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**‘Online’ integration of sensory and fear memories**

*Abstract:*

How does a stimulus never associated with danger become frightening? When elements of a past sensory memory become integrated into a new fear memory. But when does this integration occur? We show that this integration occurs ‘online’ as the fearful event is encountered.

Text:

Imagine the following sequence of events. First, you walk through the tropical rainforests of Australia and hear an (unfamiliar) booming sound then see an (unfamiliar) bird-like animal. Some days later, you see a photograph of the bird (the cassowary) with the caption ‘extremely dangerous.’ Finally, days later again, you are walking through the rainforest and hear the booming sound again: it makes you feel apprehensive, perhaps even a little bit frightened. Why does the booming sound that has never been associated with the dangerous element come to be frightening? Clearly, information about the sound-bird and bird-danger relationships have been integrated within the memory system to generate fear of the sound. But ***when*** does this integration occur?

There are two possibilities. The first is that, during the middle event in the sequence, the photograph of the bird triggers the memory of the booming sound, so when you learn the bird is dangerous, the booming sound also becomes frightening. We refer to this as online integration. The second possibility is that the booming sound is frightening because hearing it again retrieves the memory of the bird, which is then linked to the memory of the bird being dangerous. We refer to this as test integration.

We set out to differentiate between these two explanations by using an animal model, sensory preconditioning in rats. This procedure has three key stages. In stage 1, rats learn that the sound leads to a light. They form a sensory memory which is stored in a region called the perirhinal cortex (PRh). The next day, in stage 2, rats learn that the light is dangerous (the light is paired with a foot-shock). Here, they form a fear memory that is stored in the amygdala (specifically the basolateral complex; BLA). Finally, in stage 3, we test whether they show fearful reactions to the sound and/or the light. Not surprisingly, rats show fear to the dangerous light; but they also show fear to the sound that has never been directly paired with the danger (foot-shock).

We examined whether the sensory and fear memories, which are stored in distinct brain regions, are integrated online or at test. Under the online integration explanation, retrieval of the past memory (e.g. the sound) is necessary for it to subsequently become integrated with the new memory in stage 2. Here, the retrieval of the sound should require activity in the PRh, as the initial memory of the sound was stored in the PRh in stage 1. However, under the test integration explanation, the retrieval of the past memory is not necessary in stage 2 but rather it becomes necessary in stage 3. Therefore, to distinguish which explanation underlies this fear to the sound, we inhibited (‘stopped’) processes in the PRh during the middle stage (stage 2) of our preconditioning protocol.

Our results demonstrate that, when the PRh is inhibited at the time the light becomes dangerous, rats learn to fear the light but do NOT show fear to the sound. This suggests that retrieval of the sound is necessary in stage 2 for the sound to become frightening. These results provide evidence that integration in this procedure occurs online: as rats learn to fear the light through its pairings with shock, the retrieved sound also becomes associated with the shock, and thus, becomes frightening. Finally, we additionally showed that retrieval of the new integrated memory (where the sound is now frightening) continues to require the PRh at the point of testing. That is, after its formation in stage 2, inhibition of the PRh at the time of testing undermined the rat’s ability to retrieve and express fear to the sound.

Integration occurs online, as the dangerous event occurs. At least, that is what our results suggest. So then how does this relate to the booming sound in the rainforest? Well, the booming sound becomes frightening at the time you discover the bird that produced the sound is dangerous! Of course, this does not exclude the possibility that, under other circumstances, integration occurs at the moment when past stimuli are re-encountered and an action must be made. In our future work, we hope to determine the conditions under which different types of integration occur, and the circuitry that underlies each form.