App, Google Glass help kids with autism read facial expressions, investigators say

By Erin Digitale

Children with autism were able to improve their social skills by using a smartphone app paired with Google Glass to help them understand the emotions conveyed in people’s facial expressions, according to a pilot study by researchers at the School of Medicine.

Prior to participating in the study, Alex, 9, found it overwhelming to look people in the eye. Gentle encouragement from his mother, Donji Cullenbline, hadn’t helped. “I would smile and say things like, ‘You looked at me three times today!’ But it didn’t really move the bar,” she said. Using Google Glass transformed how Alex felt about looking at faces, Cullenbline said. “It was a game environment in which he wanted to win — he wanted to guess right.”

The therapy, described in findings published online Aug. 2 in npj Digital Medicine, uses a Stanford-designed app that provides real-time cues about other people’s facial expressions to a child wearing Google Glass. The device, which was linked with a smartphone through a local wireless network, consists of a glasses-like frame equipped with a camera to record the wearer’s field of view, as well as a small screen and a speaker to give the wearer visual and audio information. As the child interacts with others, the app identifies and names their emotions through the Google Glass speaker or screen. After one to three months of regular use, parents reported that children with autism made more eye contact and related better to others.

The treatment could help fill a major gap in autism care: Right now, because of a shortage of trained therapists, children may wait as long as 18 months after an autism diagnosis to begin receiving treatment.

‘Really important unmet need’

“We have too few autism practitioners,” said the study’s senior author, Dennis Wall, PhD, associate professor of pediatrics and of biomedical data science. Early autism therapy has been shown to be particularly effective, but many children aren’t treated quickly enough to get the maximum benefit, he said. “The only way to break through the problem is to create reliable, home-based treatment systems. It’s a really important unmet need.”

Autism is a developmental disorder that affects 1 in 8-10 percent of the United States and the world, affecting families and communities at all income levels. It is characterized by social and communication deficits and repetitive behaviors.

The researchers named the new therapy “Superpower Glass” to help make it appealing to children. The therapy is based on applied behavior analysis, a well-studied intervention for autism that includes consulting with the clinician to create a treatment plan and then practicing it in the child’s own environment, using real-life situations.

Clinical depression linked to low blood levels of acetyl-L-carnitine

By Bruce Goldman

People with depression have low blood levels of a substance called acetyl-L-carnitine, according to a School of Medicine scientist and her collaborators in a multicenter study.

Naturally produced in the body, acetyl-L-carnitine is also widely available in drugstores, supermarkets and health food catalogs as a nutritional supplement, and that may help patients for whom existing treatments don’t work or have stopped working. Natalie Rasgon, MD, PhD, professor of psychiatry and behavioral sciences at Stanford, described the findings as “an exciting addition to our understanding of the mechanisms of depressive illness.”

“As a clinical psychiatrist, I have treated many people with this disorder in my practice,” she said. Depression, also called major depressive disorder or clinical depression, is the most prevalent mood disorder in the United States and the world, affecting 8-10 percent of the population.

Rasgon and her collaborators conducted the first rigorous indication that the link between acetyl-L-carnitine levels and depression may apply to people, too. And they point the way to a new class of antidepressants that could be free of side effects and faster-acting than those in use today, and that may help patients for whom existing treatments don’t work or have stopped working.

Diabetic-level glucose spikes seen in healthy people, researchers find

By Hanae Armitage

A device that keeps extra-close tabs on the ups and downs of blood glucose levels reveals that most people see only a partial picture of the sugar circulating in their blood, according to a study by researchers at the School of Medicine. It turns out that the level of sugar in an individual’s blood — especially in individuals who are considered healthy — fluctuates more than traditional means of monitoring, like the one-and-done finger-prick method, would have us believe.

Often, these fluctuations come in the form of “spikes,” or a rapid increase in the amount of sugar in the blood, after eating specific foods — most commonly, carbohydrates.

“There are lots of folks running around with their glucose levels spiking, and they don’t even know it,” said Michael Snyder, PhD, professor and chair of genetics at Stanford and senior author of the study. The covert spikes are a problem because high blood sugar levels, especially when prolonged, can contribute to cardiovascular disease risk and a person’s tendencies to develop insulin resistance, which is a common precursor to diabetes, he said.

“We saw that some folks who think they’re healthy actually are misregulating glucose — some are.”

A continuous glucose-monitoring device takes frequent readings of blood-sugar concentrations.
Deep-brain stimulation for drug-resistant epilepsy

Devices that administer deep-brain stimulation, or DBS, are now in widespread use for the treatment of various neurological disorders, including movement disorders and some psychiatric conditions. Development of DBS for epilepsy, which stimulates by a different method than the devices used for movement disorders and psychiatric conditions, has been an area of focus for researchers in recent years.

A clinical trial led by Stanford neurologist Robert Fisher, who holds the Maslah Saul, MD, Professorship, has been studying the use of DBS in the treatment of refractory epilepsy for several years. The trial, which began in 2010, showed that DBS can be used to treat seizures in patients who are refractory to medication. In 2010, the FDA approved DBS for the treatment of patients with refractory epilepsy, and Stanford is leading the world in neurostimulation. The treatment of epilepsy by DBS is an important new option, and Stanford is a leader in this field.

Osteoporosis and fracture risk predicted with genetic screen

By Krista Conger

A new genetic screen may predict a person’s future risk of osteoporosis and bone fracture. The test was developed by a researcher in the field of genetics to identify people who are at risk for osteoporosis, a disease that results in a reduction in bone density and fracture.

The test identifies people who are at risk for osteoporosis by identifying genetic markers associated with the disease. These markers are used to develop a computer algorithm to identify people who are at risk for osteoporosis.

The test was developed by a team of scientists at Stanford University. The team included Paul Costello, an expert in genetics, and Susan Ipakchian, a student of Dr. Robert Tibshirani, a leading expert in statistical genetics.

The test was validated in a study of 1,000 people who were followed for an average of 10 years. The results showed that people who were identified as having a high risk of osteoporosis were 17 times more likely to have a bone fracture than people who were identified as having a low risk.

The test is currently available to the public, and it is expected to be used by doctors to identify people who are at risk for osteoporosis.

Developing an algorithm

Kam analyzed the genetic data and health information of nearly 400,000 people in the UK Biobank — a vast compendium of de-identified information freely available to public health researchers around the world. For each participant, Kam collected data on bone-mineral density, age, height, weight, and sex, as well as participants’ genome sequence.

She then used a computer algorithm to identify naturally occurring genetic differences among people found with low bone-mineral density.

Using the algorithm, Kam was able to identify a new gene, called SLC22A21, that is associated with bone density. She also identified several other genes, such as calcium, in a person’s hip, spine, or heel. But bone-mineral density tests are usually only performed on people with a family history of osteoporosis or those who have experienced a recent fracture from a simple fall.

The most common clinical algorithm used to detect or predict osteoporosis is called FRAX, Kam said. “But the catch is that the two largest components of the FRAX algorithm are bone-mineral density and prior fracture. So it’s kind of a circular argument.”

FISHER: It’s marketed by Medtronic but is not yet approved for reimbursement by American insurance companies. It should be available at experienced epilepsy centers by early 2019. About 70 other countries have already been using DBS to treat uncontrolled seizures for several years.

5 How would you categorize Stanford’s academic and clinical strengths regarding the application of DBS for treating refractory epilepsy?

FISHER: Stanford is the world leader in neurostimulation for epilepsy, and one of the leaders for neurostimulation in a variety of other neural and psychiatric diseases. Martha Morrell in the Stanford Comprehensive Epilepsy Program led the successful trial for the FDA-approved responsive neurostimulation therapy for epilepsy, which stimulates by a different method from DBS that is applicable to some epilepsy patients. I led the U.S. trial of the latest generation of vagus nerve stimulators for epilepsy available for prescription. Other researchers at Stanford, including Jamie Henderson, Casey Halpern and Lawrence Shure have developed important techniques for stimulation.

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2 What is deep-brain stimulation, and how can it be used to treat seizures?

FISHER: DBS entails sending electrical signals to a target in the brain. This is done by implanting electrodes in the brain and supplying power to these electrodes via wires threaded to a pulse-generating device placed under the skin of the chest. For this therapy, the wires are placed in the part of the brain that controls the movement disorder, which can influence widespread regions of brain.

I led a trial in 2010 that showed DBS in the anterior thalamus can reduce seizures in epilepsy patients for whom other therapies have failed. Compared with surgery to remove parts of the brain, which can also eliminate or reduce the frequency of recurrent, or refractory seizures, DBS is adjustable and reversible. It also spares brain tissue. However, surgery may be more effective in some cases.

3 Can you briefly discuss the clinical trial you led in which DBS was approved for the treatment of patients with refractory epilepsy?

FISHER: The trial was performed at 17 centers on 110 patients with medication-resistant focal-onset seizures that occurred, on average, about 20 times per month. Half of these patients were randomized to active stimulation and half to placebo stimulation. Patients who could not feel the stimulation so could not tell which group they were in.

In 2015, another study I led showed that the long-term results of this procedure were very favorable. Over time, numbers continued to improve, reaching a 70 percent reduction of seizures. About 15 percent of the participants receiving active stimulation became seizure-free for at least one year by 2016.

This was the first proof in a large, controlled trial that electrical brain stimulation could reduce seizures.

In 2020, we published the final results of this trial showing that DBS can reduce seizures in patients with refractory epilepsy. The device’s use for epilepsy is now commercially available.

4 Now that the FDA has approved this device for this indication, is it commercially available?

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Researchers at the School of Medicine have identified a molecule that serves as a natural protection against one of the most common intestinal pathogens.

Propionate, a byproduct of gut bacteria, protects against Salmonella infection. Most cases are caused by contaminated food, according to the U.S. Centers for Disease Control and Prevention. Each year, the pathogen causes about 1.2 million illnesses, 23,000 hospitalizations and 450 deaths nationwide.

The study is an example of Stanford Medicine’s focus on precision health. It was made possible by the use of a unique laboratory model for reprogramming that tightly synchronizes the earliest steps of the process.

The protein, NKX3-1, has previously been identified in specific bacteria in the gut that are responsible for specific characteristics like resistance to pathogens.

From mice to men

The scientists started with an observation that has been recognized in the field for years: Two inbred strains of mice harbor different levels of Salmonella in their guts after being infected with the pathogen. “The biggest challenge was to determine why this was happening,” den Boer said.

First, they determined that the differences in Salmonella growth could be attributed to differences in the microbial community in the intestines of each mouse strain. They did this by performing fecal transplants, which involved giving mice from one strain the feces from the other. The researchers found that the unique composition of gut bacteria and then replacing the microbial community with the feces of other mice, some of whom were resistant to Salmonella infection, convinced the researchers which microbes were responsible for increased resistance to Salmonella infection in mice.

Instead of the molecule prolonging the time it takes the immune response to thwart the pathogen, it inhibits the growth of bacteria called the Bacteroides, said Denise Monack, PhD, professor of microbiology and immunology and the senior author of the paper. “It has been a real mystery to understand why we see these differences among people. Our findings may shed some light on this phenomenon,” she said.

Denise Monack

Researchers at the School of Medicine have identified a new protein critical to the production of induced pluripotent stem cells, or iPS cells. The protein, NKKX3-1, has previously been shown to play a role in progenitor development and tumor suppression. It can substitute for one of the four Yamanaka factors — Oct4, Sox2, Klf4 and cMyc — the four factors first identified in 2007 by stem cell researchers Shinya Yamanaka, MD, PhD, as sufficient to reprogram somatic cells and turn them into iPS cells.

This is a crucial regulator that would not have been discovered any other way, said Helen Blau, PhD, professor of microbiology and immunology. “It appears within two hours of the initiation of reprogramming, and then it’s gone. But it’s absolutely critical. If we eliminate it, reprogramming doesn’t happen.”

Blau, the Donald E. and Delia B. Baxter Foundation Professor and director of the Baxter Foundation Laboratory for Stem Cell Biology, is the senior author of the research, which was published online July 16 in Nature Cell Biology. The study was supported by the National Institutes of Health, the Paul Allen Stanford Discovery Center on Systems Modeling of Infection and the National Science Foundation.

By Krista Conger


gut bacteria byproduct protects against Salmonella, study finds

By Kimber Price


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Patients with advanced cancer who spoke with a trained nonclinical worker about personal goals for their care were more likely to talk with doctors about their care preferences, report higher satisfaction with their care and incur lower health costs in their final month of life, School of Medicine researchers report.

Manali Patel created a curriculum to train a nonclinical health worker on conducting goals-of-care conversations.

The findings, from a pilot study of 213 patients, suggest that patients with a serious illness are more at ease with decisions about their care and more likely to mention their care preferences to health care providers when they discuss those preferences soon after their diagnosis, and on an ongoing basis, with someone outside the medical context, said Manali Patel, MD, assistant professor of medicine at Stanford and the study’s lead author.

She and her colleagues employed a lay health worker to conduct conversations with patients about their personal desires for care and to encourage them to share this information with providers. The intervention was based on prior research conducted by Patel, when she was a fellow at Stanford’s Clinical Excellence Research Center, in which patients and their proxy decision-makers meet for having these discussions with nonclinical workers. Though more research is needed, the new study is another step toward improving the quality of end-of-life cancer care while lowering the costs, she said.

“A goals-of-care conversation is not about prognosis. It’s a holistic approach to understanding the patient’s wishes and how they want to be treated and to give them this experience,” Patel said. “You don’t need higher-level training to have that conversation. You just need a very supportive ear.”

The lay health worker had participated in a training curriculum created by Patel that included an 80-hour online seminar, as well as four weeks of observational training with the hospital's palliative care team. During several telephone and in-person conversations, the worker led patients through a structured program that addressed questions, such as, “What is your understanding of your cancer?” “What is important to you?” “Have you thought about a time when you could be sicker?” “How would you want to spend your time in this situation?” Together, the worker also established care preferences, identified a surrogate decision-maker and filed an advance directive.

“We trained the worker to address these questions over multiple time periods and to revisit the conversation when unexpected events occurred, such as an emergency department visit or bad scan results,” Patel said. “How a patient feels and what they express as their desires to doctors may make a huge difference in how they may feel a week from now, if they had a really horrible side effect from the chemotherapy that they’re receiving and they’re finding themselves in the hospital for two weeks rather than spending the time with their family.”

Patients in the intervention group also rated their oncology care higher, giving it an average satisfaction score of 9.16 out of 10, compared with the average of 7.83 from the control group. They also posted higher satisfaction scores when queried about their care-related decision-making.

“This indicates that patients in the intervention were better off overall than patients who had been in the control group. It’s an intervention that can be activated to discuss really difficult situations,” Patel said. “This is consistent with what other studies have shown indicating that patients value honest and open communication regarding their prognosis.”

Use and cost of health care

The researchers also monitored health-care costs and use among patients in the two groups.

They found few significant differences over 15 months; however, for patients who died during the study, the final 30 days diverged markedly. Those who discussed goals of care with the lay health worker were six times less likely to visit the emergency department or be hospitalized than members of the control group, and twice as likely to use hospice services. Their median health care cost within 30 days of death was $1,048, compared with $23,482 for the control group.

Overall, patients who participated in conversations with the lay health worker used hospice at higher rates than the control group — a finding that tracks with other research, Patel said.

“Consistently, patients who understand that they have an incurable cancer are more likely to choose less aggressive care, and we see that same result here,” she said. “Communication and listening to patients seem to be the common theme because when providers listen to patients and they’re receiving care that’s concordant with their goals, they seem to have better outcomes, especially at the end of life.”

Other Stanford co-authors of the study are hematologist Vindoo Sundaresh, Manisha Desai, PhD, professor of medicine and of biomedical data science; Vij Periyakoil, MD, professor of medicine; James Kahn, MD, professor of medicine; Amrita Bhattacharya, MD, PhD, professor of medicine; Steven Asch, MD, professor of medicine, and Arnold Milestone, MD, professor of medicine.

Patel is a member of the Stanford Cancer Institute.

The research was funded by the California Health Care Foundation, Veterans Affairs Office of Healthcare Transformation Specialty Care and the National Institutes of Health.

This work was also supported by Stanford’s departments of Medicine and of Health Research & Policy. 

"You just need a very supportive ear.”

A video that accompanied the magazine about transgender youth received a bronze award in the news and research category. Video director Mark Hanlon produced the video, which told the story of a transgender teen and his family. “The video frames Dani’s challenges and joy as part of the broader issue of gender research and care of transgender patients for which Stanford Medicine is at the forefront,” the judges wrote. “It juxtaposes the soft image through the glass and the sharp focus on the eye was dramatic and interesting,” the judges wrote.


Stanford Medicine magazine earned one of two silver awards for periodical staff writing (the other silver award went to Stanford Magazine). Judges for CASE’s annual Circle of Excellence Awards said the magazine stories were “highly readable from a non-specialist's perspective, and we noted how well the articles spoke to a wide range of audiences from physicians to policy makers to the general public.” The magazine’s editor is Rosanne Spector.

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Cells continue from page 3

stem cells, even beginning to express Oct4 on their own. There are concerns about this process, however, because cMyc and Oct4 are oncogenes that can cause cancers when overexpressed in normal cells. It is not yet clear if there is an understanding of how reprogramming occurs might allow them to identify new ways to differentiate stem cells that are safer for clinical use.

Unfortunately, much of what goes on during the first hours of reprogramming has remained a mystery because of the unpredictability of the condition leaves parents feeling uncertain about the child is doing, and what might trigger a flare-up. The unpredictability of the condition leaves parents feeling as though asthma is controlling their lives.”

Helen Blau

The researchers also found that NKX3-1 expression was necessary to trigger the cells’ expression of their own Oct4 protein and to promote other genetic changes that facilitate reprogramming.

Delving deeper

On October 14, Blau and her colleagues, in collaboration with assistant professor of genetics and of computer science Anshul Kundaje, PhD, plan to continue their studies into the earliest steps of reprogramming to pluripotency using a multi-staged ‘omics-based’ approach.

“When the technology, Harris told the story of a 9-year-old boy the met during a clinical study: “He was having an asthma exacerbation roughly once a month. In the prior year, his flare-ups were so severe that he had to be to the emergency room twice and was hospitalized once. But by the third month of using our service, he was symptom-free, and his mother felt more knowledgeable and empowered to manage his asthma.”

A need-driven approach

Yock, an interventional cardiologist and renowned medical device innovator, founded Stanford Biodesign in 2000 as part of both the School of Medicine and the School of Engineering. The center’s focus on deeply understanding the need first, rather than starting with an idea for a new technology, has become a model for health technology training programs around the world. Recognizing this contribution, the National Academy of Engineering awarded Yock the 2018 Bernard M. Gordon Prize for Innovation in Technology Education. To date, 47 companies have been founded by the center’s trainees based on technologies they initiated during their training. Other alumni have gone on to drive innovation initiatives within larger medical-technology companies, launch innovation training programs at other universities, or pursue technology innovation within their clinical practice. Information about the center is available online at biodesign.stanford.edu. #w

About us

Cells continue from page 3

Cell’s are able to differentiate into many types of cells, such as those in the liver and skin, could express muscle-specific genes when joined with muscle fibers. At the time, the results provided the first evidence that adult cells could be reprogrammed to assume entirely different cell fates.

In the new study, Mai and his colleagues investigated short cells called fibroblasts to mouse embryonic stem cells. After fusion, factors in the developing embryo convert the human fibroblasts, indicating NKX3-1’s crucial role in the conversion of adult cells to stem cells. The researchers also found that externally added NKX3-1 can replace Oct4 to reprogram cells without any loss of efficiency.

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Delving deeper

Now Blau and her colleagues, in collaboration with assistant professor of genetics and of computer science Anshul Kundaje, PhD, plan to continue their studies into the earliest steps of reprogramming to pluripotency using a multi-staged ‘omics-based’ approach. ‘Our goal is to study all facets of the regulatory logic, or ‘grammar,’ that underlies cellular reprogramming to pluripotency,” Blau said. “Reprogramming completely changes a cell’s fate. We want to understand the mechanistic and signaling pathways that mediate such a remarkable change.”

Other Stanford co-authors are post-doctoral scholars Glenn Markov, PhD, and Adelaida Palla, PhD; former post-doctoral scholar Jennifer Brady, PhD, current post-doctoral researcher Heng Zeng, MD, PhD; and assistant professor of obstetrics and gynecology Vittorio Sebastiani, PhD. Blau is a member of Stanford’s Institute for Stem Cell and Regenerative Medicine, Bio-X, Cardiovascular Institute, Child Health Research Institute, Cancer Institute and Neurosciences Institute.

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Stem cells, even beginning to express Oct4 on their own. There are concerns about this process, however, because cMyc and Oct4 are oncogenes that can cause cancers when overexpressed in normal cells. It is not yet clear if there is an understanding of how reprogramming occurs might allow them to identify new ways to differentiate stem cells that are safer for clinical use.

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Delving deeper

Now Blau and her colleagues, in collaboration with assistant professor of genetics and of computer science Anshul Kundaje, PhD, plan to continue their studies into the earliest steps of reprogramming to pluripotency using a multi-staged ‘omics-based’ approach. ‘Our goal is to study all facets of the regulatory logic, or ‘grammar,’ that underlies cellular reprogramming to pluripotency,” Blau said. “Reprogramming completely changes a cell’s fate. We want to understand the mechanistic and signaling pathways that mediate such a remarkable change.”

Other Stanford co-authors are post-doctoral scholars Glenn Markov, PhD, and Adelaida Palla, PhD; former post-doctoral scholar Jennifer Brady, PhD, current post-doctoral researcher Heng Zeng, MD, PhD; and assistant professor of obstetrics and gynecology Vittorio Sebastiani, PhD. Blau is a member of Stanford’s Institute for Stem Cell and Regenerative Medicine, Bio-X, Cardiovascular Institute, Child Health Research Institute, Cancer Institute and Neurosciences Institute.

The research was supported by the National Institutes of Health, the California Institute for Regenerative Medicine, the Voyager Foundation, the National Science Foundation, Bio-X, the GSK Sir James Black Prize for Innovation in Technology Education.
Autism
continued from page 1

cases such as flash cards depicting faces with different emotions. Other traditional applied behavior analysis helps children with autism, it has limitations: It must be delivered one-on-one by trained therapists, flash cards can’t always capture the full range of human emotion and children struggle to transfer what they learn to their daily lives.

Eight core facial expressions
Wall’s team decided to try using applied behavior analysis principles in a way that would bring parents and everyday situations into the treatment process. They built a smartphone app that uses machine learning to recognize eight core emotions: happiness, sadness, anger, disgust, surprise, fear, neutral and contempt. The app was trained with hundreds of thousands of photos of faces showing the eight expressions, and also had a mechanism to allow people involved in the study to calibrate it to their own “neutral” faces if necessary.

Typically developing children learn to recognize emotions by engaging with people around them. For children with autism, it’s different. “They don’t pick those things up without focused treatment,” Wall said.

In the study, 14 families tested the Superpower Glass setup at home for an average of 10 weeks each. Each family had a child between the ages of 3 and 7 with a clinically confirmed autism diagnosis.

The families used the therapy for at least the first two and a half sessions per week. At the start and end of the study, parents completed questionnaires to provide detailed insights into their children’s social skills. In interviews, parents and children also gave feedback about how the technology affected their families.

The researchers designed three ways to use the face-recognition program: In “free play,” children wear Google Glass while interacting with family members and their families. The software provides the wearer with a visual or auditory cue each time it recognizes an emotion on the face of someone in the field of view. There are also two game modes. In “guess my emotion,” a parent acts out a facial expression corresponding to one of the eight core emotions, and the child tries to identify it. The game helps families and researchers track children’s identification of emotions. In “capture the smile,” children give another person clues about the emotion they want to elicit, until the person acts it out, which helps the researchers gauge the children’s understanding of different emotions.

Good reviews from families
Families told the researchers that the system was engaging, useful and fun. Kids were willing to wear the Google Glass, and the devices withstood the wear and tear of being used by children.

Twelve of the 14 families, including Alex’s, said their children made more eye contact after receiving the treatment. A few weeks into the trial, Alex began to realize that people’s faces hold clues to their feelings.

“He told me, ‘Mommy, I can read minds!’” Cullenbine said. “My heart sang, I’d like other parents to have the same experience.”

Families whose children had more severe autism were more likely to choose the game modes rather than free play, the researchers reported.

The children’s mean score on the SRS-2, a questionnaire completed by parents to evaluate a child’s social skills, decreased by 3.78 points during the study, indicating less severe symptoms of autism. None of the participants’ SRS-2 scores increased during the study, meaning nobody’s autism symptoms worsened. Six of the 14 participants had large enough declines in their scores to move down one step in the severity of their autism classification. Four from “severe” to “moderate,” one from “moderate” to “mild” and one from “mild” to “normal.”

The results should be interpreted with caution since the study did not have long-term compliance.”

The research was funded by grants from the National Institutes of Health, Stanford’s Clinical and Translational Science Award, the David and Lucile Packard Foundation, the Beckman Center for Molecular and Genetic Medicine, the Hong Kong Jockey Club, software developer Aaron Kline; Carl Feinstein, MD, professor emeritus of psychiatry and behavioral sciences; and Terry Winograd, PhD, professor emeritus of computer science.

Wall, Feinstein and Winograd are members of Stanford Bio-X and the Stanford Child Health Research Institute. Wall is also a member of the Stanford Neurosciences Institute.

Depression
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do not predict outcomes among patients with different mental disorders,” McEwen said. "What’s the appropriate dose, frequency? Duration? We need to answer many questions before proceeding with clinical testing." But he added, "We are developing that knowledge, which will require large-scale, carefully controlled clinical trials."

Rasgon is a member of the Stanford Neurosciences Institute.

Researchers at Weil Cornell Medical College, the Icahn School of Medicine at Mount Sinai, Duke University and the Karolinska Institute in Stockholm, Sweden, also contributed to the work. Stanford University shares in a multi-institutional agreement concerning intellectual property generated by this research.

The study was funded by the Hope for Depression Research Foundation, the Michael J. Fox Foundation for Parkinson’s, Autism Speaks, the Robertson Foundation and the Beckman Center for Molecular and Genetic Medicine.

Stanford’s Department of Psychiatry and Behavioral Sciences also supported the work.

As McEwen noted, “Even subjects who are clinically depressed, at least persons who are clinically depressed, can have periods of normal mood.”

He said researchers are exploring whether the levels can be restored in people who have been depressed in the past, and who are now in remission, and whether the levels can be maintained in people who are currently depressed.

McEwen said it’s not known if the levels predicted by the study are good enough to be useful. But he said it’s possible that the levels could be used to predict who is likely to respond to treatment. And it’s possible that people who have low levels of the amino acid may respond better to certain treatments.

McEwen said the study is a step toward determining whether the results are clinically meaningful. "We are at the beginning of the process," he said. "We need more research to confirm our findings and to determine how to use the findings in clinical practice."

In the future, McEwen said, researchers could study how the levels change over time and how they change in people who are treated with different medications. And they could study how the levels change in people who are treated with different types of therapy.

He said the study is also a step toward determining whether the results are clinically meaningful. "We are at the beginning of the process," he said. "We need more research to confirm our findings and to determine how to use the findings in clinical practice."

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Social reward circuit in the brain impaired in kids with autism

By Erin Digita

Children with autism have structural and functional abnormalities in the brain circuit that normally makes social interaction feel rewarding, according to a new study from the School of Medicine.

The study, which was published July 17 in Brain,做梦的，found that children with autism have a brain circuit that "is not a constant; it ebbs and flows depending on what the person has eaten" and is not a "systemic process that captures only a snapshot in time."

The problem with this method is that it reads out the blood glucose concentration at a single point in time. It's a "quick lance to the finger and a device that continuously takes a reading," said Snyder.

And the results from the first groups could not be replicated in a second, independent cohort. In the second cohort, the group studied was 8-13 years old. Children with autism had their diagnosis confirmed by standard clinical testing for the disorder, and all children had their IQ tested.

The density of nerve-fiber tracts in the mesolimbic reward pathway was lower in children with autism than in those without, there were no differences between the children with and without autism when researchers examined an emotion-related brain pathway as a control. Among the children who had autism, lower density of nerve-fiber tracts was linked to greater social impairment on a standard clinical evaluation of their social skills.

"Our findings suggest that this is a brain system that should be targeted early in clinical treatments," he added.

Social reward circuit in the brain impaired in kids with autism

Glucose continued from page 1

times at the same severity of people with diabetes — and they have no idea," Snyder said.

"The first time we have had concrete brain evidence to support this theory," said the study's lead author, Kaustubh Supekar, PhD, a research scientist at Stanford's Translational Neurosciences Incubator.

Disrupting the mesolimbic reward pathway in mice reduces their social behavior, prior research has shown, but no one knew how closely the pathway was tied to social skills in people. "This is the first time we have neurological evidence in children that this mechanism might explain their social impairments," Supekar said.

"Human social cognition is complex," said the study's senior author, Vinod Menon, PhD, professor of psychiatry and behavioral sciences. "We were surprised we could trace deficits in social skills to a very simple, almost primordial circuit."

A vicious cycle

The brain difference could launch a vicious cycle that makes it harder for children with autism to acquire complex social skills, according to the researchers.

"Social interaction is usually inherently rewarding. If it's not rewarding enough to a child with autism, that could have cascading effects on other brain systems," Menon, who is the Rachel L. and Walter F. Nichols, MD, Professor. In order to develop social-commu-

nication skills and the ability to infer others' thoughts and actions, "a child needs to understand and show repetitive behaviors and restricted interests. The Centers for Disease Control and Prevention's criteria for a developmental disorder affects 1 in 59 children.

To conduct the study, the researchers collected MRI brain scans of 40 children with autism and 44 children without autism.

They examined brain wiring in 24 children with autism and 24 children who had it, and functional connections in the brain in 16 children with autism and 20 children without the disorder as they looked at social or nonsocial images — pictures of faces or of scenery — while having their brains scanned.

"The team also conducted MRI scans of brain wiring in an additional 17 children with the disorder and 17 children without it to see if the results from the first groups could be replicated in a second, independent cohort. All of the children studied were 8-13 years old. Children with autism had their diagnosis confirmed by standard clinical testing for the disorder, and all children had their IQ tested.

The density of nerve-fiber tracts in the mesolimbic reward pathway was lower in children with autism than in those without, there were no differences between the children with and without autism when researchers examined an emotion-related brain pathway as a control. Among the children who had autism, lower density of nerve-fiber tracts was linked to greater social impairment on a standard clinical evaluation of their social skills. The results were the same in the second, independent cohort of children the team studied. Children with autism also had weaker functional connections in the mesolimbic reward pathway than did typically developing children. The degree of functional deficit was also correlated to social impairment.

Findings could aid treatment search

The research provides a useful link between prior work in animal models of autism and human data, the researchers said, and in future work, prior animal studies were replicated in two groups of research participants. Next, the researchers want to determine whether the brain circuit deficits can be detected in younger children with autism.

The discovery also provides a good starting point for future studies of autism treatments. Some existing, effective autism therapies use various rewards to help children engage in social interaction, but it is not known if those treatments strengthen the brain's social reward circuits.

"It would be exciting to conduct a clinical interven-

tion study to determine whether the structural and functional integrity of this pathway can be altered through a reward-based learning paradigm," Menon said.

The study's other Stanford authors are graduate student John Korchalak; former visiting scholar Ma-

rie Schaefer, MD, PhD; former research assistant Holly Wakeman; Shaosheng Qin, PhD, former instructor; and Aarthi Padmanabhan, PhD, academic program professional. Menon is a member of Stanford's Child Health Research Institute and Stanford Bio-X.

The research was supported by the Brain & Behav-
or Research Foundation and the National Institutes of Health, the Stanford Child Health Research Institute, the Autism Science Foundation, the Swiss National Foundation, and the Simons Foundation for Autism Research.

Stanford’s Department of Psychiatry and Behavioral Sciences also supported the work.

Social reward circuit in the brain impaired in kids with autism

Michael Snyder and his colleagues found that glucose dysregulation is more common than previously thought.

Findings could aid treatment search

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Our findings suggest that this is a brain system that should be targeted early in clinical treatments.
By Beth Duff-Brown

Malaria claims nearly a half-million lives worldwide each year, yet scientists still know little about the immunology of the disease that has plagued humanity for thousands of years.

There were 216 million cases in 2016, according to the World Health Organization. Sub-Saharan Africa carries 80 percent of the global burden of this mosquito-borne infectious disease, which devastates families, disrupts education and promotes the cycle of poverty.

It is particularly brutal to pregnant women, who are three times more likely to suffer from a severe form of the disease, leading to lower birthweight among their children and higher rates of miscarriage, premature birth and stillbirth.

“Pregnant women and their unborn children are more susceptible to the adverse consequences of malaria, so we are working to investigate new strategies and even lay the foundation for a vaccine to prevent malaria in pregnancy,” said Prasanna Jagannathan, MD, an assistant professor of medicine and this year’s recipient of the Dr. George Rosenkranz Prize for Health Care Research in Developing Countries.

The Freeman Spogli Institute for International Studies and Stanford Health Policy gives the $100,000 prize each year to a young Stanford researcher who is trying to improve health care in underserved countries. It was established in 2009 by the family of George Rosenkranz, PhD, a chemist who first synthesized cortisone in 1951, and later progesterone, the active ingredient in birth control pills.

Jagannathan, an infectious disease specialist who is also a member of Stanford’s Child Health Research Institute, said the prize will allow his lab members to ramp up their research in Uganda. His team is particularly interested in how strategies that prevent malaria might actually alter the development of natural immunity to malaria.

“With support from the Rosenkranz Prize, we hope to identify maternal immune characteristics and immunologic targets that are associated with protection of malaria in pregnancy and infancy,” Jagannathan said.

Goal: Vaccine for pregnant women

Jagannathan has been traveling to Uganda for a decade to study malaria. He’s seen firsthand the relentless, grueling impact the disease has on daily life.

“Before I went to Uganda I really didn’t understand the burden that malaria causes in communities — and it’s just incredible,” he said.

Jagannathan and his collaborators at the University of California-San Francisco and in Uganda are currently conducting a randomized controlled trial of 782 Ugandan women who are receiving intermittent preventive treatment with a fixed dose of dihydroartemisinin-piperaquine, or IPTp-DF, a medication that has dramatically reduced the risk of maternal parasitemia, anemia and placental malaria. Their preliminary data suggests that among 684 infants born to these women, maternal receipt of IPTp-DF may lead to a reduced incidence of malaria in the first year of life.

“Having the discretionary support of the Rosenkranz Prize will allow us to generate some preliminary ideas from this trial that could lead to larger studies to push this agenda further along,” Jagannathan said.

That agenda is to create a vaccine that prevents malaria in pregnant women and by extension, their infants, giving them a better start in life.

Lisa Goldman Rosas, PhD, MPH, was appointed assistant professor (research) of health research and policy and of medicine, and the associate director of the Stanford Center for Population Health Sciences, effective May 1. She is also the associate faculty director for the center’s Office of Community Engagement. Her research focuses on reducing the prevalence of obesity and related chronic diseases among low-income minority communities and on effectively engaging these communities in research to improve health.

Vittorio Sebastiani, PhD, assistant professor of obstetrics and gynecology, and Katja Weinacht, MD, PhD, assistant professor of pediatrics, were awarded $865,929 by the California Institute for Regenerative Medicine. The grant will support their research on generating human stem cells to help children born with a severe form of DiGeorge syndrome — a condition caused by the loss of a small piece of DNA on chromosome 22.

Natalie Tokor, MD, was appointed professor of medicine, effective July 1. Her research focuses on understanding the molecular pathways that cause inflammation and fibrosis in the liver, particularly those leading to nonalcoholic and alcoholic steatohepatitis.

JULIA CHANDLER, MD, a resident in general surgery, has been named the Ernest and Amelia Gallo Endowed Post-doctoral Fellow by the Stanford Child Health Research Institute. Chandler will receive $105,000 to support her study of screening and secondary prevention for post-traumatic stress in pediatric trauma patients.

GREGORY CHARVILLE, MD, PhD, was appointed assistant professor of pathology, effective July 1. He specializes in the classification and study of disorders related to the gastrointestinal and hepatoportalbiliary systems, and has a special interest in the diagnosis of rare tumors that derive from bone and soft tissues.

EDWARD DAMROSE, MD, was promoted to professor of otorhinolaryngology-head and neck surgery, effective June 1. His research focuses on laryngeal physiology and function, with a particular interest in the role of advanced imaging techniques to study vocal fold physiology. He is the chief of staff at Stanford Health Care.

ROBERT DODD, MD, PhD, was promoted to associate professor of neurosurgery and of radiology, effective May 1. He specializes in endoscopic skull base surgery, with a clinical focus on minimally invasive techniques to treat brain tumors and cerebrovascular disease. His research interests include pituitary tumors and stroke.

IRIS GIBBS, MD, professor of radiation oncology, was elected as an American Society for Radiation Oncology Fellow. The ASTRO Fellows program annually recognizes individuals who have made significant contributions to radiation oncology through research, education, patient care and service to the field.

SABINE GIRDO, MD, DDS, PhD, was promoted to professor of surgery, effective June 1. Her clinical and research interests are maxillofacial surgery and computer-assisted maxillofacial surgery. She is the chief of the oral and maxillofacial surgery service.

ESTHER JOHN, PhD, was appointed professor (research) of medicine, effective May 1. Her research focuses on the epidemiology of cancer, with an emphasis on causes and outcomes of common cancers, such as breast and prostate cancer, in racial and ethnic minority populations, and on addressing cancer-health disparities. She is the chief of the Stanford Cancer Institute’s population sciences program.

PURVESH KHATRI, PhD, was promoted to associate professor (research) of medicine, effective May 1. His research focuses on developing new bioinformatics approaches to improve clinical care related to autoimmunity, infection and inflammation.

ALEX MACARIO, MD, professor of anesthesiology and perioperative medicine, was elected to the board of directors of the American Board of Anesthesiology. He will chair the ABAn Research Committee and serve as a member of the Maintenance of Certification, In-Training Examination and Objective Structured Clinical Examination committees.

ROBBIE MAIJZNER, MD, instructor of pediatric hematology and oncology, received a $350,000 grant from the St. Baldrick’s Foundation. The three-year grant will fund his work to develop multi-specific chimeric antigen receptor T cells for pediatric high-grade gliomas (brain tumors) and use new cell-engineering methods developed at Stanford to introduce the receptors into the cells.

STEPHENVONKRONSTEDT, MD, PhD, was promoted to associate professor of pathology and of genetics, effective July 1. His research focuses on understanding the effects of genetic variation on molecular and cellular phenotypes, as well as on the molecular modeling of disease using genomics.

LISA GOLDMAN ROSAS, PhD, MPH, was appointed assistant professor (research) of health research and policy and of medicine, and the associate director of the Stanford Center for Population Health Sciences, effective May 1. She is also the associate faculty director for the center’s Office of Community Engagement. Her research focuses on reducing the prevalence of obesity and related chronic diseases among low-income minority communities and on effectively engaging these communities in research to improve health.

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