Research Article

A Cross-Species Investigation of Acetylcholine, Attention, and Feature Binding

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ABSTRACT—*The binding problem is the brain's fundamental challenge to integrate sensory information to form a unified representation of a stimulus. A recent nonhuman animal model suggests that acetylcholine serves as the neuromodulatory substrate for feature binding. We hypothesized that this animal model of cholinergic contributions to feature binding may be an analogue of human attention. To test this hypothesis, we conducted a cross-species study in which rats and humans learned comparable intramodal feature-conjunction (FC) and feature-singleton (FS) tasks. We challenged the cholinergic system of rats using the muscarinic antagonist scopolamine (0.2 mg/kg) and challenged the attentional system of humans by dividing attention. The two manipulations yielded strikingly similar patterns of behavior, impairing FC acquisition, while sparing FS acquisition and FC retrieval. These cross-species findings support the hypothesis that cholinergically driven attentional processes are essential to feature binding at encoding, but are not required for retrieval of neural representations of bound stimuli.*

The mammalian brain is organized in a modular fashion such that distinct regions are primarily responsible for processing the different features of a stimulus, such as its color and shape. Feature binding, the cognitive process by which a unified neural representation of a stimulus is formed, has been shown to depend on attention (Treisman & Gelade, 1980). Although feature-singleton (FS) tasks require only the processing of single features, feature-conjunction (FC) tasks require the binding of multiple features. Patients with attentional impairments are impaired at FC, but not FS, tasks (Bernstein & Robertson, 1998; Cohen & Rafal, 1991; Foster, Behrmann, & Stuss, 1999; Friedman-Hill, Robertson, & Treisman, 1995; Tales et al., 2002), and functional magnetic resonance imaging (fMRI) studies have implicated fronto-parietal networks in feature binding (Corbetta, Shulman, Miezin, & Petersen, 1995; Luck & Ford, 1998; Reynolds & Desimone, 1999; Treisman, 1998).

Although the cognitive mechanisms and functional neuroanatomy of feature binding have been well examined in the literature on human cognition, the neurochemistry of feature binding remains unknown. Research on nonhuman animals suggests that the neuromodulator acetylcholine (ACh) may be critical to feature binding given its presumed role in modulating attention (Sarter, Hasselmo, Bruno, & Givens, 2005). Recent work showed that the muscarinic cholinergic antagonist scopolamine selectively impaired the ability of rats to learn a cross-modal odor-texture FC task, but not their ability to learn an FS task. In addition, scopolamine left the retrieval of previously learned FC stimuli intact (Botly & De Rosa, 2007). Such an encoding-retrieval dissociation is consistent with a model in which high cortical ACh levels set the stage for encoding, whereas low cortical ACh levels set the stage for retrieval (Hasselmo & McGaughy, 2004).

We hypothesized that this animal model of cholinergic contributions to feature binding may be an analogue of human attention. As feature binding is traditionally assessed intramodally in humans, a test with intramodal stimuli would provide a stronger test of this hypothesis. Accordingly, we designed intramodal versions of the FC and FS tasks for rats (using odors) and a homologue for humans (using colored shapes), and conducted a cross-species study to assess whether muscarinic cholinergic blockade in rats is an appropriate model for impairment in human attention.

During performance of the FC and FS tasks, we challenged the cholinergic system of rats (Experiment 1) using the muscarinic antagonist scopolamine and challenged the attentional system of humans (Experiment 2) using a concurrent task. If the animal model of cholinergic contributions to feature binding is analogous to human attention, then challenging the attention of

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human participants behaviorally with a divided-attention task and challenging the cholinergic system of rats with scopolamine should result in similar effects on feature binding. We predicted that both manipulations would impair acquisition of FC stimuli, leaving acquisition of FS stimuli relatively intact. In addition, our hypothesis predicted a novel behavioral dissociation in feature-binding performance in humans: Under diminished attention, encoding of FC stimuli should be impaired, but retrieval of previously bound FC stimuli should remain intact.

EXPERIMENT 1

Method

Participants

Eight experimentally naive adult male Long-Evans rats (Charles River, Quebec, Canada) were maintained at 90% of *ad libitum* free-feeding weight for the duration of the experiment. This study was approved by the University of Toronto's Institutional Animal Care Committee.

Stimuli

The stimuli were presented in bowls containing the granular commercial bedding Bed-o'cobs (The Andersons, Maumee, OH). At the bottom of each odor-odor bowl was a small metal cap with small holes. Each metal cap contained cotton gauze, which was injected with 0.1 ml of the appropriate scented mineral oil each day (Aveda®, Blain, MN; The Body Shop®, Wake Forest, NC). This oil constituted one odor stimulus. The second odor stimulus was provided by mixing ground herb or spice with the bedding and filling the bowl with this mixture. Table 1 lists the odorants from which the experimental stimuli were created.

On each trial, rats were simultaneously presented with two digging bowls in a testing arena: an odor-odor bowl and a blank bowl containing Bed-o'cobs bedding (see Fig. 1). On target trials, the reward (half piece of Kellogg's Froot Loops cereal) was buried in the odor-odor bowl, and on distractor trials, the reward was buried in the blank bowl. Finely ground pieces of Froot Loops cereal were added to the bedding of all bowls to mask the location of the food reward. (For similar methods, see Botly & De Rosa, 2007.)

Each FC stimulus set contained four conjunction odor-odor bowls, along with the blank bowl. Two of the odor-odor bowls were designated target bowls (T1 and T2) and were presented on target trials. The remaining two odor-odor bowls were designated distractor bowls (D1 and D2) and were presented on distractor trials. In a forced-choice design, rats were allowed only one bowl choice on each trial. Binding of odors was required to determine the correct bowl choice as each individual odor was associated with either the target or the distractor, depending on its feature pairing, and the different pairings occurred equally often across trials. That is, each odor was used in one target bowl and one distractor bowl, such that no single odor could be used to select the correct bowl (see Fig. 2).

TABLE 1
Odorants, Colors, and Shapes From Which the Experimental Stimuli Were Created

Experiment 1		Experiment 2	
Mineral oils	Herbs and spices	Colors	Shapes
Vanilla	Cumin	Red	Triangle
Peach	Ginger	Blue	Square
Ylang-ylang	Cinnamon	Green	Cross
Geranium	Sage	Yellow	Circle
Tangerine	Cocoa	Brown	Cylinder
Peppermint	Nutmeg	Pink	Hexagon
Bergamot	Garlic	Orange	Diamond
Musk	Coffee	Purple	Trapezoid
Passion fruit	Coriander		
Jasmine	Oregano		
Sandalwood	Mustard		
Strawberry	Dried coconut		
Chamomile	Dill		
Lilac	Turmeric		
Lavender	Rosemary		
Eucalyptus	Ground almonds		
Tea tree	Onion		
Frankincense	Basil		
Papaya	Curry		
Tobacco flower	Paprika		
Melon	Celery salt		

Each FS stimulus set contained four nonconjunction odor-odor bowls, along with the blank bowl. Two of the odor-odor bowls were designated target bowls (T1 and T2), and the remaining two were designated distractor bowls (D1 and D2). Feature binding was not required to determine the correct bowl choice as each odor-odor bowl was characterized by two distinct odors. That is, rats could use a single odor or the distinct combination of two odors to select the correct bowl (see Fig. 2).

Pharmacological Manipulation

A within-subjects pharmacological design was used. Each rat participated in each of two drug conditions: scopolamine hydrobromide (0.2 mg/kg dissolved in sterile 0.9% physiological saline, pH = 7.4) and physiological saline (injection control). Rats were given an intraperitoneal injection 15 min prior to testing, and experimenters were blind to the drug condition. Given that rats in our cross-modal study performed comparably under the influence of the peripheral antagonist methylscopolamine (a control for the peripheral effects of scopolamine) and when injected with saline (Botly & De Rosa, 2007), we used only saline and scopolamine in the present study to best equate the drug conditions with the full- and divided-attention conditions used with the human participants in Experiment 2.

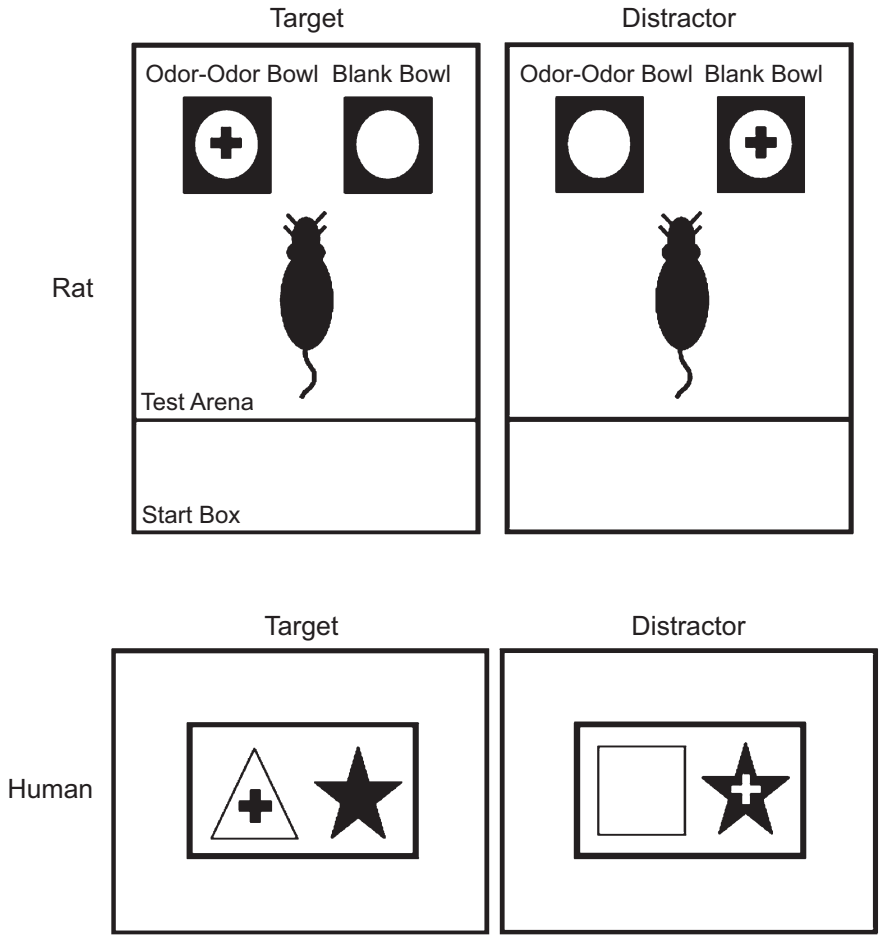

Fig. 1. Illustration of the two different trial types (target and distractor) of the forced-choice tasks. On target trials, the rewarded (+) stimulus was the odor-odor bowl (for rats) or the colored shape (for humans), shown here in white. On distractor trials, the rewarded stimulus was the blank bowl (for rats) or the black star (for humans).

Training Procedure

Each session consisted of 12 trials, half of which were target trials (3 T1, 3 T2), and half of which were distractor trials (3 D1, 3 D2). Within a session, trials were presented in a pseudorandom order, such that no more than 3 consecutive trials were of the same type (target or distractor). First, the rats learned an initial FC stimulus set, which we refer to as the *learning-to-learn* set, without injections. The rats received one session per day until all rats reached a criterion of at least 5 out of 6 correct responses on target trials and 5 out of 6 correct responses on distractor trials for at least two nonconsecutive sessions.

After acquiring the learning-to-learn set to criterion, the rats retrieved these same FC stimuli for two sessions under each drug condition, given the rats' excellent retrieval performance. Next, the rats acquired novel FC stimuli under each drug condition until rats under the influence of scopolamine reached asymptotic performance, which took nine sessions. Finally, the rats acquired novel FS stimuli under each drug condition until rats under the influence of scopolamine reached asymptotic performance, which took six sessions. The sequence of drug conditions was always counterbalanced across rats.

Results

Task accuracy was assessed using proportion of correct responses. For statistical analyses, acquisition data were binned into three-session blocks and retrieval data remained unblocked. All statistical analyses were conducted using SPSS Version 14 with an alpha level of .05.

Acquisition of FC Stimuli

Figure 3a depicts the results for FC acquisition. A two-way repeated measures analysis of variance (ANOVA) using drug condition (saline or scopolamine) and block as within-subjects factors revealed significant main effects of drug condition, $F(1, 7) = 21.29$, $p < .01$, $p_{rep} = .99$, $\eta_p^2 = .75$, and block, $F(2, 14) = 28.90$, $p < .001$, $p_{rep} = .99$, $\eta_p^2 = .81$, and a significant interaction, $F(2, 14) = 4.92$, $p < .05$, $p_{rep} = .94$, $\eta_p^2 = .41$ Within-subjects simple contrasts revealed that accuracy differed significantly between the saline and scopolamine conditions during all three blocks of acquisition ($p_{rep} = .93$, $\eta_p^2 = .49$; $p_{rep} = .99$, $\eta_p^2 = .84$; and $p_{rep} = .98$, $\eta_p^2 = .70$, respectively).

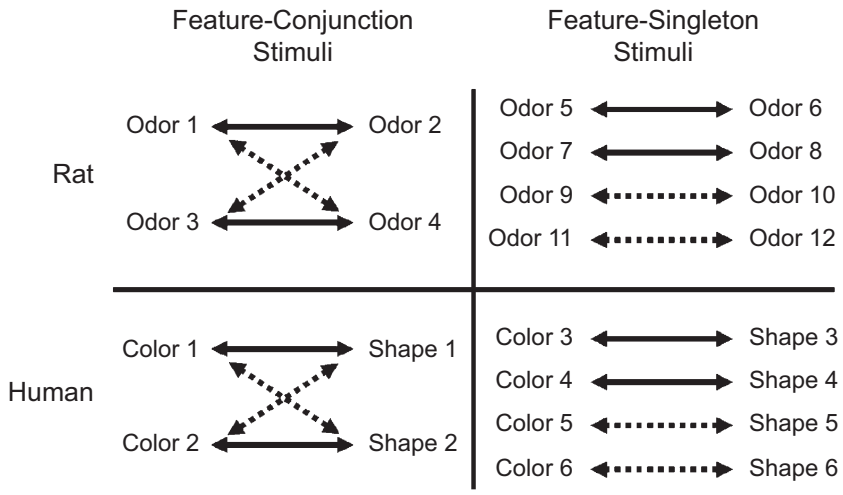

Fig. 2. Illustration of the features defining the feature-conjunction (FC) and feature-singleton (FS) stimuli. Solid lines indicate pairings of features in target stimuli, and dashed lines indicate pairings of features in distractor stimuli. The FC task required feature binding because the features of target and distractor FC stimuli overlapped. In contrast, the FS task did not require feature binding because each FS stimulus was a combination of two unique odors (for rats) or a unique color and a unique shape (for humans). The FC stimuli in each stimulus set comprised four distinct features, and the FS stimuli in each stimulus set comprised eight distinct features, so that the number of feature pairs to be learned was equated (i.e., four).

Acquisition of FS Stimuli

Figure 3b depicts the results for FS acquisition. A two-way repeated measures ANOVA using drug condition (saline or scopolamine) and block as within-subjects factors revealed a significant main effect of block, $F(2, 14) = 23.64$, $p < .001$, $p_{rep} = .99$, $\eta_p^2 = .77$, but no significant effect of drug condition ($F < 2.5$, $p_{rep} = .83$, $\eta_p^2 = .24$) and no significant interaction ($F < 1$, $p_{rep} = .62$, $\eta_p^2 = .06$). A within-subjects ANOVA comparing starting performance (Block 1) on the FC and FS tasks in the saline condition revealed that the effect of task was not significant ($F < 2$, $p_{rep} = .80$, $\eta_p^2 = .19$), which suggests that spared acquisition of the FS task under scopolamine was not simply due to the FS task being less difficult than the FC task at the outset of training.

Retrieval of FC Stimuli

Twelve sessions were required for all rats to reach criterion performance during initial drug-free acquisition of the learning-to-learn FC stimulus set. Accuracy during subsequent retrieval of these stimuli in the drug conditions was examined in a two-way repeated measures ANOVA using drug condition (saline or scopolamine) and session as within-subjects factors. This analysis revealed nonsignificant main effects of drug condition ($F < 2$, $p_{rep} = .81$, $\eta_p^2 = .22$) and session ($F < 1$, $p_{rep} = .57$, $\eta_p^2 = .01$) and no significant interaction ($F < 1$, $p_{rep} = .81$, $\eta_p^2 = .21$).

Effects of Scopolamine on Performance of the FC and FS Tasks

Figure 4a compares the effects of scopolamine on performance during the last block of FC acquisition, the last block of FS acquisition, and FC retrieval. The cost of scopolamine was computed by calculating a difference score (accuracy in the saline condition – accuracy in the scopolamine condition) for each task. A one-way repeated measures ANOVA using task (FC acquisition, FS acquisition, or FC retrieval) as a within-subjects factor revealed a significant effect of task, $F(2, 14) = 6.89$, $p < .01$, $p_{rep} = .99$, $\eta_p^2 = .50$. Within-subjects simple contrasts revealed a significant difference between the difference scores for FC acquisition and FC retrieval ($p_{rep} = .96$, $\eta_p^2 = .61$), and between the difference scores for FC acquisition and FS acquisition ($p_{rep} = .92$, $\eta_p^2 = .45$).

Discussion

Rats under the influence of scopolamine were significantly impaired at acquiring FC stimuli relative to acquiring FS stimuli and retrieving previously bound FC stimuli. These findings provide support for a critical role for the muscarinic cholinergic system in feature binding at encoding. We contend that this rat model of the role of ACh in feature binding at encoding may be an analogue of human attention. Experiment 2 tested this hypothesis using a human version of our rat feature-binding paradigm and a behavioral manipulation of attention.

EXPERIMENT 2

We predicted that if manipulations of the cholinergic system in rats are analogous to manipulations of human attention, then human participants in a divided-attention condition would exhibit impaired FC acquisition, but relative sparing of FS

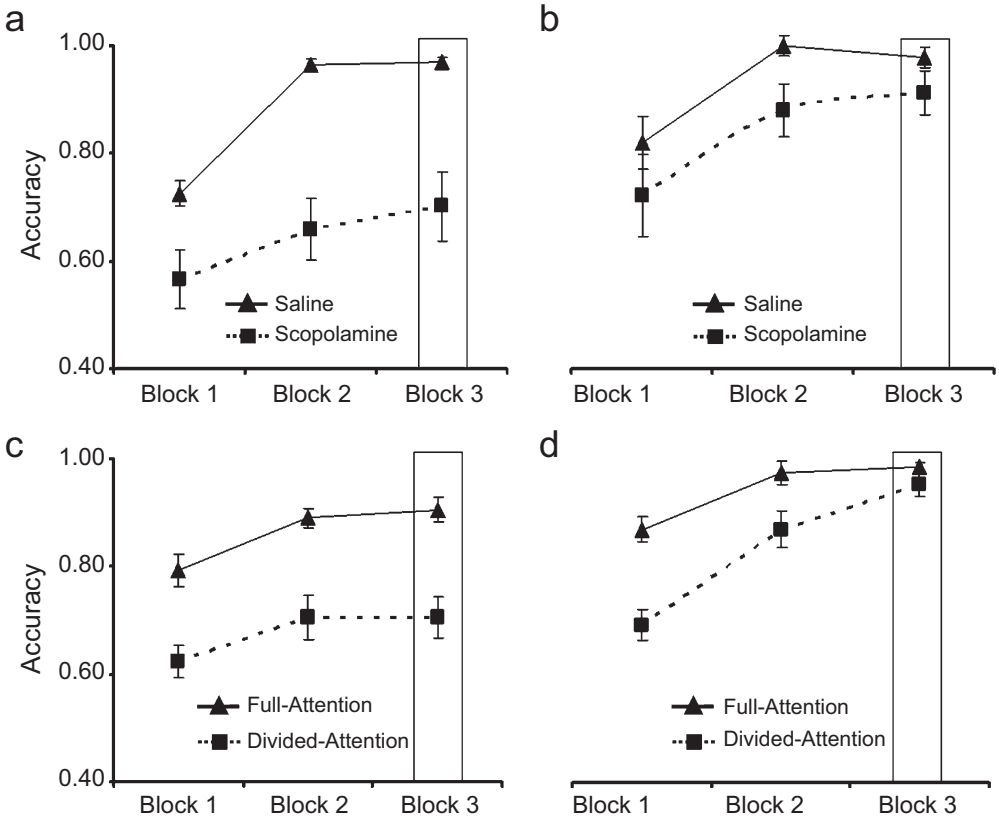

Fig. 3. Acquisition of the feature-conjunction (FC) and feature-singleton (FS) tasks in Experiment 1 (rats) and Experiment 2 (humans). The graphs in the top row show rats' accuracy on the (a) FC and (b) FS tasks in the saline and scopolamine conditions. The graphs in the bottom row show humans' accuracy on the (c) FC and (d) FS tasks in the full-attention and divided-attention conditions. Results are shown as a function of block (rats: three-session blocks for the FC task and two-session blocks for the FS task; humans: 30-trial blocks). Error bars show ± 1 *SEM*. The boxes highlight the final level of performance attained by rats and humans on the FC and FS tasks.

acquisition and FC retrieval, just as rats under the influence of scopolamine do.

Method

Participants

One hundred two undergraduate students (mean age = 20.0 years, *SD* = 3.82; 57 females, 45 males) at the University of Toronto gave written informed consent to participate in return for course credit or remuneration. Participants were randomly assigned to one of six conditions: full-attention FC acquisition, divided-attention FC acquisition, full-attention FC retrieval, divided-attention FC retrieval, full-attention FS acquisition, and divided-attention FS acquisition. There were 17 participants in each condition.

Stimuli

On each trial, a computer screen simultaneously presented two visual stimuli: a colored shape and a black star; the star served as the analogue of the blank bowl in the rat paradigm (see Fig. 1). Both stimuli were presented within a centrally located rectangle (12 × 8.5 cm); the colored shape always appeared in the left half of the rectangle, and the black star always appeared in the right half of the rectangle. The stimuli subtended 2.5° × 2.5° of visual angle. On target trials, the correct response was to select the colored shape, and on distractor trials, the correct response was to select the black star. Table 1 lists the colors and shapes from which the experimental stimuli were created.

The FC stimulus set contained four conjunction colored-shape stimuli, along with the black star. Two of the colored shapes were designated target stimuli (T1 and T2) and were presented on target trials. The remaining two colored shapes were designated distractor stimuli (D1 and D2) and were presented on distractor trials. In a forced-choice design, participants were allowed only one stimulus choice on each trial. Binding of color and shape was required to determine the correct stimulus choice, as each individual color and shape was associated with either the target or the distractor, depending on its feature pairing, and the different pairings occurred equally often across trials. That is, each color and shape was used in one target

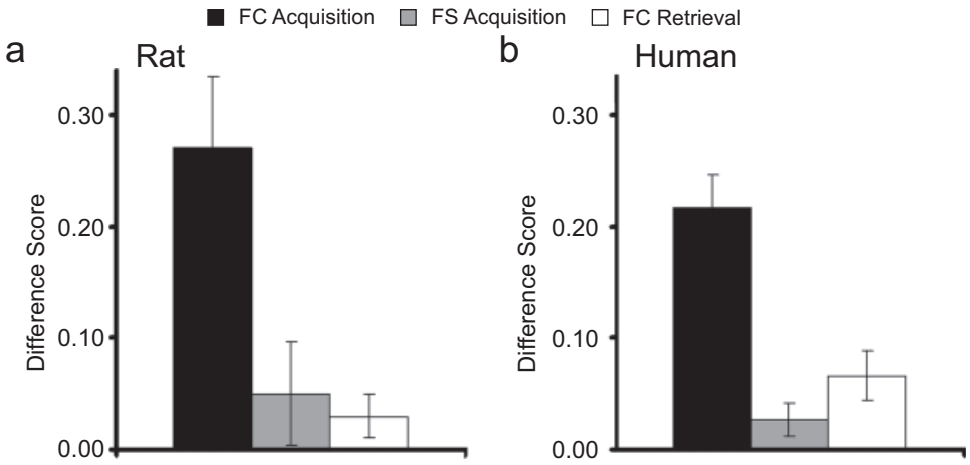

Fig. 4. Performance costs of the cholinergic and attentional challenges in the feature-conjunction (FC) and feature-singleton (FS) tasks. The cost of the cholinergic challenge (a) was calculated by subtracting rats' accuracy in the scopolamine condition from their accuracy in the saline condition; the cost of the attentional challenge (b) was calculated by subtracting humans' performance in the divided-attention condition from their performance in the full-attention condition. Results are shown separately for acquisition of the FC stimuli, acquisition of the FS stimuli, and retrieval of the FC stimuli. Error bars show ± 1 *SEM*.

bowl and one distractor bowl, such that neither color nor shape could be used by itself to determine the correct stimulus choice (see Fig. 2).

The FS stimulus set contained four nonconjunction colored-shape stimuli and the black star. Two of the colored shapes were designated target stimuli (T1 and T2), and the remaining two were designated distractor stimuli (D1 and D2). Feature binding was not required for stimulus selection, as the color and shape of each colored shape were both unique. That is, participants could use either color or shape alone or the distinct combination of the two features to determine which stimulus to choose (see Fig. 2).

Attentional Manipulation

In the concurrent letter-matching task, participants had to indicate whether two letters that flanked the centrally presented colored shapes were the same or different. This task is similar to a classic method of dividing attention in studies of human cognition (Treisman & Schmidt, 1982).

Training Procedure

Each session consisted of at least 116 trials, half of which were target trials (29 T1, 29 T2), and half of which were distractor trials (29 D1 and 29 D2). Within a session, trials were presented in a pseudorandom order, such that no more than 3 consecutive trials were of the same type (target or distractor). A performance criterion of 18 correct responses in 20 consecutive trials (90%) was employed. If this criterion was not met by the 116th trial, the session continued until the criterion was met.

Full-Attention Conditions. Full-attention FC and FS trials commenced with a fixation cross presented for 250 ms in the middle of the screen. The FC or FS stimuli then appeared. Participants selected the colored shape or black star, pressing one of two keyboard buttons using their right hand. The FC or FS stimuli disappeared from the screen as soon as a response was made, and were followed by a 25-ms colored mask to clear any afterimages. If participants failed to respond within 1,000 ms, the colored mask was presented, and then a screen prompting a response replaced the mask, remaining until a response was made. Participants received auditory feedback, a 500-ms high-pitched tone after every correct response and a low-pitched tone of the same duration after every incorrect response.

Divided-Attention Conditions. The trial structure of the divided-attention conditions was identical to that of the full-attention conditions except for the addition of a concurrent letter-matching task during which participants indicated whether two letters that flanked the centrally presented colored shapes were the same or different. (One letter was uppercase, and the other was lowercase, to prevent simple visual matching.) Participants indicated their response by pressing one of two keyboard buttons using their left hand. Participants had to respond to the letter-matching task first in order for a response to the FC or FS stimuli to be counted. The FC or FS stimuli disappeared from the screen as soon as a response to the flanking letters was made, and then the 25-ms colored mask was presented. If there was no response to the letter-matching task within 1,000 ms, the colored mask was presented, and then a screen prompting a response replaced the mask, remaining until a response was made. Following responses to the two tasks, feedback was provided to encourage strong performance on the divided-attention task; a percentage score indicating cumulative accuracy on the letter-matching task and an auditory tone reflecting performance on the FC or FS task were presented simultaneously for 500 ms.

Practice Trials. All participants practiced the divided-attention letter-matching task, and then they acquired a set of learning-to-learn FC stimuli, distinct from those used during subsequent FC acquisition and retrieval, until criterion performance was met (at least 116 trials).

Acquisition of the FC or FS Stimuli. After the completion of practice training, participants in the FC-acquisition and FS-acquisition conditions began training with novel FC or FS stimuli, under either full-attention or divided-attention conditions. Training continued until criterion performance was met (at least 116 trials).

Retrieval of the FC Stimuli. Participants in the FC-retrieval conditions completed practice training and subsequently acquired novel FC stimuli under full-attention conditions, continuing this training until they reached criterion performance (at least 116 trials). After a delay of 2 to 3 min, they retrieved these same FC stimuli, under either full-attention or divided-attention conditions, until criterion performance was met (at least 116 trials).

Results

Task accuracy was assessed using proportion of correct responses. All statistical analyses were conducted using SPSS Version 14 with an alpha level of .05. We used only the first 90 trials of each session so that the data could be binned into 30-trial blocks for ease of comparison with the rat data. Across all six conditions, there were no significant differences between performance during the last 26 trials of a session (i.e., Trials 91–116) and performance during the preceding 30 trials (i.e., Trials 61–90).

Participants' accuracy scores for the last 30-trial block of each session, when performance was most stable, were transformed into standardized z scores, and participants with z scores greater than $+1.96$ or less than -1.96 were removed from analyses: 1 from the full-attention FS-acquisition condition, 2 from the divided-attention FC-acquisition condition, 1 from the divided-attention FS-acquisition condition, and 2 from the divided-attention FC-retrieval condition.

Acquisition of FC Stimuli

Figure 3c depicts the results for FC acquisition. A two-way mixed ANOVA using attention condition (full attention or divided attention) as a between-subjects factor and block as a within-subjects factor revealed significant main effects of attention condition, $F(1, 30) = 26.19$, $p < .001$, $p_{rep} = .99$, $\eta_p^2 = .47$, and block, $F(1.60, 47.88) = 13.61$, $p < .001$, $p_{rep} = .99$, $\eta_p^2 = .31$, but no significant interaction ($F < 1$, $p_{rep} = .62$, $\eta_p^2 = .01$). At the end of training (Block 3), performance was still impaired in the divided-attention condition, $t(30) = 4.57$, $p < .001$, $p_{rep} = .99$, $\eta_p^2 = .41$.

Acquisition of FS Stimuli

Figure 3d depicts the results for FS acquisition. A two-way mixed ANOVA using attention condition (full attention or divided attention) as a between-subjects factor and block as a within-subjects factor revealed significant main effects of attention condition, $F(1, 30) = 16.91$, $p < .001$, $p_{rep} = .99$, $\eta_p^2 = .36$, and block, $F(2, 60) = 47.75$, $p < .001$, $p_{rep} = .99$, $\eta_p^2 = .61$, and a significant interaction, $F(2, 60) = 7.29$, $p < .01$, $p_{rep} = .99$, $\eta_p^2 = .20$. Further analysis revealed a significant difference between the full- and divided-attention conditions during the first block of acquisition, $t(30) = 5.00$, $p < .001$, $p_{rep} = .99$, $\eta_p^2 = .46$; this difference diminished to nonsignificance by the end of training (Block 3; $t < 2$, $p_{rep} = .80$, $\eta_p^2 = .01$).

A one-way ANOVA comparing starting performance (Block 1) on the FC and FS tasks in the full-attention condition revealed that the effect of task was nonsignificant ($F < 2$, $p_{rep} = .82$, $\eta_p^2 = .05$); this suggests that spared acquisition of the FS task in the divided-attention condition was not simply due to the FS task being less difficult than the FC task at the outset of training.

Retrieval of FC Stimuli

To examine the effects of the attention manipulation on FC retrieval, we conducted a two-way mixed ANOVA using attention condition (full attention or divided attention) as a between-subjects factor and block as a within-subjects factor. This analysis revealed a significant main effect of block, $F(2, 60) = 10.64$, $p < .001$, $p_{rep} = .99$, $\eta_p^2 = .26$, but no significant effect of attention condition ($F < 3$, $p_{rep} = .89$, $\eta_p^2 = .10$) and no significant interaction ($F < 1$, $p_{rep} = .59$, $\eta_p^2 = .01$).

Because this was a between-subjects design, we conducted a two-way mixed ANOVA on FC acquisition using cohort (full-attention or divided-attention retrieval) as a between-subjects factor and block as a within-subjects factor, to ensure that there were no performance differences in participants' initial acquisition (under full-attention conditions) of the FC stimulus set prior to its retrieval. The ANOVA confirmed a significant main effect of block, $F(2, 58) = 9.55$, $p < .001$, $p_{rep} = .99$, $\eta_p^2 = .25$, and revealed no significant effect of cohort ($p_{rep} = .82$, $\eta_p^2 = .05$) and no significant interaction ($p_{rep} = .82$, $\eta_p^2 = .05$).

Effects of Divided Attention on Performance of the FC and FS Tasks

To examine the performance of participants in the divided-attention condition during the last block of FC acquisition, the last block of FS acquisition, and FC retrieval, we conducted a one-way ANOVA using task (FC acquisition, FS acquisition, or FC retrieval) as a between-subjects factor. This analysis revealed a significant effect of task, $F(2, 45) = 16.37$, $p < .001$, $p_{rep} = .99$, $\eta_p^2 = .42$. Further analysis revealed a significant difference between performance in the divided-attention FC-acquisition condition and performance in the divided-attention FC-retrieval condition, $t(30) = -2.40$, $p < .05$, $p_{rep} = .95$, $\eta_p^2 = .16$, and

between performance in the divided-attention FC-acquisition condition and performance in the divided-attention FS-acquisition condition, $t(30) = -5.65, p < .001, p_{rep} = .99, \eta_p^2 = .52$. Figure 4b compares the effect of divided attention on performance during the last block of FC acquisition, the last block of FS acquisition, and FC retrieval. For display purposes, the cost of divided attention was computed by calculating a mean difference score (mean accuracy of participants in the full-attention condition − mean accuracy of participants in the divided-attention condition) for each task.

Letter-Matching Task

Average accuracy on the concurrent divided-attention task was 90%, 92%, and 94% (collapsed across blocks) in the FC-acquisition, FS-acquisition, and FC-retrieval conditions, respectively. A two-way mixed ANOVA using task (FC acquisition, FS acquisition, or FC retrieval) as a between-subjects factor and block as a within-subjects factor revealed a significant main effect of block, $F(2, 86) = 3.96, p < .05, p_{rep} = .95, \eta_p^2 = .08$, but no significant effect of task ($F < 2, p_{rep} = .79, \eta_p^2 = .06$) and no significant interaction ($F < 2, p_{rep} = .87, \eta_p^2 = .08$).

Discussion

The effects of the attention manipulation mirrored those of the scopolamine manipulation in Experiment 1. In the divided-attention condition, human participants were significantly impaired in acquiring intramodal FC stimuli, whereas both FS acquisition and retrieval of previously bound FC stimuli were relatively spared.

GENERAL DISCUSSION

This cross-species study of feature binding suggests that cholinergically driven attentional processes are essential to feature binding at encoding. In a strikingly similar manner, rats under the influence of scopolamine and human participants under divided attention were impaired at acquiring FC stimuli, whereas their ability to acquire FS stimuli and to retrieve previously bound FC stimuli remained intact relative to performance under saline and full-attention conditions, respectively. Our FS findings are consistent with those of studies demonstrating that single-feature processing constitutes a low attentional load for humans (Bernstein & Robertson, 1998; Cohen & Rafal, 1991; Corbetta et al., 1995; Foster et al., 1999; Friedman-Hill et al., 1995; Luck & Ford, 1998; Treisman & Gelade, 1980). In addition, the invulnerability of the feature-binding retrieval process to a cholinergic or divided-attentional challenge suggests that once an FC stimulus is well learned, it has a bound and stable neural representation, which reduces the need for an attentionally demanding feature-binding process during retrieval.

Our retrieval findings are in agreement with a considerable body of research on human cognition showing that disrupting attention is selectively detrimental to the encoding, relative to the retrieval, of episodic memories (Craik, Govoni, Naveh-Benjamin, & Anderson, 1996; Logie, Della Sala, MacPherson, & Cooper, 2007; Naveh-Benjamin, Craik, Guez, & Dori, 1998; Naveh-Benjamin, Craik, Perretta, & Tonev, 2000; Naveh-Benjamin, Kilb, & Fisher, 2006). Furthermore, our data are consistent with a well-supported model of cholinergic function (Hasselmo & McGaughy, 2004) proposing that high levels of ACh facilitate encoding by boosting sensory input, whereas low levels facilitate retrieval by allowing reactivation of neural connections representing previously learned information (Anagnostaras, Maren, & Fanselow, 1995; McGaughy, Koene, Eichenbaum, & Hasselmo, 2005; Orsetti, Casamenti, & Pepeu, 1996; Pepeu & Giovannini, 2004; Safer & Allen, 1971; Schon et al., 2005; White & Ruske, 2002).

Although there is no direct evidence that dividing attention reduces cholinergic levels in humans, it has been shown that increasing cholinergic levels results in the behavioral and neural correlates of increased attention. Specifically, it has been demonstrated that administration of the cholinergic-enhancing drug physostigmine during fMRI results in enhanced visual working memory performance by augmenting activation of sensory cortices and decreasing reliance on fronto-parietal attentional networks (Bentley, Husain, & Dolan, 2004; Furey, Pietrini, Alexander, Schapiro, & Horwitz, 2000; Furey, Pietrini, & Haxby, 2000). There is, however, direct evidence from nonhuman animals to support the more general proposition that disruptions to the cholinergic system are akin to disruptions of attention. This evidence has come from studies in which pharmacological (Chiba, Bucci, Holland, & Gallagher, 1995; Mirza & Stolerman, 2000; Sarter, Bruno, & Givens, 2003) and *in vivo* microdialysis techniques were used to measure the amount of frontal cortical ACh efflux while animals performed attentional tasks (Arnold, Burk, Hodgson, Sarter, & Bruno, 2002; Hata, Kumai, & Okaichi, 2007; Himmelheber, Sarter, & Bruno, 2000, 2001; Pepeu & Giovannini, 2004). Our cross-species data are consistent with the premise that the blockade of muscarinic cholinergic function in rats is analogous to imposition of an attentional load in humans (i.e., divided attention) and suggest that ACh may provide the attentional "glue" for feature binding.

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