Non-human animal neuroscience research has offered much information concerning the circuitry involved in the acquisition and expression of conditioned responses to stimuli that predict biologically-relevant outcomes. The obvious strength of this work lies in its ability to assert control over a given subject’s reinforcement history. But the human volunteers come to our studies with a reinforcement history of her/his own and this is a related but distinct area of research in its own right. Given that human faces constitute a rich source of predictive social information, we present our human subjects with pictures of facial expressions of emotion with the assumption that the past predictive value of these expressions will command the respect of circuits involved in the acquisition and/or expression of biologically-relevant learning. For example, we have documented that the human amygdala is activated robustly to presentation of certain facial expressions, most notably fear. This occurs whether or not subjects report having a strong emotional response to presentation of these stimuli and even occurs when subjects report not having seen these stimuli. In this talk, I will present data showing how facial expressions can be used to understand the role of the amygdala in normal socio-emotional functioning. In addition, we will see that facial expressions can also be used to evoke activity through a prefrontal-amygdala circuit that, when compromised, is hypothesized to play a role in the breakdown of emotional regulation prevalent in mood and anxiety disorders.