Dissociation between the neural correlates of recollection and familiarity in the striatum and hippocampus: across-study convergence

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Highlights

- Recollected and familiar recognition test items elicit dissociable striatal responses
- Recollection elicits enhanced activity in ventral striatum and subgenual cortex
- Familiarity and recollection elicit activity in dorsal striatum
- Retrieval-related activity in the striatum does not track hippocampal activity

Abstract

In tests of recognition memory, neural activity in the striatum has consistently been reported to differ according to the study status of the test item. A full understanding of the functional significance of striatal 'retrieval success' effects is impeded by a paucity of evidence concerning whether the effects differ according to the nature of the memory signal supporting the recognition judgment (recollection vs. familiarity). Here, we address this issue through an analysis of retrieval-related striatal activity in three independent fMRI studies (total N = 88). Recollection and familiarity were operationalized in a different way in each study, allowing the identification of test-independent, generic recollection- and familiarity-related effects. While activity in a bilateral dorsal striatal region, mainly encompassing the caudate nucleus, was enhanced equally by recollected and 'familiar only' test items, activity in bilateral ventral striatum and adjacent subgenual frontal cortex was enhanced only in response to items that elicited successful recollection. By contrast, relative to familiar items, activity in anterior hippocampus was enhanced for both recollected and novel test items. Thus, recollection- and familiarity-driven recognition memory judgments are associated with anatomically distinct patterns of retrieval-related striatal activity, and these patterns are at least partially independent of recollection and novelty effects in the hippocampus.

Key words: Familiarity, Novelty, Recollection, Recognition Memory, Reward, Subgenual, Striatum

Introduction

According to dual-process models of recognition memory (Mandler,1980; Yonelinas, 2002), accurate recognition of a test item can be supported by two different memory signals, which are frequently termed ‘recollection’ and ‘familiarity’. Recollection refers to retrieval of qualitative information about a past episode. This includes information both about whether the test item has been encountered previously, and about the study episode more generally, including spatio-temporal information unique to the episode. By contrast, familiarity supports judgments of prior occurrence in the absence of contextual or other information diagnostic of a specific study episode.

It has been widely argued that recollection and familiarity are functionally dissociable, and that their respective component processes rely on at least partially distinct neural regions and networks (e.g. Aggleton and Brown, 2006; Skinner and Fernandes, 2007). Consistent with this view, fMRI studies have reported largely non-overlapping patterns of neural activity in association with recollection- and familiarity-based memory judgments (e.g. Johnson et al., 2013; see for review Kim, 2010, 2013). When recollection is operationalized by the contrast between correctly recognized memory test items for which recollection either succeeded or failed, enhanced activity is evident in a characteristic brain network (the ‘core recollection’ network) that includes the hippocampus and medial prefrontal, posterior cingulate, middle temporal and ventral parietal cortex (Rugg and Vilberg, 2013; King et al., 2015). Familiarity (operationalized either by the contrast between recognized but unrecollected items and unstudied items, or by activity that covaries with subjective ratings of familiarity strength) is associated with enhanced activity in a different set of regions, including the intra-parietal sulcus (IPS), precuneus, and dorsal medial, left lateral and left anterior PFC (e.g. Johnson et al., 2013; Kim, 2013). Familiarity has also been associated with *reductions* in activity relative to new items. Such ‘novelty effects’ are especially prominent in perirhinal cortex, where they have been linked with signals supporting familiarity-driven recognition (Henson et al., 2003), and the anterior hippocampus, where the effects are frequently interpreted as correlates of encoding novel item-context associations (Nyberg, 2005; Stark and Okado, 2003). [Note that when we refer to ‘familiarity’ and ‘novelty’ effects below, we are using these terms simply to define the direction of the respective contrasts (familiar>novel, and vice-versa), without any implication that the effects reflect qualitatively distinct mnemonic processes].

Whereas dissociations between recollection- and familiarity-related neural activity in the hippocampus and neocortex are well documented, less attention has been paid to the possibility of analogous dissociations in subcortical regions that have been implicated in mnemonic processing, such as the striatum. Retrieval-related modulation of striatal activity has been noted in reviews and meta-analyses dating back over several years (Spaniol et al., 2009; Kim, 2010, 2013; Sciemeca and Badre, 2012), but little research has directly addressed whether the location or magnitude of this activity differs when memory judgments are based on recollection versus familiarity. Instead, recent studies aimed at elucidating the functional significance of retrieval-related striatal activity (Han et al., 2010; Schwarze et al., 2013; Clos et al., 2015) have mainly employed variants of 'yes/no' recognition that did not permit judgments to be segregated according to whether they were recollection- or familiarity-driven. Perhaps as a consequence of this, Han et al. (2010) were able to interpret their findings in terms of a single role for the striatum in recognition memory ('goal-satisfaction'). Both Schwarze et al. (2013) and Clos et al. (2015) argued however that their findings suggested that striatal activity during recognition judgments reflects two distinct sources of 'subjective value'. These are derived from 'perceived oldness' and response confidence respectively.

Unlike in the three studies just mentioned, Elward et al. (2015) employed a source memory procedure rather than a test of item (recognition) memory. Subjects were informed that accurate retrieval of one of two study contexts (sources) would result in high monetary reward ($2), while correct retrieval of the other context would lead to low reward (2c). They were also informed that inaccurate judgments would lead to corresponding losses. Regardless of the value of the associated reward, accurate source judgments (assumed to be supported by recollection) elicited greater activity in ventral and lateral striatum than did inaccurate judgments (when recollection was assumed to be weak or absent), replicating prior findings (Spaniol et al., 2009; Sciemeca and Badre, 2012). Additionally, adjacent ventral striatal regions demonstrated enhanced activity for judgments associated with high versus low reward, irrespective of the accuracy of the source judgment, while no regions were identified where the factors of recollection success and reward value interacted. These findings suggest that retrieval-related activity in the striatum is sensitive not only to 'retrieval success' in tests of item recognition, but also to whether recollection of the study context of a recognized item succeeds or fails (see also Sciemeca and Badre, 2012). The findings further

suggest that this recollection-related activity can be dissociated from striatal responses linked to the prospect of reward ('goal satisfaction' in the terminology of Han et al., 2010). Elward et al. (2015) did not, however, examine striatal activity during familiarity-based recognition.

Here we take advantage of three independent data sets (described originally in Elward et al., 2015; de Chastelaine et al., 2016, in press; Wang et al. 2016) to examine whether memory judgments based on recollection or familiarity are associated with dissociable patterns of striatal activity. The three studies employed memory tests that differed markedly in their operationalization of recollection and familiarity (see Table 1 and Methods) and used diverse experimental materials. We assume that fMRI effects shared across the three studies reflect general, rather than material- or test-specific, effects that provide insight into the neural regions and networks linked to different classes of memory process (see King et al., 2015, for an analogous approach). To anticipate the results, we find compelling evidence that previously reported dissociations between recollection- and familiarity-driven neural responses extend to the striatum and closely adjacent regions. The findings constrain proposals about the role or roles of the striatum in memory retrieval.

Results

Behavioral Findings

Accuracy data for each of the three experiments have been fully described previously (Elward et al., 2015; de Chastelaine et al., 2016, in press; Wang et al. 2016; see also King et al., 2015). In each case estimates of recollection and familiarity were robustly above chance. Reaction time (RT) data were however not fully reported in Wang et al., (2016) and de Chastelaine et al. (2016). Accordingly, we report these data here (Table 2). For each experiment, the RT data were subjected to one-way repeated measures ANOVA (Geisser-Greenhouse corrected for non-sphericity). The ANOVAs revealed main effects of trial type ($F_{1.92,44.1} = 26.00$, $F_{1.88,65.8} = 46.69$, $F_{1.4,26.2} = 59.85$ for experiments 1, 2 and 3 respectively, min $p < .001$). Post-hoc contrasts (Bonferonni corrected) indicated that in each experiment RTs for recollected and new items were reliably shorter than those for familiar items. However, whereas in experiments 1 and 2 RTs for new items were longer than those for recollected items, this difference was reversed in experiment 3.

fMRI Findings

For the reasons outlined in the Introduction, we focus here on results for each of the contrasts of interest (recollection, familiarity and novelty) that were common to the three experiments. Common effects were defined as those that survived our conjoint height and cluster extent thresholds for the main effect across experiments (see Methods), as well as inclusive masking with the simple effect in each experiment, thresholded at $p < .05$ uncorrected. The masking procedure was employed to limit the results to voxels where effects were shared across the experiments. Along with the outcome of the masked across-experiment ANOVA, the key finding (the dissociation between memory effects in the dorsal and ventral striatum) is illustrated in Figures 1a, 1b and 1c for each experiment separately.

Striatal familiarity and recollection effects are illustrated in Figure 1 and, along with novelty effects, are documented in Table 3. As is evident from the figure, relative to new items, familiar test items elicited enhanced activity in dorsal (caudate) and, to a more limited extent, ventral striatum. By contrast, relative to familiar items, successfully recollected items did not elicit any additional activity in the caudate, but instead elicited enhanced activity in the most ventral aspects of the striatum and the adjacent subgenual frontal cortex (corresponding mainly to Brodmann's Area 25; Palomero-Gallagher et al., 2015). For each subject, the parameter estimates representing the magnitude of the responses elicited by recollected, familiar, and novel items were extracted from the voxels in the left and right striatum where familiarity or recollection effects were maximal ('peak' parameter estimates; see Table 3 for their MNI co-ordinates). The across-subjects means of these estimates are plotted in Figures 2d and 2e. The novelty contrast (N > F) identified an effect in the posterior aspect of the right putamen (not illustrated).

We employed exclusive masking to further assess the independence of the different striatal retrieval effects. To remove voxels where effects may not have been uniquely sensitive to only one contrast we exclusively masked each contrast illustrated in Figure 1 with the other contrasts (thresholded at $p < .05$). The novelty effect in the right putamen did not survive this procedure, but as is evident from Figures 2a and 2b, the dissociation between familiarity and recollection effects remained.

Figure 1 suggests there is little overlap between striatal familiarity and recollection effects. An inclusive mask of the two contrasts confirmed this impression, identifying only a single

overlapping voxel in right ventral striatum. It is possible however that the lack of overlap is exaggerated because of the relatively strict thresholds applied to the respective contrasts ($p<.0001$). In support of this possibility, inclusive masking of the two contrasts at a threshold of $p<.01$ revealed a cluster (101 voxels) spanning left and right ventral striatum where familiarity and recollection effects overlapped [MNI co-ordinates of the centers of mass in each hemisphere for each contrast pair were -11 12 -7 (peak Zs = 3.83 and 5.93, for the recollection and familiarity contrasts respectively)), and 9 8 -7 (peak Zs = 3.94 and 5.22)]. These overlapping effects survived experiment-wise inclusive masking (see above), indicating that the tendency toward overlap was independently present in each of the experiments. The effects and the relevant parameter estimates from their centers of mass are plotted in Figures 2c and 2f respectively. As is evident from Figure 2f, the response profile is graded: smallest for novel items, intermediate for familiar items, and largest for recollected items.

The analyses presented thus far identify three anatomically segregated patterns of effects: i) a dorsal striatal region where recollected and familiar items elicited responses that differed from the response elicited by novel items, but not from one another, ii) a ventral region where responses to familiar and novel items did not differ, but were smaller than the responses elicited by recollected items, and iii) an intermediate region where responses were graded (recollected > familiar > novel). These findings do not however license the conclusion that the response profiles in the three regions differ qualitatively; this requires the demonstration of an appropriate pattern of region x item interaction effects. Accordingly, after collapsing across experiment and hemisphere, the parameter estimates summarized in Figure 2 were subjected to a 3 (region) x 3 (item type) ANOVA. The region x item type interaction was highly significant ($F3.1, 267.3 = 53.52$, $p < .001$). We followed up this result with subsidiary 2 (region) x 2 (item type) ANOVAs, which examined whether interactions were evident for four important combinations of region and item type (dorsal vs. ventral x familiar vs. novel; dorsal vs. ventral x familiar vs. recollected; dorsal vs. intermediate x familiar vs. recollected; and ventral vs. intermediate x familiar vs. recollected). In each case the interaction was significant (minimum $F1,87 = 14.48$, max $p < .001$). To ensure that none of these interactions resulted from scaling artifacts caused by inter-regional differences in the overall magnitudes of the parameter estimates, we repeated all of these ANOVAs after z-scoring the parameter estimates across items separately for each region, hemisphere, and experiment. Each of the

interaction effects reported above remained highly significant. Together, these findings indicate that the response profiles for recollected, familiar and novel items did indeed differ qualitatively across regions, in keeping with the impression given by Figure 2.

Discussion

We identified a common pattern of dissociations between recollection- and familiarity-related fMRI BOLD responses within the striatum in three independent experiments that employed different operationalizations of recollection and familiarity. Relative to correctly detected novel items, responses in the dorsal striatum were robustly and equivalently enhanced whether the responses were elicited by recollected or familiar test items. In striking contrast, responses in a ventral striatal region and adjacent subgenual frontal cortex did not reliably discriminate between novel and familiar test items, but were enhanced for recollected items. At a more lax statistical threshold, we also identified an area lying between these dorsal and ventral regions where retrieval-related activity demonstrated a graded profile.

These findings add to existing evidence that retrieval-related striatal activity is a reflection of multiple cognitive processes (Schwarze et al., 2013; Clos et al., 2015; Elward et al., 2015; see also Sciemeca and Badre, 2012). We begin however by discussing an account of the present findings that is compatible with the view that retrieval-related striatal activity reflects only a single process. By this account, although the inter-regional dissociations illustrated in Figure 2 indicate that retrieval-related BOLD responses have different profiles across the striatum, the dissociations are not necessarily indicative of distinct profiles of neural activity. Rather, the findings might merely reflect inter-regional differences in the non-linearity of the hemodynamic response function (HRF) that mediates between neural activity and the resulting BOLD response. According to this account (first advanced by Squire et al., 2007 as an explanation for dissociations between recollection- and familiarity-related BOLD responses in hippocampus and perirhinal cortex), recollection- and familiarity-based memory judgments are reflections not of functionally distinct mnemonic processes, but of differences in the ‘strength’ of a unitary, continuously varying memory signal. If the HRF in seemingly familiarity-sensitive neural regions causes the BOLD signal to asymptote when neural activity and, correspondingly, memory strength, is low, while in seemingly recollection-sensitive regions the BOLD signal is sensitive only to high levels of neural activity (and memory

strength), the present findings can be accommodated without recourse to the idea that dorsal and ventral striatal regions support functionally distinct cognitive processes.

Since there is currently no evidence as to how HRFs vary within the striatum this account cannot be rejected definitively. It is, however, entirely *ad hoc*. Moreover, while their specific roles are debated, there is ample evidence from domains other than episodic memory that the dorsal and ventral striatum are functionally dissociable (e.g. Robbins and Everitt, 1992; Liljholm and O'Doherty, 2012; Haber, 2015). Together with the large body of human and animal evidence indicating that recognition memory depends on at least two functionally and neurally distinct memory signals (Aggleton and Brown, 2006), this leads us to conclude that a 'strength-based' account of the present findings is logically possible but implausible.

Before going on to discuss the implications of our findings from a dual-process perspective, we note an important methodological caveat. This concerns the ventral striatal region where a graded response profile was identified (Figure 2c). It is possible that this 'intermediate' region was responding to something akin to a continuously varying memory signal (or to a process tied to such a signal). We cannot rule out the possibility however that the graded profile demonstrated in the region merely reflects the relatively low spatial resolution of our scanning protocol (3mm isotropic voxels) and, consequently, a failure to cleanly delineate the border between two functionally distinct regions. This could have led to within-voxel mixing of their respective response profiles and hence to the semblance of a graded response (see Vilberg and Rugg, 2009, for a similar concern in respect of the response profile of an area lying between familiarity- and recollection-sensitive regions of lateral parietal cortex). Further research employing higher resolution scanning protocols will be necessary to resolve this issue. In the meantime, we refrain from further discussion of the response profile here.

As already noted, activity in a dorsal striatal region, overlapping primarily with bilateral caudate nucleus, was enhanced to an equivalent extent whether the activity was elicited by familiar or recollected test items. Importantly, this finding rules out the possibility that retrieval-related activity in the dorsal striatum is merely a reflection of the fact that the judgments to familiar items were significantly slower than those to novel items in each of the three experiments (see *Behavioral Findings* and Table 2), and hence that it represents a difficulty or 'time-on-task' effect. In Experiments 1 and 2, RTs to recollected items were reliably *faster* than those to novel items, but these items nonetheless elicited enhanced

dorsal striatal activity (see Figure 1). (We further note that analogous reasoning can be applied to the response profile evident in the ventral striatum/subgenual cortex: despite large differences in their associated RTs, familiar and novel items elicited equivalent responses in these regions, as is illustrated in Figure 2e).

The response profile observed in the caudate led us to identify the region as 'familiarity-sensitive'. We acknowledge however that this may be something of a misnomer. While undeniably responsive to test items recognized on the basis of familiarity alone, the present findings cannot adjudicate between the possibilities that the region is exclusively familiarity-sensitive (the majority of recollected items are likely also to have elicited a familiarity signal; Johnson et al., 2013), or that it is equally responsive when a memory judgment is either familiarity- or recollection-based. From the perspective of the first possibility, one might interpret the findings as the reflection of a signal that acts as a 'call' for engagement of cognitive control or resources following the detection of a familiar test item. For instance, there is evidence that people attempt to reduce the cognitive demands of recollection-dependent memory tests by adopting the strategy of 'familiarity-gated recollection' (Dudukovic and Wagner, 2007). By this account, effortful search processes directed toward retrieval of qualitative mnemonic information (recollection) are engaged only if the familiarity of the retrieval cue is high enough to indicate that the item was previously studied. It is possible that the caudate plays a role in initiating the engagement of these search processes (see also Sciemeca and Badre, 2012).

Proposals that the caudate plays a role in functions such as action selection (Grahn et al., 2008) are more compatible with the second of the two possibilities mentioned above, that is, that the region is equally sensitive to familiarity and recollection. From this perspective, the present findings might indicate a role for the caudate in selecting between response alternatives associated with retrieval cues that elicit *any* memory signal that is diagnostic of 'oldness'. This view is also compatible with prior findings that the caudate demonstrates retrieval success effects in tests of simple item recognition memory, when it is equally responsive to items attracting hits and false alarms; that is, the region responds to 'perceived' rather than 'objective' oldness (Sciemeca and Badre, 2012).

A factor that complicates both of these proposed accounts is that the dorsal striatal region identified here corresponds closely with the region identified by Han et al. (2010) as being

sensitive to incentive. Han et al. reported that retrieval success effects (greater activity for items attracting old rather than new judgments) reversed direction when ‘new’ judgments were linked with monetary reward. On the basis of this finding, the authors proposed that retrieval-related striatal activity was a reflection not of mnemonic processing, but of ‘goal satisfaction’. They argued that while goal satisfaction in standard recognition memory tests is typically higher when old rather than new items are detected (accounting for the retrieval success effects consistently identified in the caudate in prior studies; Sciemeca and Badre, 2012), this asymmetry is reversed when new judgments are given sufficiently high motivational significance.

Whether the findings of Han et al. (2010) generalize to the more complex memory tests that are the focus here remains to be established. Indeed, it will be of considerable interest to examine whether retrieval-related striatal activity varies according to how reward levels are distributed across familiarity-driven, recollection-driven and ‘new’ judgments. Nonetheless, on the face of it, Han et al.’s findings are difficult to reconcile with the first of the two accounts discussed above, in which dorsal striatal ‘familiarity effects’ are linked to familiarity-gated recollection, and hence to familiarity strength rather than the subjective value or motivational significance of a memory judgment. Their findings are arguably more compatible with the second account. If the caudate is preferentially engaged during the selection of goal-relevant actions (Grahn et al., 2008), but the goal-relevance of different memory judgments (and hence the ensuing action) can be modified by extrinsic reward, the present and prior findings are not in conflict.

In contrast to the response profile demonstrated by the dorsal striatum, more ventral regions demonstrated an enhanced response that was exclusively associated with recollected items. It has been suggested (Spaniol et al., 2009; Sciemeca and Badre, 2012) that recollection-related striatal responses are more likely to be observed when recollection is operationalized ‘objectively’ (as in tests of source memory) rather than ‘subjectively’ (as in the Remember/Know procedure), and this suggestion is consistent with the impression given in Figure 1 of more robust ventral effects in experiments 2 and 3 than in experiment 1. However, not only were the effects highly reliable in each case (all $p <= .002$), but an ANOVA contrasting the effects across experiments failed to identify a significant effect of experiment ($F_{2,85} = 2.00$, $p > .1$).

In light of extensive evidence that the ventral striatum and subgenual frontal cortex (with which it is strongly interconnected; Johansen-Berg et al., 2008; Neubert et al., 2015) are implicated in reward and affective processing (e.g. Barta et al., 2013; Palomero-Gallagher et al., 2015; Price and Drevets, 2010), it is tempting to interpret the present findings for these regions as evidence that recollection is intrinsically rewarding (cf. Kim, 2013). There are two reasons to treat this proposal with caution. First, it lacks direct empirical support and hence depends heavily on a potentially problematic reverse inference (Poldrack, 2006). Second, the little empirical evidence we are aware of that is relevant to the proposal is not encouraging. As was noted in the Introduction, Elward et al. 2015 (the present experiment 3) examined the influence of the factors of monetary reward and source memory accuracy on fMRI BOLD activity. Although there was a region in the ventral striatum where reward- and accuracy-related responses overlapped, there were other regions, extending into subgenual cortex and overlapping the regions identified here, where activity was exclusively recollection-related (Figure 3). These findings do not of course rule out the possibility that recollection-related responses in this region signal the receipt or the prospect of reward of some kind, but it would appear to be a signal that is distinct from the one associated with monetary reward. A fuller understanding of the functional significance of this hitherto unrecognized neural correlate of successful recollection will require research in which recollection effects in the region are compared with those elicited by different types of reward. It would also benefit from studies that examine the effects of lesions to the region on memory performance (cf. Manohar and Husain, 2016; Pujara et al., 2016).

That being said, one possibility that seems unlikely on the basis of the present findings is that the ventral striatal/subgenual responses identified here merely parallel analogous responses in the hippocampus (a region with which both subgenual cortex and ventral striatum are strongly inter-connected; Johansen-Berg et al., 2008; Lisman and Grace, 2005; Haber, 2015). As we have reported previously (King et al., 2015), and illustrate in the present Figure 4, across the three experiments anterior hippocampal activity was robustly enhanced for recollected relative to familiar items. And as is also illustrated in Figure 4, relative to familiar items, novel items elicited robust enhancement of activity in the same anterior hippocampal region (consistent with prior findings; Kim, 2013). By contrast, enhanced activity in ventral striatum/subgenual cortex was evident exclusively for recollected items (see Figure 2a); the activity elicited by novel items in these regions did not reliably differ from that elicited by

familiar items. Thus, in itself, enhanced activity in the hippocampus is unlikely to be the driver of the recollection effects observed here in the ventral striatum/subgenual cortex (or *vice versa*). As we note below, however, this does not mean that these regions do not functionally interact to share information specifically about successful recollection.

In conclusion, the present findings demonstrate that retrieval-related activity in different striatal regions dissociates according to whether a memory judgment is based on recollection or familiarity. Relative to the activity elicited by novel items, activity in the dorsal striatum is enhanced irrespective of whether it is elicited by items attracting familiarity- or recollection-based memory judgments. By contrast, activity in the ventral striatum and adjacent subgenual cingulate cortex is enhanced only when an item is recollected. Regardless of their exact functional significance, these dissociable retrieval effects are likely a reflection of the differing inputs to the two regions (Haber, 2015). The ventral striatum and subgenual cortex receive significant input from the hippocampus (which as just discussed, is also recollection-sensitive; see Figure 4a). By contrast, input to the dorsal striatum derives largely from lateral PFC, a region that consistently demonstrates robust familiarity-related activity (e.g. Yonelinas et al., 2005; Johnson et al., 2013; de Chastelaine et al., in press). How the striatum exploits or augments these different memory signals are key questions for the future.

Finally, we acknowledge that the extent to which the recollection/familiarity dichotomy captures the critical computational distinctions between memory signals that support different kinds of recognition memory judgments remains to be determined (see, for example, Norman, 2010; Wixted and Squire, 2011; Rugg et al., 2012). Nevertheless, the present findings strongly suggest that future efforts to delineate the role of the striatum in memory retrieval will benefit from the adoption of this or a related dual process perspective.

Methods

Participants

Data from three previously published studies (Elward et al., 2015; de Chastelaine et al., 2016, in press; Wang et al. 2016) were analyzed, each of which employed a sample of healthy, right-handed young adults (aged 18 – 30 yrs), with Ns of 24, 36 and 28 in experiments 1, 2 and 3 respectively (see King et al., 2015, for description of analyses of this data-set in respect of recollection-related modulation of functional connectivity). All subjects

gave informed consent prior to participation and were compensated for their time. The studies were approved by the Institutional Review Boards of UT Southwestern and UT Dallas. Experiments 1 and 2 included samples of older participants also. The data from these participants are not included in the analyses presented here. The findings for the recollection contrasts in these studies have been described previously, both singly (Elward et al., 2015; de Chastelaine et al., 2016; Wang et al. 2016) and together (King et al., 2015), but the findings for the familiarity/novelty contrasts have been previously reported only for Experiment 2 (de Chastelaine et al., in press). Comparisons of striatal recollection and familiarity effects are reported here for the first time.

Materials and Procedures

Recollection and familiarity were examined using a different behavioral paradigm in each of the three experiments (see Table 1). Experiment 1 employed a Remember/Know procedure (Tulving, 1985). Experimental items consisted of 216 pictures and 216 corresponding object names. Of the 216 picture-word pairs, 144 were randomly selected for presentation during the study phase. For 72 of the pairs, it was the picture that was presented, while for the remainder it was the word. During encoding, subjects made one of two judgments (fit inside a shoebox? found inside or outside a house?) about the denoted object depending on whether it was presented as a picture or a word. At test, the 144 studied items and an additional 72 new items were presented as words only. The test task was to judge whether each test word corresponded to a studied item, regardless of its study format. There were three response options. Subjects were instructed to respond ‘Remember’ on trials where recognition was accompanied by retrieval of a specific detail or details from the study episode. ‘Know’ responses were to be used when an item was recognized in the absence of the retrieval of any specific detail about the study event. ‘New’ judgments were to be given if a test item was not recognized from the study phase. Here, behavioral and fMRI data were analyzed after collapsing over the format of the studied items. Recollection effects were identified by the contrast between the fMRI BOLD activity elicited by test items endorsed ‘Remember’ and items endorsed ‘Know’. Familiarity and novelty effects were identified by the contrasts Know > New, and New > Know, respectively.

Experiment 2 employed an associative recognition procedure. During the study phase, subjects studied 240 visually presented pairs of concrete words, judging which of the two

denoted objects was more likely to fit into the other. At test, 120 of the studied word pairs were re-presented (intact pairs). A further 80 test pairs comprised studied words that had been re-paired from study (rearranged pairs). There were also 80 new pairs, consisting of unstudied words. The retrieval task was to judge whether each test pair was ‘Intact’, ‘Rearranged’, or ‘New’. For the purpose of fMRI analyses, successful recollection was operationalized as the contrast between activity elicited by intact test pairs correctly judged as such (associative hits), and activity elicited by intact pairs wrongly judged as rearranged (associative misses), familiarity effects were identified by the contrast associative miss > correctly judged new pairs (correct rejections), and novelty effects by the contrast correct rejection > associative miss.

Experiment 3 involved a source memory task. Experimental items consisted of 240 color pictures of objects. During the study phase, 160 of the objects were presented, 80 in association with the depiction of one type of coin (a Lira), and 80 with the depiction of another (a Deutschmark). The requirement was to make an ‘indoor/outdoor’ judgment about each object. At test, each studied picture was re-presented along with the 80 unstudied pictures. The task was to judge whether each picture had been studied in association with a Lira or a Deutschmark or whether it was unstudied; correct source judgments were differentially rewarded ($2 vs. 2c) according to the identity of the coin. Unlike in the original report, here test items were collapsed across the two study contexts (reward levels). This allowed us to analyze data from more subjects (N=28) than in the original analysis (N=20), when limitations on trial numbers led to the exclusion of eight of the subjects who are included here (see Elward et al., 2015, for a description of reward effects). Recollection was operationalized by the contrast between fMRI responses to studied items attracting correct versus incorrect source judgments, familiarity was operationalized by the contrast between incorrect source judgments and new items, and novelty effects were identified by the new > incorrect source judgment contrast.

MRI Data Acquisition and Preprocessing

In each experiment, MRI data were acquired with the same 3T Philips Achieva MRI scanner (Philips Medical Systems, Andover, MA, USA) equipped with a 32 channel receiver head coil. Functional images were acquired using a T2*-weighted, blood oxygen level-dependent echoplanar (EPI) sequence (SENSE factor 1.5, flip angle 70º, 80 x 80 matrix, FOV = 24 cm,

TR = 2000 ms, TE = 30 ms) and T1-weighted anatomical images were acquired with a magnetization-prepared rapid gradient echo (MPRAGE) pulse sequence (FOV= 240×240, 1mm3 isotropic voxels).

MRI data were preprocessed in SPM8 (Wellcome Department of Cognitive Neurology, London, UK). Briefly, functional scans were realigned to the mean EPI image, subjected to slice timing correction, reoriented to approximate the Montreal Neurological Institute (MNI) reference template, spatially normalized to MNI space, and smoothed using an 8mm full-width half maximum Gaussian kernel. Anatomical images were similarly normalized to MNI space.

fMRI Data Analysis

A standard two-stage procedure was employed to identify voxels where fMRI BOLD activity varied according to the three critical contrasts in each experiment (see above). Statistical Parametric Mapping (SPM8, Wellcome Department of Cognitive Neurology, London, UK) based on a General Linear Model (GLM) was used to analyze fMRI data. At the individual subject level, a number of events of interest were modeled. Crucially, these events included i) recollected items (studied items endorsed as R, studied pairs correctly endorsed as intact, and studied items receiving a correct source memory judgment, in experiments 1, 2 and 3 respectively), ii) correctly recognized items for which recollection failed (studied items endorsed as K, studied pairs wrongly endorsed as rearranged, and studied items receiving an incorrect source judgment), and iii) correctly rejected unstudied items. The neural response was modeled as a delta function at the onset of each trial. The delta functions were convolved with a canonical hemodynamic response function to model the predicted BOLD response. Other covariates entered into the first-level models included six parameters that represented the motion-related variance in the data (three for rigid-body translation and three for rotation), and regressors representing each of the separate scan sessions. An AR(1) model was employed during parameter estimation to correct for time-series correlations in the data. Individual subjects' parameter estimates for the three events of interest ('recollected', 'familiar' and 'novel' test items; see above) from these first-level analyses were entered into an ANOVA model that treated experiments as a between-subjects fixed effects factor, item type as a repeated measures factor and subjects as a random effects factor. As is standard in SPM, effects were assessed using a single, pooled error term.

For the principal analyses, the across-experiment main effects for the contrasts of interest were height thresholded at $p < .0001$ one-sided with a cluster extent threshold (k) of 29 voxels (to give a cluster-wise FWE of $p<.05$). As is described in the Results section, these contrasts were supplemented by additional inclusive and exclusive masking procedures. Inclusive masking identifies voxels that survive a given statistical threshold across two or more contrasts. Exclusive masking identifies the voxels in a given contrast that are *not* shared with above-threshold voxels in a 'masking' contrast. Note that the more liberal the statistical threshold applied to the masking contrast, the more conservative is the exclusive masking procedure.

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Table 1. Summary of the three experiments contributing data to the present analyses

	Retrieval Test	**N**	**Critical trials**
Expt. 1	Remember/Know	24	Remember, Know, New
Expt. 2	Associative Recognition	36	Intact judged intact, Intact judged rearranged, New judged new
Expt. 3	Source Memory	28	Source correct, source incorrect but item correct, New

Table 2 Mean (SD) RTs (ms) for recollected (R), familiar (F) and new (N) items in each experiment

	R	**F**	**N**
Expt. 1	2140 (769)	3060 (1083)	2920 (994)
Expt. 2	1855 (388)	2274 (468)	2075 (464)
Expt. 3	1573 (276)	1741 (389)	1122 (147)

Table 3. Coordinates of the peak effects in the striatum identified by each contrast

Contrast	Region	coordinates	peak Z
F > N	L Caudate	-12 14 1	7.39*
	R Caudate	12 11 -2	6.76*
R > F	L Vent. Striat/Subgen	-12 11 -17	5.54*
	R Vent. Striat/Subgen	9 14 -17	5.25*
N > F	R. Putamen	30 -13 10	4.22

F = Familiarity, R = Recollection, N = New. L = left, R = Right. Vent Striat = Ventral striatum, Subgen = Subgenual frontal cortex. * = significant at $p<.05$ after whole brain FWE correction.

Figure Legends

Figure 1. Across-experiment overlap of Recollection (R>F) and Familiarity (F>N) contrasts. The effects are shown for each experiment individually in a) Exp. 1; b) Exp. 2; and c) Exp. 3. Individual experiment contrasts were height thresholded at $p < .01$, uncorrected, with a cluster extent threshold of $k = 9$ voxels. The across experiments main effects of recollection and familiarity are shown in d) and e). These effects were thresholded at $p < .0001$ ($k=29$ voxel extent threshold), inclusively masked with the simple effect in each experiment (thresholded at $p < .05$ in each case). Coronal sections are displayed for MNI coordinate $y = 14$, and the saggital section is displayed for $x = 6$. Effects are overlaid on the SPM8 canonical T1-weighted image.

Figure 2. a) Outcome of exclusively masking the main effect of recollection (R>F) with the main effects of both familiarity (F>N), and novelty (N>F). b) Outcome of exclusively masking the main effect of familiarity with the main effect of recollection. In each case, the principal contrasts were height thresholded at $p < .0001$, $k=29$ voxel extent threshold, and the exclusive masks were thresholded at $p < .05$. c) Outcome of inclusively masking the main effects of recollection and familiarity (each thresholded at $p <. 01$, $k=29$ voxel extent threshold). All sections displayed at MNI coordinate $y = 11$. d-f: peak parameter estimates (see text), collapsed across experiments and hemispheres, for recollected (R), familiar (F) and novel (N) trials. Standard errors were estimated across participants and experiments ($N=88$) after averaging across hemispheres.

Figure 3. Data from Elward et al. (2015). Outcome of the contrast between accurate and inaccurate source judgments (thresholded for display purposes at $p<.005$, uncorrected, $k=50$ voxel extent threshold) masked exclusively with the contrast between trials associated with high vs. low monetary reward (thresholded at $p < .1$). The subgenual recollection effect is indicated by the white arrows. Sections at MNI coordinates of $y = 14$, and $x = 3$ respectively. Peak $Z = 4.18$ ($p < .0001$) at MNI co-ordinates 6,14, -14.

Figure 4. Recollection (R>F) and Novelty (N>R) effects in anterior hippocampus. Main effects, collapsed across the three experiments, of a) recollection and b) novelty, each

thresholded at p <.0001, uncorrected, k=29 voxel extent threshold. Sections at MNI co-rodinate y = -11.

Figure 1.

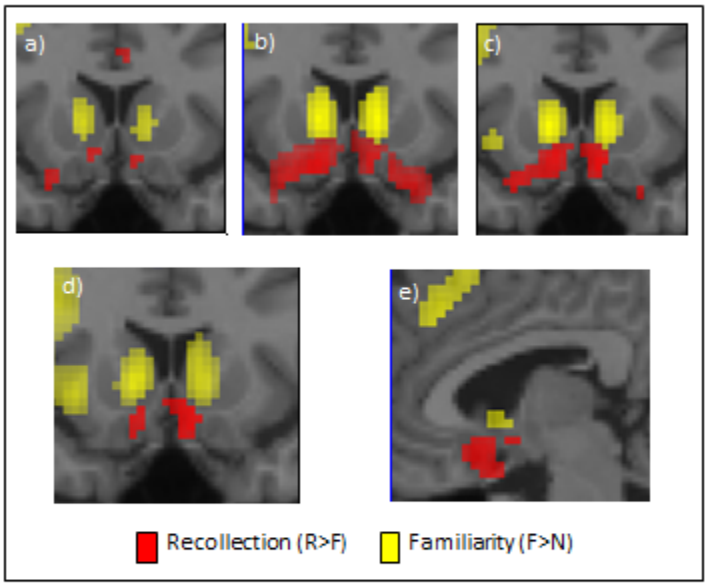

Figure 2

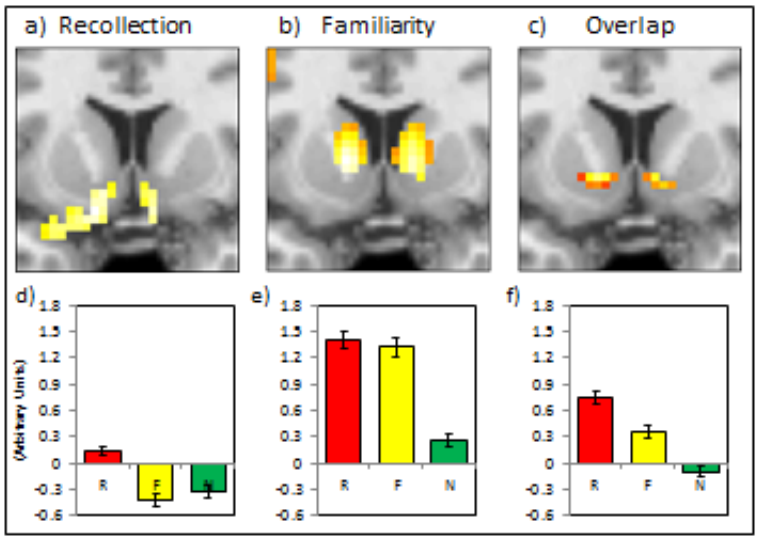
a) Recollection
b) Familiarity
c) Overlap
d)
e)
f)
(Arbitrary Units)
1.8
1.5
1.2
0.9
0.6
0.3
0
-0.3
-0.6
R
F
N

Figure 3

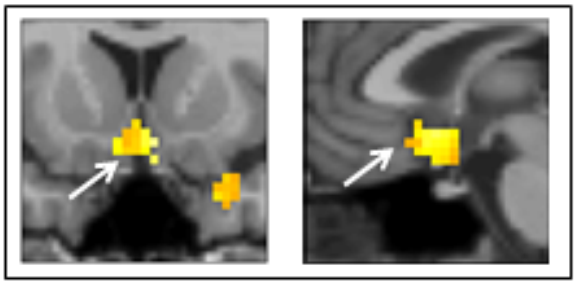

Figure 4