Reducing anxiety and stress with pupil feedback

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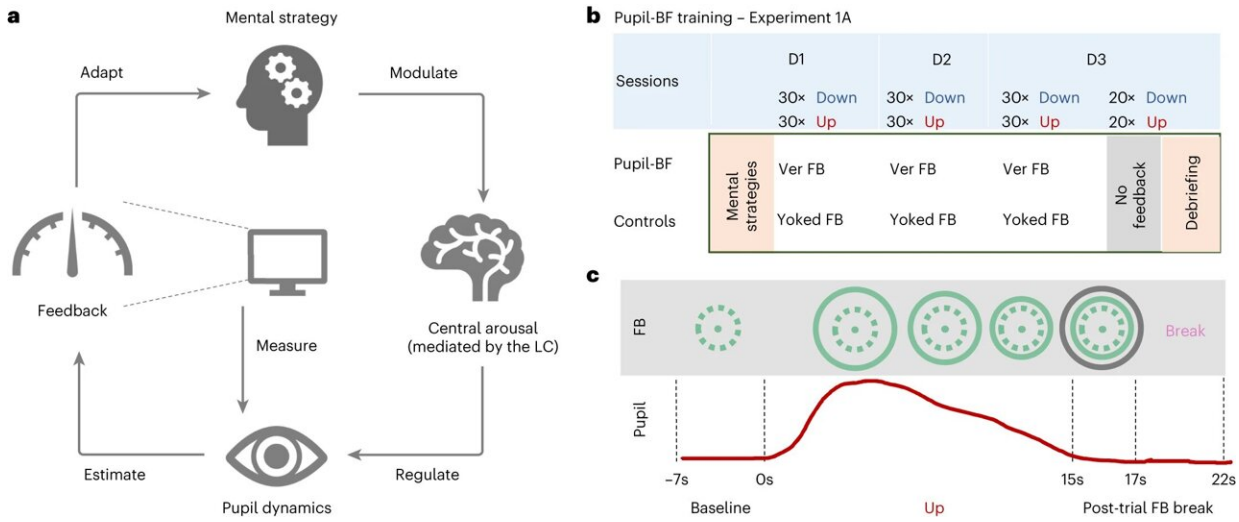

a, Participants apply mental strategies that are believed to modulate the brain's arousal levels mediated by nuclei such as the LC. Pupil size was measured by an eye tracker and fed back to the participant via an isoluminant visual display. **b**, In experiment 1A, healthy volunteers were informed about potential mental strategies of arousal regulation and then participated in 3 days (D1, D2, D3) of upregulation and downregulation trainings (30 trials each) while receiving either veridical pupil feedback (Ver FB) (pupil-BF group) or visually matched input/yoked feedback (Yoked FB) (control groups I and II). At the end of day 3, all participants performed 20 Up and 20 Down trials without receiving any feedback and were debriefed on which strategies they have used. **c**, Example trial of the experiment. Each trial consisted of (1) 7 s baseline measurements, (2) 15 s modulation phase where the pupil-BF group sees a circle that dynamically changes its diameter as a function of pupil size (veridical feedback), (3) 2 s of color-coded post-trial performance feedback (green, average circle size during

modulation; black, maximum (Up) or minimum (Down) circle size during modulation) and (4) 5 s break. The upper panel shows an example of what participants would see on their screen, while the red line in the lower panel indicates measured pupil size. Note that the control groups I and II see a circle that changes independently of pupil size but resembles that for a participant in the pupil-BF group. Credit: *Nature Human Behavior* (2023). DOI:10.1038/s41562-023-01729-z

Our pupils are a mirror of our state of arousal: they dilate when we are tense, stressed or even panicky, and constrict when we calm down. Key to this is an area of the brain measuring about 15 millimeters: a nucleus in the pons of the brainstem known as locus coeruleus. Located deep in the brain, it regulates our state of arousal via the neurotransmitter noradrenaline.

Up until now, it had been unclear whether information about pupil size can also be used to volitionally influence the arousal centers in the brain. A new study conducted at ETH Zurich now shows that this is indeed possible. "With the right biofeedback, people can better learn to control their state of arousal through mental relaxation and activation techniques," explains Nicole Wenderoth, Professor of Neural Control of Movement at ETH Zurich.

The results of the study open up new possibilities in the treatment of stress- and anxiety-related disorders.

Pupil feedback is key

To investigate the relationship between pupil size and the brain's state of arousal, the researchers first taught a group of 27 subjects to volitionally control their pupil size. Using mental relaxation and activation

techniques, such as focusing on breathing and visualizing stressful or threatening situations, the subjects were asked to alternately constrict and dilate their pupils. They sat in front of a screen with an eye tracker that recorded how well they were doing.

The researchers showed this feedback to some of the subjects in the form of a circle on the screen. A shrinking circle indicated to the subjects that their pupils were constricting: a sign of relaxation. An expanding circle, by contrast, indicated dilating pupils and rising arousal.

The researchers found that individuals who received real-time feedback about their pupil size were better able to control their state of arousal and pupil size. This pupil feedback allowed subjects to identify the relaxation and activation techniques that worked best for them. By contrast, the control group either received a false feedback signal unrelated to their own pupil size or were instructed to focus purely on the use of mental strategies.

MRI shows activity in the locus coeruleus

The researchers then repeated the experiment, except this time they recorded the subjects' brain activity using magnetic resonance imaging. "We saw that volitional changes in pupil size are actually accompanied by changes in activity in brainstem regions that regulate the brain's state of arousal," says Sarah Meissner, a postdoctoral researcher in Wenderoth's research group.

A look at the subjects' heart rates revealed that the change in pupil size also physically relaxed or roused them. The pulse of those who were able to control their pupils better due to the feedback fell or rose more at the end of the training compared to the beginning of the training and more than the pulse of those in the control group.

The ETH researchers' method translates well to commercially available VR headsets that provide real-time feedback on pupil size. "Our goal is for people to learn to control their pupils in a playful way and, in doing so, find out which relaxation or activation techniques work best for them," Wenderoth says. The researchers have already founded an ETH spin-off, Mindmetrix, to bring this technology to market.

The research is published in *Nature Human Behavior*.

More information: Meissner, S.N. et al, Self-regulating arousal via pupil-based biofeedback, *Nature Human Behavior* (2023). DOI: 10.1038/s41562-023-01729-z.
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