The power to...
Adapt our brains to fit today's world

Our society and environment are changing faster than ever before, making it harder for our brains to adapt. We must learn how our natural neural protections work so we can build resilience in the face of stress, aging and disease.

The challenge
Every day we face a myriad of stresses that can challenge our mental health—everything from our electronic devices bombarding us with information to global issues such as pandemics, mass shootings, war and climate change.

Our brains allow us to experience, interpret, interact with and change the world around us. And our brains manage to cope amazingly well with the many stresses and challenges we experience every day—most of the time.

But eventually, age and relentless overload exceed the brain’s ability to cope. What determines the tipping point between coping and crisis? And how can we prevent or treat mental health crises?

The Salk approach
Neuroscience research has long been a strength at Salk. The concepts of adaptation and resilience in the brain and spinal cord have long been embedded in our studies of movement, sensation, learning, memory and neurodegenerative diseases.

Salk scientists are now studying how some brains adapt well and others don’t, and what tips the balance between acute and chronic mental health issues. To do this, they:

Look at the big picture. To understand the brain—at any level—Salk scientists study not just individual cells or molecules but the brain as a dynamic, interconnected whole that interacts with the entire body, the external environment and other people.

Collaborate. Salk scientists collaborate across disciplines, coming together in “think tanks” of cell biologists, geneticists, behavioral scientists, computational biologists and other experts all tackling the same research questions from different perspectives.

Develop new technologies. New approaches and new questions require cutting-edge tools—often some that don’t even exist yet. To overcome that hurdle, Salk biologists work with engineers to customize and build new tools. Salk scientists recently invented Social LEAP Estimates Animal Poses (SLEAP), a novel computational tool that allows researchers to simultaneously track the locations of multiple body parts in multiple animals in motion, and sonogenetics, a noninvasive tool that allows researchers to control brain cells with sound waves.

With these approaches, we are better equipped to find the mechanisms that tip a healthy brain to an unhealthy one so we can nudge them back—instanting resilience and, ultimately, improving our mental health, cognitive abilities, memory and movement long into old age.

See the Salk approach at work: How social isolation affects our health

According to the World Health Organization, the three biggest influences on a person’s health are diet, exercise and social interaction.

We know a lot about the first two. Now, according to Salk researchers, it’s time to shine a light on the third. While social isolation has been linked to increased mood disorders, shortened life spans and worsened cancer and heart disease outcomes, we don’t know how.

COVID-19 quarantines highlighted the importance of social interaction. As people stayed home more often and isolated when sick, they clearly suffered in many ways. In one example of neuroscience research at Salk, scientists are now addressing a number of critical questions about the role social interaction and isolation play in our mental and physical health. Answers to these questions may ultimately pave the way for new ways to prevent or treat anxiety, depression, aggression and other mental health conditions.

What causes social isolation? Some causes of social isolation may be extrinsic—imposed upon us by a pandemic, say—but some are intrinsic, or self-imposed. For example, anxiety and autism spectrum disorders can be intrinsically isolating conditions. In contrast, children with a rare genetic condition known as Williams syndrome tend to be hyper-social—overly friendly and trusting, even with strangers.

Professor Rusty Gage and the late Professor Emerita Ursula Bellugi long studied autism spectrum disorders and Williams syndrome as two sides of the same coin. They used leading-edge stem cell technologies to re-create the conditions in the
laboratory—essentially generating “mini-brains” in a dish that preserved each patient’s unique genetic background. This approach helped them connect specific genetic variations with visible changes in brain structure. By studying neurodivergent cases such as these, Salk scientists are providing new insights into the human social brain and the genetic changes that may predispose a person to social interaction or isolation.

**How does the brain perceive—and respond to—social interaction and isolation?** Professor Kay Tye and collaborators have found that isolation impacts some of the same brain regions affected by hunger. In other words, while isolated, we may crave social interaction the way we crave food when we’re hungry.

Now Tye is using some of the world’s most advanced research tools to better understand the role social isolation plays in mental health. She is collecting a parts list and a wiring diagram to build a predictive model that details the brain circuitries that might explain, for example, why short-term isolation tends to end with pro-social behaviors, whereas long-term isolation more often results in withdrawal and anti-social behaviors.

**How might we restore pro-social behaviors after isolation?** Associate Professor Kenta Asahina studies genes and neurons that reduce anti-social behaviors, such as aggression, that often increase after social isolation. His group found that when fruit flies lose proteins that regulate gene expression in a small number of neurons, they act as though they were socially isolated even after they are allowed to interact with other flies. One possibility is that these proteins are necessary for restoring normal, pro-social behavioral patterns when an animal transitions from social isolation to a socially connected environment.

Flies are much simpler than humans, of course, but they are useful tools for unraveling molecular pathways involved in health and disease. Once researchers know which genes are involved in outcomes such as social isolation-related conditions, they can study those genetic counterparts in humans.

**What are the effects of social isolation, and how can we better adapt to or recover from it?** The sense of touch is a constant source of input from our environment, and it can have a large influence on how we interact with the world around us. When we’re startled by something we touch or feel, it may be a survival instinct, or it may be due to an internal state of fear or anxiety.

When rodents are socially isolated, their feelings of fear and anxiety are heightened, which can in turn change how the animals react to touch. Associate Professor Eiman Azim and his team are now identifying the parts of the brain that trigger this negative response, and they are exploring how manipulating those circuits might alleviate isolation-related stress and touch response.

**Why Salk**
For more than 60 years, the Salk Institute has pursued Jonas Salk’s vision of fearless, interdisciplinary science tackling some of the biggest challenges facing humankind.