

# **Fear and panic in humans with bilateral amygdala damage**

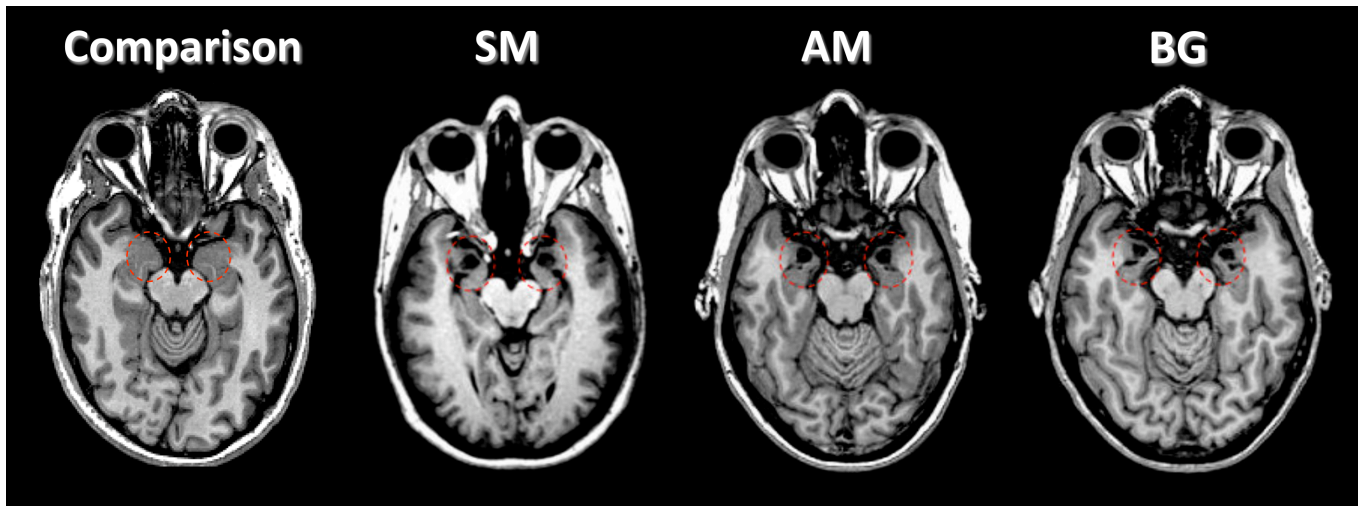
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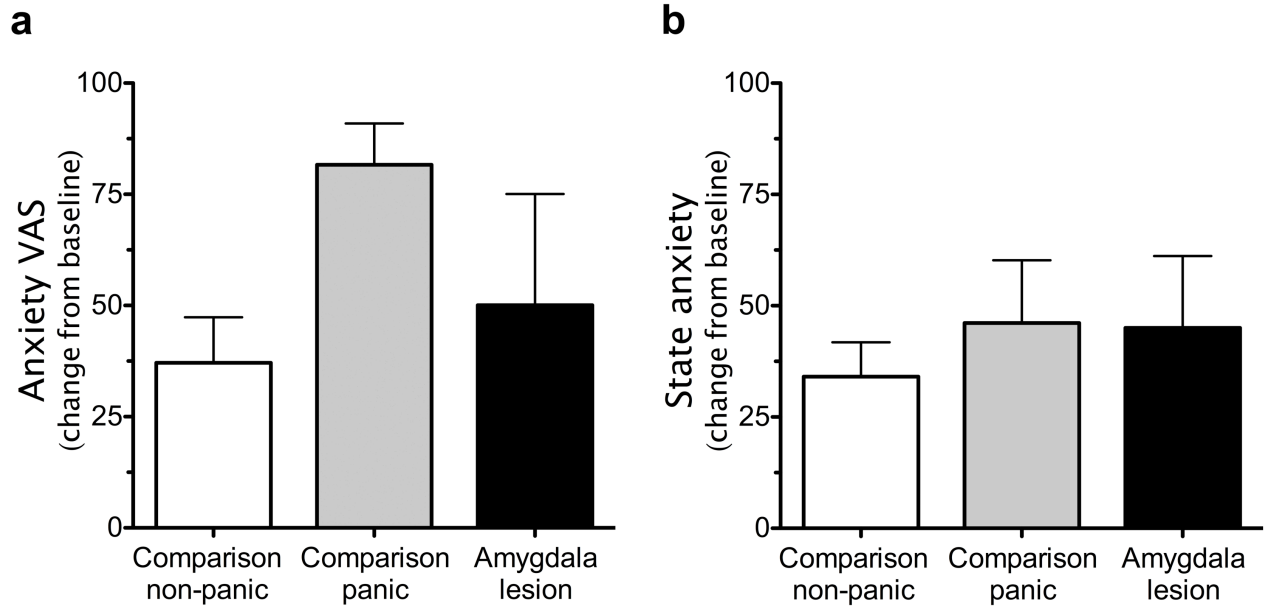
## **Supplementary Information**

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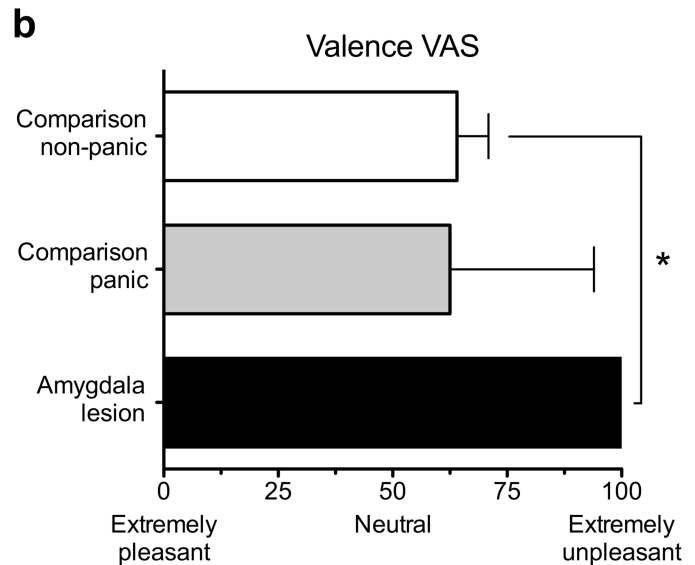
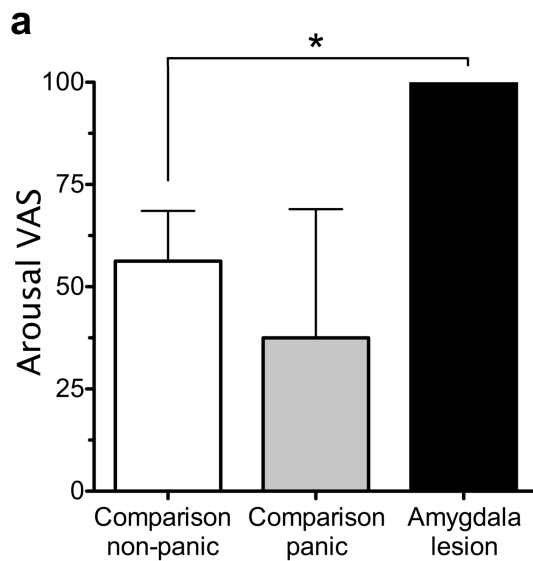
**Supplementary Fig. 1.** MRI scans acquired during the same time period as the CO<sub>2</sub> experiment revealed focal bilateral amygdala lesions in patients SM, AM, and BG (as highlighted by the red-dashed circles). For comparison, the amygdala of a healthy, neurologically-intact individual is also shown. Detailed neuroanatomical analyses of each patient's amygdala lesion have been previously published. Importantly, other key neural structures related to emotion remain intact, including the insular cortices, ventromedial prefrontal cortices, hypothalamus and brainstem (including the periaqueductal gray).



**Supplementary Fig. 2.** Change from baseline in self-reported anxiety during the first CO<sub>2</sub> inhalation as measured by (a) an anxiety visual analog scale (VAS), and (b) the Spielberger State Anxiety Inventory. Error bars represent the standard error of the mean.



**Supplementary Fig. 3.** Level of self-reported arousal and valence during the first CO<sub>2</sub> inhalation. **(a)** The amygdala-lesion patients rated the CO<sub>2</sub> inhalation as significantly more arousing than the comparison participants who did not panic (\*p<0.05; Mann-Whitney U-test). **(b)** The amygdala-lesion patients rated the CO<sub>2</sub> inhalation as significantly more unpleasant than the comparison participants who did not panic (\*p<0.05; Mann-Whitney U-test). Error bars represent the standard error of the mean.



**Supplementary Table 1.** DSM-IV panic symptoms endorsed by each patient during the panic attack evoked during the first CO<sub>2</sub> inhalation challenge (Panic #1), and during a subsequent CO<sub>2</sub> inhalation challenge (Panic #2).

	<b>Panic #1</b>	<b>Panic #2</b>
<b>SM</b>	<ul style="list-style-type: none"> <li>-sensations of shortness of breath and smothering</li> <li>-palpitations</li> <li>-derealization (feelings of unreality)</li> <li>-fear of losing control</li> </ul>	<ul style="list-style-type: none"> <li>-sensations of shortness of breath and smothering</li> <li>-trembling and shaking</li> <li>-feeling unsteady</li> <li>-chills and hot flushes</li> </ul>
<b>AM</b>	<ul style="list-style-type: none"> <li>-sensations of shortness of breath and smothering</li> <li>-palpitations</li> <li>-trembling</li> <li>-feeling dizzy</li> <li>-fear of dying</li> </ul>	<ul style="list-style-type: none"> <li>-sensations of shortness of breath and smothering</li> <li>-palpitations</li> <li>-trembling</li> <li>-feeling dizzy</li> <li>-fear of going crazy</li> </ul>
<b>BG</b>	<ul style="list-style-type: none"> <li>-sensations of shortness of breath and smothering</li> <li>-feeling of choking</li> <li>-palpitations and accelerated heart</li> <li>-sweating</li> <li>-trembling</li> <li>-feeling dizzy and faint</li> <li>-derealization (feelings of unreality)</li> <li>-chills</li> <li>-fear of dying</li> </ul>	<ul style="list-style-type: none"> <li>-sensations of shortness of breath and smothering</li> <li>-feeling of choking</li> <li>-palpitations</li> <li>-trembling</li> <li>-feeling dizzy and faint</li> <li>-derealization (feelings of unreality) and depersonalization (being detached from oneself)</li> <li>-paresthesias (numbness or tingling sensations)</li> <li>-fear of dying</li> </ul>

## Supplementary Panic Descriptions

All patients were video recorded during the CO<sub>2</sub> inhalation. Below are detailed behavioral observations of each patient's first CO<sub>2</sub>-induced panic attack, followed by excerpts taken from an interview conducted after the inhalation.

### **Patient SM**

Immediately following the inhalation, SM began breathing at a rapid pace and gasping for air. Approximately 8 seconds following the inhalation, her right hand started waving frantically near the air mask. At 14 seconds post-inhalation, SM exclaimed, "Help me!" while her right hand gestured toward the mask. The experimenter immediately removed the mask from SM's face. As this was happening, her body became rigid, her toes curled, and her fingers on both hands were flexed toward the ceiling. As soon as the mask was removed, SM grabbed the experimenter's hand and in a relieved tone said, "Thank you." The skin on her face was flushed, her nostrils were flared, her eyes were opened wide, and her upper eyelids were raised. At 30 seconds post-inhalation, SM's breathing began to return to a normal rate, she let go of the experimenter's hand, and then said, "I'm alright."

SM: It felt like my throat was closing up... I couldn't breathe.

Clinician: What kind of emotions did that cause?

SM: Panic mostly, cause I didn't know what the hell was going on.

Clinician: This [feeling] was really bad?

SM: Yeah, this was the most, number one, worst.

Clinician: Were you surprised that you reacted the way you did?

SM: I was cause usually nothing happens to me.

Clinician: [During the inhalation] what were you worried about?

SM: Suffocating.

### **Patient AM**

At the very beginning of the inhalation, AM's entire upper body (including both arms) slightly jumped as if startled, her left hand clenched into a fist, and her breathing became pronounced. Her facial expression formed into a grimace with eyebrows furrowed, eyelids tightly shut, mouth stretched downward and horizontally, and neck muscles tightened. At 10 seconds post-inhalation, AM attempted to escape from underneath the mask by contorting her head down and to the left, while trying to grab the mask with her left hand. At 15 seconds post-inhalation, she stopped trying to escape, but her eyes remained closed, and her left hand remained near the mask. By 22 seconds post-inhalation, her body posture and facial expression became more relaxed, as did her breathing.

Clinician: Can you verbally describe what that experience was like for you?

AM: Yes, fear. A strong fear of suffocation.

Clinician: Did you ever feel this before?

AM: No, never.

Clinician: Is this the strongest feeling of fear you have ever had?

AM: Yes, definitely.

Clinician: Did you have any thoughts that came to your mind during the peak of this experience?

AM: I was overwhelmed by the panic and fear of dying. There was nothing else.

Clinician: Did you actually have the thought that you might be dying.

AM: Yes.

### **Patient BG**

During the inhalation, BG's eyelids closed and her eyebrows lowered and furrowed. At 8 seconds post-inhalation, she gasped for air, as her neck muscles clenched, and her facial expression became even more contorted with both eyes tightly shut and her mouth opened and stretched horizontally. Her hands briefly flailed upwards and then rested back down on top of her stomach. At 16 seconds post-inhalation, she ripped the mask off with both hands and started to take deep inhalations followed by quick exhalations as her fingertips gently touched her upper chest and her head slowly rocked back and forth on the headrest. At 36 seconds post-inhalation, BG moved her hands back down to her stomach and her breathing became less labored.

BG: When I breathed in, I didn't get any air. I thought that if it went on then it ends.

Clinician: Could you describe it in a bit more detail? What do you mean by it ends?

BG: Well, that if it went longer, then, I go away.

Clinician: Death?

BG: Yes.

Clinician: Have you ever had such a feeling in your life before?

BG: Totally new.

Clinician: What best describes what you experienced?

BG: Panic... the feeling of suffocation.