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Report

The Human Amygdala and the Induction and Experience of Fear

 Justin S. Feinstein¹, , Ralph Adolphs², Antonio Damasio³ and Daniel Tranel¹
¹ University of Iowa, Iowa City, IA 52242, USA

² California Institute of Technology, Pasadena, CA 91125, USA

³ University of Southern California, Los Angeles, CA 90089, USA

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Summary

Although clinical observations suggest that humans with amygdala damage have abnormal fear reactions and a reduced experience of fear ([1], [2] and [3]), these impressions have not been systematically investigated. To address this gap, we conducted a new study in a rare human patient, SM, who has focal bilateral amygdala lesions [4]. To provoke fear in SM, we exposed her to live snakes and spiders, took her on a tour of a haunted house, and showed her emotionally evocative films. On no occasion did SM exhibit fear, and she never endorsed feeling more than minimal levels of fear. Likewise, across a large battery of self-report questionnaires, 3 months of real-life experience sampling, and a life history replete with traumatic events, SM repeatedly demonstrated an absence of overt fear manifestations and an overall impoverished experience of fear. Despite her lack of fear, SM is able to exhibit other basic emotions and experience the respective feelings. The findings support the conclusion that the human amygdala plays a pivotal role in triggering a state of fear and that the absence of such a state precludes the experience of fear itself.

Highlights

- ▶ Case study of patient SM, a rare human patient with focal bilateral amygdala lesions
- ▶ First investigation of the induction and experience of fear in such a patient
- ▶ SM failed to exhibit fear behaviors, and her fear experience was highly impoverished
- ▶ The human amygdala plays a pivotal role in triggering a state of fear

Article Outline

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Acknowledgements

Supplementary content for this Article



Document S1. Supplemental Data, Three Figures, and Two Tables.

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Results and Discussion

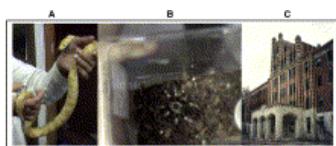
The amygdala is involved in multiple aspects of fear processing, ranging from fear conditioning [[5] and [6]] to the modulation of attention and memory for fear-related stimuli [[7], [8] and [9]], all the way to fear recognition [10] and the induction of fear-related behaviors [[11], [12], [13], [14], [15], [16], [17], [18], [19] and [20]]. Much less is known about the amygdala's role in the conscious experience of fear, in large part because nonhuman animals with amygdala lesions are unable to verbally report on their internal subjective experience, and humans with focal bilateral amygdala damage are extremely difficult to find. An exception is patient SM, a 44-year-old woman who is one of the best-characterized human cases with bilateral amygdala damage [10] (see [Figure S1](#) available online for a description of SM's brain damage). SM's neuropsychological profile has been stable for the past two decades. She performs within the normal range on standardized tests of IQ, memory, language, and perception [10] yet is severely impaired in fear conditioning [21], in recognizing fear in facial expressions [[4], [10] and [22]], and in aspects of social behavior thought to be mediated by emotions related to fear [[23], [24] and [25]]. Importantly, none of the previous studies specifically assessed the induction and experience of fear in patient SM, and it is these two aspects of fear that form the basis for the current report. We predicted that without the amygdala, the action sequence that constitutes a state of fear would fail to be induced in SM, thereby preempting her experience of fear.

Throughout this study, we define fear induction as the exposure to stimuli capable of triggering a state of fear. Fear experience, on the other hand, is the subjective feeling of fear, and it was measured by SM's self-report of her internal experience. The success of a fear induction was gauged based on the intensity of fear experience in addition to the presence of any overt behavioral manifestations of fear, especially signs of avoidance behavior or withdrawal in response to fear-provoking stimuli. Because much of the testing occurred in real-world settings, we did not have the opportunity to collect complementary psychophysiological data. However, we note that previous studies [[21] and [26]] have shown impairments in SM's conditioned skin conductance response and startle reflex.

Fear Induction

When exposed to dangerous stimuli, such as potential predators, animals with amygdala lesions typically display a lack of the behaviors normally associated with the action program of fear [[11], [12], [13], [14], [15], [16], [17], [18], [19] and [20]]. We used a comparable approach in SM by directly confronting her with fear-inducing stimuli and observing her behavior while also querying her subjective state. For ethical reasons, we chose three situations capable of inducing fear with little to no risk of direct harm to the subject: (1) visiting an exotic pet store with snakes and spiders, (2) walking through a haunted house, and (3) watching film clips of scary movies. SM provided her informed written consent to participate.

The first fear-inducing situation entailed direct exposure to snakes and spiders, two of the most commonly feared species in the animal kingdom. Interestingly, for many years, SM has repeatedly told us that she "hates" snakes and spiders and "tries to avoid them." To test her real-life behavior, we took her to an exotic pet store and focused on probing for external manifestations of fear with a particular eye toward any signs of avoidance behavior. Upon entering the store, SM was spontaneously drawn to the snake terrariums and appeared visually captivated by the large collection of snakes. A store employee asked SM whether she would like to hold a snake, and she agreed ([Figure 1A](#)). SM held the snake for over 3 min while displaying a wide range of exploratory behaviors: she rubbed its leathery scales, touched its flicking tongue, and closely watched its movements as it slithered through her hands. Her verbal behavior revealed a comparable degree of fascination and inquisitiveness: she repeatedly commented, "This is so cool!" and asked the store employee numerous questions (e.g., "When they look at you, what do they see?"). During this time period, we asked SM to rate her fearfulness on a scale from 0 (no fear at all) to 10 (extreme fear). Her reported experience of fear never surpassed a rating of 2. Moreover, SM displayed a compulsive desire to want to "touch" and "poke" the store's larger and more dangerous snakes, even though the store employee repeatedly told her that these snakes were not safe and could bite. In total, SM asked 15 different times whether she could touch one of the larger snakes. She also attempted to touch a tarantula ([Figure 1B](#)), but had to be stopped because of the high risk of being bitten. When asked why she would want to touch something that she knows is dangerous and that she claims to hate, SM replied that she was overcome with "curiosity." The disconnection between SM's verbally stated aversion to snakes and spiders and her actual real-life behavior was striking. She did not display any signs of avoidance, but instead exhibited an excessive degree of approach (a pattern highly reminiscent of the behavior in monkeys with Kluver-Bucy syndrome [12]). We note that SM's behavior was not merely the result of her feeling comfortable in the relatively safe environment of the pet store, because we later discovered that, in the past, SM encountered a large snake outdoors and behaved in a similar manner (see [Supplemental Data](#)).



[Full-size image \(40K\)](#)
[High-quality image \(363K\)](#)

Figure 1.

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Fear Induction in Patient SM

(A–C) Still-frame photos of SM handling a snake (A), the tarantula that SM tried to touch (B), and the Waverly Hills Sanatorium Haunted House (C).

In the second fear-inducing situation, we attempted to scare SM in a setting professionally designed for such a purpose. During Halloween, we took SM to the Waverly Hills Sanatorium (Figure 1C), ranked as one of the “most haunted” places in the world (http://en.wikipedia.org/w/index.php?title=Waverly_Hills_Sanatorium&oldid=324971912). On an annual basis, the sanatorium hosts a haunted house, elaborately decorating the inside with eerie scenes, airing scary music and loud noises, and featuring people dressed as monsters, murderers, and ghosts. Upon arrival, SM and the research team were paired with a group of five women (all of whom were strangers). From the outset, SM voluntarily led the entire group through the haunted house, showing no signs of hesitation while walking around corners or into dark hallways. As the other members of the group lagged behind her, she would repeatedly call out, “This way guys, follow me!” The hidden monsters attempted to scare SM numerous times, but to no avail. She reacted to the monsters by smiling, laughing, or trying to talk to them. In contrast, their scare tactics typically elicited loud screams of fright from the other members of the group. More than showing a lack of fear, SM exhibited an unusual inclination to approach and touch the monsters. Ironically, SM scared one of the monsters when she poked it in the head because she was “curious” as to what it would feel like. Before, during, and after the haunted house, SM was queried about her current level of fear. She never reported experiencing any elevations in fear, and her fear ratings were at 0 throughout. She did, however, report feeling a high level of excitement and enthusiasm. When asked to elaborate, she said her excitement was similar to the feeling she gets while riding on a rollercoaster, an activity she claims to enjoy. In sum, SM was highly aroused by the haunted house, but did not feel any sense of fear, showed no signs of nervousness or apprehension while walking through dark passageways, and was never visibly frightened by any of the numerous attempts to scare her.

Lastly, we used a film induction procedure, widely considered one of the most effective and reliable ways to induce emotions in a laboratory setting ([27] and [28]). SM viewed a set of ten different fear-inducing film clips (Table S2). Interspersed between the fear clips were films aimed at inducing other types of emotion, including disgust, anger, sadness, happiness, and surprise. During the non-fear-related films, SM exhibited behaviors compatible with those emotions (e.g., laughter during happiness, shouts of revulsion during disgust) and reported experiencing high levels of the appropriate emotion (Figure S2). By contrast, SM exhibited no fear responses and reported experiencing little to no fear across the entire battery of fear-inducing films (Figure 2). Nonetheless, she found the fear films to be exciting and entertaining, and in one case, she inquired about the name of the movie so she could rent it from the video store later that day. Of note, SM commented that most people would likely feel scared by the content of the films, even though she did not; this provides evidence that her impoverished experience of fear cannot be fully accounted for by a fear recognition deficit or a failure to understand the concept of fear (see Supplemental Data).

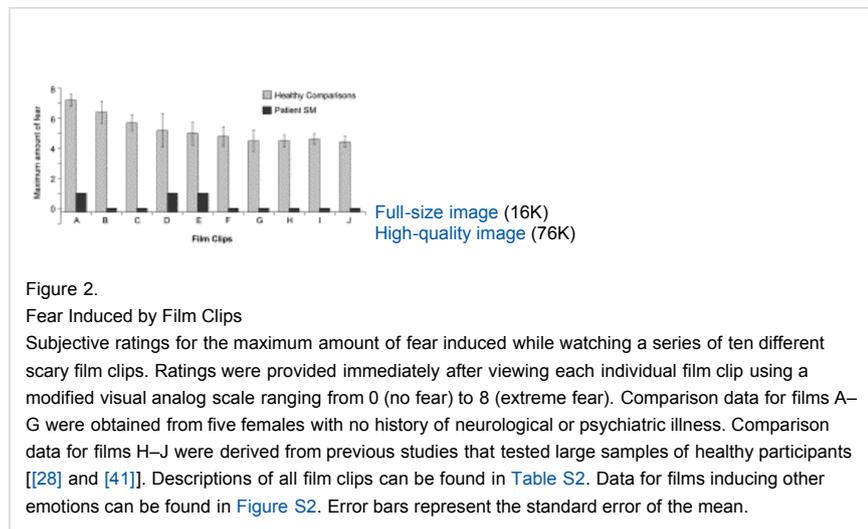


Figure 2.

Fear Induced by Film Clips

Subjective ratings for the maximum amount of fear induced while watching a series of ten different scary film clips. Ratings were provided immediately after viewing each individual film clip using a modified visual analog scale ranging from 0 (no fear) to 8 (extreme fear). Comparison data for films A–G were obtained from five females with no history of neurological or psychiatric illness. Comparison data for films H–J were derived from previous studies that tested large samples of healthy participants ([28] and [41]). Descriptions of all film clips can be found in Table S2. Data for films inducing other emotions can be found in Figure S2. Error bars represent the standard error of the mean.

Fear Experience

We assessed SM's general experience of fear using eight well-validated self-report questionnaires that cover topics ranging from phobias and panic symptoms all the way to fear in relation to specific situations such as public speaking or dying (Table S1). SM completed the questionnaires multiple times over the course of 3 years. A previous study [29] that used one of these questionnaires suggested that amygdala damage does not impair fear experience; however, the patients in this sample all had incomplete (and mostly unilateral) amygdala lesions. Despite the fact that most of these questionnaires were created for detecting abnormally high, rather than low, levels of fear, SM consistently scored near the floor level and well below the normative mean on all occasions (Figure 3 and Table S1). Together with our other data, these findings from self-report questionnaires corroborate a profound and reliable reduction in SM's experience of fear.

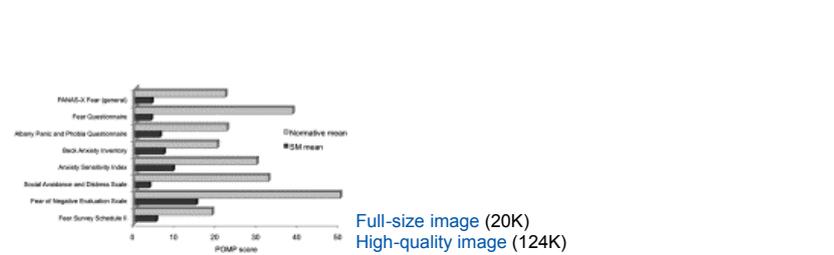


Figure 3.

Fear Experience in Patient SM

Self-report questionnaires comparing patient SM's experience of fear to normative samples comprised of healthy individuals. All scores have been converted to POMP units [42], representing the "percent of maximum possible" for each questionnaire. Raw scores and additional information about the questionnaires can be found in [Table S1](#). Data from the experience-sampling study can be found in [Figure S3](#).

To further investigate SM's emotional experiences in everyday life, we used the experience-sampling method, which captures emotional experiences in real time as they unfold in the subject's natural environment [[30] and [31]]. SM was provided with a handheld computerized emotion diary that prompted her at three random times each day to rate her current emotional state using a set of 50 randomly presented emotion terms. The emotion terms covered a broad range of both positive and negative affects, and ratings were provided on a 5-point scale. Both the emotion terms and rating scale were derived from the Positive and Negative Affect Schedule – Expanded Form (PANAS-X) [32]. Across 156 sampling time points collected over a 3 month period, there were only six items (out of the 50) that SM consistently rated feeling at the lowest possible level: afraid, nervous, scared, guilty, ashamed, and fearful. Likewise, her average PANAS-X fear composite score was at the floor level (mean score = 0% of maximum possible; [Table S1](#)). For all basic emotions other than fear, SM reported numerous instances of experiencing the emotion, with intensity levels varying from "a little" to "quite a bit" ([Figure S3](#)). Interestingly, out of the 50 different emotion terms, the item that received the highest average rating over the entire 3 month period was "fearless" (mean score = 45% of maximum possible). Although we did not collect comparable experience-sampling data from healthy individuals, precluding quantitative statements about SM's abnormality, the striking pattern observed and its consistency with the other questionnaires provides strong evidence that SM fails to experience fear, even though she can experience other emotions.

Fear in SM's Past

In modern-day developed societies, fear-provoking situations are not commonly encountered [33]. To assess the possibility that SM's lack of fear can be attributed to a lack of fear-provoking encounters, we queried her about past life experiences (including experiences during childhood; see [Supplemental Data](#)). As it turned out, SM has encountered numerous events that would be considered fear-inducing or even traumatic in nature. For instance, she has been held up at knife point and at gun point, she was once physically accosted by a woman twice her size, she was nearly killed in an act of domestic violence, and on more than one occasion she has been explicitly threatened with death (see [Supplemental Data](#) for a detailed account of one of these events). What stands out most is that, in many of these situations, SM's life was in danger, yet her behavior lacked any sense of desperation or urgency. Police reports obtained from the local police department further corroborate SM's recollection of these events and paint a picture of an individual who lives in a poverty-stricken area replete with crime, drugs, and danger. Of note, SM has never been convicted of any crime, but rather has been the victim of numerous crimes. Moreover, it is evident that SM has great difficulty detecting looming threats in her environment and learning to avoid dangerous situations, features of her behavior that have in all likelihood contributed to her high incidence of life-threatening encounters.

When asked to recollect how she felt during the aforementioned situations, SM denied feeling fear but did report feeling upset and angry about what had happened. Without fear, it can be said that SM's distress lacks the deep heartfelt intensity endured by most survivors of trauma. Such an interpretation is consistent with a previous study [34], in which two experienced clinical psychologists interviewed SM without having any knowledge of her condition. To the psychologists, SM came across as a "survivor," as being "resilient" and even "heroic" in the way that she had dealt with adversity in her life. Taken together, this evidence illuminates the possibility that because of her amygdala damage, SM is immune to the devastating effects of posttraumatic stress disorder, an intriguing hypothesis that has recently found support in war veterans with amygdala lesions [35].

Conclusions

The findings from this study indicate that patient SM, a woman with focal bilateral amygdala lesions, has a profound and pervasive impairment in the induction and experience of fear across a wide range of situations and measures. By contrast, SM appears entirely capable of triggering and feeling emotions other than fear (see [Figures S2 and S3](#)). Her inability to generate fear across the range of situations probed in this study supports the conclusion that the amygdala is a critical brain region for triggering a state of fear when an individual encounters threatening stimuli in the external environment. There is no reason to expect that fear, or even panic, induced by internal stimuli (e.g., the interoceptively conveyed pain caused by myocardial infarction) would be mediated by the amygdala. On the contrary, structures in the brainstem

would likely be the direct trigger region for interoceptive fear-inducing stimuli, a prediction that our group is in the process of investigating and for which there is some factual support [36]. Such a conclusion is consistent with what is known about the functional neuroanatomy of the amygdala. Sensory and association cortices required for representing external stimuli are intact in SM's brain, as are the brainstem and hypothalamic circuitry necessary for orchestrating the action program of fear. SM's amygdala lesions in effect disconnect these two components, making it improbable, if not impossible, for sensory representations to trigger fear responses. Our framework for thinking about emotion and feeling argues that many different cognitive, autonomic, and behavioral changes comprise a state of fear, and the induction of such a state is required in order to experience a feeling of fear. In short, we view SM's lack of experienced fear as a direct consequence of her failure to mount a normal fear response (see [Supplemental Data](#) for additional explanation).

Interestingly, SM's reaction to fear-inducing stimuli was not characterized by a loss of responsiveness, but rather manifested as a heightened arousal and interest in the face of a near-complete lack of avoidance and caution. Moreover, SM's lack of avoidance was often accompanied by an excess of exploratory approach behavior that she verbally described as an overwhelming feeling of "curiosity." This striking pattern of behavior is consistent with reports in amygdala-lesioned monkeys [20] but is not easily reconciled with emerging accounts of the amygdala as critical in detecting the saliency of stimuli. At a minimum, our findings argue that fear-inducing stimuli are still capable of eliciting changes in attention and arousal through structures other than the amygdala [37].

Finally, our findings suggest that the amygdala's role in the induction and experience of emotion is specific to fear [38]. To say that SM is emotionless or unable to feel emotion is simply false. Her emotional deficit is primarily circumscribed to the behaviors and experiences that characterize a state of fear. Although this study has several limitations inherent to any case study (see [Supplemental Data](#)), the results are remarkably consistent with previous work in nonhuman animals [[11], [12], [13], [14], [15], [16], [17], [18], [19] and [20]], as well as with other case reports documenting diminished fear in humans with amygdala damage [[1], [2] and [3]]. The unique case of patient SM provides a rare glimpse into the adverse consequences of living life without the amygdala. For SM, the consequences have been severe. Her behavior, time and time again, leads her back to the very situations she should be avoiding, highlighting the indispensable role that the amygdala plays in promoting survival by compelling the organism away from danger [39] and [40]. Indeed, it appears that without the amygdala, the evolutionary value of fear is lost.

Acknowledgments

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