

pairs had distinct handedness by observing how the spectra changed with the strength of the tunneling current. Theoretical analysis showed that a chiral superconductor should have a zero-bias Andreev peak that is unaffected by the strength of the tunneling current. However, the peak split into two satellites as the tunneling current increased, implying that the Cooper pairs had no distinct handedness.

The study of Gu *et al.* helps settle a long debate about the symmetry of the superconducting state in uranium ditelluride and contributes to theoretical modeling of superconductivity in this material. However, many questions remain unanswered. The properties of the nonsuperconducting state of uranium ditelluride are still poorly understood. Likewise, several measured quantities, such as specific heat and magnetic response, in a superconducting state depend on how the crystals were grown. In particular, the question of whether Cooper pairs are chiral has received contradictory answers from probing the change in polarization of light reflected off a uranium ditelluride crystal (9, 10). Other reports have shown unusual vortices on the surface of uranium ditelluride under an applied magnetic field (11, 12) that suggest a nonchiral nature of the Cooper pairs, corroborating the conclusions of Gu *et al.* Further, a sharp zero-energy tunneling peak in the cores of these vortices may also imply a topological nature of superconductivity in uranium ditelluride (12).

What makes understanding uranium ditelluride more challenging is the pronounced variation in its superconducting properties under a strong applied magnetic field and pressure. This has led to a conjecture that there may be as many as four or five different superconducting phases in this material (13). Can some of these phases be chiral? Although this could be true under strong magnetic fields (14), further experimental and theoretical studies are needed to address this issue. The quest to understand the remaining puzzles surrounding the superconductivity of uranium ditelluride centers around two universal questions: What is the symmetry of the superconducting order parameter? And what is the “glue” that enables electrons to pair up? The study of Gu *et al.* may help answer the first question; at the same time, the nature of the pairing in uranium ditelluride remains as elusive as ever. □

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## NEUROSCIENCE

# A wave of emotion

Sustained brainwide patterns of activity enable emotions to outlast their triggers

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**E**motions shape how individuals experience the world. Some emotions appear and fade away in seconds or minutes, whereas others linger for longer. Acute fear might dissipate quickly upon escape to safety or could transform into enduring anxiety. The grief caused by bereavement may persist for even longer, affecting an individual for many months. Whether fleeting or lasting, emotions influence perceptions, behavior, and decisions well beyond the experience that set them in motion. Yet very little is known about how the brain holds onto these internal states. Explaining the biological basis of their enduring nature is crucial for building a mechanistic understanding of emotion. On page 933 of this issue, Kauvar *et al.* (1) report an evolutionarily conserved brainwide response to an emotional stimulus that serves as the early-stage neural substrate of an emotion state. Thus, they identify a fundamental process that may help explain how emotions emerge.

A flash of light in the eye, a sudden noise, or a shooting pain can produce a neural response—a signature of the stimulus that bursts and disappears in milliseconds. However, the emotions that such stimuli can evoke are sustained at longer timescales, from seconds to minutes, and sometimes through to hours or even days (2). Not much is known about what facilitates the transformation of a brief stimulus-induced burst of activity into an enduring brainwide state. Kauvar *et al.* aimed to address this gap in knowledge. They shot puffs of air into the eyes of humans and mice to induce an aversive internal state. This precisely timed stimulus caused members of both species to squint their eyes reflexively. When the puff was over, the squint subsided, but did so slowly. The timing of this late-stage eye closure correlated with the negative emotional response reported by human participants. The authors also carried out intracranial electrophysiological recordings to measure brain activity during the task. The human participants underwent recordings as part of epilepsy treatment, so target brain regions were selected on the basis of clinical need but spanned the forebrain, with dense representation of areas such as the insular, premotor cortices and the hippocampus. In mice, recordings were collected from thousands of individual neurons across the whole brain.

The puffs of air caused a sudden burst of neural activity in humans and mice. These initial sharp responses were detected almost everywhere in the brain; however, they decayed within hundreds of milliseconds in areas that are involved early in the hierarchy of sensory processing, such as in parts of the midbrain and thalamus. Notably, Kauvar *et al.* also witnessed a slower wave of neuronal activity: Coordinated clusters of sustained activity echoed through the forebrain limbic and sensorimotor cortical areas over the following seconds. This slower wave of activity followed the dynamics of the nonreflexive eye closure, suggesting that it could be involved in the emotional experience. To test this possibility, the authors administered ketamine, a drug that can evoke a temporary state of dissociation and can flatten emotional responses (3). In this state of reduced emotionality, both mice and humans squinted, but not beyond the end of the stimulus. The reflex was there, but as was confirmed by the reports of the human participants, the longer-lasting aversive state didn't follow. And in the brains of both species, the short sharp neural response was observed, but the longer-lasting wave was absent.

Does the slower wave of activity observed by Kauvar *et al.* account for the persistence of emotions once the stimulus is no longer pres-

ent? It may be a crucial prerequisite. At the fastest scale, neurons communicate with millisecond precision through fast neurotransmitter receptors. Such activity could be responsible for quickly broadcasting a sensory event. Ketamine, however, blocks a slow-acting neurotransmitter receptor that integrates bursts of neuronal activity that occur over tens to hundreds of milliseconds. With this receptor inactivated, many networks across the brain are incapable of persistent activity (4). The findings of Kauvar *et al.* indicate that this integration might be required for the initiation of an emotion state. Very little is known about how a global emotional context is maintained. In the mouse hypothalamus (an area of the brain involved in homeostatic control), a fear trigger causes neural activity that lasts for tens of seconds. That activity likely sustains itself by a combination of slow neurotransmission and even slower neuromodulatory input (5). The neural activity of a neighboring population of hypothalamic cells, which are involved in the expression of aggression in mice, shows stereotyped dynamics that unfold over tens of seconds to minutes. This network likely captures angry intent and its transformation into aggression (6, 7).

More broadly, signals from one brain area to another can change the behavior of a brainwide neuronal network (8). For example, interventional experiments in mice show that, when performed at the correct frequency, manipulations of neuronal activity at the circuit-level have the power to extinguish or prolong an appetitive state of social engagement (8, 9). At the brainwide level, activity across groups of brain regions, especially when constrained to particular frequencies, appears to show coherence and may become self-reinforcing at longer timescales (10). Some motivationally and emotionally charged states, such as hunger, thirst, or malaise, may persist because of their own dedicated molecular and circuit mechanisms. For example, two peptides involved in hunger and satiety (the feeling of fullness) were recently shown to dampen each other's impact, effectively preventing sudden fluctuations in the activity of the neurons responsible for the hunger state (11). This process works alongside what appears to be a dedicated molecular mechanism controlling the rate of satiation. Slow endocrine signaling and brain-body feedback loops could also play a key role, especially at the later stages of an emotional experience (12). For example, in mice, a stereotyped breathing pattern contributes to the maintenance of freezing in response to fear, perhaps reflecting a self-reinforcing physiological-behavioral loop (13).

Understanding what makes emotions last will require an integrative approach that draws on knowledge of the mechanisms that enable persistence at different timescales. The findings of Kauvar *et al.* improve the understanding of what happens in the brain in the first seconds during the formation of an emotion. Future work should investigate what information is carried on the observed wave of neural activity and its effects on how an emotion is maintained and changed. □

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## HYPOTHESIS

# Growing anxious— Are preschoolers matched to their futures?

Evolutionary and developmental factors may contribute to anxiety in young people

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Anxiety is an emotion that, in evolutionary terms, can have an adaptive role in ensuring alertness to potential danger. In animals, stresses such as population density, predators, and food availability can act, through maternal cues, on the prenatal and early postnatal development of stress responses in offspring (1). Such maternal and perinatal effects, which operate across a wide range of taxa, lead to predictive adaptive responses in offspring, promoting Darwinian fitness (2). Mechanistically, epigenetic changes in neural pathways have been implicated in explaining how environmental factors can affect gene expression and thus development (3). What if anticipated conditions do not match those that triggered a predictive adaptive response? For example, over- or inappropriate expression of anxiety later in human life can turn out to be maladaptive, reducing an individual's own or social functionality. Perhaps anxiety disorders can be understood as inappropriate socioemotional regulation in relation to actual, perceived, or anticipated challenges.

There is growing evidence that the incidence of anxiety disorders has risen considerably in recent years in adolescents (between 12 and 19 years old), particularly in developed countries (for example, the United States) (4). Although this trend is well documented in the years preceding the COVID-19 pandemic (5), there was only a small increase in the incidence of anxiety in children (younger than 12 years old) and adolescents during the pandemic by comparison (6). This suggests that contemporary stressful situations such as those operating during the pandemic do not fully explain a contemporaneous increase in anxiety in adolescents.

Environmental factors during the early years of development can have profound and lasting effects on a child's executive functions and emotional development, affecting socioemotional regulation, especially if these factors are deleterious and prolonged (7). But there are indications of more subtle effects on the development of executive functions, even in the prenatal and early postnatal periods (8). Such early life impacts could contribute to the increased prevalence of anxiety later in life, triggered by current social and environmental challenges.

Executive functions in humans depend on the development of fronto-thalamic and limbic systems in the brain, which are the critical foundations for socioemotional and attentional regulation. Much of this neural substrate develops in the first 4 years after conception, but there are also prenatal and postnatal modifications of these neural systems that occur in response to environmental cues (9). Although matu-