Scientists home in on origin of human, chimp facial differences

By Krista Conger

The face of a chimpanzee is decidedly different from that of a human, despite the fact that the apes are our nearest relative in the primate tree. Now researchers at the School of Medicine have begun to pinpoint how those structural differences could arise in two species with nearly identical genetic backgrounds.

The key lies in how genes involved in facial development and human facial diversity are regulated — how much, when and where the genes are expressed — rather than dissimilarities among the genes themselves. In particular, the researchers found that chimps and humans express different levels of proteins known to control facial development, including some involved in jaw and nose length and skin pigmentation.

“We are trying to understand the regulatory changes in our DNA that occurred during recent evolution and make us different from the great apes,” said Joanna Wysocka, PhD, associate professor of developmental biology and of chemical and systems biology. “In particular, we are interested in craniofacial structures, which have undergone a number of adaptations in head shape, eye placement and facial structure that allow us to house larger brains, walk upright and even use our larynx for complex speech.”

The researchers coined the term “cellular anthropology” to explain how some steps of early primate development can be mimicked in a dish, and thus used to study gene-expression changes that can shed light on our recent evolutionary past.

A study describing the research was published online Sept. 10 in Cell. Graduate student Sara Prescott is the lead author. Wysocka and senior research scientist Tomasz Swiogot, PhD, share senior authorship of the study.

Although chimps and humans have almost identical genomes, their genes make different amounts of proteins known to control facial development, including some involved in jaw and nose length.

The role of enhancer regions

For their comparison, the researchers focused on areas of DNA known as enhancer regions in human and chimpanzee genomes. These regions contain chemical tags and proteins bound to the DNA that control when, where and how nearby genes are expressed. Prescott and her colleagues wondered whether differences in the way proteins bind to these enhancer regions during development could explain morphological differences between humans and chimpanzees.

“We wanted to look at how the activity of these enhancer regions may have changed during recent evolution,” said Wysocka. “Many recent studies have shown that changes in the DNA sequences of enhancers could arise in two species with nearly identical genetic backgrounds.”

A study published in Science in 2014 found that human and chimp genomes have different numbers of copies of a particular DNA sequence. This multiplicity, or “copy number variation,” may be a significant factor in how our facial structures differ.

“Healthy people have two to five repeats of this six-nucleotide pattern,” said Aaron Gitler, PhD, associate professor of genetics. “But in some people, a mutation linked to amyotrophic lateral sclerosis interferes with the transport of proteins in and out of a cell’s nucleus. ALS, or Lou Gehrig’s disease, is the first to document an effective treatment for math anxiety in children. The study, published Sept. 9 in The Journal of Neuroscience, is the first to open a window into the molecular causes of the deadly condition. The most exciting aspect of our findings is that cognitive tutoring not only improves performance, but is also anxiety-reducing,” said the study’s senior author, Vinod Menon, PhD, professor of psychiatry and behavioral sciences. “It was surprising that we could, in fact, get remediation of math anxiety.”

Even if they are good at math, many children feel anxious about doing math problems. For some, the anxiety persists throughout life, discouraging them from pursuing advanced math and science classes as well as careers that rely on mathematical expertise. Yet almost no attention has been paid to how math anxiety is treated.

The study, known as the Math Anxiety Remediation Effectiveness Study (MARES), found that cognitive tutoring fixed abnormal responses in the brain’s fear circuits. The findings are among the first to document an effective treatment for math anxiety in children.

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Girls and boys with autism differ in behavior, brain structure

By Erin Digitale

Girls with autism display less repetitive and restricted behavior than boys do, according to a study by researchers at the School of Medicine.

The study, which was published online Sept. 3 in Molecular Autism, gives the best evidence to date that boys and girls exhibit the developmental disorder differently.

“We wanted to know which specific clinical manifestations of autism show significant gender differences, and whether patterns in the brain’s gray matter could explain behavioral differences,” said the study’s senior author, Vinod Menon, PhD, professor of psychiatry and behavioral sciences. Knowledge of the difference could help clinicians better recognize and treat autism in both sexes, he added. “Understanding this is really quite clinically.”

“We found strong evidence for gender differences in autism,” said postdoctoral scholar Kaurtahk Supetak, PhD, the study’s lead author. The researchers used two large, public databases to examine nearly 800 children with high-functioning forms of autism in the United States, he said.

Restrictive and restricted behavior is perhaps the most widely recognized of the three core features of autism. It can show up as a child’s preoccupation with a narrow, inflexible interest, repetition of routines or rituals, or hand-flapping. The other core features of autism are social and communication deficits.

More boys with high-functioning autism

Among children diagnosed with the high-functioning form of autism, boys outnumber girls by four to one currently. But what factors could underlie the differ-

ence in core features of the disorder between sexes be-
cause they have long suspected girls with autism may display symptoms differently, causing them to be un-
derdiagnosed or making it harder for them to get the most appropriate treatment.

“Autism has primarily been studied from the view-
point of boys with the disorder,” said Menon, who holds the Rachael L. and Walter F. Nichols, MD, Pro-
fessorship. “Understanding gender differences can help in identifying the behavioral skills that are most impor-
tant to remediate in girls vis-a-vis boys.”

The study examined the severity of autism symptoms in 128 girls and 614 boys registered with the National Database for Autism Research. The children ranged in age from 7 to 13, had IQ scores above 70, and had been evaluated with standard tests for autistic behavior. The boys and girls were matched for age, and had the same average IQ. Girls and boys had similar scores for so-
cial behavior and communication skills, but that girls

had less-severe repetitive and restricted behaviors. “This replication provides the strongest evidence to date for gender differences in a core phenotypic feature of au-
tism,” Menon said.

Brain-structure differences

The brain-scan analysis revealed several gender dif-
ferences in brain structure between typically develop-
ing boys and girls, consistent with the findings of earlier studies.

Children with autism, however, had a dissimilar set of gender differences in their brains—specifically, the motor cortex, supplementary motor area and a portion of the cerebellum. These regions affect motor function and planning of motor activity. The researchers noted that many repetitive behaviors, such as hand-flapping, have a motor component. The study demonstrated that patterns of gray matter in these mo-

tor regions could account for the differences in autistic behaviors.

“As you look at the brain-scan analysis, you see that Hispanic families of low socioeconomic status were more likely to communicate in the same-length language: For instance, less information can be communicated in the same-length language. “There is a big cultural impediment,” Menon said. “We need bilingual and bicultural staffing to help improve our ability to provide patient-centered care.”

Other Stanford-affiliated authors of the study include Jonathan Dunlap and Joshua Jaramillo, Raji Kop-

colo, a nurse practitioner in surgical education, and Supekar, the study’s first author.

The research was funded by the His-
panic Center of Excellence at Stanford Health Research Institute.

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

When families of patients prefer Spanish at the hospital

By Erin Digitale

Spanish-speaking families are more satisfied with and better understand their children’s surgical care when they communicate with the surgical team in their native language, according to a new study from the School of Medicine and Lucile Packard Children’s Hospital Stanford.

The study, which appears in the Sep-

ember issue of the Journal of Pediatric Surgery, examined outcomes in the His-

panic Center for Pediatric Surgery at the children’s hospital. All staff members at the center, including the receptionists, triage staff, nurse practitioners and pediatric general surgeon, interact with patients and their family members in flu-

ent Spanish. Families receive all of their medical care without the need for an interpreter.

“Even though the interpreters are great, being able to look someone in the eye and tell them how we feel and hear directly how they feel about us, makes for such a different interaction,” said the study’s senior author, Matias Bruzoni, MD, assistant professor of surgery. Bru-

zoni is the surgeon for the center, which is part of Stanford Children’s Health.

Hispanics form a large and growing part of the U.S. population, particularly in California, and 25 percent speak little or no English. Even though professional medical interpreters can help bridge the language gap, there are drawbacks to using an interpreter compared with communicating in the patient’s native language: For instance, less information can be communicated in the same-length appointment because everything that is said must be interpreted.

The study compared patient satis-

faction among three groups of families

whose children received surgical care at the hospital between November 2011 and July 2013. The two experimental groups were made up of Hispanic, exclu-

sively Spanish-speaking families, 43 of which were about the same number of English-

speaking caregivers via a medical inter-

preter, and 78 of which communicated directly in Spanish with their caregivers. The control group was 56 English-speaking

families of any race or ethnicity who spoke with their caregivers in English.

The verbal interaction between the caregivers and families included patient registration; the induction, history, physical, explanation of the patient’s di-

agnosis and management plan; surgical consent; and pre- and post-operative in-

structions for the patient and parents.

All families included in the experi-

ment answered a questionnaire to as-

dess their general satisfaction with their care, their feelings about the importance of speaking the same language as their child’s caregivers, and their feelings about the quality of information they received from hospital staff.

The study found that families prefer Spanish when they are more satisfied and feel more comfortable communicating in the same language. “We need to provide care in the language more highly than English-

speaking families do,” Menon said. “We can improve the quality of information they receive from our staff.”

Interacting in Spanish

Spanish-speaking families that dis-
cussed their children’s care in Spanish reported a higher level of satisfaction compared with families of higher ratings of the quality of information they received compared with the English-speaking group and the group that worked through an interpreter.

Spanish-speaking families rated the im-
por-tance of discussing care in their native language as more highly than English-

speaking families, the study found.

Although socioeconomic status was not studied in this research, Bruzoni said that Hispanic families of low socioeco-

nomic status may have an even greater need for caregivers to provide care in their native language. “There is a big cultural barrier,” Bruzoni said. “Because of these language barriers, it is even more important to work with them using their own language.”

He said he wants to encourage other clinics and hospitals, particularly those who serve large numbers of Hispanic patients, to create similar teams catering to Spanish speakers. “Not only is the pa-

tient population growing, the physician population is growing,” he said, adding that he sees a growing number of surgical

fellowships of Hispanic background receiving training. “We need bilingual and bicultural staff to help improve our ability to provide patient-centered care.”

Other Stanford-affiliated authors of the study include Jonathan Dunlap and Joshua Jaramillo, Raji Kopp-

olo, a nurse practitioner in surgery; and Supe-

kar, the study’s first author.

The research was funded by the His-
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Stanford’s Department of Surgery also supported the work.
Carlos Bustamante named chair of new Department of Biomedical Data Science

By Jennie Dusheck

Carlos Bustamante, PhD, professor of genetics and founding director of the Stanford Center for Computational, Evolutionary and Human Genomics, has been appointed chair of the new Department of Biomedical Data Science.

The department will build on the School of Medicine’s strengths in biostatistics, bioinformatics and mathematical genetics, among other things.

Bustamante, who was involved in planning the department, said he is enthusiastic about its new possibilities. He said he hopes the new role will "bring together our exceptional faculty with expertise in statistics, information technology to advance precision health and work to find common solutions to the challenges of analyzing biomedical data from varied sources, including omics data, electronic medical records and genomic sequencing.

Bustamante said he plans to begin populating the new department with a core of 15-20 faculty from across the medical school and add up to 10 "associate investigators," in the coming five years to build the department, large-scale biological data sets, and precision health. His goal is to marry rigorous methods development with the ombudsperson. To Stanford's credit, it was among the first to establish an ombudsperson.

Ombudsperson. He is the founder of Concilium, a San Francisco-based mediation firm with an ombudsperson. He is the founder of Concilium, a San Francisco-based mediation firm.

LafLiN: The Office of the Ombudsperson serves as a confidential resource for the entire medical school community, including faculty, staff, students and post-docs, regarding any School of Medicine-related problem or issue that arises. Typical examples are workplace conflicts arising between colleagues and/or supervisors, mistreatment, harassment and bullying, authorship and scientific misconduct disputes, re-appointment and promotion concerns, favoritism and/or discrimination (based on age, race, gender, religion, national origin, etc.), and unfairness in the application of school policy, among other things.

The ombudsperson acts informally, as a neutral and independent voice for fairness, not as an advocate, but in the interests of all sides. Some refer to this as being unbiased. How do you manage socially?

LafLiN: This is a great job, one that I'm grateful for and that I thoroughly enjoy coming to every day. Once people understand what it is that I do, they're nearly always appreciative of having someone to talk to off the record, someone who can enthrall further involvement of the ombudsperson, and sometimes not. Where it does, that involvement can take the form of mediation, facilitated conversations, dialogue, shuttle diplomacy, coaching, or some combination thereof. Importantly, the office does not become involved in formal processes, such as investigations, grievances and appeals. Never the less, I can often facilitate actions of those processes and how to engage them.

Why is it important to have an ombudsperson?

LafLiN: It's important to have an ombudsperson so that problems are addressed in a timely, effective and fair way for all parties concerned. This simply doesn't happen unless organizations such as the medical school proactively support and implement informal channels, such as the ombudsperson, specifically focused on that goal. I'm not arguing that formal investigatory, appeal and grievance processes aren't legitimate or that they don't have their place. They are and they do. However, the informal tools of the ombudsperson are more appropriate and effective when it comes to improving communication, restoring trust, building relationships and setting more responsible relationships and curing internal narrative over and over again. I call this default thinking. Trust because it's the foundation of the relationship between the ombudsperson and the individuals who come for help. It's something I never take for granted. I have to earn it with every person I work with. And that takes time, effort, honesty and compassion.

LafLiN: Default thinking is another big challenge. By Jennie Dusheck

Carlos Bustamante is pre-adapted for developing the new department, which was established in June. "I've been interested in large-scale data analysis since I was in large school," he said. He is a population geneticist whose work has encompassed analyzing genome-wide patterns of variation within and between species. He has used such genomic analysis to answer basic questions in biology, anthropology and medicine, and has long worked at the interface of genomics, computational biology and mathematical genetics. Pioneers in the field, who were training a new generation of researchers at Stanford, hosted the symposium.

Partnering with Ruijing Hospital, the Shanghai Jiao Tong University School of Medicine and the Salk Institute for Biological Studies, Stanford Medicine will host researchers, scientists, industry experts and policymakers from China and the United States.

The symposium is designed to transcend medical research and facilitate opportunities in precision health, education, training and large-scale computing and data analysis. The theme of this year's event is big data in health care and how to use large-scale computing and data analysis to improve health. The symposium also aims to foster long-term collaborations among researchers and clinicians in the United States and China.

Other keynote speakers include Xu Tianle, PhD, president of the basic medical faculty at Shanghai Jiao Tong University; Bill Brody, MD, PhD, president of the Salk Institute; and Michael Levitt, PhD, Stanford professor of structural biology and 2013 Nobel laureate in chemistry.

To learn more or to register for the conference, visit http://med.stanford.edu/sino-us.html. The registration fee is $195 for university faculty and postdoctoral scholars, students and trainees, and $295 for the general public.
New medical students ponder life-and-death questions

By Tracie White

SILENCE fell in Berg Hall when Alvaro Galdos stood amid a crowd of new medical students and their family members and recalled the decision to end life support for his youngest son, Luis, who was 8 years old.

“Eleven years ago we lost a son at a hospital in Texas due to a congenital heart defect,” Galdos said. His oldest son, Francisco, a first-year medical student at Stanford who was 11 at the time, hopes to become a pediatric cardiologist.

“He was the love of my life, we didn’t want him to suffer anymore,” Galdos said. “We knew the end of his life was coming. We made the decision to stop everything. Was this euthanization? We still wonder.”

The book describes health-care workers treating patients in a way that could arguably violate tenets of the Stanford Affirmation. “You will be reciting this later today after you receive your white coats and stethoscopes,” Prober said. “Hopefully, the affirmation will have more meaning to you. It will help you to reflect more deeply on the words as you ponder it in the future.”

Written by Pulitzer Prize-winning investigative reporter and Stanford-trained physician Sheri Fink, Five Days at Memorial is filled with ethical conundrums about what constitutes humane health care.

The new cohort of 90 students was chosen from an applicant pool of 7,200. Twenty-six were born inside the United States. Nine entered with graduate degrees — eight with master's degrees, one with a PhD — and 60 have published in peer-reviewed journals.

Donning the white coats

The discussion, inspired by the book Five Days at Memorial, a grim recounting of the horror at a New Orleans hospital following Hurricane Katrina 10 years ago, was part of a three-day orientation for new students in preparation for the start of classes Aug. 24.

Each year, new medical students receive their white coats and stethoscopes during a ceremony on the last day of orientation. Then they stand together as a group and read the Stanford Affirmation, which is a pledge written in the spirit of the Hippocratic Oath — an ancient vow to uphold certain ethical standards of caregiving.

Five days after the storm, a number of the dead were victims of homicide. The Louisiana Attorney General maintained that “at the other extreme, murder” was committed.

Can euthanasia be justified?

Prober and Minor posed the question to the audience, “Is involuntary euthanasia ever justifiable?” The general consensus was that involuntary euthanasia is impossible or at the other extreme, murder.

According to the book, it was clear that physicians administered life-ending injections of morphine or the sedative midazolam, or both, in about half of the patients. The Louisiana Attorney General maintained that a number of the dead were victims of homicide.

“It was definitely hard to know what was right or wrong,” Minor said. “They showed a lot of courage staying behind and working. Lack of communication and leadership was a big problem. If there is a villain in this book, it was the parent hospital chain for Memorial. The crew was told, ‘We can’t do anything. You have to wait for the military and the Coast Guard.’”

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New medical students ponder life-and-death questions at stethoscope ceremony

By Tracie White

As 112 new graduate students in the biosciences prepare to begin classes Sept. 21, Will Talbot, PhD, professor and chair of developmental biology, is settling into the position of senior associate dean for graduate education and postdoctoral affairs.

Talbot was appointed to the post Sept. 1, replacing Daniel Herschlag, PhD, professor of biochemistry.

“I am very excited about my new role,” Talbot said. “We are all inspired by the accomplishments of our graduate students and postdoctoral fellows, at Stanford and beyond. It is privilege to have a role in their training.”

Lloyd Minor, MD, dean of the School of Medicine, said, “Will has shown a strong commitment to graduate education and postdoctoral training. Under his leadership, I am confident that the Office of Graduate Education and Postdoctoral Affairs will enjoy a bright future and will continue guiding and empowering the next generation of leaders and innovators in academia and industry.”

The first-year students were selected from a pool of 1,985 applicants. Seventy of the students are men, and 42 are women. Twenty-four of the 112 students were born outside the United States, including Myanmar, the Ukraine and Ghana, and 31 are considered underrepresented minorities in the biosciences. Eighteen hold advanced degrees, including 11 with master’s degrees and two with doctorates in veterinary medicine.

“The arrival of our new graduate students is a wonderful way to start our academic year,” Talbot said. “This incoming class represents our most diverse cohort ever, and we are all excited about the great discoveries they will make as students and in the future.”

The Office of Graduate Education, in collaboration with Alumni Affairs, will hold the annual PhD lab coat ceremony Sept. 30 at the Li Ka Shing Center for Learning and Knowledge. At the event, each new student is introduced by his or her program chair and presented with a lab coat.

space to accommodate seating for an ongoing series of free community lectures by Stanford physicians.

“There are so many people in the community who were born in this building. They come up to me and thank me for bringing it back. The library brings people back into the building and makes it a real community resource again,” Tingwald said.

Community service

“We started in a nonclinical setting to provide evidence-based information people could trust,” Cain said. “We have access to libraries and databases not available to the general public and can customize packets to any level of expertise.”

The library staff respond to about 600 requests a month, with most inquiries revolving around cancer, aging, nutrition and chronic conditions like diabetes, arthritis and heart disease. Requests come in by phone, by email and in person, with the library’s resources available to anyone in the community — not just patients and their families, Cain said. Librarians and volunteers also work closely with several Silicon Valley companies’ wellness programs.

The lobby of the Hoover Pavilion — left, as it looked in the 1960s — is now home to the Stanford Health Library, right, a free community resource for medical and health information.
Students at Zilla Parishad High School, in the south Indian metropolis of Hyderabad, gather to watch an educational video about HIV/AIDS.

with culturally sensitive animated videos, as well as interactive versions for use on smartphones, that use the voices and faces of celebrity icons to teach the basics of HIV biology, how the virus is spread and how individuals can protect themselves.

**AIDS continued from page 1**

has the third-highest number of AIDS cases in the world, knowing about the disease is very low. Sex, the primary mode of HIV transmission, is a taboo subject, and there is no sex education in the schools, so students know precious little about a virus that has infected more than 2 million people in India, according to the United Nations Joint Programme on HIV/AIDS.

TeachAIDS, a nonprofit organization that began as a graduate student’s thesis project at Stanford, aims to fill that gap but they are in countries where talking about these things has been taboo or very, very limited. And she’s done it in this very culturally sensitive, appropriate way. It’s really quite effective.

Each version is carefully tailored to the local culture, featuring recognizable local celebrities in local dialects. The organization, supported by private philanthropy, donates the materi- als to governments, which then copy them free of charge to schools, hospitals and counseling centers. In 2012, the nonprofit was honored with the United Nations’ TR35 Award from MIT, which recogn- izes innovations that could have a dramatic impact on the world.

First launched in the hard-hit countries of sub-Saharan Africa, TeachAIDS brought its message to India in 2009, at a time when the disease was rapidly spreading there.

“I was reading reports that India was to be a hot zone for HIV,” said Sorcar, an adjunct affiliate at the School of Medicine and lecturer in the School of Education. “I was on an interview over coffee near her office in downtown Palo Alto. Millions of dol- lar passes were poured into this problem, but knowledge levels were very low…. It was disturbing how much was unknown about the virus.”

On a visit to India that year, she man- aged to secure a five-minute interview with Nirajguna, hoping he would agree to be featured in TeachAIDS videos. By sheer coincidence, Nirajguna’s wife, actress and activist Amala Akki- neni, was scheduled just before a heated public debate over the expulsion of HIV-positive students from medical schools in the fourth-most populous city, with some 7 million people.

Though the AIDS video cannot be transmitted through casual contact, un- educated parents were demanding that their children not sit side by side in class with children infected with the virus. Akkineni, herself a mother, managed to persuade the parents to back down from their demands by assuring them that the schools would introduce materials to edu- cation students about HIV.

Akkineni was at a loss; the govern- ment had banned previous HIV materi- als as pornographic, and some had been burned in public bonfires. She fretted about where to find AIDS information even without the video. So Sorcar’s visit could not have been more auspicious: “My husband came home and told me you were coming. You have to mention this to your wife, Piya Sorcar,” Akkineni said. “It was cosmic.”

Within the year, TeachAIDS had re- leased its first productions in the Indian state of Andhra Pradesh, which has a population of more than 83 million and one of the highest rates of HIV in the country. Akkineni agreed to serve as trustee for the organization.

Star power

It was not Akkineni’s first foray into the epidemic. Once a major Bollywood actress, she had starred in 54 movies by the time she was in her mid-20s, but then decided to give up full-time acting and instead moved into her social activism. As an animal lover, she founded Blue Cross of Hyderabad, the city’s first and only ani- mal shelter, in 1992. Shortly after, she was approached by Karl Sequeira, an AIDS activist, who was looking to estab- lish the city’s first AIDS hospice. It was a period in which people living with the disease were literally being wrapped up in blankets and tossed in the garbage, Ak- kineni recalled. So Sequeira, who had moved by the dire need for humane care,

It was already known as this noto- rious ex-actress who was running this hospice for animals,” Akkineni said in an interview in her office at the animal shelter. “So he thought I was a kindred soul.

In one evening, they raised 2.5 million rupees, about $45,000 in today’s currency, to start the project, among the wide-ranging HIV/AIDS and substance- abuse services provided now by Freedom From Addiction.

The state of Andhra Pradesh had a crying need for such services; it claims to have the highest prevalence of HIV in all of India. A high rate of heterosexual sex outside of marriage, low condom use and the large migrant labor force are among the factors that have contributed to the spread of the virus, according to a report by the United Nations Population Fund.

In contrast, another gene known to be in- volved in determining the shape of the beaks of closely related species was studied. The cebal sid was expressed at higher levels in humans than in chimpanzees. In mice, overexpression of this gene in the facial nerve caused the natural crest cells to change shape in a skin squi, surrounding a rouding of the skull and eyes that are more front the face. Of interest, this project, as well as these more interesting species-biased en- hancers to better understand how they im- pact morphological traits, which are emerging as becoming clear that these cellular pathways can be used in many ways to affect facial shape.

One of the authors of the study is re- search assistant Rajini Srinivasan.

The research was supported by the National In- stitutes of Health, the California Institute for Regen- erative Medicine, the W.M. Keck Foundation and the Innovation Fund. Stanford’s departments of Chemical and Systems Biology and of Developmental Biology also supported the work. **ms**

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Students at Zilla Parishad High School, in the south Indian metropolis of Hyderabad, gather to watch an educational video about HIV/AIDS.
to help alleviate this problem. “Math anxiety has been under the radar,” said the study’s lead author, research associate Karen Menon, a PhD candidate in the PhD candidate in the Department of Neuroscience. “People think it will just go away, but it doesn’t.”

Measuring math anxiety

The new research was based on the idea that the presence of exposure-based therapy for creating a bias might also apply to alleviation of math anxiety. Phobias, such as the fear of spiders, can be relieved in people by repeatedly exposing them to their fear. The researchers wondered if the same might be true for math anxiety.

The study included 46 children in third grade. Before tutoring, each child took a test that assessed their math anxiety. The children were then divided into two groups — one with high math anxiety, the other with low math anxiety — based on whether they performed above or below the median score for all of the children. They also completed standardized neuropsychological assessments and were instructed to imagine math problems that they found difficult. They were then given a task to solve two math problems that were repeatedly exposed in a social context plays a role, or whether computerized tutoring can result in the same benefits and brain circuit changes.

“The tutoring has a standard protocol, but it is also personalized,” said Menon, who holds the Rachael L. and Walter F. Nichols, MD, Professorship. “If a child is stuck at a particular concept, the tutor tries to get the child beyond the bottleneck in a non-negative, encouraging way.” Because the tutoring happens one-on-one, children do not have the opportunity to feel fearful about not performing as well as their peers, which may also help. “We need more research to understand that,” Menon added.

The researchers also want to investigate whether the anxiety-reducing effects of tutoring will persist as children move on to learn more complex problem-solving skills.

Other Stanford-affiliated authors of the paper are graduate students Neori Chai, Shizuka Yamada, Gregor Bieri and Nicholas Kramer, and undergraduate student Joseph Paul III.

The research was supported by the National Institutes of Health, the Packard Center for ALS Research at Johns Hopkins, a Target ALS Springboard Fellowship, the J.P. Foundation, the Helsmeyer Foundation, the Mathers Foundation, the University of Leuven, the European Research Council, the Fund for Scientific Research Flanders, the Belgian Science Policy Office, the Association Beige contre les Maladies Neuro-Musculaires and the ALS League Belgium.

Stanford’s Department of Genetics also supported the work.

Math anxiety

before tutoring, replicating a finding that Menon and colleagues published in 2012. After the first (MRI) scan, children participated in an intensive, eight-week tutoring program consisting of 22 lessons involving addition and subtraction problems. Tutors gave the lessons to each child individually. After tutoring, the math anxiety test and MRI scans were repeated.

All of the children performed better on the addition and subtraction problems after tutoring. The children who started the study with high levels of math anxiety had a reduction in their anxiety, while those in the low-math-anxiety group had no change in their anxiety level.

Anxiety alleviated

After tutoring, the fear circuits and amygdala were no longer activated in children with a history of math anxiety, confirming that tutoring alleviated the anxiety itself, rather than providing the children with a coping mechanism that relies on other brain circuits.

“It’s reassuring that we could actually help these children reduce anxiety by mere exposure to problems,” Supcar said.

The researchers plan to conduct future studies to figure out what aspects of the one-on-one tutoring were helpful. Menon wants to test whether the interaction between tutors and students in a social context plays a role, or whether computerized tutoring can result in the same benefits and brain circuit changes.

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By Jennie Dusheck

Thomas Stamey, expert on prostate cancer and PSA test, dies at 87

By Jennie Dusheck

Thomas A. Stamey, MD, a professor emeritus of urology at the School of Medicine and a noted leader for many years to come, and I feel privileged to have known him.”

A strongly knit department

Born in North Carolina in 1928, Stamey graduated from Vanderbilt University and went on to earn a medical degree in 1952 from Johns Hopkins University. He also did his internship and a residency. After serving as a urological consultant for the U.S. Army in the United Kingdom, he joined the faculty of Johns Hopkins in 1958. In 1961, he came west to Stanford Department of Urology and led it for more than 25 years. He was truly one of the giants in academic urology, with his biggest impact in the area of prostate cancer, said Eila Skinner, MD, chair of urology and the Thomas A. Stamey Research Professor in Urology. “His research collaborations with John McNeal formed the basis of much of what we know about prostate cancer today. He trained over 100 residents and fellows, many of whom went on to be leaders in urology in their own right. His influence on the department will go on for many years to come, and I feel privileged to have known him.”

Stamey was the founding father of the Stanford Department of Urology and led it for more than 25 years. He was truly one of the giants in academic urology, with his biggest impact in the area of prostate cancer, said Eila Skinner, MD, chair of urology and the Thomas A. Stamey Research Professor in Urology. “His research collaborations with John McNeal formed the basis of much of what we know about prostate cancer today. He trained over 100 residents and fellows, many of whom went on to be leaders in urology in their own right. His influence on the department will go on for many years to come, and I feel privileged to have known him.”

A strongly knit department

Born in North Carolina in 1928, Stamey graduated from Vanderbilt University and went on to earn a medical degree in 1952 from Johns Hopkins University. He also did his internship and a residency. After serving as a urological consultant for the U.S. Army in the United Kingdom, he joined the faculty of Johns Hopkins in 1958. In 1961, he came west to Stanford’s medical school as associate professor of surgery and chair of the Division of Urology. In 1990, he was appointed founding chair of the newly created Department of Urology and worked to develop it into one of the top programs in the nation.

Stamey’s wife, Kathryn, noted that her husband worked with the late Duncan Gowan to create the department. Gowan, MD, PhD, a professor emeritus of urology, died in 2007. “They built the department from scratch, and it became, at its high point, the most

sought-after urology residency in the country,” Kathryn Stamey said. “It was a very strong, family-oriented department. We had lots of parties, and everybody came with their children. It became a strongly knit depart-

ment and very successful.”

Stamey authored or co-authored more than 225 scientific papers, four books, 30 textbook chapters and seven monographs. Among many other awards, he received the Hugh Hamp-

ton Young Award (1972) and the Ra-


“People talk about translational medicine now, but he was doing it back then.” That research fo-

cus was the reason, she said, he was the first urologist and one of the first surgeons to be elected to the Insti-

tute of Medicine. “Tom instituted one year of a med-

ical residency to be a laboratory year, where residents worked on research,” Kathryn Stamey said.

Authoritative voice

Shortliffe has vivid memories of working with Stamey and, in particular, of his authoritative voice. She said that many of Stamey’s former residents wrote to her in response to news of his death, reporting, “I still hear his voice.”

He had a distinct North Carolina accent, which was not that common on the West Coast,” she said. “It was like hearing your father’s voice all the time, even though we were not that much younger than he was. It was a voice you could hear in your sleep.” Even today, she said, many of his former surgical residents say they hear his voice while operating in the operating room.

Many of the residents that Stamey trained went on to become departmental chairs around the country, said Kathryn Stamey. Stamey was also one of the first to show the value of the PSA test for prostate cancer, but then, ironically, he was also a vocal opponent against the test’s use to justify unnecessary prostate surgery. In the late 1980s, he pio-

neered the development of the prostate specific antigen, or PSA, blood test for prostate, which allowed physi-

cians to estimate the risk that a male patient had prostate cancer. PSA levels correspond to the size of the prostate. As men age, it’s com-

mon for the prostate to become larger, leading to higher levels of PSA in the blood. When surgeons biopsied the prostate to assess PSA levels, they frequently found cancer. How-

ever, what was not obvious at the time was that both an enlarged prostate and small prostate cancers are common among all men and usually not lethal. That is, most men with a prostate cancer will die of something else, and treating the prostate cancer can need-

lessly lead to a much-reduced quality of life. To Stamey’s credit, he recognized this, and in 2004 published a study showing that the PSA test predicted the size of the patient’s prostate, but not the severity of the cancer.

As Stamey said at the time, “Our job now is to stop removing every man’s prostate who has prostate cancer. We originally thought we were doing the right thing, but we are now figuring out how we went wrong. Some men need prostate treatment but certainly not all of them.” The 2004 paper was one the last papers he wrote. Kathryn Stamey said. But that kind of strong language was typical of Shortliffe. Stamey said, “There was never any question about where he stood.”

“He was a compassionate, kind gentleman,” his wife added. “He thought his patients were his heroes, and he loved medicine. He loved learning, he loved everything about his work. He used to say that he did work in his day, he was just a very kind and loving man.”

In addition to his work at Stanford, he loved fly-fish-

ing, music and travel, she said. In addition to his wife, Stamey is survived by his five children — Frederick Stamey, Charline Stamey, Alex Stamey, Thomas Cooper and Allison Stamey and grandchildren Suzy Quist, George Quist, Heather Magrin, Robin Magrin and Alexis Stamey. A service for Stamey was held Sept. 12 in Menlo Park. 

OF NOTE

- Leah Backhus, MD, MPH, was ap-

pointed associate professor of cardio-

thoracic surgery, effective July 1. Backhus specializes in general thoracic surgery, head and neck surgery, effective July 1. Desser served as residency program chief for the now-controversial PSA blood test for prostate cancer, died of Alzheimer’s disease Sept. 4 at his home in Portola Val-

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