women; mean age = 25 years; $SD = 3$ years; range = 21–31 years). For 18 of these participants, intelligence was assessed in a separate session by means of Ravens Standard Progressive Matrices (Raven, 1958). Written consent was provided by all participants prior to the scanning session. All participants were right-handed as assessed by the Edinburgh Handedness Scale (Oldfield, 1971), had normal or corrected-to-normal vision, and were native German speakers. No participant had a history of neurological, major medical, or psychiatric disorder; none were taking medication at the time of measurement. The experimental standards were approved by the local ethics committee of the University of Leipzig in Germany.

Experimental Task

The participants' task was to respond to a presented stimulus (1 out of 3 different geometrical shapes in 1 out of 3 different colors) by pressing the corresponding button with the index, middle, or ring fingers of their right hands (Figures 1 and 2). Each trial started with a task cue which was presented for 250 msec and indicated which of the four tasks was to be performed in the present trial. Following a 150-msec fixation interval, the stimulus was presented for 500 msec. Responses were to be delivered within a time window of 2000 msec starting at stimulus onset. Valid feedback was given immediately following a response. The four types of tasks differed with respect to the rule that had to be applied to determine the correct response. Two first-order rules defined how to respond to either the stimulus color irrespective of its shape (color rule), or the stimulus shape irrespective of its color (shape rule). The second-order rule defined the correct response according to the combination of stimulus color and shape, on the basis of a match or mismatch of the two first-order rules (Figure 2). In the fourth task, which was used as a control, the task cue indicated which finger the participants should press as soon as the stimulus would come up, irrespective of its color or shape. In the sense that the stimulus dimensions were not to be used to determine the correct response, this condition realized simple motor behavior.

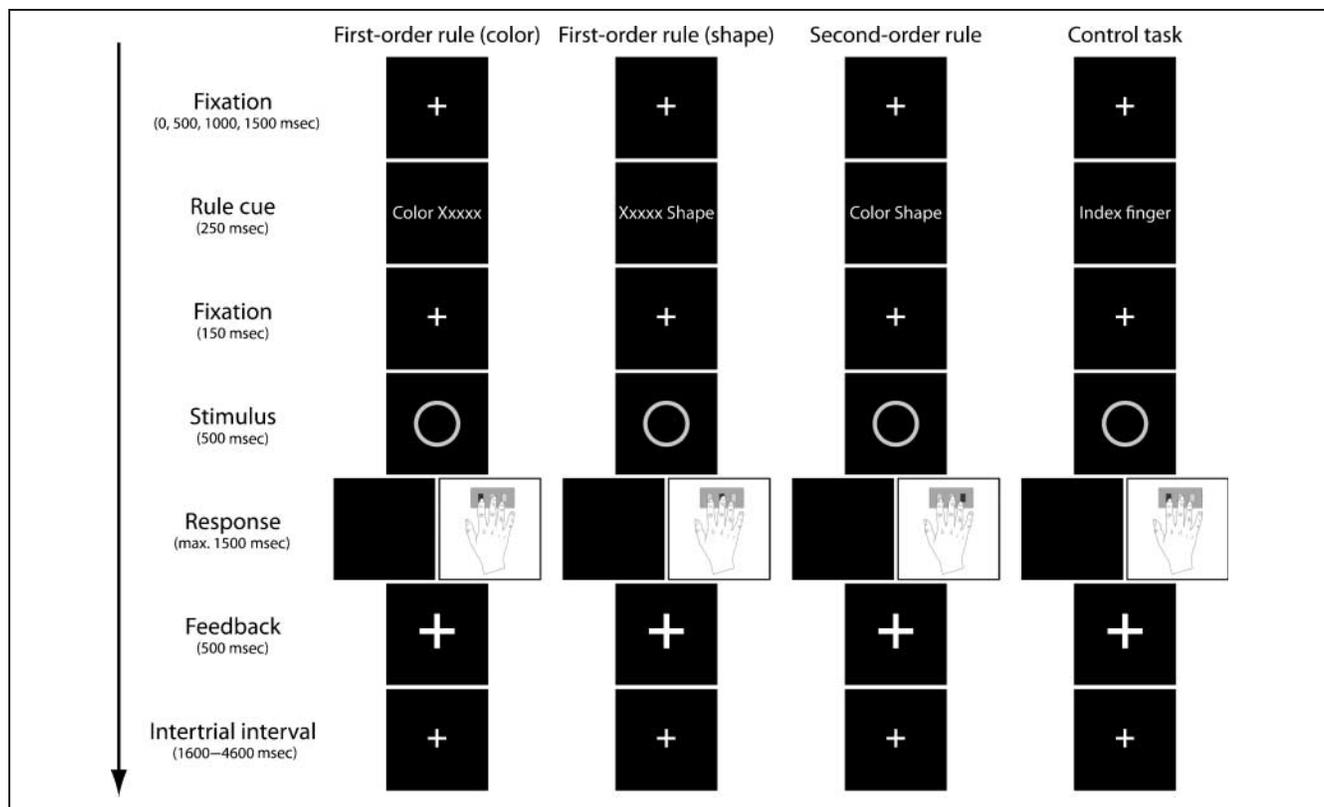


Figure 1. Experimental task. The timing for one trial is shown for the three experimental conditions and the control task. In the control task (right), the cue did not instruct a rule, but rather directly instructed a certain movement. Apart from that, the control task was completely comparable to the experimental conditions.

Arbitrary S–R rules					
Congruent			Incongruent		
first-order rule (color)			first-order rule (color)		
					
first-order rule (shape)			first-order rule (shape)		
					
second-order rule			second-order rule		
					
IF	MF	RF	IF	MF	RF

Figure 2. Arbitrary S–R rules. Depicted are the first-order rules (color, shape) and second-order rules, separately for the congruent and incongruent cases. Congruent refers to the fact that a stimulus would require the same button press (e.g., index finger) in the two first-order rules, which would result in a rule match during rule integration as required by the second-order rules. Incongruent refers to the fact that a stimulus would require different responses in the two first-order rules (e.g., index and ring fingers), which would result in a rule mismatch during rule integration. When applying one of the two first-order rules, the currently not relevant dimension could be ignored, whereas for the second-order rules both dimensions had to be considered to come up with a correct response. In case of a rule match, this correct response would be the response required by both first-order rules (e.g., the index finger). In case of a rule mismatch in turn, the correct response would be the response required by neither of the two first-order rules (e.g., the middle finger). IF = index finger; MF = middle finger; RF = ring finger.

The stimuli were unfilled squares, triangles, and circles with red, yellow, or blue colored outlines. All the centrally presented stimuli were matched in size (47.1 mm^2 ; square: $11.7 \times 11.7 \text{ mm}$; circle: diameter 15 mm ; triangle: $15.7 \times 13.5 \text{ mm}$), thus not exceeding a visual angle of 1.8° in height and width at a viewing distance of 100 cm . The trials were further subdivided into congruent and incongruent types. In congruent trials, first-order color and shape rules, as well as the second-order rule, would require the same response, whereas in incongruent trials, the first-order color and shape rules and the second-order rule would require three different responses. The four tasks were presented in mini-blocks of seven to eight trials (due to random insertion of empty trials), and were separated by intertrial intervals varying in length between 1600 and 4600 msec due to varying response times and jittered initial fixation intervals ($0, 500, 1000, 1500 \text{ msec}$) to enhance the resolution of the BOLD signal sampling rate (Figure 1). The order of congruent and incongruent trials within mini-blocks was pseudo-randomized such that the transition frequencies were balanced and exact stimulus repetitions were excluded. In total, 382 experimental trials (48 trials of each of the 8 conditions) and 32 empty trials were presented in 52 mini-

blocks. To eliminate task switching effects, the initial trials in all blocks (52 block switching trials) were excluded from the behavioral and the fMRI data analysis. After completing the experiment, all 25 participants (including the participant for whom imaging data could not be used due to technical problems) were debriefed on the strategies they applied in a semistructured interview.

Scanning Procedure

Participants lay supine on the scanner bed, with the index, middle, and ring fingers of the right hand positioned over the three buttons of a response box. The participants' hands were carefully stabilized, and form-fitting cushions were used to prevent arm, hand, and head motion. Stimuli were presented via a head-mounted mirror system. To attenuate scanner noise, participants were provided with earplugs.

Imaging was performed at the MPI for Human Cognitive and Brain Sciences, at a 3-T scanner (Siemens TRIO, Erlangen, Germany) equipped with the standard birdcage head coil. Twenty-two axial slices (64×64 pixel matrix, field of view = 192 mm , thickness = 4 mm , spacing = 1 mm) positioned parallel to the bicommissural plane (AC–PC) were acquired using a single-shot gradient-echo EPI sequence (TE = 30 msec , flip angle = 90° , repetition time = 2000 msec). In total, 1256 functional images were acquired in a single run. Prior to the functional run, 22 two-dimensional anatomical images (256×256 pixel matrix, MDEFT sequence) and T1-weighted EPI images were acquired.

Data Analysis

Functional data were motion-corrected off-line with the Siemens motion correction protocol (Siemens, Erlangen, Germany). Further processing of the fMRI data was performed using the software package LIPSIA (Lohmann et al., 2001). In the preprocessing, low-frequency components of the signal (i.e., baseline drifts) were suppressed by applying a $1/100\text{-Hz}$ high-pass filter. To correct for the temporal offset between the slices acquired in one image, a sinc-interpolation algorithm based on the Nyquist–Shannon sampling theorem (Press, Teukolsky, Vetterling, & Flannery, 1992) was employed.

Subsequently, the functional data were aligned with the high-resolution three-dimensional (3-D) reference datasets (160 slices, 1 mm thickness) by rigid linear registration with six degrees of freedom (3 rotational, 3 translational). These rotational and translational parameters were acquired by registering the two-dimensional functional data of one selected time step with the individual 3-D reference dataset. Subsequently, the rotational and translational parameters were transformed to standard size (Talairach & Tournoux, 1988) by linear scaling.

Transformed parameters were then used to align all functional slices with the stereotactic coordinate system by means of trilinear interpolation, thus generating output data with a spatial resolution of $3 \times 3 \times 3$ mm (27 mm^3). Subsequently, a 3-D spatial smoothing was performed using a Gaussian kernel with an FWHM of 4.24 mm. The alignment of the individual brains was further improved by nonlinear normalization (Thirion, 1998).

The fMRI data were modeled implementing an event-related design, with the event set to the stimulus onset. The eight regressors of interest comprised correctly answered congruent and incongruent trials for first-order rules (color or shape, respectively), second-order rule (color and shape), and the control task. Empty trials, as well as incorrectly answered trials along with the first trials in each mini-block (switch trials), were modeled as two separate regressors of no interest. The design specifications were convolved with a hemodynamic response function using a gamma function as well as its first derivative (Glover, 1999) including a delay of 6 sec. The statistical analysis was based on a least squares estimation using a general linear regression with prewhitening (Worsley et al., 2002). In a first step, autocorrelation parameters were estimated from the least squares residuals using the Yule-Walker equations and were applied to the data and the design matrix. In a second step, the linear model was re-estimated using least squares on the whitened data to produce estimates of effects and their standard errors.

To reveal the network generally engaged in conditional motor behavior, contrast images were generated for each participant based on the estimated raw-score differences between the control task and (a) the first-order rules (collapsed across color and shape trials) and (b) second-order rules. To separately test for congruent rule integration and incongruent rule integration, contrast images were generated for congruent first-order versus second-order rules, and for incongruent first-order versus second-order rules, respectively. Second-level analyses were done in several steps. One-sample *t* tests across the contrast images of all participants were computed for the control task contrasts. For congruent and incongruent rule integration, one-sample *t* tests were computed separately for two subgroups of participants that showed different behavioral patterns (see Results section). After converting these *t* values into *Z* scores, the results were corrected for multiple comparisons at the cluster level ($p = .05$) employing an initial voxelwise *Z* threshold of 2.58 ($p = .005$).

To statistically assess differences between the groups, the individual rule integration contrast images were additionally subjected to two-sample *t* tests. Any group differences were considered to be valid only if they were based on a significant effect in one or the other group (exceeding an uncorrected voxelwise $p = .005$, and a minimum cluster size of $216 \text{ mm}^3/8$ voxels), by inclusively masking the two-sample *t*-test map with the rule integration *Z* maps. Hence, differences due to effects with opposite directions in the two groups that were nonsignificant

on the single-group level are neglected. Finally, the modulating influence of the behavioral congruency effect on the brain areas engaged in congruent and incongruent rule integration was tested across the entire sample of participants by introducing the individual behavioral congruency effect as a second-level covariate. Again, any correlations were considered to be valid only if they were based on a significant effect in one or the other group (exceeding an uncorrected voxelwise $p = .005$, and a minimum cluster size of $216 \text{ mm}^3/8$ voxels), by inclusively masking the correlation map with the rule integration effect *Z* maps.

RESULTS

Behavioral Results

Congruency effects in reaction times for first-order rules were more consistent across participants (color: $M = 145$ msec, $SD = 82$ msec; shape: $M = 128$ msec, $SD = 74$ msec) than the congruency effects for second-order rules ($M = 172$ msec, $SD = 199$ msec). Inspection of the individual data revealed that a subgroup of participants showed no or even reversed congruency effects for second-order rules (Figure 3A). To take this observation into account, we subdivided the sample in participants who did show a substantial positive Congruency effect for second-order rules and can thus be argued to have applied a rule integration (RI) strategy (RI group, $n = 14$, 7 women) and those who did not show a substantial positive Congruency effect for second-order rules and can thus be argued to have applied a different strategy (No-RI group, $n = 10$, 4 women). This was done by means of a one-sample *t* test against zero, taking the lower 95% confidence interval boundary as the classification criterion (88 msec). Note that the two groups were comparable with respect to an intelligence measure obtained in a separate session as revealed by a *t* test for independent samples [RI group: $n = 11$, mean percentile rank = 93.7, $SE = 2.1$; No-RI group: $n = 7$, mean percentile rank = 96.3, $SE = 2.1$, $t(17) = 0.68$, $p = .50$].

Error rates and response times were then entered into a separate repeated measures ANOVAs with three-level factor Integration (first-order color, first-order shape, second-order), two-level factor Congruency (incongruent vs. congruent), and between-subject factor Group (RI, No-RI). Regarding error rates (Figure 3C), the analyses revealed a significant main effect for congruency only [$F(2, 22) = 21.86$, $p < .001$], showing that participants made more errors when responding to incongruent stimuli (5.8%) than when responding to congruent stimuli (0.6%). There were no between-group effects.

With respect to response times, the analysis revealed significant main effects for Integration [$F(2, 44) = 34.9$, $p < .001$] and Congruency [$F(1, 22) = 79.3$, $p < .001$], as well as Congruency \times Group [$F(1, 22) = 9.7$, $p < .01$] and Integration \times Congruency \times Group interactions

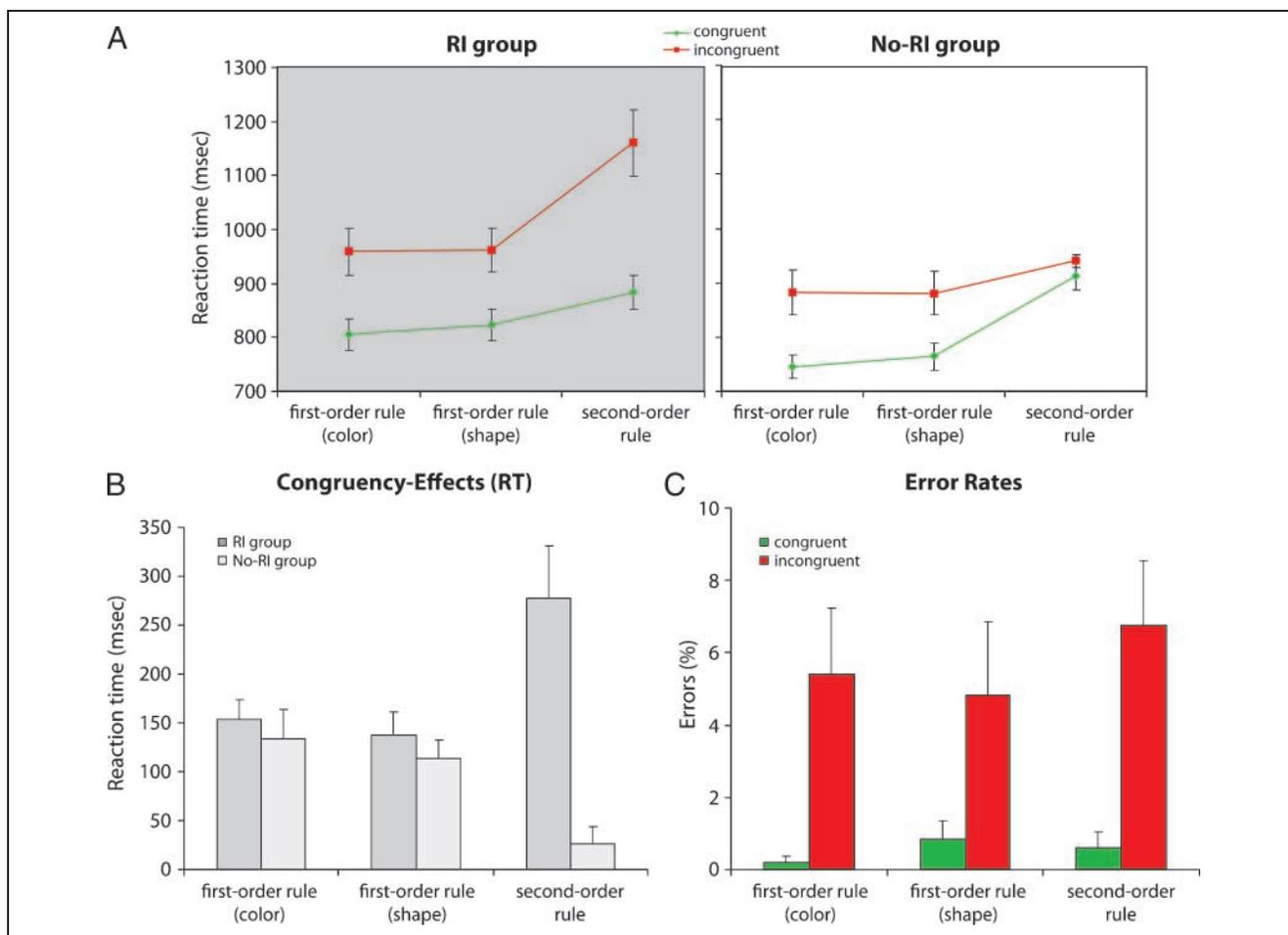


Figure 3. Behavioral results. (A) Reaction times are depicted separately for the group showing a behavioral congruency effect during rule integration (RI group) and the group not showing a substantial congruency effect (No-RI group). (B) Congruency effects on RT (incongruent vs. congruent) are shown for the RI and No-RI groups. (C) Error rates are depicted for the whole sample, as the overall ANOVA did not reveal any group-related effects. Error bars denote the standard error of the mean.

[$F(1.4, 30.1) = 10.3, p < .01$]. Follow-up repeated measures ANOVAs performed separately for the two subgroups of participants confirmed the main effects for Integration ($F > 14, p < .001$) and Congruency ($F > 55, p < .001$) in both groups (Figure 3A). Participants took longer to respond in second-order rule trials (No-RI: 922 msec; RI: 1044 msec) than in first-order rule trials (No-RI color: 809 msec, shape: 820 msec; RI color: 879 msec, shape: 887 msec). They also took longer to respond to incongruent stimuli (No-RI: 897 msec; RI: 1027 msec) than to congruent stimuli (No-RI: 805 msec; RI: 837 msec).

Furthermore, there were significant Integration by Congruency interactions in both groups [No-RI group: $F(2, 18) = 6.11, p < .005$; RI group: $F(1.3, 16.5) = 6.23, p < .05$], which had opposite directions. The congruency effect for second-order rules was significantly larger in the RI group than in the No-RI group ($t = 4.5, p < .001$), which is to be expected given the classification procedure. However, the groups did not differ with respect to their congruency effects when implementing either of the two first-order rules ($t < 0.78, p > .45$). Importantly, the con-

gruency effect for second-order rules was significantly larger than the congruency effects for both first-order rules only for the RI group ($t > 2.46, p < .05$; see Figure 3B). Also, the RI group did not answer more accurately to rule-mismatch stimuli than the No-RI group (RI group: 8.9%, No-RI group: 4.6%, $p > .05$), as would be expected if the enhanced RT to these stimuli reflected different speed-accuracy tradeoffs in two groups.

Self-reported Strategies

In order to quantify the debriefing data, six independent raters classified a certain description as (a) rule-based strategy (where the correct response is selected based on determining rule match or mismatch), (b) an item-based strategy (where the correct response is directly associated with each stimulus), or (c) an unclassifiable description. Five participants' descriptions could not be classified as one specific strategy, either because the raters indicated that the description was unclassifiable or because the ratings differed immensely between raters (e.g., out of 6,

Table 1. Cerebral Network Commonly Engaged in Conditional Motor Behavior Based on First-order and Second-order S–R Rules Compared to a Motor Control Task

<i>Anatomical Specification</i>	<i>Size (mm³)</i>	<i>Talairach Coordinates</i>			<i>Z_{max}</i>
		<i>x</i>	<i>y</i>	<i>z</i>	
Presupplementary motor area (pre-SMA)	9180 ^a	–5	7	48	4.97
L Anterior cingulate gyrus	l.m. ^a	–11	22	24	3.54
R Anterior cingulate gyrus	l.m. ^a	1	34	18	3.78
L Middle frontal gyrus	23,652 ^b	–35	34	21	4.51
L Inferior frontal sulcus (posterior portion)	l.m. ^b	–35	16	18	4.45
L Precentral gyrus (PMv)	l.m. ^c	–38	–2	33	4.32
R Precentral gyrus (PMv)	837	43	–2	27	3.58
L Superior precentral sulcus (PMd)	l.m. ^c	–23	–2	48	3.63
R Superior precentral sulcus (PMd)	2079	25	–5	54	3.67
L Precentral gyrus (MI)	l.m. ^c	–38	–26	48	4.67
L Intraparietal sulcus	l.m. ^c	–26	–56	42	5.04
R Intraparietal sulcus	60,480 ^c	22	–53	33	5.63
L Angular gyrus (IPL)	l.m. ^c	–44	–38	42	4.65
R Angular gyrus (IPL)	l.m. ^c	31	–35	33	4.01
L Precuneus	l.m. ^c	–11	–65	45	4.82
R Subcallosal sulcus	3861	4	–35	27	4.58
L Thalamus	l.m. ^b	–11	–11	6	4.12
R Thalamus	l.m. ^b	10	14	12	4.01
L Putamen and pallidum	l.m. ^b	–23	1	3	3.56
L Calcarine sulcus	l.m. ^c	–11	–95	9	3.62
R Calcarine sulcus	l.m. ^c	13	–92	3	4.45
Anterior cerebellar lobe	l.m. ^d	1	–53	6	4.63
L Anterior cerebellar lobe	l.m. ^d	–29	–65	–21	4.19
R Anterior cerebellar lobe	31,563 ^d	19	–53	–21	4.92
Posterior cerebellar lobe	l.m. ^d	7	–74	30	4.10
L Posterior cerebellar lobe	l.m. ^d	–11	–74	–15	4.67
R Posterior cerebellar lobe	l.m. ^d	7	–68	–18	4.51

The reported effects were obtained by a conjunction analysis on the whole sample group averages for first-order rules (vs. control task) and second-order rules (vs. control task). All activation survived cluster-level correction ($p < .05$). IPL = inferior parietal lobule; L = left; l.m. = local maximum; MI = primary motor cortex; PMd = dorsal premotor cortex; PMv = ventral premotor cortex; R = right. Letters a–d denote the cluster identity of a local maximum.

3 indicated a rule-based strategy and 3 indicated an item-based strategy). In terms of the behavioral data pattern, the remaining 20 subjects comprised 7 No-RI group and 13 RI group subjects. Six of 7 No-RI group subjects' descriptions were classified as an item-based strategy, and 10 of the 13 RI group subjects' descriptions were classified as a rule-based strategy, adding up to a correct classification rate of 80%. A frequency analysis revealed that the strategies, as classified based on the subjects' descriptions, were not equally distributed in the RI group and the No-RI group ($\chi^2_{\text{Yates-corrected}} =$

4.90, $p < .05$). Thus, if the participants provided a description that allowed a classification, this classification was mainly in line with the classification based on the behavioral data pattern.

Imaging Results

In a first step, we determined the areas that were engaged in conditional responses based on first- and second-order rules as compared to a motor control task by means of a

conjunction analysis. In general, conditional responses were associated with activation in a large predominantly bilateral fronto-parietal network including lateral prefrontal and premotor areas, pre-SMA, and inferior parietal lobule and superior parietal lobule (SPL), as well as basal ganglia, visual cortex, and cerebellum (see Table 1).

Following up on the behavioral dissociation of two subgroups of participants differing with regard to their congruency effects for second-order rules and, hence, putatively with respect to the applied strategy, the fMRI effects of congruent and incongruent rule integration were investigated separately for these groups. Congruent rule integration resulted in stronger activation only in right angular gyrus for the RI group, and in bilateral SPLs including precuneus, as well as left cerebellum for the No-RI group (Table 2, Figure 4A). Subsequent analyses of the percent signal change extracted from all of these areas revealed group-related effects for left and right SPLs only [Integration \times Congruency \times Group: $F(1, 22) = 10.2$, $p < .01$]. In these areas, substantial effects for congruent rule integration were revealed only for the No-RI group (left SPL: 0.13%, right SPL: 0.06, $p \leq .001$) but not for the RI group (0.05%, $p > .20$). However, a two-sample t test did

Table 2. Congruent Rule Integration (Congruent Second-order Rule vs. First-order Rules)

Anatomical Specification	Size (mm ³)	Talairach Coordinates			Z_{max}
		x	y	z	
<i>No-RI Group</i>					
L Angular gyrus	1.m. ^a	-35	-59	42	3.50
L Superior parietal lobule	2376 ^a	-14	-65	57	4.29
R Superior parietal lobule	2997 ^b	19	-62	51	4.44
R Precuneus	1.m. ^b	4	-59	36	3.88
L Posterior cerebellar lobe	486	-29	-59	-30	5.05
<i>RI Group</i>					
R Angular gyrus	1620	34	-66	45	3.99

Reported effects for congruent rule integration in the No-RI group and RI group result from separate one-sample t tests, and were corrected for multiple comparisons at the cluster level ($p = .05$). L = left; l.m. = local maximum; R = right. Letters a and b denote the cluster identity of a local maximum.

Figure 4. Imaging results. (A) Effects of congruent rule integration as revealed by contrasting the congruent second-order rules versus congruent first-order rules for the RI group (left) and the No-RI group (right). Activations were corrected for multiple comparisons at the cluster level ($p = .05$). (B) Effects of incongruent rule integration as revealed contrasting the incongruent second-order rule versus incongruent first-order rule contrasts for the RI group. For the No-RI group, no area displayed effects of incongruent rule integration. Activations were corrected for multiple comparisons at the cluster level ($p = .05$). (C) Group differences (RI vs. No-RI) during incongruent rule integration as revealed by a two-sample t test. To exclude group differences based on differences in first-order rule application in the groups, the results of the group comparison were inclusively masked with the RI group average for incongruent rule integration. Areas were only considered if they were activated above $Z < 2.58$ ($p = .005$, uncorrected) in both t tests and comprised at least 8 contiguous voxels (216 mm³). All activations are depicted on the individual brain from the investigated sample which had been used for nonlinear normalization. L = left; R = right; MFG = middle frontal gyrus; PMd = dorsal premotor cortex; SMG = supramarginal gyrus; SPL = superior parietal lobule.

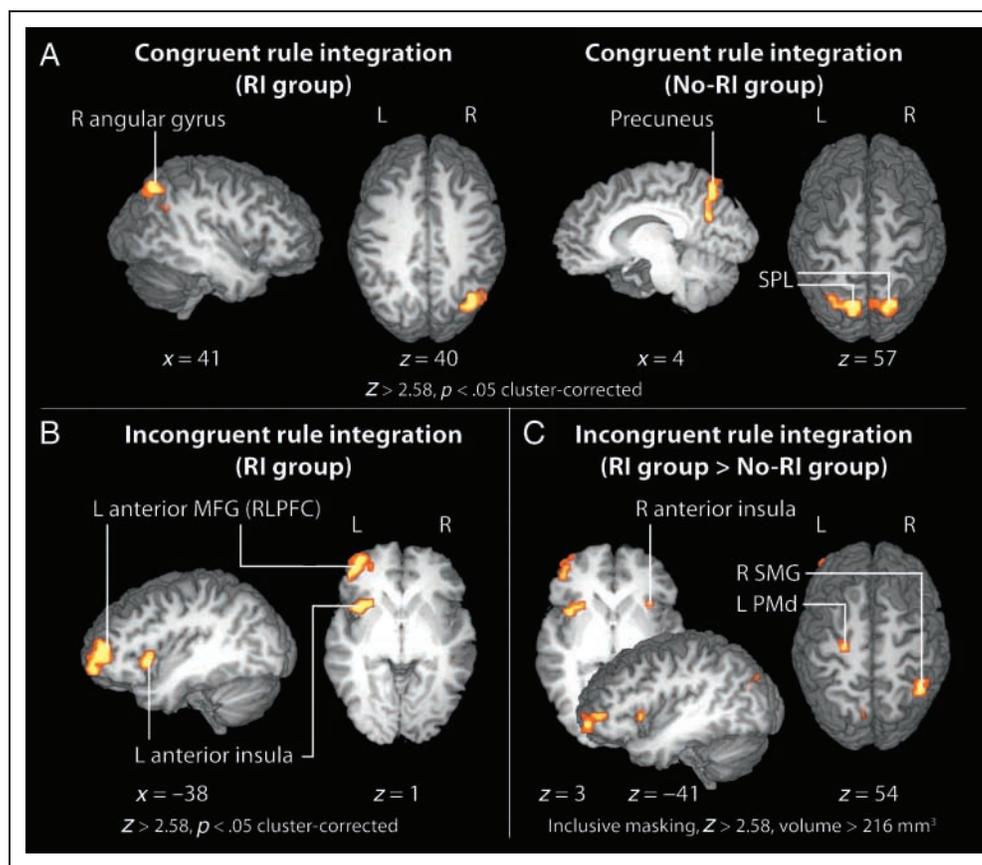


Table 3. Incongruent Rule Integration (Incongruent Second-order Rule vs. First-order Rule)

Anatomical Specification	Size (mm ³)	Talairach Coordinates			Z _{max}
		x	y	z	
<i>RI Group</i>					
L Anterior middle frontal gyrus (RLPFC)	1.m. ^a	-38	48	9	3.82
L Orbito-frontal cortex	3240 ^a	-32	54	-6	4.39
L Anterior insula	1161	-35	15	0	4.40
<i>RI Group > No-RI Group</i>					
L Anterior middle frontal gyrus (RLPFC)	1.m. ^a	-41	39	3	3.08
L Orbito-frontal cortex	1242 ^a	-32	54	-9	4.00
R Orbito-frontal cortex	243	22	51	-12	5.05
L Anterior insula	648	-32	15	0	4.07
R Anterior insula	216	28	12	9	3.24
L Precentral gyrus	324	-23	-18	54	2.99
R Supramarginal gyrus	702	34	-48	54	3.75
L Precuneus	243	-8	-63	51	3.14
L Middle temporal gyrus	270	-35	-72	27	3.95

Reported effects for incongruent rule integration in the RI group result from a one-sample *t* test, and were corrected for multiple comparisons at the cluster level ($p = .05$). Group differences were tested by means of a two-sample *t* test and inclusively masked with the RI group average for incongruent rule integration, thereby ensuring that significant effects did not result from differences in first-order rule application. Areas were only considered if they comprised at least 8 contiguous voxels (216 mm³) in both contrast maps ($Z > 2.58, p = .005$, uncorrected). Inclusive masking with the No-RI group average for incongruent rule integration did not reveal any results. L = left; l.m. = local maximum; R = right; RLPFC = rostralateral prefrontal cortex. The letter a denotes the cluster identity of a local maximum.

not reveal any differences between the groups on the whole-brain level.

Effects of incongruent rule integration were observed in the RI group only, resulting in stronger activation of left RLPFC, the ventrally adjacent orbito-frontal cortex, and left anterior insula (Table 3, Figure 4B). The two-sample *t* test revealed group differences in these three areas and additionally revealed stronger activation for the RI group in right orbito-frontal cortex, right anterior insula, and left PMd (see Table 2, Figure 4C). These results were confirmed by ANOVAs revealing significant Integration \times Congruency \times Group interactions in all these regions (all $F > 4.8, p < .05$; see Figure 5 displaying the effect for RLPFC). These interactions were mostly driven by the RI group displaying an increase in activation during incongruent rule integration (second-order $>$ first-order rules, $t > 2.60, p < .05$, right anterior insula, $p = .10$). In some of the areas, additional effects were observed for the No-RI group, such that they displayed a decrease in activation during incongruent integration (second-order $<$ first-order rules: bilateral orbito-frontal cortex, right anterior insula $t < -2.02, p \leq .05$) or an increase in activation during congruent rule integration (left RLPFC, right orbito-frontal cortex, left anterior insula, $t > 2.59, p < .05$).

Finally, we tested for a correlation between the BOLD effects during congruent and incongruent rule integration

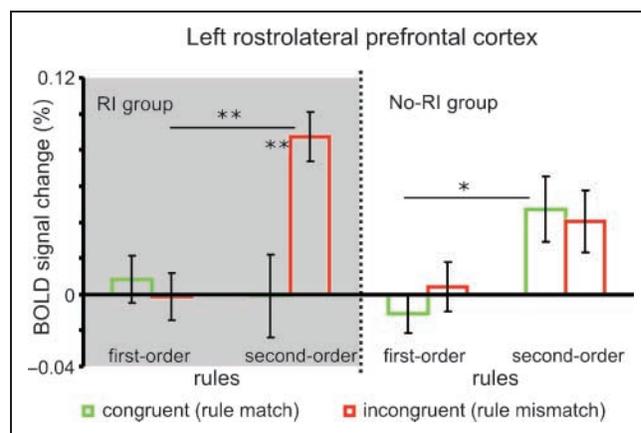


Figure 5. Rule integration in left RLPFC. Mean BOLD signal changes associated with the four conditions of interest, namely, congruent and incongruent first- and second-order rules, are shown separately for the RI group and the No-RI group. The BOLD signal was extracted from left RLPFC including the peak voxel and six adjacent voxels and the mean signal change associated with each condition was obtained by averaging across the interval from 4 to 8 sec after stimulus onset. Asterisks denote significant differences ($*p < .05, **p < .01$).

Table 4. Brain–Behavior Correlation during Incongruent Rule Integration

Anatomical Specification	Size (mm ³)	Talairach Coordinates			Z _{max}	ρ
		x	y	z		
<i>Positive Correlation</i>						
L Orbito-frontal cortex	297	-32	49	-9	3.04	.51
R Orbito-frontal cortex	216	22	52	-9	4.02	.44
L Anterior insula	567	-29	19	0	4.72	.49
R Anterior insula	351	28	19	6	4.14	.43
L Superior precentral sulcus	405	-20	-8	57	3.93	.50
R Superior precentral sulcus	270	25	-2	54	3.55	.51

Reported areas displayed a significant correlation between the cerebral effects of incongruent rule integration as obtained by contrasting incongruent second-order rule versus incongruent first-order rules and the individual behavioral congruency effect for second-order rules. To ensure that significant effects did not result from differences in first-order rule application, the RI group average for incongruent rule integration was used as an inclusive mask. Areas were only considered if they comprised at least 8 contiguous voxels (216 mm³) in both contrast maps ($Z > 2.58$, $p = .005$, uncorrected). Inclusive masking with the No-RI group average for incongruent rule integration did not reveal any results. Nonparametric Spearman's Rho (ρ) correlation coefficients are given in the leftmost column for each area. These values were derived from analyses on the extracted percent signal change after excluding outliers (one per region, two for right orbito-frontal cortex). L = left; R = right.

and the size of the behavioral congruency effect for second-order rules for all participants. Analyses revealed a modulating influence of the behavioral congruency effect on activation associated with incongruent rule integration in orbito-frontal cortex, anterior insula, and anterior portions of PMd, bilaterally (Table 4, Figure 6A). We also assessed

the brain–behavior correlation in left RLPFC that was engaged for incongruent rule integration in the RI group only (Figure 6B). Here, the nonsignificant positive correlation in the whole sample (Spearman's $\rho = .244$, $p = .262$) arose from the combination of a negative correlation in the No-RI group (Spearman's $\rho = -.62$, $p = .054$) and a positive correlation in the RI group (Spearman's $\rho = .60$, $p < .05$).

DISCUSSION

The overall aim of the present study was to shed more light on the cerebral implementation of arbitrary S–R rules. More specifically, we were interested in higher-order S–R rules, which require the integration of two rules in order to come up with a correct response, asking what happens if one stimulus dimension does not sufficiently determine the correct response. The general brain activation patterns for both the first- and second-order rules replicate established findings by showing the engagement of a network of cortical and subcortical areas involved in conditional motor behavior (Hadj-Bouziane et al., 2006; Bunge et al., 2005; Hoshi et al., 2000; Wise & Murray, 2000). More specifically, the present fMRI findings lend support to the assumption that rule integration would lead to an enhanced or additional recruitment of cortical areas such as posterior parietal cortex, PMd, and RLPFC. We demonstrate further functional differentiations when taking into account whether a second-order rule refers to a match or mismatch of two first-order rules and is therefore congruent or incongruent with both. Importantly, however, the behavioral data revealed impressive interindividual differences in terms of how congruency affects reaction times during rule integration. Only a subgroup of participants displayed substantial congruency effects for second-order rules, whereas another subgroup of participants did not, despite

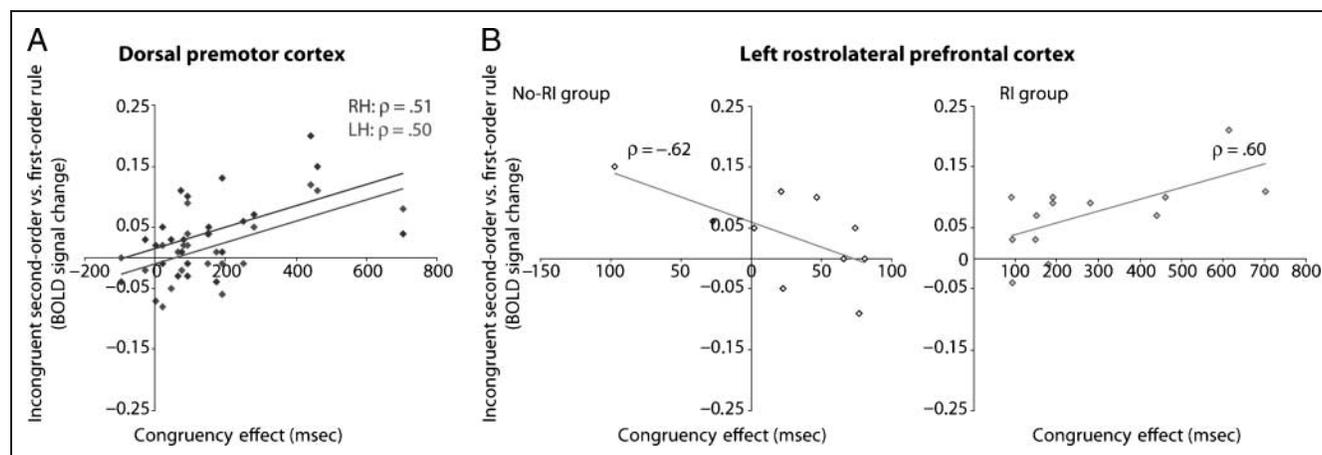


Figure 6. Brain–behavior correlations. The correlation between the behavioral congruency effect for combined rules, indicative of strategic differences and the BOLD effect of incongruent rule integration (incongruent second-order rule vs. incongruent first-order rule application) is plotted for the whole sample for right and left PMd (A) and separately for the No-RI and RI group for left rostrolateral prefrontal cortex (B). The pattern in anterior insula and orbito-frontal cortex resembled the pattern depicted for PMd. For Talairach coordinates of the plotted areas, please see Table 4 (PMd) and Table 2 (RLPFC). Nonparametric Spearman's rho (ρ) correlation coefficients are reported.

displaying normal congruency effects for first-order rules. Apparently, the participants adopted different strategies when implementing complex S–R rules, and only a part of the sample displayed a rule integration strategy. This does not, of course, exclude a certain amount of strategy overlap, such as for instance, adopting the rule integration strategy for some stimuli, and a more item-based strategy for others, or adopting different strategies at different stages of the experiment. In light of these interindividual differences at the behavioral level, congruency effects during second-order rule application on brain activation (i.e., the second question of the experiment) cannot be discussed without also considering the influence of strategy differences, that is, the third question at the same time. Therefore, the present findings regarding congruent and incongruent rule integration will be discussed separately, alongside with the corresponding findings on strategy effects.

Congruent Rule Integration—Rule Match

Posterior parietal cortex was more strongly engaged during congruent rule integration, which was based on a rule match, referring to the fact that the two dimensions of a presented stimulus matched in terms of S–R associations. Although the exact focus of the posterior parietal activation differed between participants with and without a substantial behavioral congruency effect during rule integration, the subsequent whole-brain group comparison and signal change analyses revealed that the pattern was predominantly comparable in both groups. Functionally, the activation could be interpreted to reflect either the process of conjoining the two perceptual features (Coull et al., 2003; Donner et al., 2000, 2002) or an enhanced demand on rule maintenance (Crone et al., 2006; Bunge et al., 2003). However, neither of these interpretations can account for the fact that the enhancement was observed for congruent rule integration only. If the enhanced activation was reflecting the necessity to conjoin two features, one would expect to find an enhancement for incongruent rule integration as well. Besides, the role of the posterior parietal in feature conjunction has been debated lately in the light of studies showing that perceptually hard single feature search and feature conjunction search engage this area to the same extent (Song & Jiang, 2006; Nobre, Coull, Walsh, & Frith, 2003). However, explaining activation differences between second-order and first-order rules in terms of detection difficulty does not apply here because the stimuli were exactly the same. If alternatively, the enhanced activation in posterior parietal cortex reflected an enhanced demand on rule maintenance due to having to maintain two rules instead of one, a similar or even more pronounced effect would also be expected for incongruent rule integration. However, this was not the case. One potential explanation is that the incongruent stimuli might automatically activate the currently invalid rule even at the first-order rule level, thereby diminishing the incongruent rule integration effect. This implies that activation in posterior parietal cortex re-

flects the amount of currently activated rules, irrespective of whether they were automatically triggered (incongruent first-order rules) or actively retrieved (congruent and incongruent second-order rules) but cannot be settled solely based on the present findings.

Incongruent Rule Integration—Rule Mismatch

The PMd and left RLPFC were more strongly engaged during incongruent rule integration, which was based on a rule mismatch, referring to the fact that the two dimensions of a presented stimulus did not match in terms of S–R associations. Most importantly, these cerebral effects were strongly modulated by the way the participants dealt with interference at the second-order rule level as indicated by their behavioral congruency effect, thereby confirming that interindividual behavioral differences during higher-order S–R rules application are accompanied by interindividual differences in the brain activation pattern.

Activation of the PMd during incongruent rule integration was influenced by the ongoing behavior in a quantitative manner, such that a larger congruency effect for second-order rules indicative of a higher susceptibility to interference, and thus, a stronger need for cognitive control, was associated with stronger activation. Functionally, PMd has been implicated in the selection of movements based on sensory cues (O’Shea, Johansen-Berg, Trief, Gobel, & Rushworth, 2007; Amiez, Kostopoulos, Champod, & Petrides, 2006; Hoshi & Tanji, 2006; Toni et al., 2001, 2002). A greater number of planned finger movements has been associated with enhanced activation in this area (Cavina-Pratesi et al., 2006). Furthermore, in line with the present data, for nonhuman primates it has been shown that PMd neurons display a preference for rules requiring a response to nonmatching stimuli (Muhammad, Wallis, & Miller, 2006; Wallis & Miller, 2003). Applying this logic to the present study, participants who applied the rule integration strategy would, in the case of incongruent rule integration, covertly select the different movements in order to determine the rule mismatch. Thereafter, they could finally come up with the correct response, namely the third one, which had not been selected for either of the first-order rules. Naturally, participants who applied a different strategy, as for instance representing the incongruent stimulus as a compound exemplar associated with a specific response, would not covertly select multiple movements and should, consequently, not show an enhanced dorsal premotor activation, which is exactly the pattern we observed. The present findings are furthermore in line with previously reported strategy effects on PMd activation during response preparation showing stronger activation in participants who were sensitive to congruency and were strategically using it to select and prepare responses in advance (Ruge & Braver, 2007).

The current activation of RLPFC for incongruent rule integration and its lateralization to the left hemisphere are

in line with several recent findings (Badre & D'Esposito, 2007; De Pisapia, Slomski, & Braver, 2007; Bunge et al., 2003; for a review, see Koechlin & Hyafil, 2007). De Pisapia et al. (2007) showed that having to integrate memorized information with an ongoing task, in this case, a mental arithmetic, is associated with left rostrolateral prefrontal activation. Here, the response associated with the present feature of one stimulus dimension, (e.g., that yellow was to be responded with the index finger) had to be memorized while deriving the response associated with the present feature of the other dimension, (e.g., that a circle was to be responded with the middle finger). Only then could the nonmatch be determined and the correct response be derived, which corresponds to combining and coordinating the outputs of at least two cognitive operations (Ramnani & Owen, 2004). Furthermore, it has been argued, that RLPFC is activated in situations where competition is induced between very abstract representations rather than very concrete representations such as responses (Badre & D'Esposito, 2007). In the present study, competition was introduced at the rule level but was apparently highly dependent on the strategy applied to implement the more complex second-order rules. In the group of participants presumably adopting the rule integration strategy as indicated by their elevated congruency effect for second-order rules, larger congruency effects were associated with stronger activation in left RLPFC during incongruent rule integration. This particular finding fits with previously reported activation in this area for the implementation of nonmatch rules on two serially presented stimuli (Bunge et al., 2003). In turn, in the group of participants presumably not adopting the rule integration strategy, smaller congruency effects were associated with stronger activation in RLPFC during incongruent rule integration, and activation of this brain region was enhanced during congruent rule integration. One might speculate that this reflects a strategy, where the mismatch stimuli are coded as an exception, thereby establishing a direct S–R link which serves as a standard to determine the correct response for a match stimulus. Following up on that, it might actually be the case that the rule integration strategy is not the most efficient one, given that it is actually slowing the participants down. Moreover, given that rule-based and item-based strategies are not mutually exclusive in the long run (Bourne, Healy, Kole, & Graham, 2006), it can be assumed that with even more task practice, the majority of the participants might shift to an item-based strategy.

Conclusion

The present study revealed striking interindividual differences in how people perform in situations, where one stimulus dimension alone does not sufficiently determine the correct response. Strategic differences in integrating matching and nonmatching rules manifested both behaviorally and on the brain level. Most importantly, these effects were tightly linked, such that the brain activation

pattern was highly dependent on the level of interference during rule integration and on the participants' strategy in coping with this interference. Elevated activation in posterior parietal cortex was restricted to rule integration based on a rule match. Elevated activation in PMd and left RLPFC pertained to rule integration based on a rule mismatch and was influenced by the applied strategy. Activation of these areas was restricted to or stronger in participants who adopted a rule integration strategy as indicated by their behavioral susceptibility to interference induced by a rule mismatch. Together, the present findings shed new light on the differential implementation of higher-order conditional motor behavior in the human brain depending on both the level of interference during rule integration and the presumably adopted strategy. Most importantly, the results of the present study suggest that even simple and well-controlled choice reaction paradigms may invoke striking interindividual differences, both behaviorally and in terms of brain activation, which have to be considered to foster our understanding of both the processes under investigation and the functionality of cortical areas taken to subserve them.

Acknowledgments

We thank Anna Abraham, Hannes Ruge, and Birte U. Forstmann for countless discussions and helpful suggestions; Mandy Jochemko, Simone Wipper, and Domenica Wifling for their assistance with the fMRI measurement; and Ramona Menger and Katja Macher for their assistance in collecting the behavioral data.

Reprint requests should be sent to Uta Wolfensteller, Section of Systems Neuroscience, Department of Psychiatry & Psychotherapy, Medical Faculty Carl Gustav Carus, Technische Universität Dresden, Wuerzburger Strasse 35, 01187 Dresden, Germany, or via e-mail: uta.wolfensteller@tu-dresden.de.

Note

1. Effects of cognitive control on rule implementation are often studied by employing task switching paradigms. Please note that the present experimental approach focuses on the rule types themselves, that is, lower- versus higher-order S–R rules. Influences of switching between tasks (here rules) were experimentally controlled.

REFERENCES

- Amiez, C., Kostopoulos, P., Champod, A. S., & Petrides, M. (2006). Local morphology predicts functional organization of the dorsal premotor region in the human brain. *Journal of Neuroscience*, *26*, 2724–2731.
- Badre, D., & D'Esposito, M. (2007). Functional magnetic resonance imaging evidence for a hierarchical organization of the prefrontal cortex. *Journal of Cognitive Neuroscience*, *19*, 2082–2099.
- Boettiger, C. A., & D'Esposito, M. (2005). Frontal networks for learning and executing arbitrary stimulus–response associations. *Journal of Neuroscience*, *25*, 2723–2732.
- Bourne, L. E., Jr., Healy, A. F., Kole, J. A., & Graham, S. M. (2006). Strategy shifts in classification skill acquisition:

- Does memory retrieval dominate rule use? *Memory & Cognition*, *34*, 903–913.
- Bunge, S. A., Kahn, I., Wallis, J. D., Miller, E. K., & Wagner, A. D. (2003). Neural circuits subserving the retrieval and maintenance of abstract rules. *Journal of Neurophysiology*, *90*, 3419–3428.
- Bunge, S. A., Wallis, J. D., Parker, A., Brass, M., Crone, E. A., Hoshi, E., et al. (2005). Neural circuitry underlying rule use in humans and nonhuman primates. *Journal of Neuroscience*, *25*, 10347–10350.
- Cavina-Pratesi, C., Valyear, K. F., Culham, J. C., Kohler, S., Obhi, S. S., Marzi, C. A., et al. (2006). Dissociating arbitrary stimulus–response mapping from movement planning during preparatory period: Evidence from event-related functional magnetic resonance imaging. *Journal of Neuroscience*, *26*, 2704–2713.
- Cho, S., Holyoak, K. J., & Cannon, T. D. (2007). Analogical reasoning in working memory: Resources shared among relational integration, interference resolution, and maintenance. *Memory & Cognition*, *35*, 1445–1455.
- Christoff, K., Prabhakaran, V., Dorfman, J., Zhao, Z., Kroger, J. K., Holyoak, K. J., et al. (2001). Rostrolateral prefrontal cortex involvement in relational integration during reasoning. *Neuroimage*, *14*, 1136–1149.
- Christoff, K., Ream, J. M., Geddes, L. P., & Gabrieli, J. D. (2003). Evaluating self-generated information: Anterior prefrontal contributions to human cognition. *Behavioral Neuroscience*, *117*, 1161–1168.
- Coull, J. T., Walsh, V., Frith, C. D., & Nobre, A. C. (2003). Distinct neural substrates for visual search amongst spatial versus temporal distractors. *Brain Research, Cognitive Brain Research*, *17*, 368–379.
- Crone, E. A., Wendelken, C., Donohue, S. E., & Bunge, S. A. (2006). Neural evidence for dissociable components of task-switching. *Cerebral Cortex*, *16*, 475–486.
- De Pisapia, N., Slomski, J. A., & Braver, T. S. (2007). Functional specializations in lateral prefrontal cortex associated with the integration and segregation of information in working memory. *Cerebral Cortex*, *17*, 993–1006.
- Donner, T. H., Kettermann, A., Diesch, E., Ostendorf, F., Villringer, A., & Brandt, S. A. (2000). Involvement of the human frontal eye field and multiple parietal areas in covert visual selection during conjunction search. *European Journal of Neuroscience*, *12*, 3407–3414.
- Donner, T. H., Kettermann, A., Diesch, E., Ostendorf, F., Villringer, A., & Brandt, S. A. (2002). Visual feature and conjunction searches of equal difficulty engage only partially overlapping frontoparietal networks. *Neuroimage*, *15*, 16–25.
- Donohue, S. E., Wendelken, C., Crone, E. A., & Bunge, S. A. (2005). Retrieving rules for behavior from long-term memory. *Neuroimage*, *26*, 1140–1149.
- Dreisbach, G., Goschke, T., & Haider, H. (2006). Implicit task sets in task switching? *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *32*, 1221–1233.
- Dreisbach, G., Goschke, T., & Haider, H. (2007). The role of task rules and stimulus–response mappings in the task switching paradigm. *Psychological Research*, *71*, 383–392.
- Forstmann, B. U., van den Wildenberg, W. P. M., & Ridderinkhof, K. R. (2008). Neural mechanisms, temporal dynamics, and individual differences in interference control in the Simon task. *Journal of Cognitive Neuroscience*, *20*, 1854–1865.
- Genovesio, A., Brasted, P. J., Mitz, A. R., & Wise, S. P. (2005). Prefrontal cortex activity related to abstract response strategies. *Neuron*, *47*, 307–320.
- Germain, L., & Lamarre, Y. (1993). Neuronal activity in the motor and premotor cortices before and after learning the associations between auditory stimuli and motor responses. *Brain Research*, *611*, 175–179.
- Glover, G. H. (1999). Deconvolution of impulse response in event-related BOLD fMRI. *Neuroimage*, *9*, 416–429.
- Grafton, S. T., Fagg, A. H., & Arbib, M. A. (1998). Dorsal premotor cortex and conditional movement selection: A PET functional mapping study. *Journal of Neurophysiology*, *79*, 1092–1097.
- Grol, M. J., de Lange, F. P., Verstraten, F. A., Passingham, R. E., & Toni, I. (2006). Cerebral changes during performance of overlearned arbitrary visuomotor associations. *Journal of Neuroscience*, *26*, 117–125.
- Hadj-Bouziane, F., Frankowska, H., Meunier, M., Coquelin, P. A., & Boussaoud, D. (2006). Conditional visuo-motor learning and dimension reduction. *Cognitive Processing*, *7*, 95–104.
- Hoshi, E., Shima, K., & Tanji, J. (2000). Neuronal activity in the primate prefrontal cortex in the process of motor selection based on two behavioral rules. *Journal of Neurophysiology*, *83*, 2355–2373.
- Hoshi, E., & Tanji, J. (2006). Differential involvement of neurons in the dorsal and ventral premotor cortex during processing of visual signals for action planning. *Journal of Neurophysiology*, *95*, 3596–3616.
- Koechlin, E., & Hyafil, A. (2007). Anterior prefrontal function and the limits of human decision-making. *Science*, *318*, 594–598.
- Lohmann, G., Muller, K., Bosch, V., Mentzel, H., Hessler, S., Chen, L., et al. (2001). LIPSIA—A new software system for the evaluation of functional magnetic resonance images of the human brain. *Computerized Medical Imaging and Graphics*, *25*, 449–457.
- Meiran, N., & Kessler, Y. (2008). The task rule congruency effect in task switching reflects activated long-term memory. *Journal of Experimental Psychology: Human Perception and Performance*, *34*, 137–157.
- Mitz, A. R., Godschalk, M., & Wise, S. P. (1991). Learning-dependent neuronal activity in the premotor cortex: Activity during the acquisition of conditional motor associations. *Journal of Neuroscience*, *11*, 1855–1872.
- Muhammad, R., Wallis, J. D., & Miller, E. K. (2006). A comparison of abstract rules in the prefrontal cortex, premotor cortex, inferior temporal cortex, and striatum. *Journal of Cognitive Neuroscience*, *18*, 974–989.
- Nobre, A. C., Coull, J. T., Walsh, V., & Frith, C. D. (2003). Brain activations during visual search: Contributions of search efficiency versus feature binding. *Neuroimage*, *18*, 91–103.
- Oldfield, R. C. (1971). The assessment and analysis of handedness: The Edinburgh Inventory. *Neuropsychologia*, *9*, 97–113.
- O’Shea, J., Johansen-Berg, H., Trief, D., Gobel, S., & Rushworth, M. F. (2007). Functionally specific reorganization in human premotor cortex. *Neuron*, *54*, 479–490.
- Press, W. H., Teukolsky, S. A., Vetterling, W. T., & Flannery, B. P. (1992). *Numerical recipes in C*. Cambridge: Cambridge University Press.
- Ramnani, N., & Owen, A. M. (2004). Anterior prefrontal cortex: Insights into function from anatomy and neuroimaging. *Nature Reviews Neuroscience*, *5*, 184–194.
- Raven, J. C. (1958). *The standard progressive matrices*. London: H. K. Lewis.
- Ruge, H., & Braver, T. S. (2007). Neural mechanisms of cognitive control in cued task-switching: Rules, representations, and preparation. In S. A. Bunge & J. D. Wallis (Eds.), *Neuroscience of rule-guided behavior*. New York: Oxford University Press.
- Sakai, K., Hikosaka, O., Miyauchi, S., Sasaki, Y., Fujimaki, N., & Putz, B. (1999). Presupplementary motor area activation

- during sequence learning reflects visuo-motor association. *Journal of Neuroscience*, *19*, RC1.
- Sakai, K., Hikosaka, O., Takino, R., Miyachi, S., Nielsen, M., & Tamada, T. (2000). What and when: Parallel and convergent processing in motor control. *Journal of Neuroscience*, *20*, 2691–2700.
- Smith, R., Keramatian, K., & Christoff, K. (2007). Localizing the rostrolateral prefrontal cortex at the individual level. *Neuroimage*, *36*, 1387–1396.
- Song, J. H., & Jiang, Y. (2006). Visual working memory for simple and complex features: An fMRI study. *Neuroimage*, *30*, 963–972.
- Talairach, J., & Tournoux, P. (1988). *Co-planar stereotaxic atlas of the human brain. 3-Dimensional proportional system: An approach to cerebral imaging*. Stuttgart: Thieme.
- Tanji, J., & Hoshi, E. (2001). Behavioral planning in the prefrontal cortex. *Current Opinion in Neurobiology*, *11*, 164–170.
- Thirion, J. P. (1998). Image matching as a diffusion process: An analogy with Maxwell's demons. *Medical Image Analysis*, *2*, 243–260.
- Toni, I., Rushworth, M. F., & Passingham, R. E. (2001). Neural correlates of visuomotor associations. Spatial rules compared with arbitrary rules. *Experimental Brain Research*, *141*, 359–369.
- Toni, I., Schluter, N. D., Josephs, O., Friston, K., & Passingham, R. E. (1999). Signal-, set- and movement-related activity in the human brain: An event-related fMRI study. *Cerebral Cortex*, *9*, 35–49.
- Toni, I., Shah, N. J., Fink, G. R., Thoenissen, D., Passingham, R. E., & Zilles, K. (2002). Multiple movement representations in the human brain: An event-related fMRI study. *Journal of Cognitive Neuroscience*, *14*, 769–784.
- Wallis, J. D., & Miller, E. K. (2003). From rule to response: Neuronal processes in the premotor and prefrontal cortex. *Journal of Neurophysiology*, *90*, 1790–1806.
- Wendelken, C., Bunge, S. A., & Carter, C. S. (2008). Maintaining structured information: An investigation into functions of parietal and lateral prefrontal cortices. *Neuropsychologia*, *46*, 665–678.
- Wise, S. P., di Pellegrino, G., & Boussaoud, D. (1996). The premotor cortex and nonstandard sensorimotor mapping. *Canadian Journal of Physiology and Pharmacology*, *74*, 469–482.
- Wise, S. P., & Murray, E. A. (2000). Arbitrary associations between antecedents and actions. *Trends in Neurosciences*, *23*, 271–276.
- Worsley, K. J., Liao, C. H., Aston, J., Petre, V., Duncan, G. H., Morales, F., et al. (2002). A general statistical analysis for fMRI data. *Neuroimage*, *15*, 1–15.