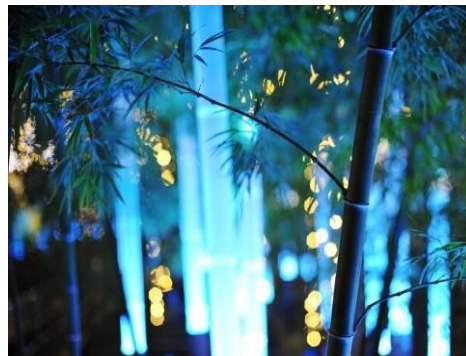


BIO NEWS

July, 2017



In-Vivo Science International Inc.

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目次

2017年6月のニュース

= 研究編 (詳細については各番号をクリックして下さい) =

1. 思春期のホルモンが学習態度/成果の変化の原因に -マウス実験
2. 褐色脂肪の役割解明 -マウス実験
3. 感覚過敏症（脆弱 X 症候群）のマウスモデルは刺激を調整できず
4. 西洋式食事は、遺伝的に素因があるマウスのアルツハイマー病を悪化させる
5. 新しい食欲調節剤 -マウス実験
6. 中枢神経の再生阻害「かさぶた」の仕組み解明 -マウス実験
7. 妊娠中のアセトアミノフェンが男児の性抑制の可能性 -マウス実験
8. フェロモンがどのようにして女性の性行為を引き起こすか -マウス実験
9. マウスのゲノム解析
10. 自閉症スペクトラム障害の遺伝について -マウス実験

2017年6月のニュース

= 企業関連ニュース他 =

- ・うつ病に關与のタンパク質特定 岡山理大グループ -マウス実験 (6/1)
- ・MannKind 社 最高販売責任者が CEO に昇進 (6/1)
- ・時価総額 74 億ドルの TESARO が売りにだされている (6/1)
- ・Eisai と Charles River Laboratories の英国拠点での創薬協力が 1 年間延長される (6/1)
- ・英国と米国のケンブリッジを拠点とする Bicycle 社が 4000 万ポンド調達 (6/2)
- ・Editas 設立 CEO・Kevin Bitterman 氏が Atlas Venture で新たなバイオテックを育てる (6/2)
- ・Lilly に 27 年間在籍の CFO が今年中で辞任 (6/3)
- ・Baxalta の CEO と R&D 長が Alexion で再びタッグを組む (6/5)
- ・がんを抑制する遺伝子の特徴発見 -慶大チーム (6/5)
- ・マリファナ使用下での運転の検出に現地での口腔液検査を導入すべき (6/6)
- ・Elan の元 CEO・Kelly Martin 氏が頓挫した Novan の暫定 CEO に就任 (6/7)
- ・飲酒はたとえ控えめな量であっても海馬萎縮を生じやすくする (6/7)
- ・中国の研究開発受託会社 WuXi Biologics が香港での IPO で 5 億 1100 万ドル調達 (6/7)
- ・国の常備薬の判断基準となる必須薬剤一揃えを WHO が発表 (6/8)
- ・AstraZeneca 片頭痛薬の権利をドイツの Grunenthal に売却 (6/8)
- ・Aimmune 社 フロリダ州の製造工場完成～ピーナツアレルギー治療製品製造予定 (6/9)
- ・Perrigo の CEO・John Hendrickson 氏が僅か 14 か月で辞任を表明 (6/9)
- ・レット症候群によく似た特徴を示す MECP2 変異サルができた (6/11)
- ・Editas 社の遺伝子編集技術の多くを築いた Feng Zhang 氏等が新会社を設立 (6/12)
- ・BMS の R&D 部門の 12 年来の古株 Douglas Manion 氏が Kleo Pharmaceuticals の CEO に就任 (6/12)
- ・日光浴びずに「日焼け」する塗り薬、10 年越しで開発 (6/14)
- ・ヘロインワクチンがアカゲザルに効いた～臨床試験の準備へ (6/14)
- ・Pfizer/Lilly の抗 NGF 抗体による慢性痛治療の開発が FDA の Fast Track 対象になった (6/14)

- ・脳のアミロイド量が多いと認知機能指標が悪化しやすい (6/15)
- ・J.P. Morgan の Stephen Berenson がバイオテック投資会社 Flagship に加わる (6/15)
- ・太り過ぎ/肥満の妊婦の子は奇形になりやすい～BMI 値上昇につれてリスクも上昇 (6/15)
- ・欧州の Medicxi が Novartis や Verily 等からバイオテックへの投資原資 3 億ドル調達 (6/15)
- ・ニューヨーク市の新規インキュベーターが開業～Neochromosome に開設記念賞 (6/16)
- ・J&J の Actelion 買収が完了 (6/19)
- ・米国マサチューセッツ州が生命科学に今後 5 年間に最大 5 億ドルを投じる (6/20)
- ・契約違反で訴えていた Luke Miels 氏の GSK 製薬事業長就任を AstraZeneca が了承 (6/20)
- ・PAREXEL を投資会社 Pamplona Capital が約 50 億ドルで買う (6/21)
- ・Akcea、IPO 調達見込みの上限を 1 億ドルから約 1 億 5,500 万ドルにかき上げ (6/21)
- ・世界最大のバイオテック代表団体 BIO の会長に Alnylam の CEO が選出された (6/21)
- ・6 歳以上小児の肥満検診が必要と米国専門家の集まり USPSTF が判断 (6/21)
- ・米国で高用量ビタミン D 補給成人が増えている (6/22)
- ・価値が大きい順に 20 位までの最終開発段階薬一覧に AbbVie から 4 つがランクイン (6/22)
- ・Merck KGaA から抗癌免疫誘導チェックポイント阻害剤開発会社がスピンアウト (6/22)
- ・卵ではなく細胞から作る Protein Sciences 社のインフルエンザワクチンがより有効 (6/22)
- ・Amgen の Epogen の Pfizer 社製バイオシミラーを FDA が承認せず (6/23)
- ・そーせいの GPCR 標的薬子会社 Heptares が英国ケンブリッジ新居に引っ越す (6/24)
- ・脳卒中の治療に光 新細胞発見 -山梨大など (6/24)
- ・GenSight Biologics、2,250 万ユーロ調達 (6/25)
- ・島津製作所、LCMS 用試薬の開発製造行うフランス Alsachim SAS 社を買収 (6/26)
- ・運動不足で認知症になるのではなく、認知症になる人が運動しなくなるらしい (6/26)
- ・イエメンが世界最悪のコレラ流行に直面～患者数が 20 万人超え (6/27)
- ・米国での大学研究は 20 年間で米国産業に最大 1.3 兆ドルの寄与 (6/27)
- ・膵臓がん、自覚症状乏しく治療困難・検査キットで早期発見へ -国立がん研究センター (6/28)
- ・Pfizer、ミズーリ州チェスターフィールドの新規 R&D 拠点の建設着工 (6/28)

- ・中国の成人の糖尿病有病率は 11% (6/28)
- ・Selexis 社の細胞株を使って融合蛋白質を開発する権利を武田薬品がライセンス (6/28)
- ・治療遺伝子を相同組換えで収めて子供の病気を治す LogicBio 社が 4,500 万ドル調達 (6/29)
- ・Merck がコンピューターネットワーク攻撃・ランサムウェアの被害に (6/29)
- ・腹膜転移の胃がん、狙い撃ち 「攻撃役」新物質合成 -量子科学技術研究開発機構 (6/29)

1. 思春期のホルモンが学習態度/成果の変化の原因に –マウス実験

2017年6月1日

カリフォルニア大学バークレー校とサンフランシスコ校の研究者らによるマウスの脳研究によって、思春期のホルモンがいかにして若者（女子）の健康と学習に影響を及ぼすか、初めて示された。

Current Biology 誌の6月1日号に掲載されたこの共同研究論文によると、思春期発症は脳の前頭皮質の「スイッチ」のようなものをオンにし学習の柔軟性を低下させる可能性がある、としている。また、思春期後のマウスは、思春期前のマウスに比べて規則の変化に適応するのがより困難であることも示されている。

この研究のために、研究者らは若い雌マウスにエストラジオールやプロゲステロンなどの思春期ホルモンを注射することで思春期を誘導し、卵巣を取り除くことで思春期をブロックした。

この研究結果が男子の脳にも当てはまるかどうかを判断するために、将来的には雄マウスの研究が必要だとしている。

英文記事：

<https://www.sciencedaily.com/releases/2017/06/170601151829.htm>

Puberty hormones trigger changes in youthful learning

Brain study of mice has broad implications for the health and education of young girls

Date:

June 1, 2017

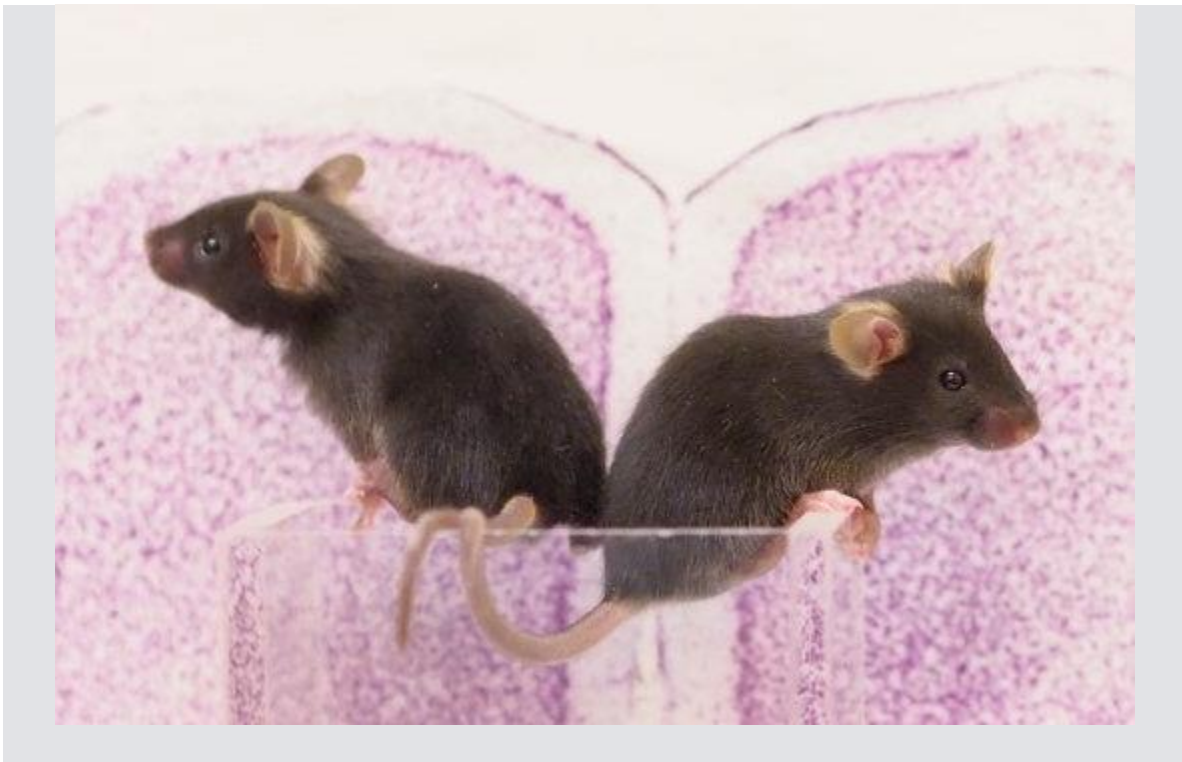
Source:

University of California - Berkeley

Summary:

A study of mice reveals, for the first time, how puberty hormones might impede some aspects of flexible youthful learning.

FULL STORY



Pre-puberty mice found to be better at exploratory learning than post-pubertal mice.

Credit: Photo by Jon Wilbrecht

A University of California, Berkeley, study of mice reveals, for the first time, how puberty hormones might impede some aspects of flexible youthful learning.

"We have found that the onset of puberty hits something like a 'switch' in the brain's frontal cortex that can reduce flexibility in some forms of learning," said study senior author Linda Wilbrecht, an associate professor of psychology and neuroscience at UC Berkeley.

While gleaned from young female mice, the findings, published in the June 1 issue of the journal *Current Biology*, may have broad educational and health implications for girls, many of whom are entering the first stage of puberty as young as age 7 and 8.

"Puberty onset is occurring earlier and earlier in girls in modern urban settings -- driven by such factors as stress and the obesity epidemic -- and has been associated with worse outcomes in terms of school and mental health," said Wilbrecht, a researcher at the campus's Center on the Developing Adolescent.

Wilbrecht and her laboratory team at UC Berkeley and UCSF discovered significant changes in neural communication in the frontal cortices of female mice after they were exposed to pubertal hormones. The changes occurred in a region of the frontal brain that is associated with learning, attention and behavioral regulation.

"To our knowledge, this study is the first to demonstrate changes in cortical neurotransmission due to hormones at puberty," said study lead author David Piekarski, a post-doctoral researcher in Wilbrecht's lab.

Overall, children have been found to have greater brain flexibility or "plasticity" than adults, enabling them to more easily master multiple languages and other elementary scholastic pursuits.

While they continue to learn after puberty, their cognitive focus in adolescence is often redirected to peer relationships and more social learning. If hormonal changes start as early as second or third grade, when children are tasked with learning basic skills, a shift in brain function could be problematic, Wilbrecht said.

"We should be more thoughtful about aligning what we know about biology and education to accommodate the fact that many girls' brains are shifting to this adolescent phase earlier than expected," she said.

For the study, researchers induced puberty in some young female mice by injecting them with pubertal hormones such as estradiol and progesterone, and blocked puberty in others by removing their ovaries.

In measuring the electrical activity of brain cells in the frontal cortices of post-pubertal mice, they observed significant changes in the synaptic activity thought to regulate brain plasticity.

They also compared the higher-order learning strategies of pre-pubertal and post-pubertal mice by testing their ability to find Cheerios hidden in bowls of wooden shavings scented with licorice, clove, thyme or lemon.

After each mouse figured out which scent was paired with the Cheerio, that pairing was changed so the mice had to use trial and error to adapt to the change and learn the new rule.

Overall, researchers found that the post-pubertal mice had a harder time adapting to the rule changes than their pre-pubertal counterparts.

"These data demonstrate that puberty itself, not just age, plays a role in frontal cortex maturation," the study concluded.

The study notes that future studies on male mice will be needed to determine if the present results apply to the male brain.

Josiah Boivin, a graduate student at UCSF, is a co-author on the study.

Story Source:

[Materials](#) provided by **University of California - Berkeley**. Original written by Yasmin Anwar. *Note: Content may be edited for style and length.*

Journal Reference:

1. David J. Piekarski, Josiah R. Boivin, Linda Wilbrecht. **Ovarian Hormones Organize the Maturation of Inhibitory Neurotransmission in the Frontal Cortex at Puberty Onset in Female Mice.** *Current Biology*, 2017 DOI: [10.1016/j.cub.2017.05.027](https://doi.org/10.1016/j.cub.2017.05.027)
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University of California - Berkeley. (2017, June 1). Puberty hormones trigger changes in youthful learning: Brain study of mice has broad implications for the health and education of young girls. *ScienceDaily*. Retrieved June 15, 2017 from

www.sciencedaily.com/releases/2017/06/170601151829.htm

University of California - Berkeley. "Puberty hormones trigger changes in youthful learning: Brain study of mice has broad implications for the health and education of young girls." *ScienceDaily*.

www.sciencedaily.com/releases/2017/06/170601151829.htm (accessed June 15, 2017).

2. 褐色脂肪の役割解明 -マウス実験

2017年6月2日

私たちの身体は、気温が下がると熱を出して体温を維持するが、この熱は、褐色脂肪組織あるいは褐色脂肪によって生成される。が、現在褐色脂肪が健康と病気の両方にどのように機能しているかは完全には理解されていない。これは適切な動物モデルがないからだとされているが、*Journal of Clinical Investigation Insight* 誌に掲載された Baylor College of Medicine を含む研究チームによる研究によると、マウスもヒトに見られる最大の貯蔵所に類似した褐色脂肪沈着を有するということが示された。

この発見は、将来肥満や2型糖尿病などの代謝疾患治療のために褐色脂肪を使用する新しい方法に繋がる可能性がある。

英文記事：

https://www.eurekalert.org/pub_releases/2017-06/bcom-mwh060217.php

PUBLIC RELEASE: 2-JUN-2017

Mice will help reveal the roles of human brown fat

BAYLOR COLLEGE OF MEDICINE

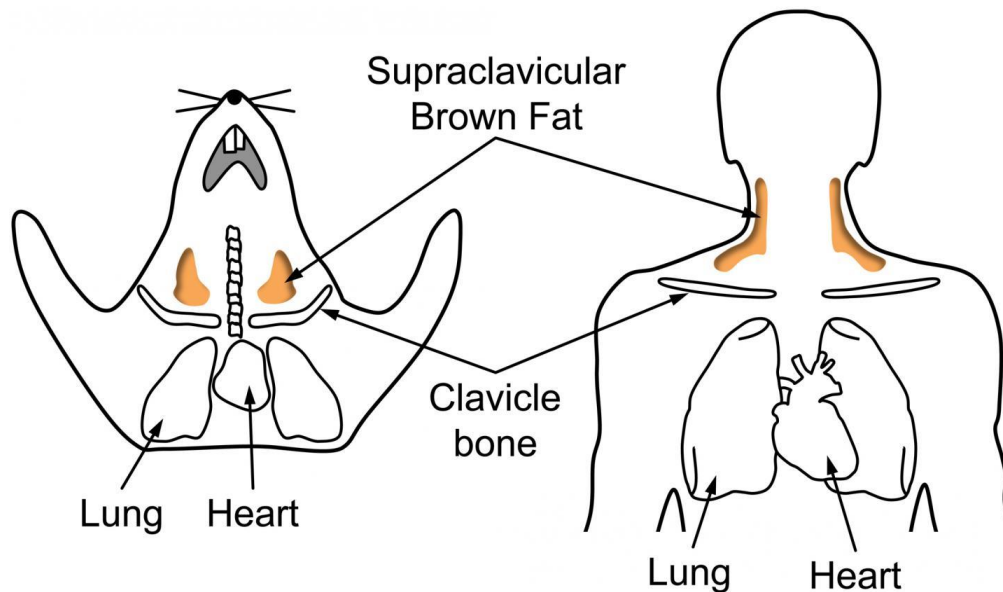


IMAGE: Adult mice have metabolically active, supraclavicular brown fat depots that share similarities with those in humans. [view more](#)

Credit: Miao-Hsueh Chen, Baylor College of Medicine

When it gets cold around you, your body turns up the heat to maintain its normal temperature. The heat is produced by brown adipose tissue, or brown fat, which also plays a role in how the body uses glucose and fat. However, scientists do not completely understand how brown fat carries out its functions both in health and disease, in part because of the lack of an appropriate animal model. In a paper published in the *Journal of Clinical Investigation Insight*, a team of researchers from several institutions, including Baylor College of Medicine, has filled this gap with the discovery that mice also have brown fat deposits similar to the largest depot found in people. The discovery opens the door to research that might lead to new ways of using brown fat to treat metabolic conditions such as obesity and type 2 diabetes in the future.

"In addition to white adipose tissue, or white fat, people have brown fat, an important contributor to the body's energy balance via the generation of body heat and the participation in metabolic processes," said senior author Dr. Miao-Hsueh Chen, assistant professor of pediatrics and nutrition at Baylor College of Medicine and the USDA/ARS Children's Nutrition Research Center at Baylor and Texas Children's Hospital.

Brown fat contains adipocytes, cells that are rich in small fat-filled droplets and in energy-producing structures called mitochondria. Brown fat adipocytes use fat and glucose as sources of energy. In mice, brown fat activated to produce heat markedly affects the energy balance. For instance, mice housed at temperatures

below their normal body temperature (20-22 degrees Celsius) would need to consume 60 percent more food to maintain their normal temperature than mice housed at 30 C. Other experiments have shown that when brown fat is dysfunctional or absent, mice decrease their energy expenditure and become obese.

A mouse model of human brown fat

Studies have indicated that most brown fat in mice is on the back, between the shoulder blades. In people, however, the main depots of brown fat are located above the collar bones and deep in the neck. Scientists think that what they learn by studying mouse brown fat might not be applicable to people because mouse and human brown fat are at different locations. In the search for a better mouse model, Chen and her colleagues analyzed mouse embryos and found brown fat surrounded by muscles in the neck, including a brown fat depot located above the collar bones, the same location of main human brown fat that had not been described before.

"Further studies showed that adult mice also have brown fat above the collar bones," Chen said. "This is important because studies will be carried out mostly in adults. In addition, mouse brown fat in the collar bone is morphologically similar to human brown fat in the same location, produces compounds involved in the production of heat and expresses genes similar to those expressed by human brown fat."

Mouse brown fat can change metabolism

In collaboration with Dr. Kristin Stanford, assistant professor of physiology and cell biology at Ohio State University Wexner Medical Center, the research team carried out brown fat transplantation experiments in mice.

"For several years, I've been interested in how to combat obesity and improve metabolic health," Stanford said. "A few years ago, my lab developed a transplantation model looking at the effects of increasing brown fat above the shoulder blade in mice, and we saw a dramatic improvement in metabolic health. When Dr. Chen showed me her data identifying brown fat above the collar bone in mice, I was excited to collaborate and apply our transplantation model."

When the researchers increased the amount of brown fat above the collar bone by transplanting more of it into healthy mice, they saw improvement on the animals' glucose tolerance. This shows that "this brown fat depot, which is remarkably similar to the main brown fat depot in humans, can be metabolically beneficial," Stanford said. "This study highlights how important this tissue most likely is in humans."

"I am most excited to bring this model to scientists in the field so they can use it to study brown fat," Chen said. "This model is the first step to improve our understanding of the role of human brown fat in metabolic processes. The model offers the possibility of carrying out studies that might result in treatments to reverse or prevent diseases such as type 2 diabetes and obesity."

###

Other contributors to this work include Qianxing Mo, Jordan Salley, Tony Roshan, Lisa A. Baer, Francis J. May, Eric J. Jaehnig, Adam C. Lehnig, Xin Guo, Qiang Tong, Alli M. Nuotio-Antar, Farnaz Shamsi Yu-Hua Tseng.

The authors are affiliated with one of more of the following institutions, Baylor College of Medicine (BCM), The Ohio State University Wexner Medical Center, Rice University and Harvard Medical School.

This study was supported by USDA/ARS CRIS 3092-5-001-059, National Institutes of Health (NIH) P30-DK079638, the American Heart Association 16GRNT30720003 and NIH K01-DK105109. RNA sequencing and data analyses were supported in part by the Genomic and RNA Profiling Core at BCM with funding from the NIH Center grant (P30-DK079638). TEM analyses were supported by the Integrated Microscopy Core at BCM with funding from the NIH (HD007495, DK56338 and CA125123).

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3. 感覚過敏症（脆弱 X 症候群）のマウスモデルは刺激を調整できず

2017 年 6 月 12 日

ヒトの自閉症の一種である、脆弱 X 症候群、を模倣するように遺伝子操作されたマウスは、通常のマウスと異なり、ほおひげに対する反復刺激に適応することができない、ということがカリフォルニア大学ロサンゼルス校（UCLA）の研究者らによって発見され、この知見は自閉症のヒトに共通の症状である感覚過敏症と密接な関係があるとして、*Journal of Neuroscience* 誌の 6 月 12 日号で報告した。

英文記事：

<https://bioengineer.org/animal-models-cant-tune-out-stimuli-mimicking-sensory-hypersensitivity-in-humans/>

June 12, 2017

Credit: Portera-Cailiau Lab/UCLA

By tickling the whiskers of mice, and recording how they respond, UCLA researchers may be closer to understanding why many children with autism cover their ears when they hear loud sounds or can't tolerate scratchy wool sweaters.

Scientists report in the June 12 issue of the *Journal of Neuroscience* that mice genetically engineered to mimic a type of autism in humans, fragile X syndrome, are unable to adapt to, or tune out, repeated stimulation to their

whiskers — unlike ordinary mice. The findings have implications for a common symptom — sensory hypersensitivity — in humans with autism.

"If we can understand more about this mechanism, or help push the brain in the direction of adaptation, we could really help children with autism," said Dr. Carlos Portera-Cailliau, professor of neurology and neurobiology at the David Geffen School of Medicine at UCLA and the paper's senior author. "Currently, their brains do not mature in a way that allows this adaptation mechanism to work properly."

Hypersensitivity to touch, sounds, taste and other sensory input is a central feature of autism, a disorder characterized by social interaction difficulties, repetitive behaviors and language impairment. Sensory hypersensitivity that leads to avoidance, or "tactile defensiveness," is important to understand because it contributes to other characteristics of autism such as anxiety, sleep disturbances and inattention.

To learn more, Portera-Cailliau and his colleagues used a genetic mouse model of fragile X syndrome, the most common genetic cause of autism and learning disabilities in humans, to determine whether mice with fragile X syndrome show the same "tactile defensiveness" seen in people with autism. The scientists studied the behavior of 14-day-old mice and adult mice running on a ball as a wire comb repeatedly touched their whiskers. The neurological development of a 14-day-old mouse roughly corresponds to the months immediately before and after birth in humans — a time when experiences shape the brain circuits involved in processing sensory input.

The researchers found that the young fragile X mice ran in response to whisker stimulation as though they were trying to escape it. By contrast, the ordinary mice ran a little and stopped, even though whisker tweaking continued, like they were able to block out the stimulus. As adults, the fragile X mice ran and changed direction to avoid the whisker stimulator, whereas typical adult mice were able to ignore it.

"Because fragile X syndrome and autism are diseases of abnormal neural development, it's really important to see what is happening at different developmental ages in the animal model," said Cynthia He, the study's first author and a Ph.D. student in Portera-Cailliau's lab.

Researchers also used a special microscope, employing a technique called two-photon calcium imaging, to observe signals from individual brain cells that are activated by stimulation like an object touching whiskers.

An analysis of these observations showed neurons firing equally in both groups of mice in the beginning, then tapering off only in the mice without fragile X. The researchers hypothesize that the fragile X group may lack chemicals that inhibit neuronal activity, a potential therapeutic target.

"You really need a solid understanding of the physiology in order to develop treatments for neurodevelopmental conditions such as autism," He said.

"This is an important step in that direction."

###

This study's other authors are Daniel Cantu, Anubhuti Goel, Shilpa Mantri and William Zeiger, all of UCLA.

The study was funded by a Paul and Daisy Soros Fellowship for New Americans and an NIH NINDS F30 Fellowship (NS093719); UCLA Neural Microcircuits training grant (T32-NS058280); a Eugene V. Cota-Robles Fellowship; the UCLA Medical Scientist Training Program (NIH NIGMS training grant GM08042; and a Developmental Disabilities Translational Research Program grant (20160969) from the John Merck Fund; a SFARI grant from the Simons Foundation (295438); and NIH NICHD grant (RO1 HD054453).

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Story Source: [Materials](#) provided by **Scienmag**

4. 西洋式食事は、遺伝的に素因があるマウスのアルツハイマー病を悪化させる

2017年6月12日

eNeuroに掲載された新しい研究によると、ヒトのアルツハイマー病（AD）に強く関連する遺伝子APOE4を有するマウスが肥満した場合に、アルツハイマー病が悪化することが示されている。この研究は、ライフスタイルを変化させることによって、この遺伝的素因を有する個体におけるAD発症の可能性を低下させることが可能であることを示唆している。

また、遺伝子APOE4を継承している個体、米国人口について言うと約12%にあたるが、この遺伝子を保有するマウスでは遅発性AD発症のリスクが高かったものの、APOE3を保有するマウスではAD関連の病理加速は観られなかった、としている。

英文記事：

<http://neurosciencenews.com/western-diet-alzheimers-6893/>

Western Diet Increases Alzheimer's Pathology in Genetically Predisposed Mice

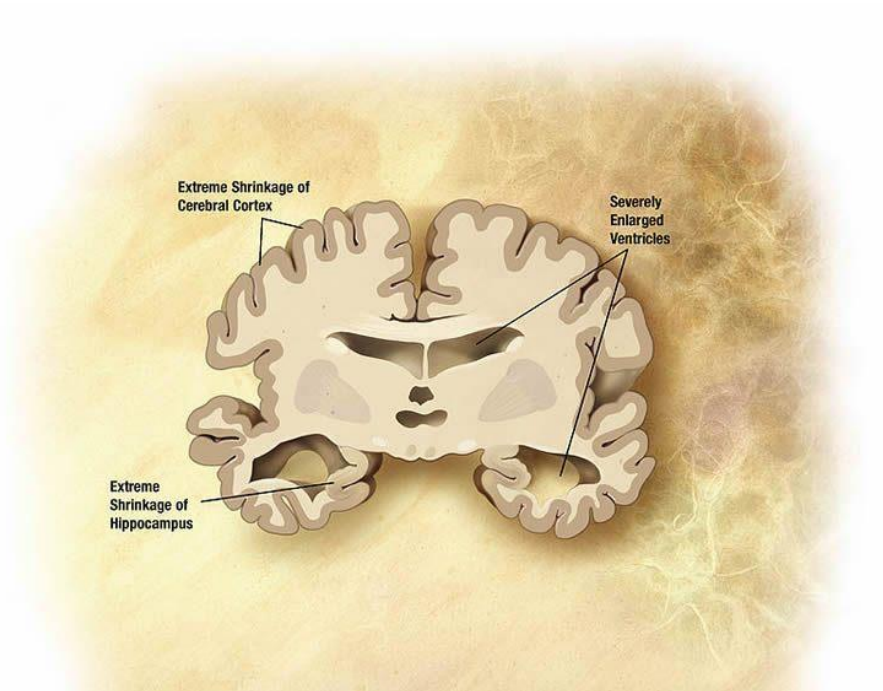
Summary: Diet and lifestyle changes could lower the risk of developing Alzheimer's disease for those who are genetically predisposed, a new study suggests.

Source: SfN.

Obese mice with a particular version of a gene strongly associated with Alzheimer's disease (AD) in humans show increased Alzheimer's pathology, according to new research published in *eNeuro*. The study suggests lifestyle changes could reduce the likelihood of developing AD in individuals with this genetic predisposition.

Individuals who inherit the gene APOE4 — approximately 12 percent of the U.S. population — have an increased risk of late-onset AD, but not all carriers develop the disease. Although the role of APOE4 in AD is not known, environmental factors that also increase risk of dementia, such as obesity, may contribute to development of AD.

Christian Pike and Alexandra Moser investigated the interaction between APOE4 and obesity in a mouse model of AD, in which some male mice carry the human version of APOE4 and others carry the more common human version APOE3. The authors found that APOE4-carrying mice fed a Western-like diet high in saturated fat and sugars for 12 weeks had increased deposits of β -amyloid protein as well as a greater number of glial cells, characteristic of AD. These changes were not observed in mice carrying APOE3, which could mean that carriers of APOE4 are more susceptible to the effects of obesity on AD.



The authors found that APOE4-carrying mice fed a Western-like diet high in saturated fat and sugars for 12 weeks had increased deposits of β -amyloid protein as well a greater number of glial cells, characteristic of AD. NeuroscienceNews.com image is for illustrative purposes only.

About this neuroscience research article

Source: [SfN](#)

Image Source: NeuroscienceNews.com image is in the public domain.

Original Research: The study will appear in *eNeuro*.

Cite This NeuroscienceNews.com Article

- [MLA](#)
- [APA](#)
- [Chicago](#)

SfN "Western Diet Increases Alzheimer's Pathology in Genetically Predisposed Mice."

NeuroscienceNews. NeuroscienceNews, 12 June 2017.

<<http://neurosciencenews.com/western-diet-alzheimers-6893/>>.

5. 新しい食欲調節剤 - マウス実験

2017年6月13日

甲状腺ホルモン受容体（TR）は身体全体に広範囲に広がり、甲状腺ホルモンの循環と相互作用して、食欲、神経系、体温、コレステロールレベル等の機能を調節している。従って、甲状腺ホルモンとその受容体を標的とする薬は、他の身体系に影響を与えないように特異的である必要がある。更に、その数も多い為個々にターゲットを絞ることが難しく、今現在これを対象とする抗肥満薬はない。

今回、Imperial College London の研究者らは、食欲を調節する脳の領域である視床下部にのみ存在する特定の TR を標的とする方法を発見し、この知見が今後新しい抗肥満薬の開発を可能にするだろう、としている。

英文記事：

<https://medicalxpress.com/news/2017-06-major-appetite-successfully-mice.html>

Major new appetite regulator successfully manipulated in mice

June 13, 2017



Credit: Martha Sexton/public domain

Researchers from Imperial College London and colleagues have found a potential way to target the receptors that specifically control appetite in mouse brains, potentially without causing other side effects.

Thyroid [hormone](#) receptors (TRs) are spread widely throughout the body and interact with circulating [thyroid](#) hormones to regulate functions such as appetite, the nervous system, body temperature, and cholesterol levels. Thus, any [drug](#) targeting thyroid hormones and their receptors needs to be specific to avoid affecting other body systems.

However, they are difficult to target individually due to their high numbers and so there are currently no anti-obesity drugs that target them.

Now, researchers from Imperial and colleagues have found a potential way to target specific TRs located only in the hypothalamus, an area of the brain that regulates appetite. The authors say the findings might lead to developing a new type anti-obesity drug in the future.

Dr James Gardiner, lead author of the research from Imperial's Department of Medicine, said: "Our hope is that these findings could ultimately lead towards drugs that target thyroid hormones as a way to reduce someone's appetite and help them control their weight. We haven't been able to target these hormones before without lots of side effects, but in this study we've been able to be very specific about which hormones we're targeting, which should greatly lessen potential side effects. We are excited to see where this might lead in the future fight against obesity."

In this [early stage](#) research, the authors divided 21 mice, who weighed roughly 20g each, into two groups. They injected mice in the first group with viruses that inactivated the brain TRs, but did not inject the second group. They then let both groups eat as much as they chose. Afterwards, the researchers examined the brains of the mice to confirm the virus had in fact inactivated the targeted receptors.

They found that the group of mice with the inactive TRs ate much more food and doubled in weight on average, doubling in size from the baseline of 20 grams to 40 grams over six weeks. The mice with active TRs maintained a stable body weight at 20 grams.

The authors say this is evidence that when targeting drugs to a specific, local, receptor in the correct [brain](#) area, they can alter appetite in these mice without causing other side effects. This could potentially be applied to humans in the future, where a drug might decrease a person's [appetite](#) by activating TRs in the hypothalamus, without causing effects in other parts of the body. Dr Gardiner said: "If our findings can be applied to humans, then we may have a new target for obesity medication."

Humans with lowered thyroid receptor activity in their brains have previously been found to be on average more obese than others. If this research continues into testing drugs on human subjects, there would be no simple test to measure levels of receptor

activity and adjust medication accordingly. Rather, treatment would be based on a system of trial and error with regard to whether the drug worked for specific individuals.

However, the authors warned that this research is at an early stage and the results should be taken with caution. Dr Gardiner added: "Due to the justifiably long and complex process of drug discovery, any potential treatment that could result from this will be far off in the future. However, the strength of our results, and the doubling in body size of these [mice](#), shows there's that the role of [thyroid hormones](#) and their [receptors](#) are definitely worth exploring further in the fight against obesity."

Explore further: [Potential obesity treatment targets the two sides of appetite: Hunger and feeling full](#)

Provided by: [Imperial College London](#)

Read more at: <https://medicalxpress.com/news/2017-06-major-appetite-successfully-mice.html#jCp>

6. 中枢神経の再生阻害「かさぶた」の仕組み解明 -マウス実験

2017年6月20日

脳や脊髄（せきずい）で、傷ついた[中枢神経](#)の再生を阻む組織ができる仕組みを、九州大のチームがマウスで解明した。この組織の形成を抑えると、マウスの脊髄で[中枢神経](#)の再生が促されることも確かめた。[脊髄損傷](#)の新しい治療法につながる可能性があるという。20日付米医学誌ネイチャーメディスン（電子版）で発表した。

脳や脊髄などを走る[中枢神経](#)は手足などの末梢（まつしょう）神経と違って、事故などでいったん損傷するとほとんど再生せず、手足のまひなどの重い後遺症が残る。損傷部の周りで、かさぶたのような組織ができて神経の再生をじゃますることが知られているが、詳しい仕組みはわかっていなかった。

チームは、わざと脊髄を傷つけたマウスの[中枢神経](#)を分析し、特定の型の[コラーゲン](#)が数十倍増えていることを発見。その[コラーゲン](#)と、アストロサイトという細胞が反応して「かさぶた」ができることを突き止めた。細胞表面にくっつく抗体を注射して反応させないようにすると、「かさぶた」の形成が抑えられ、神経が再生し、マウスが足をひきずらなくなった。

[脊髄損傷](#)の根本的な治療法はまだない。九大の岡田誠司准教授（[整形外科](#)）は「損傷しても『かさぶた』ができないようにする治療が、ヒトでも可能になるかもしれない」と話す。

[脊髄損傷](#)の治療をめぐるには、[神経幹細胞](#)などを移植して再生させる臨床研究が始まっているが、受傷後時間が経つと「かさぶた」が厚くなり、効果があがらない問題があるという。岡田さんは「かさぶたの形成を抑えられれば、幹細胞移植の効果がより高められるのではないかと話す。

（小林舞子）

朝日新聞
DIGITAL

<http://www.asahi.com/articles/ASK6J648MK6JTIP037.html?ref=rss>

[目次に戻る](#)

7. 妊娠中のアセトアミノフェンが男児の性抑制の可能性 -マウス実験

2017年6月22日

パラセタモール（アセトアミノフェン）は痛みを和らげるとして人気があるが、コペンハーゲン大学健康科学部の研究者らによる新しい研究によると、妊娠中のパラセタモールはその母から産まれた雄マウスの「男性行動」の発達を抑制する可能性があるとしている。

以前のマウス実験での研究では、パラセタモールが男性胎児における男性ホルモンのテストステロンの発達を阻害し、睾丸の奇形リスクを高める可能性があることを示していたが、今回は胎児期のテストステロンレベルの低下は、成人男性の行動にも重要であることを示した。

実験はマウスに限定されているため、結果を直接ヒトに当てはめることはできないが、ヒトに対して同じ実験を試みるのは不適切である、ともしている。

英文記事：

<https://www.sciencedaily.com/releases/2017/06/170622082522.htm>

Acetaminophen during pregnancy can inhibit masculinity

Date:

June 22, 2017

Source:

University of Copenhagen The Faculty of Health and Medical Sciences

Summary:

Paracetamol during pregnancy can inhibit the development of 'male behavior' in mice. New research shows that it can reduce sex drive and aggressive behavior.

FULL STORY

Paracetamol (acetaminophen) is popular for relieving pain. But if you are pregnant, you should think twice before popping these pills according to the researchers in a new study. In an animal model, Paracetamol, which is the pain-relieving substance found in the pills, actually damages the development of male behaviours.

Previous studies have shown the paracetamol can inhibit the development of the male sex hormone testosterone in male foetuses, thus increasing the risk of malformation of the testicles in infants. But a reduced level of testosterone at the fetal stage is also significant for the behaviours of adult males, says Ph.D. David Møbjerg Kristensen, a researcher employed during the studies at the Department of Biomedical Sciences and the Novo Nordisk Foundation Center for Protein Research at the Faculty of Health and Medical Sciences.

"We have demonstrated that a reduced level of testosterone means that male characteristics do not develop as they should. This also affects sex drive. In a trial, mice exposed to paracetamol at the fetal stage were simply unable to copulate in the same way as our control animals. Male programming had not been properly established during their fetal development and this could be seen long afterwards in their adult life. It is very worrying," says David Møbjerg Kristensen.

The dosage administered to the mice was very close to the recommended dosage for pregnant women. Because the trials are restricted to mice, the results cannot be transferred directly to humans. However, the researchers' certainty about the harmful effects of paracetamol means it would be improper to undertake the same trials on humans, explains David Møbjerg Kristensen.

Markedly reduced male behaviour

Testosterone is the primary male sex hormone that helps develop the male body and male programming of the brain. The masculine behaviours in mice observed by the researchers involved aggressiveness to other male mice, ability to copulate and the need for territorial marking. The mice reacted significantly more passively than normal for all three parameters. They did not attack other males, they were unable to copulate and behaved more like female mice when it come to urinary territorial marking.

After observing the changed behavioural patterns, Prof. Anders Hay-Schmidt, who was employed at the then Department of Neuroscience and Pharmacology during his studies at the University of Copenhagen,

investigated the specific effects of a lack of testosterone on the brain. The results showed up clearly here, too.

"The area of the brain that controls sex drive -- the sexual dimorphic nucleus -- had half as many neurons in the mice that had received paracetamol as the control mice. The inhibition of testosterone also led to a halving of the activity in an area of the brain that is significant for male characteristics," he explains.

Also affects female fertility

This study focused on the effect of paracetamol on masculine characteristics but paracetamol during pregnancy also has the potential to influence the subsequent lives of female mice. In 2016, the researchers published a study showing that female mice had fewer eggs in their ovaries if their mothers had had paracetamol during pregnancy. This led to the mice becoming infertile more quickly. But even if paracetamol is harmful, that does not mean it should never be taken, even when pregnant.

"I personally think that people should think carefully before taking medicine. These days it has become so common to take paracetamol that we forget it is a medicine. And all medicine has side effects. If you are ill, you should naturally take the medicine you need. After all, having a sick mother is more harmful for the fetus," says David Møbjerg Kristensen.

He emphasizes that pregnant women should continue to follow the guidelines given by their country's health authorities and recommends people to contact their GP if in doubt about the use of paracetamol.

Story Source:

[Materials](#) provided by **University of Copenhagen The Faculty of Health and Medical Sciences**. *Note: Content may be edited for style and length.*

Journal Reference:

1. Anders Hay-Schmidt, Olivia T Ejlstrup Finkielman, Benjamin A H Jensen, Christine F Høgsbro, Jacob Bak Holm, Kristoffer Haurum Johansen, Tina Kold Jensen, Anderson Martino Andrade, Shanna H Swan, Carl-Gustaf Bornehag, Søren Brunak, Bernard Jegou, Karsten Kristiansen, David Møbjerg Kristensen. **Prenatal exposure to paracetamol/acetaminophen and precursor aniline impairs masculinisation of male brain and behaviour.** *Reproduction*, 2017; 154 (2): 145 DOI: [10.1530/REP-17-0165](https://doi.org/10.1530/REP-17-0165)
-

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- [MLA](#)
- [APA](#)
- [Chicago](#)

University of Copenhagen The Faculty of Health and Medical Sciences. "Acetaminophen during pregnancy can inhibit masculinity." ScienceDaily. ScienceDaily, 22 June 2017.

<www.sciencedaily.com/releases/2017/06/170622082522.htm>.

University of Copenhagen The Faculty of Health and Medical Sciences. (2017, June 22).

Acetaminophen during pregnancy can inhibit masculinity. *ScienceDaily*. Retrieved June 27, 2017 from www.sciencedaily.com/releases/2017/06/170622082522.htm

University of Copenhagen The Faculty of Health and Medical Sciences. "Acetaminophen during pregnancy can inhibit masculinity." ScienceDaily.

www.sciencedaily.com/releases/2017/06/170622082522.htm (accessed June 27, 2017).

[目次に戻る](#)

8. フェロモンがどのようにして女性の性行為を引き起こすか - マウス実験

2017年6月22日

東京大学農学生命科学研究科応用生物化学研究室（東原和成教授）の研究者グループは、匂いやフェロモンなど化学感覚シグナルに関する研究をテーマにしているが、今回、オスのフェロモンがどのようにしてメスの性行為を引き起こすか、またオスの異なる行動や攻撃性をどのようにして高めるか、マウス実験で示し *Neuron* 誌上で発表した。

この発見は、生き物における性別に固有の生得的行動がどのように制御されるか調査をさらに深めていく上での方向性を示すものだとしている。

記事：

<https://www.sciencedaily.com/releases/2017/06/170622143104.htm>

How pheromones trigger female sexual behavior

Distinct neural circuits convert chemical signals into specific behavior

Date:

June 22, 2017

Source:

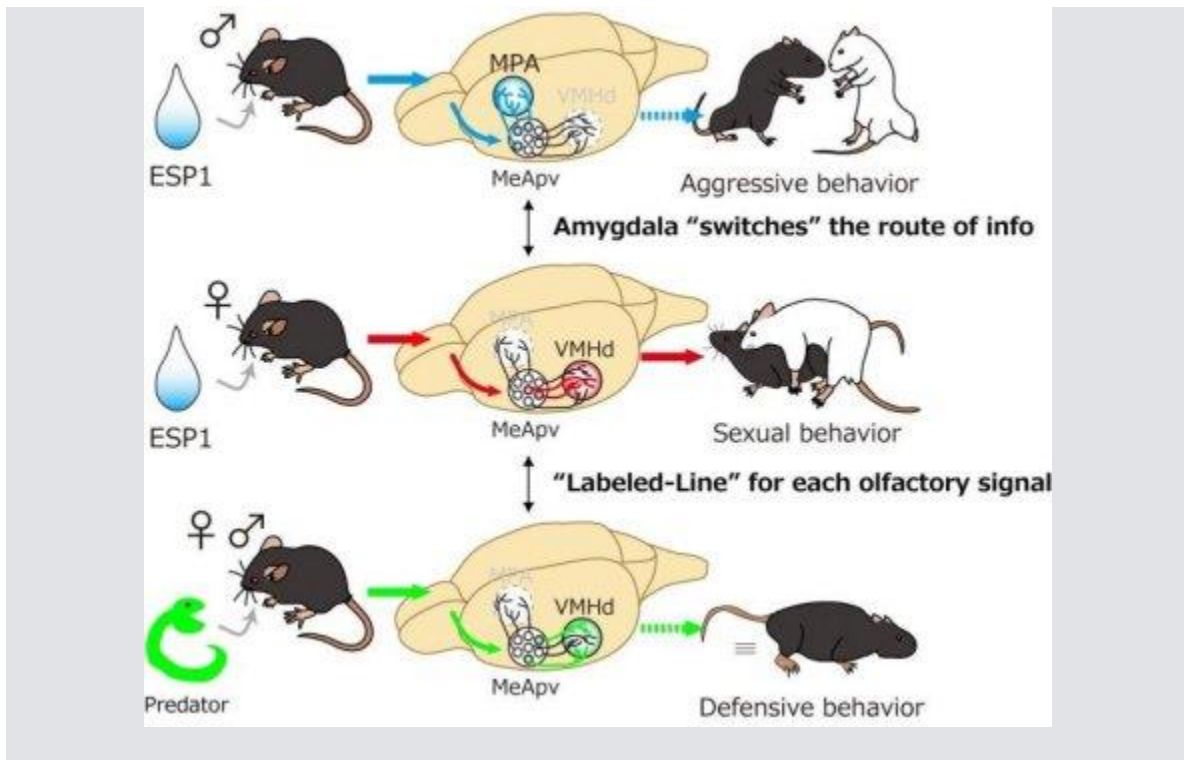
University of Tokyo

Summary:

A new study showed how a male pheromone in mice enhances sexual behaviors in females -- and how it may enhance a different behavior, aggression, in males -- by identifying distinct neural circuits and neurons that generate a particular behavioral response to specific chemical

signals. The findings point to a model for further investigating how sex-specific innate behaviors in living things are controlled.

FULL STORY



Top: When male mice detect the ESP1 sex pheromone, they display enhanced aggressive behavior toward other male mice. A region referred to as MeApv in the part of the brain called the amygdala acts as a 'switch' that passes ESP1 information to different regions of the hypothalamus, another area of the brain, depending on the sex of the recipient mouse: the MPA subregion in males and VMHd subregion in females. Middle: ESP1 enhances sexual behaviors in female mice. The neural circuit, identified in the study, is responsible for this effect. Bottom: ESP1 and a predator cue (snake skin), which elicits defensive behaviors, use intermingled but mostly different neural circuits, extending from the peripheral receptive organ to the hypothalamus.

Credit: 2017 Kazushige Touhara

A study by a group of Japanese scientists showed how a male pheromone in mice enhances sexual behaviors in females -- and how it may enhance a different behavior, aggression, in males -- by identifying distinct neural circuits and neurons that generate a particular behavioral response to specific chemical signals. The findings point to a model for further investigating how sex-specific innate behaviors in living things are controlled.

In most animals, the sense of smell and other sensory perception of chemical stimulus play a critical role in controlling instinctive behaviors. For instance, chemical signals from a partner, competitor or predator elicit specific behavior in mice, namely mating, aggression and defensive behaviors, respectively.

Ever since a pheromone secreted by a female moth that attracts the opposite sex was identified in 1959, scientists have pinned down numerous chemicals that affect behavior in a wide variety of animal species, from insects to mammals to humans. Despite their growing database of known pheromones, scientists knew little about how the brain actually converts certain sensory input into appropriate behavioral output, especially in mammals.

"It is widely known that some chemicals, especially odors, can impact an animal's instinctive behaviors even on first contact," says Kazushige Touhara, a professor at the University of Tokyo's Graduate School of Agricultural and Life Sciences, who supervised the study. "We assumed there was a neural mechanism in the brain that correctly connects important sensory information to appropriate behavioral centers in the brain," he adds.

In its study, the research group used a male pheromone, secreted from the tear gland, called ESP1 that has been shown to enhance sexual behaviors in female mice, while promoting aggression in males exposed to ESP1 in conjunction with unfamiliar male urine. Unlike other pheromones, which tend to be composed of a complex web of substances, ESP1 is a single purified chemical that is detected by a sole corresponding receptor, making it comparatively easy to track.

The group employed various viral tracing methods -- infecting receptor-expressing neurons with a virus strain and watching them spread as they label infected cells with a fluorescent protein -- to visualize the neural circuit downstream of the ESP1 receptor, as well as providing an image of nerve fibers belonging to specific neurons in the brain and synapses relaying impulses from neuron to neuron, to map the anatomical foundation that conveys ESP1 signals in the brain. Using this method, researchers found that

the information of ESP1 was routed differently in males and females by neurons in a region of the brain called the amygdala.

The researchers also found that activation of ESP1-responding neurons in the region of the brain called the hypothalamus enhanced sexual behavior in female mice, even in the absence of actual ESP1, by using various tools to chemically or optically control neural activities, combined with a process called the TRAP method, which allows them to selectively manipulate neurons responding to a particular stimulus. In contrast, activation of neurons that responded to snake skin, a predator cue that elicits defensive behaviors, in the same brain area showed no change in sexual behaviors.

"This finding suggests that there are two different types of neurons, ESP1 and predator neurons, and only the former controls sexual behaviors in female mice," explains Touhara.

A similar discovery in fruit flies, reported in an earlier independent study, which shows that a particular sex pheromone enhances female sexual behaviors and male aggression via separate neural circuits between the sexes, suggests that a sexually distinct circuit may be a universal strategy for converting male pheromone information into appropriate behavioral output. Further understanding the neural basis underlying the control of female sexual behaviors could also provide insights into the origin of sexual dysfunctions.

Story Source:

Materials provided by **University of Tokyo**. *Note: Content may be edited for style and length.*

Journal Reference:

1. Kentaro K. Ishii, Takuya Osakada, Hiromi Mori, Nobuhiko Miyasaka, Yoshihiro Yoshihara, Kazunari Miyamichi, Kazushige Touhara. **A Labeled-Line Neural Circuit for Pheromone-Mediated Sexual Behaviors in Mice**. *Neuron*, 2017; DOI: [10.1016/j.neuron.2017.05.038](https://doi.org/10.1016/j.neuron.2017.05.038)
-

Cite This Page:

- [MLA](#)
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University of Tokyo. "How pheromones trigger female sexual behavior: Distinct neural circuits convert chemical signals into specific behavior." ScienceDaily. ScienceDaily, 22 June 2017.

<www.sciencedaily.com/releases/2017/06/170622143104.htm>.

University of Tokyo. (2017, June 22). How pheromones trigger female sexual behavior: Distinct neural circuits convert chemical signals into specific behavior. *ScienceDaily*. Retrieved June 27, 2017 from www.sciencedaily.com/releases/2017/06/170622143104.htm

University of Tokyo. "How pheromones trigger female sexual behavior: Distinct neural circuits convert chemical signals into specific behavior." ScienceDaily.

www.sciencedaily.com/releases/2017/06/170622143104.htm (accessed June 27, 2017).

9. マウスのゲノム解析

2017年6月26日

実験用マウスの遺伝子カタログからの研究結果が初めて生物医学界で共有され、珍しい疾患に対して新しい洞察、また新しい治療法や精密医療の発展が加速される可能性が明らかにされた。

Queen Mary University of London によるこの研究では、2千万個以上のデータが生成され、360種の新疾患モデルを発見、マウスの生物学と疾患に対する遺伝子の影響について28,406もの新しい記述を提供している。

Nature Genetics 誌に掲載されている結果は、最初の3,328遺伝子（たんぱく質をコードするマウスのゲノムの15%）の解析に基づいている。

英文記事：

<https://www.sciencedaily.com/releases/2017/06/170626124438.htm>

Characterizing the mouse genome reveals new gene functions and their role in human disease

Date:

June 26, 2017

Source:

Queen Mary University of London

Summary:

The first results from a functional genetic catalogue of the laboratory mouse has been shared with the biomedical research community, revealing new insights into a range of rare diseases and the possibility of accelerating development of new treatments and precision medicine.

FULL STORY

The first results from a functional genetic catalogue of the laboratory mouse has been shared with the biomedical research community, revealing new insights into a range of rare diseases and the possibility of accelerating development of new treatments and precision medicine.

The research, which generated over 20 million pieces of data, has found 360 new disease models and provides 28,406 new descriptions of the genes' effects on mouse biology and disease. The new disease models are being made available to the biomedical community to aid their research.

The International Mouse Phenotyping Consortium (IMPC) is aiming to produce a complete catalogue of mammalian gene function across all genes. Their initial results, now published in *Nature Genetics*, is based on an analysis of the first 3,328 genes (15 per cent of the mouse genome coding for proteins).

Lead author Dr Damian Smedley from Queen Mary University of London (QMUL) and a Monarch Initiative Principal Investigator, said: "Although next generation sequencing has revolutionised the identification of new disease genes, there is still a lack of understanding of how these genes actually cause disease.

"These 360 new disease models that we've identified in mice represent the first steps of a hugely important international project. We hope researchers will be able to use this knowledge to develop new therapies for patients, which is ultimately what we're all striving to achieve."

With its similarity to human biology and ease of genetic modification, the laboratory mouse is arguably the preferred model organism for studying human genetic disease. However, the vast majority of the mouse genome remains poorly understood, as scientists tend to focus their research on a few specific areas of the genome linked to the most common inherited diseases.

Development of therapies for rare disease lags far behind, with over half of diagnosed rare diseases still having no known causative gene. This is why the IMPC is aiming to build a complete database that systematically details the functions of all areas of the mouse genome, including neurological, metabolic, cardiovascular, respiratory and immunological systems.

Terry Meehan, IMPC Project Coordinator at European Bioinformatics Institute (EMBL-EBI) said: "Mouse models allow us to speed up patient diagnosis and develop new therapies. But before that can work, we need to understand exactly what each gene does, and what diseases it is associated with. This is a significant effort in data collection and curation that goes well beyond the capabilities of individual labs. IMPC is creating a data resource that will benefit the entire biomedical community."

The project involves going through the mouse genome systematically and knocking out a particular gene, one by one, in different mice. By looking at the mouse's resulting characteristics in a variety of standardised tests, the team then see if and how the gene knockout manifests itself as a disease, and link their findings to what is already known about the human version of the disease. The 'one by one' knockout approach lends itself to rare gene discovery, as often these diseases are caused by variants of a single gene.

More than half of the 3,328 genes characterised have never been investigated in a mouse before, and for 1,092 genes, no molecular function or biological process were previously known from direct experimental evidence. These include genes that have now been found to be involved in the formation of blood components (potentially involved in a type of anemia), cell proliferation and stem cell maintenance.

For the first time, human disease traits were seen in mouse models for forms of Bernard-Soulier syndrome (a blood clotting disorder), Bardet-Biedl syndrome (causing vision loss, obesity and extra fingers or toes) and Gordon Holmes syndrome (a neurodegenerative disorder with delayed puberty and lack of secondary sex characteristics).

The team also identified new candidate genes for diseases with an unknown molecular mechanism, including an inherited heart disease called 'Arrhythmogenic Right Ventricular Dysplasia' that affects the heart muscle, and Charcot-Marie-Tooth disease, which is characterised by nerve damage leading to muscle weakness and an awkward way of walking.

Dr Smedley added: "In addition to a better understanding of the disease mechanism and new treatments for rare disease patients, many of the lessons we learn here will also be of value to precision medicine, where the goal is to improve treatment through the customisation of healthcare based on a patient's genomic information."

Story Source:

[Materials](#) provided by **Queen Mary University of London**. *Note: Content may be edited for style and length.*

Journal Reference:

1. Terrence F Meehan, Nathalie Conte, David B West, Julius O Jacobsen, Jeremy Mason, Jonathan Warren, Chao-Kung Chen, Ilinca Tudose, Mike Relac, Peter Matthews, Natasha Karp, Luis Santos, Tanja Fiegel, Natalie Ring, Henrik Westerberg, Simon Greenaway, Duncan Sneddon, Hugh Morgan, Gemma F Codner, Michelle E Stewart, James Brown, Neil Horner, Melissa Haendel, Nicole Washington, Christopher J Mungall, Corey L Reynolds, Juan Gallegos, Valerie Gailus-Durner, Tania Sorg, Guillaume Pavlovic, Lynette R Bower, Mark Moore, Iva Morse, Xiang Gao, Glauco P Tocchini-Valentini, Yuichi Obata, Soo Young Cho, Je Kyung Seong, John Seavitt, Arthur L Beaudet, Mary E Dickinson, Yann Herault, Wolfgang Wurst, Martin Hrabe de Angelis, K C Kent Lloyd, Ann M Flenniken, Lauryl M J Nutter, Susan Newbigging, Colin McKerlie, Monica J Justice, Stephen A Murray, Karen L Svenson, Robert E Braun, Jacqueline K White, Allan Bradley, Paul Flicek, Sara Wells, William C Skarnes, David J Adams, Helen Parkinson, Ann-Marie Mallon, Steve D M Brown, Damian Smedley. **Disease model discovery from 3,328 gene knockouts by The International Mouse Phenotyping Consortium.** *Nature Genetics*, 2017; DOI: [10.1038/ng.3901](https://doi.org/10.1038/ng.3901)
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- [MLA](#)
- [APA](#)
- [Chicago](#)

Queen Mary University of London. "Characterizing the mouse genome reveals new gene functions and their role in human disease." ScienceDaily. ScienceDaily, 26 June 2017.

<www.sciencedaily.com/releases/2017/06/170626124438.htm>.

Queen Mary University of London. (2017, June 26). Characterizing the mouse genome reveals new gene functions and their role in human disease. *ScienceDaily*. Retrieved June 27, 2017 from www.sciencedaily.com/releases/2017/06/170626124438.htm

Queen Mary University of London. "Characterizing the mouse genome reveals new gene functions and their role in human disease." *ScienceDaily*. www.sciencedaily.com/releases/2017/06/170626124438.htm (accessed June 27, 2017).

10. 自閉症スペクトラム障害の遺伝について -マウス実験

2017年6月27日

カリフォルニア大学デイビス校の研究者らは、遺伝子技術の進歩を利用して、自閉症に関与する特定の遺伝子の果たす役割について更なる理解を深めており、この研究が6月26日の *Nature Neuroscience* 誌に掲載されている。

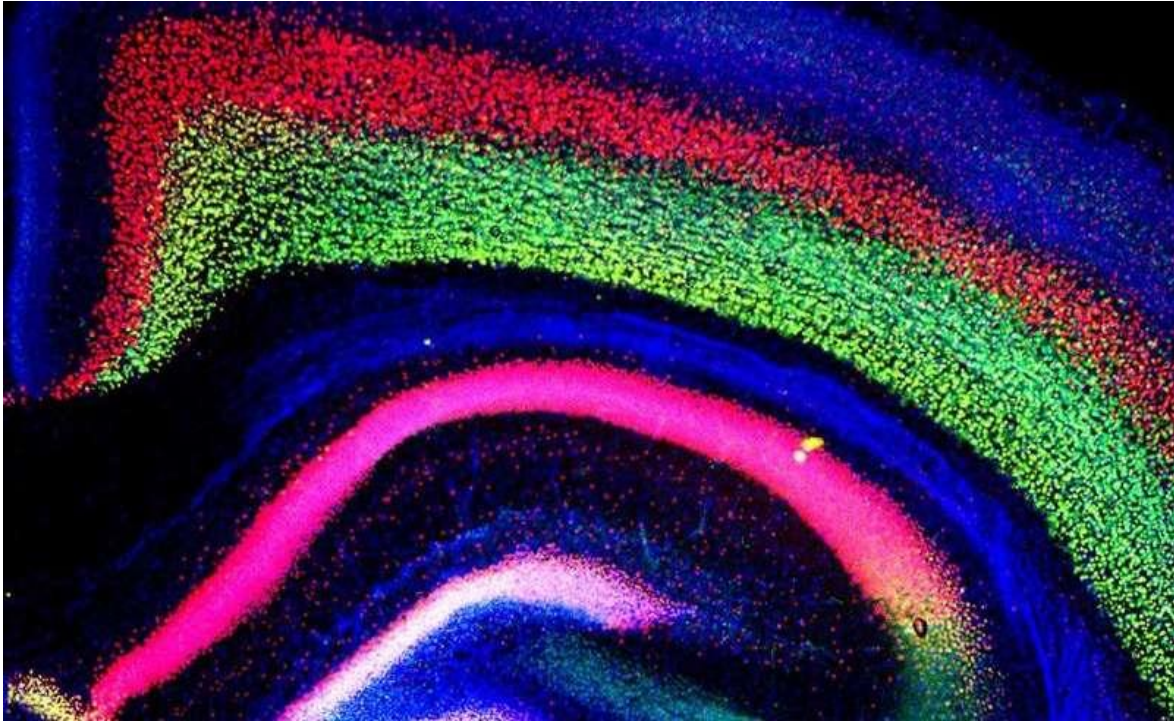
CHD8 遺伝子は、ヒトの自閉症のいくつかの症例と関連しているとされるが、この研究によると、突然変異した CHD8 を有するマウスは脳の発達および行動変化に欠陥を示しており、このことから自閉症スペクトラム障害の遺伝的要因を洞察することができるとしている。

英文記事：

<https://medicalxpress.com/news/2017-06-mice-insight-genetics-autism-spectrum.html>

Mice provide insight into genetics of autism spectrum disorders

June 27, 2017 by David Slipher



In this mouse cortex, a mutation in the CHD8 gene caused increased brain size, or megalencephaly, a condition also present in people with autism spectrum disorder. The colored sections correspond to different layers of the developing cortex.

Credit: Alex Nord/UC Davis

While the definitive causes remain unclear, several genetic and environmental factors increase the likelihood of autism spectrum disorder, or ASD, a group of conditions covering a "spectrum" of symptoms, skills and levels of disability.

Taking advantage of advances in genetic technologies, researchers led by Alex Nord, assistant professor of neurobiology, physiology and behavior with the Center for Neuroscience at the University of California, Davis, are gaining a better understanding of the role played by a specific gene involved in autism. The collaborative work appears June 26 in the journal *Nature Neuroscience*.

“For years, the targets of drug discovery and treatment have been based on an unknown black box of what’s happening in the [brain](#),” said Nord. “Now, using genetic approaches to study the impact of specific mutations found in cases, we’re trying to build a cohesive model that links genetic control of brain development with behavior and [brain function](#).”

The Nord laboratory studies how the genome encodes brain development and function, with a particular interest in understanding the genetic basis of neurological disorders.

Mouse brain models

There is no known specific genetic cause for most cases of autism, but many different genes have been linked to the disorder. In rare, specific cases of people with ASD, one copy of a gene called CHD8 is mutated and loses function. The CHD8 gene encodes a protein responsible for packaging DNA in cells throughout the body. Packaging of DNA controls how genes are turned on and off in cells during development.

Because [mice](#) and humans share on average 85 percent of similarly coded [genes](#), mice can be used as a model to study how genetic mutations impact brain development. Changes in mouse DNA mimic changes in human DNA and vice-versa. In addition, mice exhibit behaviors that can be used as models for exploring human behavior.

Nord’s laboratory at UC Davis and his collaborators have been working to characterize changes in brain development and behavior of mice carrying a mutated copy of CHD8.

“Behavioral tests with mice give us information about sociability, anxiety and cognition. From there, we can examine changes at the anatomical and cellular level to find links across dimensions,” said Nord. “This is critical to understanding the biology of disorders like autism.”

By inducing mutation of the CHD8 gene in mice and studying their brain development, Nord and his team have established that the mice experience cognitive impairment and have increased brain volume. Both conditions are also present in individuals with a mutated CHD8 gene.

New implications for early and lifelong brain development

Analysis of data from mouse brains reveals that CHD8 gene expression peaks during the early stages of brain development. Mutations in CHD8 lead to excessive production of dividing cells in the brain, as well as megalencephaly, an enlarged brain condition common in individuals with ASD. These findings suggest the developmental causes of increased brain size.

More surprisingly, Nord also discovered that the pathological changes in gene expression in the brains of mice with a mutated CHD8 continued through the lifetime of the mice. Genes involved in critical biological processes like synapse function were impacted by the CHD8 mutation. This suggests that CHD8 plays a role in brain function throughout life and may affect more than [early brain development](#) in autistic individuals.

While Nord's research centers on severe ASD conditions, the lessons learned may eventually help explain many cases along the autism spectrum.

Collaborating to improve understanding

Nord's work bridges disciplines and has incorporated diverse collaborators. The genetic mouse model was developed at Lawrence Berkeley National Laboratory using CRISPR editing technology, and co-authors Jacqueline Crawley and Jill Silverman of the UC Davis MIND Institute evaluated mouse behavior to characterize social interactions and cognitive impairments.

Nord also partnered with co-author Konstantinos Zarbali of the Institute for Pediatric Regenerative Medicine at UC Davis to examine changes in cell proliferation in the brains of mice with the CHD8 mutation, and with Jason Lerch from the Mouse Imaging Centre at the Hospital for Sick Children in Toronto, Canada, to conduct magnetic resonance imaging on mouse brains.

"It's the act of collaboration that I find really satisfying," Nord said. "The science gets a lot more interesting and powerful when we combine different approaches. Together we were able to show that mutation to CHD8 causes changes to brain [development](#), which in turn alters brain anatomy, function and behavior."

In the future, Nord hopes to identify how CHD8 packages DNA in neural cells and to determine the specific impacts to early [brain development](#) and synaptic function. Nord hopes that deep exploration of CHD8 mutations will ultimately yield greater knowledge of the general factors contributing to ASD and intellectual disability.

Explore further: [Study shows connection between key autism risk genes in the human brain](#)

More information: Andrea L Gompers et al. Germline Chd8 haploinsufficiency alters brain development in mouse, *Nature Neuroscience* (2017). [DOI: 10.1038/nn.4592](#)

Journal reference: [Nature Neuroscience](#)

Provided by: [UC Davis](#)
