

## VENTRAL STRIATUM IS RELATED TO WITHIN-SUBJECT LEARNING PERFORMANCE

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**Abstract**—Learning from feedback involves a network of various cortical and subcortical regions. Although activation in this network has been shown to be especially strong in successful learners, it is currently unclear which of these regions are related to within-subject variation in learning performance. To this aim, 21 subjects performed a probabilistic feedback-learning task consisting of multiple independent Learning blocks and non-learning Control blocks, while functional magnetic resonance imaging data were acquired. In agreement with previous studies, activation in anterior, lateral and medial left prefrontal cortex, insula and superior and inferior parietal cortical regions were found when contrasting Learning and Control blocks. Furthermore, activation in the supplementary motor area, anterior cingulate cortex and bilateral striatum was associated specifically with the learning phase and not the application phase during Learning blocks. Finally, activation only in the ventral striatum was associated with within-subject learning performance across the Learning blocks. Taken together, these latter two results are argued to provide the answer to the main research question: ventral striatum activation is associated with within-subject variations in learning performance. The ventral striatum appears to play a vital role in learning by adjusting behavior based on feedback. © 2013 IBRO. Published by Elsevier Ltd. All rights reserved.

**Key words:** feedback learning, fMRI, ventral striatum.

### INTRODUCTION

For any organism that needs to engage in adaptive goal-directed behavior, the ability to learn from feedback is

crucial. Specifically, feedback learning allows organisms to use previous experiences to make predictions about the consequences of their actions. This process is often conceptualized as consisting of three steps: encoding the current state, selecting a response, and adjusting subsequent selection based on the outcome (Bunge, 2004; Seger, 2008). In humans, previous research has pinpointed several brain regions involved in this learning cycle. The ventromedial prefrontal cortex (PFC) appears to be involved in encoding the reward value associated with states (Blair et al., 2006). Punishment results in increased activation in the insula and anterior cingulate cortex (ACC) (Ullsperger and von Cramon, 2003) and may result in deactivation in the ventral striatum (Becerra et al., 2001). The basal ganglia are particularly important in selecting responses based on expected outcomes, given the current state. These regions appear to be essential for the use of value information for the selection of goal-directed responses (O'Doherty et al., 2007; Brovelli et al., 2008; Shohamy, 2008). Subsequently, they shape responses by biasing response competition in the supplementary motor area (SMA) (Seger, 2008; Vink et al., 2005a; Zandbelt and Vink, 2010; Zandbelt et al., 2012a). After response selection, feedback is used to fine-tune existing stimulus–response mappings, and, when necessary, to learn novel ones (Boettiger and D'Esposito, 2005). Prediction errors related to the expectation versus the receipt of rewarding outcomes have been disentangled and shown to be associated with activation in the ventral striatum and medial PFC, respectively (Knutson and Wimmer, 2007). In turn, adjustments of behavior in response to changes in reward likelihood are associated with activation in the ventral PFC and ventral striatum (Delgado et al., 2005; Day and Carelli, 2007; Van Hell et al., 2010). Finally, the ACC has been argued to integrate input signaling prediction errors, and use this information to select responses (Holroyd and Coles, 2008). Moreover, the functional role of the ACC is not merely restricted to processing errors, but instead is related to behavioral adjustments based on evaluative functions, in order to avoid losses (Magno et al., 2006).

Previous studies have shown relationships between individual differences in learning performance and activation in the striatum and ACC (Schonberg et al., 2007; Santesso et al., 2008). These studies mark an important step in the understanding of the neural underpinnings of feedback learning, as they pinpoint the brain mechanisms that are most proximally involved in shaping learning performance. It is important to note,

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Abbreviations: ACC, anterior cingulate cortex; fMRI, functional magnetic resonance imaging; PFC, prefrontal cortex; SMA, supplementary motor area.

though, that these studies investigated between-subject differences in learning behavior. In the present research, complementing previous studies, we explore which brain regions covary with performance within individuals. Specifically, by comparing multiple independent learning periods within subjects, we examine which brain regions are associated with fluctuations of individual learning performance over time.

Subjects performed a probabilistic feedback-learning task that consisted of multiple independent Learning blocks and non-learning Control blocks, while being scanned with functional magnetic resonance imaging (fMRI). In each Learning block, subjects had to learn the rule describing which button (left, right) was associated with a particular colored cue (two colors per block). As there were multiple independent Learning blocks (each with new color cues), the learning process could be measured repeatedly. To identify regions associated with learning, intended to provide a basic verification that the task activated learning-related regions as expected, we contrasted activation during Learning blocks to that of Control blocks. Next, we contrasted trials at the beginning of each Learning block to those at the end (controlled for the same within-block contrast in Control blocks), so we could identify regions associated with learning the stimulus–response rule (Learning phase) as compared to applying that rule (Application phase). Since subjects had to establish a new stimulus–response rule in each Learning block, each block could be assigned a score for performance reflecting the successful acquisition of that rule. This allowed us to determine activation related to the within-subject variation in learning performance across the experiment as a predictor for brain activation. Note, importantly, that it is the combination of the two contrasts described above that will provide the essential information on learning-related activation. In the Learning phase versus Application phase contrast, activation during the Learning phase will covary with learning-related processes, but also with lower accuracy and more negative feedback. In the final, parametric, contrast, higher activation will again covary with learning-related processes, but now with higher accuracy and more positive feedback. So, if activation turns out to be present in both contrasts, this indicates that the activation that is found is related to learning, rather than to the valence of feedback.

## EXPERIMENTAL PROCEDURES

### Participants

Twenty-one right-handed subjects (10 male, mean age 22, standard deviation 2 years) were tested. Informed consent was obtained from all subjects and the study was approved by the local ethics committee of the UMC Utrecht, the Netherlands.

### Task

The feedback-learning task (see Fig. 1) consisted of 12 Control and 12 Learning blocks, presented in alternation

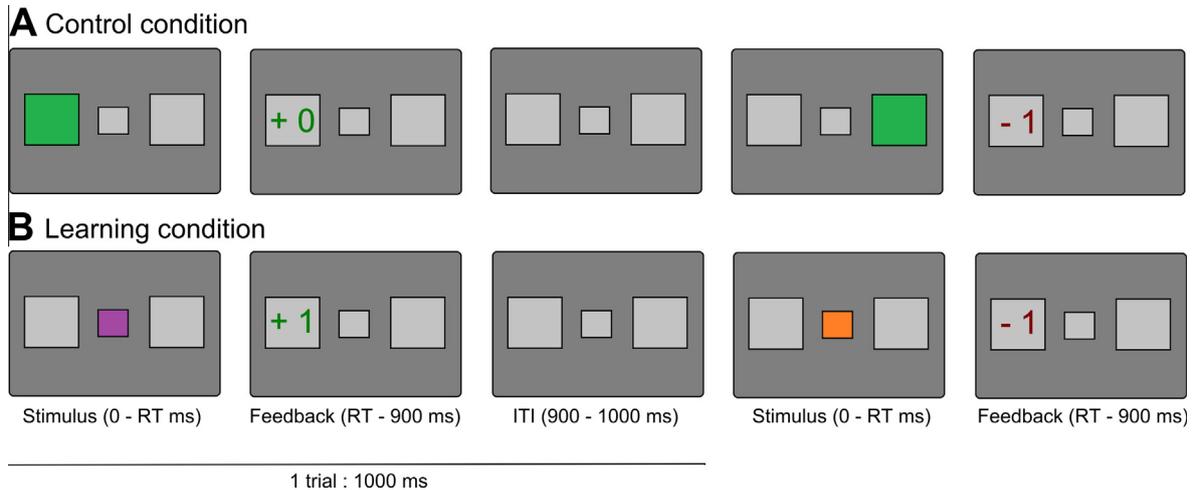
with the exception of the first two blocks that were both Control blocks. Each block had a duration of 20 s (20 trials), and began with a small central fixation square and two empty squares (left and right of the screen). In Control blocks, one of the peripheral squares changed color, whereas in Learning blocks, the central fixation square changed color, indicating to the subject that a response had to be made. Responses were given using the right thumb and had to be made within 700 ms after stimulus onset. Immediately following the response, feedback was presented up to 900 ms after stimulus onset. Next, the display was cleared for 100 ms until the next trial.

During Control blocks, indicated by a gray-colored central fixation square, subjects had to press the response button corresponding to the location of the stimulus (left or right). Feedback in this condition was either neutral or negative: after a correct response, a green '+0' was shown, otherwise a red '-1'. During Learning blocks, the central fixation square was filled by one of two colors. These were determined pseudo-randomly per block, such that they were easy to distinguish. Subjects then had to learn which response (either left or right) was associated with that particular color. Feedback followed immediately after responding. After a correct response, a green '+1' was presented; an incorrect response was followed by a red '-1' in the square corresponding to the pressed button. Feedback was based on a probabilistic model. That is, feedback was provided according to the proper mapping on 75% of the trials, and according to the reverse mapping in 25% of the trials. Trials with feedback according to the reverse mapping were distributed randomly across the 20 trials of each block. As a result, pressing the correct response resulted in positive feedback on three out of four trials (i.e. 75%).

Prior to the fMRI session, subjects were trained to become familiar with the task. First, they performed a simplified version of the task in which feedback was deterministic: a stimulus was associated with a response, and if and only if that response was given the resulting feedback was positive. Then, they performed the task with probabilistic feedback (75% valid), but were informed of the correct response on each trial. This was done to acquaint subjects with the concept of probabilistic feedback. Finally, subjects performed the task using only feedback to determine correct responses. This latter task was identical to the task used in the fMRI session, although it featured different colors. Note that subjects did not learn the set of stimulus–response mappings per se, but were only acquainted with the task. In this way, we could identify neural correlates of the acquisition of new stimulus–response mappings during the fMRI session, for each of the 12 Learning blocks separately.

### Behavioral analysis

In Learning blocks, subjects responded according to an implicit stimulus–response mapping, based on the color of the central fixation square. The stimulus–response mappings were different for each Learning block.



**Fig. 1.** Schematic representation of the probabilistic feedback-learning task. The task consisted of 12 non-learning Control blocks and 12 Learning blocks of 20 trials each. (A) In the Control condition, each trial started with the presentation of a green square either on the left or right side of the screen. Subjects were instructed to press either the left or right button corresponding to the location of the green square. Immediately after responding, feedback was presented in the square corresponding to the response. If the response was correct, a green '+0' appeared, otherwise a red '-1' appeared. (B) In the Learning condition, each trial started with the presentation of a colored cue in the center of the screen. Subjects had to learn which button to press (left or right) in response to that cue. In each Learning block, there were two colors used as cue, and these were different for each block. Feedback was given in a similar fashion as for the non-learning Control condition. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Learning blocks were divided into Learning and Application phases based on the last switch between stimulus–response mappings evidenced by the responses. That is, Learning phase ended when the subject started to consistently respond according to one stimulus–response mapping. Control blocks were also divided into two phases, based on the average trial duration of these phases in Learning blocks. Accuracy and reaction time were calculated for and compared between these two phases of Control and Learning blocks.

### Image acquisition

Data were acquired on a 3T Philips Achieva MRI scanner (Philips Medical Systems, Best, The Netherlands). Foam padding was used to restrict head motion. Functional scans were acquired using a two-dimensional echo-planar imaging (2D-EPI) sequence and SENSE factor 2.4 (anterior–posterior), with the following parameters: TE = 23 ms, TR = 1600 ms, voxel size = 4 mm isotropic, flip angle = 72.5°, reconstructed matrix = 64 × 64, 36 axial slices per volume, field of view 192 × 256 × 96. A total of 225 functional volumes were acquired in about 8 min.

### fMRI analysis

Preprocessing and statistical analyses were performed using SPM5 (<http://www.fil.ion.ucl.ac.uk/spm/>). Functional scans were realigned using rigid-body transformation. The anatomical scan was co-registered to the functional scans, and both the anatomical and functional scans were normalized to match the MNI-152 T1-template. Finally, the functional scans were smoothed using a full-width-half-maximum 8-mm

Gaussian kernel. For each individual subject, regression-coefficients for each voxel were obtained from a General Linear Model (GLM) regression analysis using a factor matrix that contained the factors modeling activation during the two phases of the Control and Learning blocks (four factors). To obtain activation related to fluctuations in individual performance across blocks, a parametric factor modeling the accuracy during each Learning block was also included. Low-frequency drifts were controlled for using a high-pass filter (discrete cosine functions) with a cutoff of 128s. Motion parameters from the realignment procedure were included as regressors of no interest to account for residual effects of head motion.

The strategy for group-wise analyses was as follows. First, to obtain basic activation associated with Learning versus Control blocks, a whole-brain group-wise paired-samples *t*-test was performed to test the difference in activation between Learning blocks and Control blocks. Next, to identify regions associated with the initial Learning phase of Learning blocks, where the stimulus–response rule had to be determined as compared to the subsequent application of the rule, a whole-brain group-wise paired-samples *t*-test was performed to test Learning versus Applying phases during Learning blocks. By contrasting this to the same contrast in Control blocks (early phase versus late phase during Control blocks), we corrected for the potential confound of time-in-block. Finally, a whole-brain group-wise one-sample *t*-test was performed to identify activations associated with within-subject performance (accuracy) variations across blocks. The accuracy of each Learning block as a whole was determined and used as a parametric modulator of the activation during the Learning phase of each of the 12 Learning blocks, per subject. This yielded a regression-coefficient map per

subject indicating where activation was related to fluctuations in Learning accuracy across the 12 Learning blocks. These maps were used in a group-wise one-sample *t*-test to reveal brain regions that consistently (over all subjects) showed higher activation when subjects performed relatively well. All group maps were tested for significance at a family-wise error (FWE) corrected cluster level of  $p = 0.05$  (cluster-defining threshold of  $p = 0.001$ , critical cluster size of 28 voxels).

## RESULTS

### Behavioral results

The average number of trials in the Learning phase of Learning block (i.e. at the beginning of each Learning block) was 10 (standard error 1). After this Learning phase, in the remainder of the trials in each Learning block, the stimulus–response rule is applied during the Application phase. Thus, on average, both the Learning and Application phases consisted of about 10 trials for each Learning block. These trial numbers were also used to divide Control blocks into two phases. Performance data are presented in Fig. 2. Mean accuracy was 95% (SD 2.3) and 98% (SD 1.2) for Control blocks, and 46% (SD 5.9) and 73% (SD 3.1) for Learning blocks, respectively. Note that given a 75% validity of feedback, an accuracy of 73% in the Application phase of Learning blocks reflects an almost perfect application of the stimulus–response mappings. Mean reaction time was 431 ms (SD 14.3) and 420 ms (SD 16.8) for Control blocks, and 452 ms (SD 21.4) and 478 ms (SD 18.5) for Learning blocks, for the Learning and Application phases, respectively.

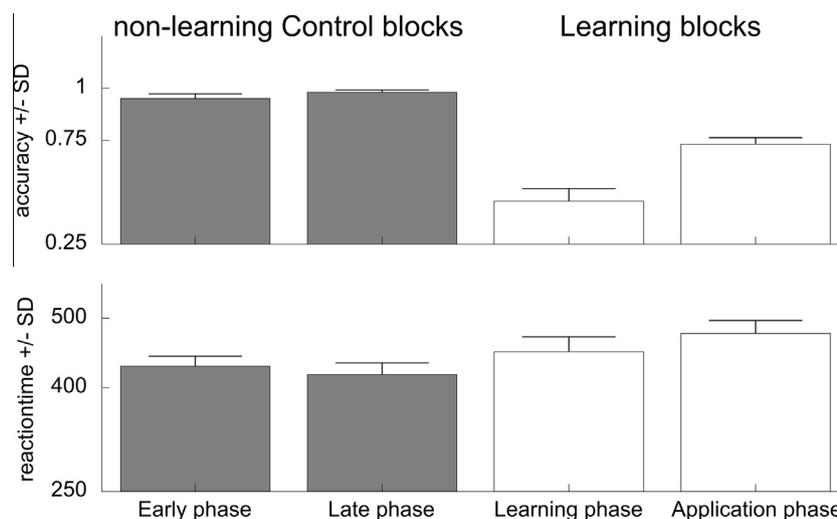
### fMRI results

As shown in Fig. 3a, activation associated with Learning versus Control blocks was found in a network consisting

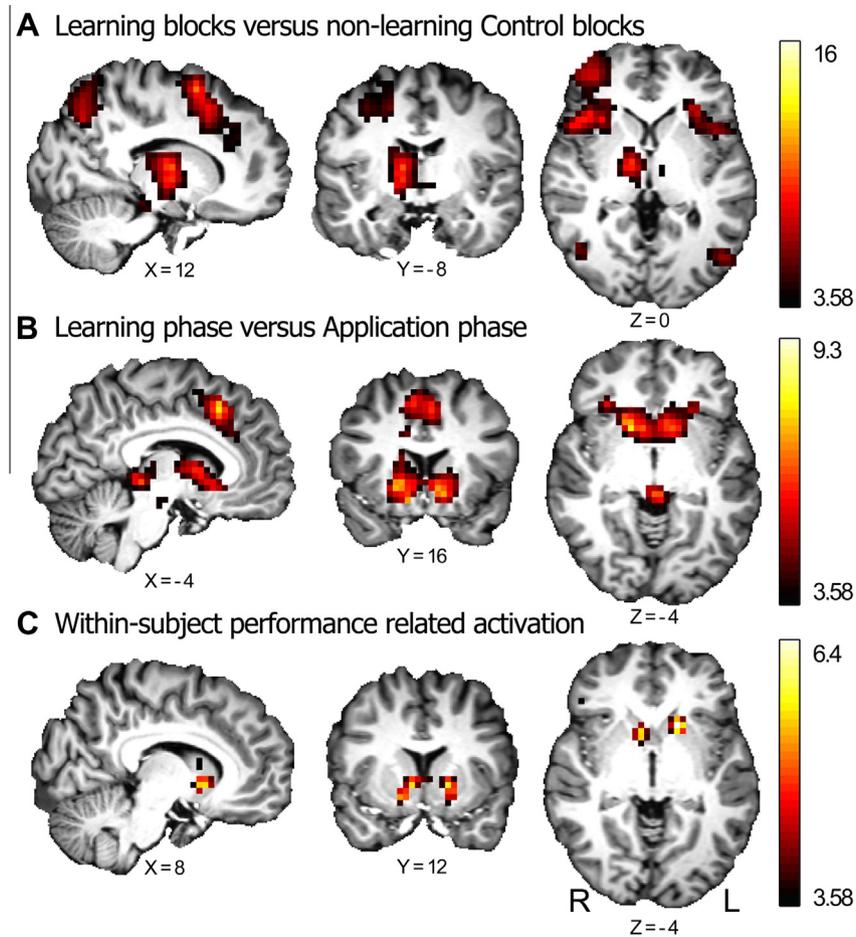
of ACC, SMA, left precentralgyrus, bilateral middle frontal gyrus (BA10), insula, inferior parietal cortex, and bilateral precuneus, and thalamus (Table 1). The contrast Learning versus Application phase revealed activation in the left and right ventral striatum, and SMA and ACC (Fig. 3b; Table 1), indicating that these areas are significantly involved in acquiring and adjusting of stimulus–response mapping based on feedback. Finally, and most relevant to the aim of the present study, activation related to within-subject performance variations across blocks was found only in the ventral striatum, bilaterally (Fig. 3c; Table 1). Even upon lowering the threshold to  $p < 0.001$  uncorrected for multiple comparisons, no additional activations appeared. There were no areas showing a significant negative relation with within-subject performance variations across blocks.

## DISCUSSION

In the current study, subjects performed a feedback-learning task, in which simple stimulus–response mappings had to be learned based on probabilistic feedback (75% valid). Increased activation was found in frontal (inferior and dorsolateral PFC, ACC and SMA and parietal (superior and inferior) cortex (Fig. 2a) when contrasting Learning blocks with non-learning Control blocks. Activation in bilateral dorsal and ventral striatum, as well as the SMA and the ACC was more prominent during the Learning phase at the beginning of each Learning block, compared to later on in the block with the mere application of stimulus–response rule (Fig. 2b). Finally, and of most interest with regard to the main research aim, individual within-subject fluctuations in performance in Learning blocks were associated with activation solely in the bilateral ventral striatum (Fig. 2c). Taken together, these data suggest that learning involves an intricate network of cortical and subcortical



**Fig. 2.** Accuracy (top) and reaction time (bottom) data for non-learning Control blocks (black bars) and Learning blocks (white bars). Accuracy and reaction times for Learning blocks were calculated for the Learning phase (first 10 trials of Learning blocks) and during the Application phase (last 10 trials of Learning blocks). Non-learning Control blocks were also split into two phases similar to Learning blocks to investigate potential within-block effects.



**Fig. 3.** Imaging results for depicting various aspects of the learning network. All brain activation maps are thresholded at a family-wise error-corrected cluster level of  $p < 0.05$ . For details see Table 1. (A) Brain activation for the contrast of Learning blocks versus non-learning Control blocks. (B) Brain activation for the contrast of the Learning phase (first 10 trials of Learning blocks) versus the Application phase (last 10 trials of Learning blocks). This was contrasted against the same contrast for non-learning Control blocks to eliminate possible within-block effects (see methods). (C) Brain activation associated with fluctuations in within-subject learning success across the 12 Learning blocks in the experiment.

**Table 1.** Overview of activations

| Region  | BA     | Side | Number of voxels | X   | Y   | Z   | Max $t$ -value |
|---|--------|------|------------------|-----|-----|-----|----------------|
| <i>Learning blocks versus non-learning Control blocks</i> |        |      |                  |     |     |     |                |
| IFG/insula  | 47     | L    | 89               | 44  | 20  | 0   | 6.38           |
| MFG   | 8/9/10 | L    | 273              | 39  | 8   | 44  | 6.14           |
|   |        | R    | 34               | -44 | 52  | 20  | 4.27           |
| Occipital lobe  | 19/37  | R    | 58               | 43  | 15  | 22  | 5.82           |
| DLPFC   | 10/46  | L    | 229              | 42  | 44  | 22  | 6.50           |
| SPL   | 7      | L    | 595              | 55  | -40 | 40  | 16.21          |
|   |        | R    | 219              | -40 | -48 | 48  | 8.48           |
| IPL   | 40     | L    | 253              | 41  | -47 | 39  | 6.49           |
| SMA   | 6      | L    | 64               | 0   | 16  | 52  | 4.97           |
| Thalamus  |        | R    | 289              | 12  | -8  | 8   | 5.71           |
| <i>Learning phase versus Application phase</i>            |        |      |                  |     |     |     |                |
| Ventral Striatum  |        | L/R  | 473              | 16  | 24  | -12 | 9.34           |
|   |        |      |                  | -12 | 16  | -12 | 7.19           |
| SMA/anterior cingulate                                    | 6      | L/R  | 182              | -4  | 20  | 44  | 7.75           |
| Superior Colliculus                                       |        | L/R  | 47               | 0   | -32 | -4  | 6.51           |
| <i>Within-subject performance related activation</i>      |        |      |                  |     |     |     |                |
| Ventral striatum  |        | L    | 32               | 16  | 12  | -12 | 5.31           |
|   |        | R    | 34               | -16 | 16  | -4  | 6.42           |

*Note:* All results are significant at a family-wise error corrected cluster level of  $p < 0.05$ ; L, left; R, right; X Y Z refer to the center of mass; IFG, inferior frontal gyrus; MFG, middle frontal gyrus; DLPFC, dorsolateral prefrontal cortex; SPL, superior parietal lobe; IPL, inferior parietal lobe; SMA, supplementary motor area.

regions. These data replicate and extend previous between-subject learning studies by showing that the ventral striatum plays a particularly pivotal role in learning as it is related to within-subject learning success.

### Learning blocks versus non-learning Control blocks

As expected, the contrast between Learning and Control blocks showed brain activation in a network of regions associated with general goal-directed behavior. Activation in the dorsolateral PFC may be due to increased working memory demands in Learning blocks. In Control blocks, a response (pressing left or right button) was directly indicated by the stimulus (presented on either the left or right side of the screen), whereas in Learning blocks, responses were based on arbitrary task demands (i.e. the color of a centrally presented stimulus indicated a response). This is consistent with the literature linking the dorsolateral PFC to establishing high-level rules guiding response selection (Koechlin et al., 2003; Hamidi et al., 2009; Kehagia et al., 2010). Furthermore, activation of the SMA throughout Learning blocks agrees with the idea that the SMA is sensitive to response conflict (Zandbelt et al., 2012b). Even after a stimulus–response mapping has been established, there will still be more response conflict than in the Control condition, as stimulus–response compatibility was always higher in this condition. Finally, we found parietal activation. As the parietal cortex is associated with visual short-term memory (Vink et al., 2005a; Kawasaki et al., 2008) and sensorimotor transformations (Grol et al., 2006; Chong et al., 2008; Coulthard et al., 2008), activation during Learning blocks could be explained by an increase in attention to the color of the central cue and the direction of responses.

### Learning versus applying stimulus–response mappings

Next, we focused on those regions showing activation more specifically related to feedback learning, by separating the acquisition and adjustment of mappings based on feedback (i.e. Learning phase of individual Learning blocks) from the application of learned stimulus–response mappings (i.e. Application phase). To correct for general time-in-block effects, we corrected for the same contrast (using the first 10 trials versus last 10 trials) in Control blocks. Our results are consistent with those reported by Eliassen et al. (2012), who reported higher activations in striatal and frontal regions during the early phases of learning as compared to the subsequent application phase. Specifically, we found increased activation during the Learning phase versus the Application phase in the bilateral striatum, and SMA extending to the ACC. The SMA and striatum are closely interconnected. The striatum is the main subcortical input region of the medial motor loop and has been associated with the initiation as well as the inhibition of movements (Vink et al., 2006, 2005b; Zandbelt and Vink, 2010; Zandbelt et al., 2011). The SMA is the main cortical region of the medial motor loop (Alexander and Crutcher, 1990). The relationship

between the SMA and response conflict (Zandbelt et al., 2012b) may also explain its activation during the Learning phase as compared to the Application phase of Learning blocks (versus the same contrast in Control blocks). In the Learning phase, at the start of Learning blocks, response conflict is high because neither response (left or right button press) has yet a clear advantage, whereas in the Application phase at the end of the block such an advantage has developed based on feedback. The difference in ACC activation found between the early and late phases of the blocks may reflect increased performance monitoring during the initial learning phase (Ridderinkhof et al., 2004), and the need to update responses based on punishment (Ullsperger and von Cramon, 2003). This explains why such activation is absent during the late application phase of stimulus–response mappings, as there is no longer a need to adjust behavior based on feedback. The involvement of the ventral part of the striatum in learning from feedback was expected based on its association with the processing of prediction errors (Becerra et al., 2001; Knutson and Cooper, 2005; O'Doherty et al., 2007; Brovelli et al., 2008) and adjustment of behavior based on feedback (Delgado et al., 2005; Tricomi et al., 2006; Day and Carelli, 2007; for an overview see Bornstein and Daw, 2011). Activation in the ventral striatum has been found to reflect prediction errors in both Pavlovian (i.e. stimulus > outcome) and operant conditioning (i.e. response > outcome, given the stimulus) (O'Doherty et al., 2007; Brovelli et al., 2008). In contrast, the dorsal striatum appears to be involved with biasing response probabilities during operant conditioning (Vink et al., 2005a,b; O'Doherty et al., 2007; Zandbelt and Vink, 2010). In addition we did not find ventral striatum activation in the Learning versus Control contrast, suggesting the ventral striatum is only active during either learning or adjusting stimulus–response mappings (Learning phase), and does not play a role during the Application phase.

### Within-subject learning performance

Finally, we found activation in the ventral striatum to covary with within-subject performance across the 12 Learning blocks, with higher activation when learning was more successful. This is consistent with findings from Schonberg et al. (2007) and Santesso et al. (2008) who showed in a between-subject design that more successful learners also showed higher activation in the ventral striatum. We extend these findings by showing this effect in individual subjects using a within-subject design. Combined with the data from the Learning versus Application contrast described above, we take our results to suggest that this ventral striatum activation reflects the use of feedback in creating and adjusting stimulus–response mappings. Indeed, as the task involved only simple stimulus–response mappings, the primary factor determining learning success was whether mappings were correctly established based on probabilistic feedback (75% correct feedback). This interpretation is consistent with results from Seger and

Cincotta (2006) and Tricomi et al. (2006) who also used within-subject blocked designs similar to our setup to investigate the regions involved in learning. However, whereas they reported activation in the dorsal caudate nucleus to be responsive to feedback during learning, we found the ventral but not the dorsal striatum to be associated with within-subject variations in learning performance. We did find activation in the dorsal striatum, but only when contrasting the Learning phase with the Application phase Learning blocks.

### Limitations

There are alternative accounts that could be argued to explain our findings. One could argue that the current results were due to a lower incidence of rewarded responses in low-accuracy blocks, leading to lower ventral striatum activation in those blocks. However, the ventral striatum also showed increased activation in the Learning phases of Learning blocks independent of performance (Fig. 3b), which contained more punished than rewarded trials compared to the later phase of these Learning blocks, when subjects performed at their maximum. We therefore argue that the correlation between activation in the ventral striatum and learning success is not likely to reflect effects of reward alone (see also Schonberg et al., 2007; Santesso et al., 2008), and that this activation is largely linked to the creation and adjustment of stimulus–response mappings. Furthermore, it has been argued that activation in the ventral striatum is associated with occurrence of prediction errors. Indeed, Schonberg et al. (2007) reported higher prediction error-related activation in the ventral striatum in subjects who were good learners compared with subjects who were poor learners. It may very well be the case that successful learners are successful because of this increased response to prediction errors, and this heightened response serves to adjust behavior accordingly. In our design we tested for within-subject effects, so that individual differences (being either a good or poor learner) cannot explain our results. In addition, in blocks in which learning was more successful there were fewer prediction errors than during lower accuracy blocks, perhaps arguing against the idea that prediction errors are the primary process driving activation in the ventral striatum.

It should be noted, that given our blocked design we are unable to determine the individual contributions from stimulus-cue, response, or outcome evaluation processes to the patterns of brain activations, or effects of feedback valence. Even using a trial-by-trial design, it is difficult to disentangle these processes given the temporal resolution of fMRI. Techniques such as EEG do provide this temporal resolution, but lack spatial resolution. One way of measuring ventral striatum activation with a high temporal resolution is via electrodes such as those used for deep-brain stimulation (Cohen et al., 2011).

Finally, we note that in the control blocks we attempted to remove either positive or negative feedback. However, the +0 feedback indicating no

change in score was positive relative to the punishment for making an error. However, the accuracy in this condition was very high and, essentially, required no feedback learning, so that we expect the effects of the feedback to have been minimal relative to the effects in Learning blocks.

Further research is needed to determine whether these results generalize. For instance, it may be that increasing the complexity by increasing the number of stimulus–response mappings would lead to Learning phase-related activation in other regions such as the dorsolateral PFC. Furthermore, we note that subjects were under relatively high time pressure to respond (700 ms from stimulus onset). This may have influenced the activation in the striatum and SMA, as these regions are sensitive to time pressure (Forstmann et al., 2008). A further fundamental question is via which mechanisms relationships between stimuli, responses and outcomes are encoded, as opposed to where in the brain. The presence of widespread changes in phase relations related to stimulus–response mapping (Gladwin and de Jong, 2005; Gladwin et al., 2008) provides tentative evidence for phase coding playing a role in the implementation of goal-directed behavior (Roelfsema et al., 1997). Finally, a potentially important question is whether fluctuations in performance in patient groups are also found to be associated with the ventral striatum, or whether other regions and hence component processes might be more relevant in those populations. For example, obsessive–compulsive disorder is known to be associated with deficient ventral striatum processing during reward (Figgie et al., 2011, 2013).

### Summary and conclusion

In conclusion, learning by establishing stimulus–response mappings is a prerequisite of adaptive goal-directed behavior. In a task with multiple independent Learning blocks per subject, the process of creating and adjusting stimulus–response mappings based on feedback involved the SMA, ACC and striatum. In addition, both activation in the ACC and the ventral striatum was only found to be significantly associated with learning the stimulus–response rules, and not with their application when the rule was successfully learned. Finally, and most notably, only the ventral striatum was found to be associated with within-subject variation in learning success. The combination of these results provides a novel kind of support for the central role of the ventral striatum in adjusting behavior using feedback, and suggests that individual fluctuations in learning performance over time may be related to processes in the ventral striatum.

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