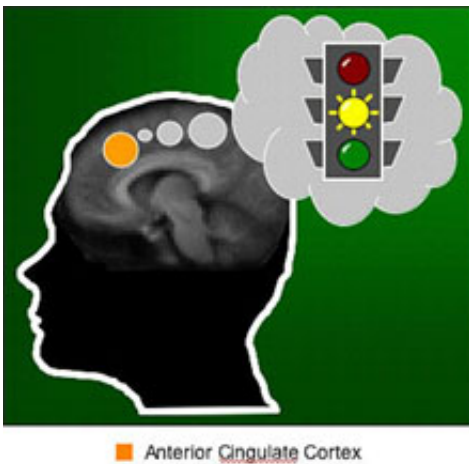


Brain region learns to anticipate risk, provides early warnings

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Following the Asian tsunami, scientists struggled to explain reports that primitive aboriginal tribesmen had somehow sensed the impending danger in time to join wild animals in a life-saving flight to higher ground.

While some scientists discount the existence of a sixth sense for danger, new research from Washington University in St. Louis has identified a brain region that clearly acts as an early warning system -- one that monitors environmental cues, weighs possible consequences and helps us adjust our behavior to avoid dangerous situations.

Image: A new theory suggests that the anterior cingulate cortex, described

by some scientists as part of the brain's "oops center," may actually function as an early warning system -- one that works at a subconscious level to help us recognize and avoid high-risk situations. Image credit: Joshua Brown, WUSTL

"Our brains are better at picking up subtle warning signs than we previously thought," said Joshua Brown, Ph.D., a research associate in psychology in Arts & Sciences and co-author of a study on these findings in the Feb. 18 issue of the journal *Science*.

The findings offer rigorous scientific evidence for a new way of conceptualizing the complex executive control processes taking place in and around the anterior cingulate cortex (ACC), a brain area located near the top of the frontal lobes and along the walls that divide the left and right hemispheres.

"In the past, we found activity in the ACC when people had to make a difficult decision among mutually exclusive options, or after they made a mistake," Brown said. "But now we find that this brain region can actually learn to recognize when you might make a mistake, even before a difficult decision has to be made. So the ACC appears to act as an early warning system -- it learns to warn us in advance when our behavior might lead to a negative outcome, so that we can be more careful and avoid making a mistake."

Implications for mental illness

The ACC has been the focus of intensive scientific research in recent years because it plays a critical role in the brain's processing of especially complex and challenging cognitive tasks. Abnormalities in the region are closely associated with a host of serious mental problems, including schizophrenia and obsessive-compulsive disorder.

By providing a clearer picture of the cognitive mechanisms by which we self monitor and control our behavior, the study is an important step in efforts to develop more effective treatments for mental illness. It also provides a new way of understanding inappropriate behaviors that often accompany mental illnesses.

"Our results suggest how impairment of the ACC mechanisms in schizophrenia can lead to breakdowns in the early warning system, so that the brain fails to pre-empt or control inappropriate behavior," Brown said. "On the other hand, in individuals with obsessive-compulsive disorder, the ACC might warn of an impending problem even when no problem is imminent."

"Interestingly, we also found evidence that the same neurotransmitter involved in drug addiction and Parkinson's disease, namely dopamine, seems to play a key role in training the ACC to recognize when to send the early warning signal," he added.

Known to be an important component of the brain's executive control system, the ACC is believed to help mediate between cold, hard, fact-based reasoning and emotional responses, such as love, fear or anticipation.

"For a long time we've been interested in how the brain figures out how to integrate cognitive information about the world with our emotions, how we feel about something," Brown said. "For many reasons, people think the ACC might be the brain structure responsible for converging these different signals. It seems to be an area that's involved in deciding what information gets prioritized in the decision-making process. It seems able to link motivational and affect information √ things like goodness or badness √ and to use this information to bring about changes in cognition, to alter how we think about things."

New paradigm for brain's "oops" center"

While there is growing consensus about the important role played by the cingulate in complex thoughts and feelings, there are competing theories regarding the cognitive mechanisms that underlie activity there.

Recent studies have documented spikes of activity in the ACC just as people realize that they've made a mistake of some kind, a sensation some describe as the "oops" moment (or, in more informal terms, as the "Oh S***" response). Theories based on these findings suggest that the primary role of the ACC is to help detect and subsequently correct mistakes or, alternatively, to detect the state of high-conflict that often accompanies mistakes"

Brown's study, co-authored with Todd Braver, Ph.D., associate professor of psychology in Arts & Sciences, offers compelling evidence that the ACC is better understood as a pre-emptive early warning system, one that is actively working to help us anticipate the potential for mistakes and thus avoid them altogether.

"We started with the premise that perhaps the cingulate was not responding to the detection of an error or state of conflict, but maybe instead what the cingulate is detecting is the likelihood of making an error," Brown said. "We wanted to see if the cingulate would become more active even in situations where no conflict is presented and no errors are made, but the potential for error is still higher than normal"

Methodolgy

To test their hypothesis, Brown and Braver developed an experiment requiring healthy young people to respond to a series of cues on a computer screen. Participants were presented with either a white or a

blue dash, which soon changed into a small arrow pointing either right or left. They were instructed to quickly push one of two buttons depending on the arrow's direction. To simulate conflict, researchers occasionally slipped in a larger second arrow that required participants to change gears and push the opposite button.

"The idea is that at some point you have these competing tendencies \surd to push the right or left button -- and both are active in brain at same time, which creates conflict," explains Brown. "Some theories suggest that whenever you see these two arrows, then that drives this state of conflict and it's the state of conflict that is being detected by the cingulate."

By increasing the delay before presentation of the larger second arrow, researchers raised the odds that an individual would reach "the point of no return" and thus be unable to change gears in time to avoid pushing the wrong button. They then adjusted the delay time over many trials so that each participant eventually exhibited error rates of about 50 percent when provided with an initial blue priming dash, compared with error rates of only 4 percent when presented with a white priming dash.

Using functional magnetic resonance imaging (fMRI), researchers captured images of brain activity at 2.5-second intervals throughout the experiment.

"We didn't tell them that the white or blue cue offered any clue about their likelihood of making an error on any particular trial, but by the end of the session, some of them had begun to figure it out, at least on a subconscious level," Brown said.

Even among those who remained relatively unaware of the blue cue's significance, researchers found that simply showing the blue color was eventually enough to spark increased activity in the cingulate, and that this effect strengthened over time as the subject became more familiar

with the task. Thus, brain imaging confirmed that the ACC had "learned" the significance of the blue cue, and had begun, at least subconsciously, to adjust behaviors accordingly, the study found.

"It appears that this area of the brain is somehow figuring out things without you necessarily having to be consciously aware of it," Brown said. "It makes sense that this mechanism exists because there are plenty of situations in our everyday lives that require the brain to monitor subtle changes in our environment and adjust our behavior, even in cases where we may not be necessarily aware of the conditions that prompted the adjustment. In some cases, the brain's ability to monitor subtle environmental changes and make adjustments may actually be even more robust if it takes place on a subconscious level."

Computer model of brain spurs new discoveries

In addition to its findings, the study is significant within scientific circles because of its use of sophisticated computer models to accurately predict the patterns of brain activation that would be sparked by the experiment, patterns only later confirmed by the imaging data from actual real-world trials.

"We started by building a detailed computer simulation of the ACC, and then we found that the computer predicted the existence of the early warning signal in ACC," Brown said. "This was an exciting result, but we still needed to test the prediction in humans to demonstrate that the model prediction was correct."

The researchers also tested their theory using another computer model that had been previously developed to support an existing theory of the ACC as a system focused on conflict resolution.

"By simulating both models we could then adjudicate between them and

do so in a way where we forced each one to make predictions that we only tested after the fact," Brown said. "By integrating the theory, the computational simulation and then the fMRI testing, we are providing other scientists with some very rigorous evidence that our new theory is accurate."

During the last two decades, as computers have become much more powerful, computer modeling has become an increasingly powerful tool for understanding the brain, said Brown, noting that findings from this study offer a nice example of how computer models of the brain can lead to new discoveries.

"In fact, our computer model also makes some other exciting predictions about how the ACC works, but we haven't had an opportunity to test them yet," Brown said. "We've got our work cut out for us."

Source: Washington University in St. Louis

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