5 Discussion

The previous three chapters provide a description of the interaction between explicit and implicit learning systems. Chapter 2 described the effects of performing a working memory task during aversive conditioning. Concurrent performance of a working memory task affects both delay and trace conditioning protocols used. Chapter 3 describes the areas of the brain involved in the explicit and implicit aspects of conditioned aversion. Activation in the amygdala correlates with implicit measures of learning, while activation in bilateral middle frontal gyri correlates with the accuracy of expectancy, our explicit measure of learning. Chapter 4 describes changes in visual cortex due to conditioning. These changes are persistent through extinction, reflecting long term changes in the representation, and potentially perception, of the face image used.

5.1 Explicit Influences on Implicit Processes

Explicit knowledge exerts a strong influence over implicit processes. Results from Chapter 2 indicate that a high level task can result in less effective conditioning. This is true even for delay conditioning which, for eye-blink conditioning, is described by Manns et al. as being independent of awareness (Manns et al., 2002). A reduction in conditioning as a result of the concurrent working memory demand argues that working memory may be necessary for both delay and trace conditioning. However, the experimental manipulations that compensated for the drop in conditioning differ for delay and trace protocols.

In trace conditioning, the deficit can be compensated for by the combination of simplifying the protocol (using only one CS instead of two) and providing explicit knowledge of the CS/US relationship. It does not seem to be affected by simplification of the protocol alone. The same deficit in delay condition is compensated for when the protocol is simplified. We did not test the effects of informing subjects in a delay protocol due to the levels of conditioning in a single cue protocol being near ceiling. It is possible that this difference in effective compensatory mechanisms reflects two different methods of working memory interference with conditioning.

During delay conditioning, prefrontal resources involved in working memory may not be necessary for conditioning, but strong prefrontal activity could still cause suppression of amygdala activity (Rosenkranz and Grace, 2001). Amygdalar suppression may be compensated for by increased activity in the amygdala when the number of stimuli is reduced. It may be true that the same process occurs during trace conditioning. However, it is also true that for trace conditioning, recovery is dependent on also receiving explicit knowledge of the CS/US relationship. This dependence on explicit knowledge for trace conditioning alone is consistent with the original results of Clark and Squire (Clark and Squire, 1998). The compensating effects for trace conditioning could be disentangled by providing explicit knowledge of the CS/US relationship to subjects in a differential (two cue) trace conditioning experiment.

Whether it is due to suppression of the amygdala or the lack of prefrontal resources, the deficit in delay conditioning due to a working memory task indicates a substantial influence of explicit activity in implicit processes – an influence that may not be necessary for the simplest associative learning, but most certainly takes place.

5.2 Implicit Influences on Explicit Processes

Conscious experience is a synthesis of implicit processes. Some implicit processes are not experienced explicitly or are greatly hindered when explicit focus is brought to them (Beilock et al., 2002). One clear example of implicitly trained differences in perception is the phenomenon called ‘cue recruitment’ (Haijiang et al., 2006). In this example of cue recruitment, subjects are conditioned to perceive a bistable stimulus in a certain way whenever a given cue is present. Eventually, the cue itself is capable of biasing the perception of the bistable stimulus.

Similar to the perceptual bias brought about by cue recruitment, Chapter 4 provided evidence that conditioning modifies the way a particular stimulus is represented. The stimulus that was behaviorally relevant elicited a greater response post training. We proposed that a modification of BOLD activity in FFA, without strong activity in any areas like the amygdala or insula, indicated a change to the saliency of the previously reinforced stimulus. An alternative hypothesis (proposed by committee member Shinsuke Shimojo) was that, similar to the somatic marker hypothesis (Damasio et al., 1991), the activity in FFA is reflective of remaining emotional association. Generally speaking, it might be expected that there would be BOLD activity in an emotional or associative area (such as the amygdala or insula) that showed the same characteristics as the visual network activated by the CS+. However, it is possible that the low level activity seen in the insula may be sufficient to maintain the network of activity as an emotional response. The connectivity analysis proposed in Chapter 4 would provide a means of differentiating these two explanations. The somatic marker proposal would be supported if the FFA still showed strong linkage to responses in the insula during extinction. If the FFA was not strongly linked to the insula, but only other visual areas, it would argue for the change in saliency proposal.

One method often used to examine differences (and potentially overlaps) between explicit and implicit learning systems is that of conditioning to masked stimuli. In these experiments, a stimulus is presented to the subject for a short duration (30 ms) and then followed by a mask image presented for a longer period of time (45 ms). The second image prevents the first image from being processed by the visual system, and the subject will often report not having seen the first image. A number of studies performed analysis of masked vs. visible conditioned expression (Morris et al., 1998a; Critchley et al., 2002) as well as comparing visible stimuli that had been previously conditioned as masked or unmasked (Morris et al., 2001). These studies identified some areas that are classically thought to be implicit (such as the amygdala and insula). They also identified some regions of the brain that are normally thought to be precursors for explicit representation (such as the FFA). This is surprising, since most discussions of non-conscious visual processing center around a potential pathway involving the superior colliculus and pulvinar nucleus (McIntosh and Gonzalez-Lima, 1998; Morris et al., 1999).

In an effort to examine the time course of learning and identify those areas directly involved in the learning process, we performed a set of experiments conditioning subjects both implicitly and explicitly using similar parameters. The protocol chosen conditioned greater than 50% of the subjects used in pilot experiments without fMRI scanning. After fMRI data collection, it became clear that the subjects being conditioned during fMRI acquisition did not develop a strong enough association to justify any fMRI results. The difference in conditioning between our pilot studies and fMRI results led us to believe that the increased number of stimuli present in the fMRI environment resulted in reduced conditioning. In hindsight, the results look similar to those described in Chapter 2. Subjects placed in a distracting environment were no longer easily conditioned. Given that the reduced conditionability depends on cross-modal factors (such as auditory noise in an MRI scanner) and that past implicit conditioning studies show changes in cortical representations, it seems likely that the classical model of a distinct explicit and implicit systems is inadequate. In fact, incorporating sensitivity measures available in an ROC analysis, amygdala responses to masked faces don’t appear to be automatic but rather related to the face’s visibility (Pessoa et al., 2006). These results argue that the difference between explicit and implicit may be more continuous than originally proposed.

5.3 Continuum or Separate Systems

Evidence from HM first led researchers to explore the potential separation between explicit and implicit learning systems (Scoville and Milner, 1957). Evidence for a non-conscious visual pathway came from blind-sight patients who seemed to be performing visual tasks without explicit knowledge (Weiskrantz et al., 1974). Work by Clark and Squire (Clark and Squire, 1998) described delay conditioning as occurring independent of awareness (Manns et al., 2002). This in spite of previous work arriving at a theoretical agreement called the “necessary gate hypothesis;” that explicit knowledge of the CS/US relationship was necessary but not sufficient for conditioning (Dawson and Furedy, 1976).

What has been described as non-conscious conditioning has been shown using masking to hide the CS and a variety of techniques to assess explicit knowledge (Soares and Ohman, 1993). Explicit assessment techniques range from expectancy reports to familiarity questionnaires. Using these techniques, groups have even described non-conscious trace conditioning when the stimuli are fear relevant (Ohman and Soares, 1998), Whether or not masked conditioning is a non-conscious process has been questioned. Arguments against masked conditioning being non-conscious mostly concern the ability to assess awareness of the masked stimuli (Lovibond and Shanks, 2002). Difficulties include memory requirements for the test, whether the test is objective or subjective and partial identification of conditioned stimuli. Recent work has also questioned whether traditional statistical assessments have the sensitivity to identify subtle differences due to conscious recognition (Pessoa et al., 2006). This debate surrounding what is conscious and what is non-conscious is suggestive of a subtle grade between the two systems rather than a sharp separation.

The work presented in this thesis fits with the possibility of a continuum of conscious experience rather than two distinct subsystems. At minimum we find interaction between the two subsystems in each study. There is the caveat that all of this work has been in healthy subjects. It is entirely possible that the explicit and implicit systems can’t be disentangled when all brain areas are functioning normally, that they function independently only when large portions of the brain have been damaged. In and of itself, this would be interesting since it would allow anatomical distinction without necessarily requiring functional separation.

5.4 Work on the Conscious Mouse

This work was begun in an attempt to better characterize the processes and substrates involved in conscious experience. Collaboration was initiated between my advisor

Christof Koch (Caltech), David Anderson (Caltech), Michael Fanselow (UCLA), and later Henry Lester (Caltech) and Tad Blair (UCLA). Beginning with Larry Squire's result that trace conditioning was related to explicit learning while delay was not, the group initiated studies of the differences between the two types of conditioning. Since trace and delay conditioning are studied both in humans and a large number of animal models, this provided a great opportunity to study the substrates required for trace conditioning with an eye toward analogues of explicit learning in humans. Efforts from human studies provided better information about the nature of explicit processes while animal model systems allowed for the use of tools (molecular, genetic, and lesion) not available when studying human subjects. The explicit distraction results described in Chapter 2 led to the use of a distraction task in mice during conditioning. Results indicated that the presentation of a cross-modal stimulus made trace conditioning less effective but did not affect delay (Han et al., 2003). The focus of the collaboration then shifted to the use of genetic tools to reversibly silence specific populations of neurons (Slimko et al., 2002). Using a combinatorial technique, the silencing could be directed toward specific neuron types that may be spatially inter-mixed with other neurons. Initial targets for silencing after verification include different nuclei in the amygdala as well as the anterior cingulate and prefrontal cortex. When these tools are fully developed, they should yield a great deal of information about implicit and explicit processes in conditioning.

5.5 Conclusion

There are robust interactions between explicit and implicit processes that provide a method of balance between the two learning systems, and, most importantly, seem to provide a method for forgetting. Specifically, areas of the prefrontal cortex are involved in extinction of conditioned associations (Milad et al., 2006; Sotres-Bayon et al., 2006). One study of functional connectivity in post traumatic stress disorder patients indicates that the disorder may be a result of excessive amygdala activity (Gilboa et al., 2004). Without suppression from prefrontal areas, the amygdala causes increasing activity in higher sensory areas, creating a feedback loop that becomes unmanageable. The necessity of these interactions is also indicated by the relative success of cognitive therapy in treating anxiety disorders.

There is evidence from a large number of areas that indicate it may be possible to sometimes separate implicit and explicit learning, the hippocampal patient HM described earlier is a good example. However, both the successful and unsuccesful work presented here indicates that explicit and implicit learning systems display little independence in practice.