Methods

Participants

Eight healthy subjects were included in this study (mean age 38.9 ± 10.1 years; 1 female; mean interval between scans 10.9 ± 2.3 months). Two additional subjects were recruited but excluded from analysis because they failed to return for the re-test visit. All volunteers gave informed consent according to procedures approved by the UCLA Office of Protection of Research Subjects. All volunteers were native English speakers, and right-handed as determined by the Edinburgh handedness inventory. Subjects had no history of neuropsychiatric disorders and were not currently taking any psychoactive medications.

Task Design

Subjects performed two distinct tasks, a probabilistic classification learning (PCL) task and cued response-inhibition task. Both experimental paradigms utilized in this study were derived from previous published work. The PCL task performed in this study was identical to that described in Aron et al. 2006. Briefly, in PCL the stimulus set consisted of four cards, each with a set of random shapes on them. In each trial of PCL, one to three of these cards were presented to the subject. Each combination of cards (irrespective of the randomized location of each individual card) comprised a 'stimulus'. The subject would then have to make a decision based on the stimulus, whether that stimulus predicted an outcome of sunshine (left button press) or of rain (right button press). Each stimulus had a particular probability with which it was associated with the rain outcome, and the frequency of presentation of each stimulus was chosen such that the associations between the four particular cards and the rain outcome were 0.18, 0.37, 0.59, and 0.82 respectively (for details see Aron, et al. 2006). In this way, both the individual cards and the individual stimuli (card combinations) were associated with the outcome (sunshine/rain) in a probabilistic manner.

In each experimental scanning session, the PCL task consisted of 50 PCL trials and 30 trials of a baseline task. These trials occurred as 10 cycles of 5 consecutive PCL trials followed by 3 consecutive baseline trials. In PCL trials, the stimuli were presented for 3 seconds, and during this time the subjects respond (left button press if they believe the stimulus predicts sunshine and right if rain). Immediately following their response, the subject received feedback in which the word 'Sunshine' or 'Rain' is displayed above the stimulus for 1 second. There is a 0.5 second interval between trials. The baseline trials were designed to control for visual stimulation, response, and feedback in the fMRI analysis. In each baseline trial a pattern of random shapes is presented in all of the three card positions for 3 seconds along with the instructions 'Press Left'. Once the subject responds with a button press, the instructions go away.

The cued response-inhibition task, commonly known as stop-signal task, was derived from a selective stop-signal paradigm introduced by Logan et al. in 1986. In this

experiment, subjects were shown arrows pointing in either the left or right direction and were instructed to press the right button when the arrow pointed right and the left button when the arrow pointed left. In some of the trials they would hear an auditory signal (stop signal) indicating that they should try to inhibit their response, but only if the arrow was pointing in a particular direction. In the first scanning session they were directed to inhibit their response when they heard the stop signal *and* the arrow was pointing left, while in the second session they were directed to inhibit their response when they heard the stop signal *and* the arrow was pointing right. Subjects were instructed to try to respond as quickly as possible but also to try their best to inhibit the response when directed to do so. The timing of the stop signal presentation was varied in relation to the presentation of the arrow indicating the proper response such that all subjects were able to successfully inhibit their response 50% of the time. An adjusting staircase method was used to ensure that each individual subject performed at this same level.

Stimulus presentation and timing, as well as response collection for both the cued response-inhibition task and the PCL task were achieved using the MATLAB (www.mathworks.com) psychophysics toolbox (www.psychtoolbox.org) on an Apple PowerBook G4 running OS X (Apple computers, Cupertino, CA). Visual stimuli were presented using MR compatible goggles (Resonance Technologies, Van Nuys, CA), and the computer was synchronized with the onset of each functional run to ensure the accuracy of event timing. Responses and timing were measured using a fiber optic button box (Current Designs, Inc).

Procedure

In each session, subjects were able to practice each task briefly to familiarize themselves with task requirements before entering the scanner. The first task performed in the scanner was the cued response-inhibition task. Each subject performed 2 to 3 runs of this task (256 trials each, 1.5 s per trial, 6-min duration) with a short break between scans. The second task performed in the scanner was the PCL task. Subjects performed 2 runs of this task (80 trials each, 4.5 s per trial, 6-min duration) separated by a short break. In the second session (roughly one year later), small changes were made to each task. The cued response-inhibition task was exactly the same as in the prior session, except that the direction of the arrow in which subjects were instructed to inhibit their response when seen in conjunction with the stop signal was changed. A small change was also made in the PCL task. The colors and shapes making up the PCL stimuli were altered in order to prevent the transference of learning from the first session.

MRI acquisition

A 3T Siemens Allegra MRI scanner was used to acquire 180 functional T2*-weighted echoplanar images (EPI) (TR= 2s, TE= 30ms, flip angle= 90°, FOV= 200, slice thickness= 4mm, 33 slices). For the purposes of registration, a matched-bandwidth scan (same slice prescription as EPI) was acquired in the Allegra scanner and a high resolution MPRAGE structural scan (TR= , TE= , FOV= , saggital plane, slice thickness= , # slices) was acquired in a separate 1.5T Siemens Sonata MRI scanner for each subject.

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