INSIGHTS

PERSPECTIVES

NEUROSCIENCE

Resilience to trauma: Just a matter of control?

Deficits in memory control may facilitate posttraumatic stress disorder

By **Karen D. Ersche**

On 13 November 2015, a group of Islamic jihadists launched a series of coordinated terror attacks across the city of Paris, France. Witness statements and police reports were almost unbearable to hear, but for people directly affected by the attacks, their traumatic experiences are unforgettable. How do people cope with the memories of such terrible experiences when reminders of the event are omnipresent? Selectively blocking memories of the event is a common coping strategy, but is it a good one? Clinicians would probably be skeptical about recommending this strategy because it is counterproductive for many patients who have experienced a traumatic event. On page 756 of this issue, Mary *et al.* (*1*) report the neural differences that control the retrieval of traumatic memories in 102 individuals who were affected by the Paris terror attacks but who dealt with these memories in different ways: 55 developed posttraumatic stress disorder (PTSD), and 47 did not.

Mary *et al.* investigated the control of memory retrieval. They first asked all participants, including 73 healthy individuals who had never experienced a traumatic event in their lives, to learn cue-target pairs of words (cues) and pictures (targets), which were completely unrelated to the terror attack, until they recalled the targets automatically in response to the presentation of the cue. Participants were then instructed to suppress the recall for some targets but not for others while their brains were being scanned. On task completion, participants were given an implicit perceptual task in which they had to actively retrieve targets they had been suppressing. All participants were able to suppress the intrusive memories of targets, as instructed, and even improved performance during the task. In the perceptual task, PTSD participants retrieved the suppressed targets much more readily than the other two groups. This "readiness" suggests a weakness in regulatory control of memory in people with PTSD.

Although all participants recruited the same neural networks during memory suppression, functional differences emerged when the authors investigated how these brain networks cooperated with one another. Successful suppression of intrusive memories was associated with increased functional

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Only some people affected by the 2015 terroristattacks in Paris went on to develop posttraumatic stress disorder.

connectivity between prefrontal inhibitory control regions, such as the medial frontal gyrus, and subcortical memory-related brain structures, such as the hippocampus, parahippocampus, and precuneus. This pattern was most pronounced in healthy individuals who had never experienced a traumatic event and in participants who did not develop PTSD after the Paris attacks, albeit to a slightly lesser degree. In participants who developed PTSD, this pattern was almost absent. In fact, top-down inhibitory control of the medial frontal gyrus on memory-related structures during memory suppression was reversed in participants who developed PTSD, indicating bottom-up control. Mary *et al.* suggest that the lack of top-down inhibitory control over memory function may contribute to ongoing PTSD symptoms.

These findings suggest that it is not the severity of the trauma but the efficacy with which unwanted memories are controlled that plays a critical role in the development of PTSD. Weak prefrontal inhibitory control over increased subcortical activity is, however, not specific to PTSD but also appears to be a core feature of many psychiatric disorders. Indeed, inefficient top-down inhibitory control over the striatum (a group of contiguous subcortical structures) when regulating behavior is characteristic of drug addiction (*2*, *3*), attention deficit hyperactivity disorder (*4*), and obsessive-compulsive disorder (OCD) (*5*). Increased activation of the amygdala (a cluster of subcortical nuclei) has been linked with inadequate regulation by the ventromedial prefrontal cortex in depressed patients (*6*), possibly contributing to ongoing negative thoughts. Although impairments of inhibitory control may affect different subcortical domains and may not rely on the same neural network, they may refer to a similar mechanism, which, if dysfunctional, might result in the distressing symptoms that are typically seen in psychiatric disorders.

External factors such as traumatic stress or the harmful effects of drugs when abused are likely to impair prefrontal inhibitory-control mechanisms (*7*), thereby facilitating unwanted memories reaching consciousness or drug-taking behaviors spiraling out of control. For individuals with poor inhibitory-control abilities, the consequences may be devastating because they do not seem to be able to compensate for the damage caused, rendering them particularly vulnerable to the development of a psychiatric disorder. Evidence from endophenotype studies, which examine genetic risk markers for psychiatric disorders in unaffected first-degree relatives of patients (*8*), have shown that inhibitory-control impairments typically seen in stimulant-addicted individuals are also evident in their biological siblings who are not addicted to drugs (*9*). This suggests that these impairments may have predated drug-taking and rendered individuals vulnerable to developing addiction, should they decide to take drugs.

Similar observations have also been reported in first-degree relatives of OCD patients (*5*, *10*) and chronic alcohol users (*11*, *12*). When addicted individuals and their nonaddicted siblings were asked to perform an inhibitory-control task in the scanner, which requires them to intermittently withhold an ongoing motor response, all participants improved their performance, but only the nonaddicted siblings were able to increase top-down control by overactivating the prefrontal inhibitory control network (*13*, *14*).

The study by Mary *et al.* nicely elucidates why blocking memory recall is an effective coping strategy for some people but not for everyone. It also confirms the skepticism toward directed forgetting as a treatment for PTSD because this challenges an already compromised system, thereby worsening clinical outcome. The idea of a preexisting vulnerability, characterized by inefficient prefrontal inhibitory control, is therefore particularly interesting. More work is warranted to elucidate the mechanisms underlying resilience, the psychological concept for a person's ability to "bounce back" from adversity. This would provide a scientific rationale for developing more efficient interventions to equip vulnerable individuals with the right strategies to cope. One of the most promising aspects of the study by Mary *et al.* is the observation that inhibition performance improved in all participants during the course of the task, raising the possibility of whether resilience can be enhanced by training. ■

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MATERIALS SCIENCE

Rectifying ionic current with ionoelastomers

A solvent-free polyanion-polycation heterojunction creates ionic diodes and transistors

By **Dace Gao** *and* **Pooi See Lee**

The formation of junctions between p- and n-type semiconductors is the elementary building block of solid-state electronics. The unidirectional transportation of electrons across the junction interface, known as rectification, is the functional basis of electronic diodes, transistors, and integrated logic circuits. By contrast, biological systems use ions as signal carriers for sensing, signal transduction, and information processing. For example, ion-selective proteins embedded in the neuronal membrane transport sodium and potassium ions asymmetrically to propagate nerve impulses (*1*). Although the pursuit of dimensional shrinkage in modern electronics is reaching its physical limitation, the development of an ionic analogy to p-n junctions is expected to bring about unconventional circuits that simulate the nervous system (*2*) and has the potential to deliver intrinsically deformable processing units. On page 773 of this issue, Kim *et al.* (*3*) report the fabrication of ionic diodes and transistors using solvent-free ionoelastomers, thereby establishing a basis for stretchable ionotronic devices.

Rectification of ionic current commenced with the work of Lovrecek *et al.* (*4*), who used an ion-exchange bipolar membrane separating polyacid and polybase aqueous solutions. Charged nanochannels (*5*) and nanofluidics (*6*) have been developed to regulate, transport, and separate ion species in electrolyte solutions with better selectivity and higher efficiency. However, the fluid nature of liquid electrolytes makes them prone to leakage and imposes challenges in device assembly and encapsulation for practical applications.

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