



Neuroscientists build case for new theory of memory formation



Existence of 'silent engrams' suggests that existing models of memory formation should be revised

Learning and memory are generally thought to be composed of three major steps: encoding events into the brain network, storing the encoded information, and later retrieving it for recall.

Two years ago, MIT neuroscientists discovered that under certain types of retrograde amnesia, memories of a particular event could be stored in the brain even though they could not be retrieved through natural recall cues. This phenomenon suggests that existing models of memory formation need to be revised, as the researchers propose in a new paper in which they further detail how these "silent engrams" are formed and re-activated.

The researchers believe their findings offer evidence that memory storage does not rely on the strengthening of connections, or "synapses," between memory cells, as has long been thought. Instead, a pattern of connections that form between these cells during the first few minutes

after an event occurs are sufficient to store a memory.

"One of our main conclusions in this study is that a specific memory is stored in a specific pattern of connectivity between engram cell ensembles that lie along an anatomical pathway. This conclusion is provocative because the dogma has been that a memory is instead stored by synaptic strength," says Susumu Tonegawa, the Picower Professor of Biology and Neuroscience, the director of the RIKEN-MIT Center for Neural Circuit Genetics at the Picower Institute for Learning and Memory, and the study's senior author.

The researchers also showed that even though memories held by silent engrams cannot be naturally recalled, the memories persist for at least a week and can be "awakened" days later by treating cells with a protein that stimulates synapse formation.

Dheeraj Roy, a recent MIT PhD recipient, is the lead author of the paper, which appears in the Proceedings of the National Academy of Sciences the week of Oct. 23. Other authors are MIT postdoc Shruti Muralidhar and technical associate Lillian Smith.

Silent memories

Neuroscientists have long believed that memories of events are stored when synaptic connections, which allow neurons to communicate with each other, are strengthened.

(Cont.) Page 4

Higher brain glucose levels may mean more severe Alzheimer's

NIH study shows connections between glucose metabolism, Alzheimer's pathology, symptoms.

For the first time, scientists have found a connection between abnormalities in how the brain breaks down glucose and the severity of the signature amyloid plaques and tangles in the brain, as well as the onset of eventual outward symptoms, of Alzheimer's disease. The study was supported by the National Institute on Aging (NIA), part of the National Institutes of Health, and appears in the Nov. 6, 2017, issue of Alzheimer's & Dementia: the Journal of the Alzheimer's Association.

Led by Madhav Thambisetty, M.D., Ph.D., investigator and chief of the Unit of Clinical and Translational Neuroscience in the NIA's Laboratory of Behavioral Neuroscience, researchers looked at brain tissue samples at autopsy from participants in the Baltimore Longitudinal Study of Aging (BLSA), one of the world's longest-running scientific studies of human aging. The BLSA tracks neurological, physical and psychological data on participants over several decades.

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Letter From The Executive Director

Welcome to 2018!

As the New Year begins this is a good time to take a wellness inventory. Many people have concerns about becoming more forgetful, for either themselves or a loved one. To alleviate concerns, a benchmark memory screening can help anyone track indicators of cognitive health.

A memory screening takes less than 30 minutes and is offered at our Anchorage, Fairbanks, Juneau and Mat-Su locations. They are confidential and there is no charge for this service. They are useful to serve as a comparison later in life, or as a first step in addressing concerns about memory loss.

Screenings test memory, language, and other cognitive abilities by asking a series of questions and having the participant do a few tasks. Recommendations are made based on the results of the test and if memory impairment is recognized during the process, it is important to then follow up with a qualified medical professional for a diagnostic evaluation. Memory loss can be caused by a number of conditions other than Alzheimer's, like vitamin deficiencies and thyroid problems that can be treated if identified.

If a full medical work-up results in a diagnosis of Alzheimer's disease and related dementias (ARD) or Mild Cognitive Impairment (MCI), early detection is extremely beneficial. Diagnosis early in the course of illness can improve the quality of life for the individual diagnosed as well as their family members. They can ease uncertainty through proactive planning, joining support groups, and taking classes to prepare. These are available for both caregivers and individuals living with dementia.

An annual wellness inventory is also a useful device for us to consider the kinds of lifestyle modifications we may want to consider to reduce our risks of developing dementia. One of our educational offerings Healthy Body, Health Brain shares how our brain, body and spirit can be affected by living and maintaining a healthy lifestyle. For more information visit page 9.

In closing, I would like to thank our donors, volunteers and community partners who supported our mission in 2017. We appreciate your commitment to Alaskans affected by ARD and those with disabilities across the state.

Best Regards,

Karl Garber
Executive Director



Neuroscientists build case for new theory *(Cont.) from page 1*

Previous studies have found that if synthesis of certain cellular proteins is blocked in mice immediately after an event occurs, the mice will have no long-term memory of the event.

However, in a 2015 paper, Tonegawa and his colleagues showed for the first time that memories could be stored even when synthesis of the cellular proteins is blocked. They found that while the mice could not recall those memories in response to natural cues, such as being placed in the cage where a fearful event took place, the memories were still there and could be artificially retrieved using a technique known as optogenetics.

The researchers have dubbed these memory cells “silent engrams,” and they have since found that these engrams can also be formed in other situations. In a study of mice with symptoms that mimic early Alzheimer’s disease, the researchers found that while the mice had trouble recalling memories, those memories still existed and could be optogenetically retrieved.

In a more recent study of a process called systems consolidation of memory, the researchers found engrams in the hippocampus and the prefrontal cortex that encoded the same memory. However, the prefrontal cortex engrams were silent for about two weeks after the memory was initially encoded, while the hippocampal engrams were active right away. Over time, the memory in the prefrontal cortex became active, while the hippocampal engram slowly became silent.

In their new PNAS study, the researchers investigated further how

these silent engrams are formed, how long they last, and how they can be re-activated.

Similar to their original 2015 study, they trained mice to fear being placed in a certain cage, by delivering a mild foot shock. After this training, the mice freeze when placed back in that cage. As the mice were trained, their memory cells were labeled with a light-sensitive protein that allows the cells to be re-activated with light. The researchers also inhibited the synthesis of cellular proteins immediately after the training occurred.

They found that after the training, the mice did not react when placed back in the cage where the training took place. However, the mice did freeze when the memory cells were activated with laser light while the animals were in a cage that should not have had any fearful associations. These silent memories could be activated by laser light for up to eight days after the original training.

Making connections

The findings offer support for Tonegawa’s new hypothesis that the strengthening of synaptic connections, while necessary for a memory to be initially encoded, is not necessary for its subsequent long-term storage. Instead, he proposes that memories are stored in the specific pattern of connections formed between engram cell ensembles. These connections, which form very rapidly during encoding, are distinct from the synaptic strengthening that occurs later (within a few hours of the event) with the help of protein synthesis.

“What we are saying is that even without new cellular protein synthesis, once a new connection is made, or a

pre-existing connection is strengthened during encoding, that new pattern of connections is maintained,” Tonegawa says. “Even if you cannot induce natural memory recall, the memory information is still there.”

This raised a question about the purpose of the post-encoding protein synthesis. Considering that silent engrams are not retrieved by natural cues, the researchers believe the primary purpose of the protein synthesis is to enable natural recall cues to do their job efficiently.

The researchers also tried to reactivate the silent engrams by treating the mice with a protein called PAK1, which promotes the formation of synapses. They found that this treatment, given two days after the original event took place, was enough to grow new synapses between engram cells. A few days after the treatment, mice whose ability to recall the memory had been blocked initially would freeze after being placed in the cage where the training took place. Furthermore, their reaction was just as strong as that of mice whose memories had been formed with no interference.

Along with the researchers’ previous findings on silent engrams in early Alzheimer’s disease, this study suggests that re-activating certain synapses could help restore some memory recall function in patients with early stage Alzheimer’s disease, Roy says.

Massachusetts Institute of Technology. “Neuroscientists build case for new theory of memory formation: Existence of ‘silent engrams’ suggests that existing models of memory formation should be revised.” ScienceDaily, 23 October 2017.



Higher brain glucose levels *(Cont.) from page 1*

Researchers measured glucose levels in different brain regions, some vulnerable to Alzheimer's disease pathology, such as the frontal and temporal cortex, and some that are resistant, like the cerebellum. They analyzed three groups of BLSA participants: those with Alzheimer's symptoms during life and with confirmed Alzheimer's disease pathology (beta-amyloid protein plaques and neurofibrillary tangles) in the brain at death; healthy controls; and individuals without symptoms during life but with significant levels of Alzheimer's pathology found in the brain post-mortem.

They found distinct abnormalities in glycolysis, the main process by which the brain breaks down glucose, with evidence linking the severity of the abnormalities to the severity of Alzheimer's pathology. Lower rates of glycolysis and higher brain glucose levels correlated to more severe plaques and tangles found in the brains of people with the disease. More severe reductions in brain glycolysis were also related to the expression of symptoms of Alzheimer's disease during life, such as problems with memory.

"For some time, researchers have thought about the possible links between how the brain processes glucose and Alzheimer's," said NIA Director Richard J. Hodes, M.D. "Research such as this involves new thinking about how to investigate these connections in the intensifying search for better and more effective ways to treat or prevent Alzheimer's disease."

While similarities between diabetes and Alzheimer's have long been suspected, they have been difficult to evaluate, since insulin is not needed for glucose to enter the brain or to get into neurons. The team tracked the brain's usage of glucose by measuring ratios of the amino acids serine, glycine and alanine to glucose, allowing them to assess rates of the key steps of glycolysis. They found that the activities of enzymes controlling these key glycolysis steps were lower in Alzheimer's cases compared to normal brain tissue samples. Furthermore, lower enzyme activity was associated with more severe Alzheimer's pathology in the brain and the development of symptoms.

Next, they used proteomics – the large-scale measurement of cellular proteins – to tally levels of GLUT3, a glucose transporter protein, in neurons. They found that GLUT3 levels were lower in brains with Alzheimer's pathology compared to normal brains, and that these levels were also connected to the severity of tangles and plaques. Finally, the team checked blood glucose levels in study participants years before they died, finding that greater increases in blood glucose levels correlated with greater brain glucose levels at death.

"These findings point to a novel mechanism that could be targeted in the development of new treatments to help the brain overcome glycolysis defects in Alzheimer's disease," said Thambisetty.

The researchers cautioned that it is not yet completely clear whether

abnormalities in brain glucose metabolism are definitively linked to the severity of Alzheimer's disease symptoms or the speed of disease progression. The next steps for Thambisetty and his team include studying abnormalities in other metabolic pathways linked to glycolysis to determine how they may relate to Alzheimer's pathology in the brain.

About the National Institute on Aging (NIA):

The NIA leads the federal government effort conducting and supporting research on aging and the health and well-being of older people.

NIA provides information on age-related cognitive change and neurodegenerative disease specifically at its Alzheimer's Disease Education and Referral (ADEAR) Center.

About the National Institutes of Health (NIH):

NIH, the nation's medical research agency, includes 27 Institutes and Centers and is a component of the U.S. Department of Health and Human Services.

NIH is the primary federal agency conducting and supporting basic, clinical, and translational medical research, and is investigating the causes, treatments, and cures for both common and rare diseases. For more information about NIH and its programs, visit www.nih.gov.



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Save Date...

Join Alzheimer's Resource of Alaska at Amblin for Alzheimer's 2018, a walk to support individuals with Alzheimer's disease and related dementia in Alaska. The walk will be held Saturday, May 5 at the Anchorage Golf Course.

Amblin is the largest awareness and fundraising event in the state dedicated to individuals with Alzheimer's disease or related dementia (ADRD). Alzheimer's Resource of Alaska hopes to reach its goal of raising \$65,000 to help frail elders throughout the state.

You can win prizes, enjoy food, activities and listen to great music all for a good cause. Registration is now open online at AlzAlaska.org.

This is the time to get involved. Alaska has one of the fastest growing aging populations in the nation. Over 8,000 Alaskans are currently affected by Alzheimer's disease and related dementia and with baby-boomers beginning to reach retirement age that number is expected to nearly double in the next ten years. Alzheimer's not only affects the individual diagnosed but also all those around them. Nearly 33,000 Alaskans provided \$463 million worth of unpaid care by providing for a loved one with dementia. It is important that we show our support by raising awareness and funds for programs and services dedicated to assisting those who need it most.

Alzheimer's Resource of Alaska is a 501(c)(3) non-profit and the state's leading source of information, services and support for individuals living with Alzheimer's disease or related dementias. The non-profit organization serves the entire state and is dedicated to ensuring quality of life until a cure is found. All funds raised from this event will remain in Alaska and go to the benefit of Alaskans.



Amblin' for Alzheimer's

Register or Sponsor Today!

www.alzAlaska.org/amblin-for-alzheimers/

May 5, 2018
at 9 a.m.

Presented By:  **Walter E. and Barbara A. Bauke Foundation**

Additional Sponsors: Anchorage Sand & Gravel Company, Sandra Hanson, The Wilson Agency
Bradley House, Davis Constructors Engineers, Inc.



Healthy Body, Healthy Brain

The research community continues their quest to identify what causes one person and not another to develop the most common form of Alzheimer's disease. Much of their attention is focused on the relationship between three factors: age, genetics and lifestyle. Our age and genetic profile can't be altered. But lifestyle can, and choices made today around health lifestyles can have an impact on the risk of developing dementia.

A recent review of the existing evidence on strategies that show promise for the prevention of cognitive decline concludes that a combined approach of regular exercise, healthy diet, control of stress, treatment of depression and reduction of vascular risk factors holds the most promise. (8 Therapeutic Advances in Chronic Disease 121 (2017)). It is clear that the best thing each of us can do for our brains today, no matter our ages or genetic profiles, is to emphasize and choose healthy lifestyles.

The components of a "brain healthy" lifestyle are:

- Good sleep hygiene
- Moderate exercise
- A diet that includes lots of plants (e.g., Mediterranean or DASH diets)
- Socialization
- Lifelong Learning
- Stress Reduction

Taking a walk with a friend while talking about the challenges you faced during the day – there's a healthy body/healthy brain prescription. It includes exercise, socialization and stress reduction. Follow it up with a bowl of soup from a new recipe you've tried and share the meal with a friend. That incorporates learning, healthy diet and socialization. Start small. Create habits. Recognize what you're doing right.

On January 18, from 7-8:30 pm Education Specialist Gay Wellman will conduct an informative webinar Healthy Body, Healthy Brain that focuses on practical ways to keep your brain and your body healthy. To register for the class contact Gay Wellman at 907-822-5620 or by email at gwellman@alzalaska.org. To view other classes being offered at all our locations visit page 10 of this newsletter.



Care Coordination
Resource of Alaska

Gain Guidance

Acquire an Advocate

Our Care Coordination team provides you with the information you need to select your own health care, financial and social services, advocating for you to help you reach your goals and maximize your independence.

www.ccralaska.org

Classes & Events around the state

ANCHORAGE

1750 Abbott Road
561-3313

ABC Presentations Activities of Daily Living

Kim Jung
Monday, 1/22
10 - 11:30 am or 5:30 - 7 pm

20 Questions & 100 Answers: Part I

Debbie Chulick
Monday, 1/29
10 - 11:30 am or 5:30 - 7 pm

20 Questions & 100 Answers: Part II

Kim Jung
Monday, 2/5
10 - 11:30 am or 5:30 - 7 pm

Decision Making

Jane Haiar
Monday, 2/12
10 - 11:30 am or 5:30 - 7 pm

Beneficial Reminiscing

Debbie Chulick
Monday, 2/19
10 - 11:30 am or 5:30 - 7 pm

Honoring Connection

Kim Jung
Monday, 3/5
10 - 11:30 am or 5:30 - 7 pm

When a Loved One Wanders

Jane Haiar
Monday, 3/12
10 - 11:30 am or 5:30 - 7 pm

Savvy Caregiver

Jane haiar
Saturday, 1/20 to 2/24
10 - 2 pm

Art Links: Friday - Every Week 11 - 12 pm.

Brain Works *

Tuesdays, 2/6 to 3/27
10 - 11:30 am

Mind Matters I *

Wednesdays, 2/7 to 3/28
10 - 11:30 am

Mind Matters II *

Mondays, 2/8 to 3/29
10 - 11:30 am

MAT-SU

10355 Palmer-Wasilla Hwy.
746-3413

ABC Presentations Home and Community Safety for Elders

Janice Downing
Tuesday, 1/9
1 - 2:30 pm or 5:30 - 7 pm

Avoiding Senior Scams & Fraud

Janice Downing
Tuesday, 2/13
1 - 2:30 pm or 5:30 - 7 pm

Avoiding Senior Scams & Fraud

Janice Downing
Thursday, 2/22
5:30 - 7:00 pm
Mat-Su Health Services,
1363 W Spruce Ave.
Wasilla, AK

What, When, and How of Assisted Living

Janice Downing
Tuesday, 3/13
1-2:30 pm or 5:30 - 7 pm

Mind Matters *

Wednesdays, 1/3 to 2/21
10:30 am-noon

Mind Matters *

Wednesdays, 3/14 to 5/2
10:30 am-noon

Savvy Caregiver *

Janice Downing
Mondays, 3/5 to 3/12
1 - 4:30 pm
Willow Sunshine Community
Health Center
24091 Long Lake Road, Willow
Registration is required

Virtual Dementia Tour *

Janice Downing
Wednesday, 2/28
12:30 - 4:30 pm
Registration required

Art Links

Fridays - Every Week
1 - 2 pm

JUNEAU

3225 Hospital Dr.
586-6044

ABC Presentations The Power of Music

Amber Smith
Thursday, 1/25
12 - 1:30 pm or 5:30 - 7 pm

Savvy Caregiver *

Amber Smith
Wednesday, 1/17 to 2/21
5:30 - 7:30 pm
Registration is required

Communication Tips for the Caregivers

Thursday, 2/22
12-1:30 pm or
5:30 - 7:30 pm

Wasilla Neighborhood Memory Café

Wasilla Area Seniors,
Inc. (WASI)

1301 S Century Cir,
Wasilla
1:00 pm – 2:30 pm

Tuesdays,
2/20 3/20 4/17

FAIRBANKS

565 University Ave. #2
452-2277

ABC Presentations Being a Friend: Staying Connected *

Joan Adams
Tuesday, 1/23
5:30 - 7 pm

Driving and Dementia *

Joan Adams
Tuesday, 2/20
5:30 - 7 pm

Decision Making for Family Caregivers *

Joan Adams
Tuesday, 3/20
5:30 - 7 pm

Art Links

Thursday,- Every Week
11 am-noon

Mind Matters *

Joan Adams
Thursdays, 1/18 to 3/8
1 - 2:30 pm
Registration required

Savvy Caregivers *

Joan Adams
Wednesdays, 1/24 to 2/28
5:30 - 7:30 pm
Registration required

Virtual Dementia Tour *

Joan Adams
Tuesday, 3/27
10 - 4 pm
Registration required

Statewide Webinars

FOR PROFESSIONALS

Contact Amber Smith
907-586-6044

Behaviors that **Challenge Us**

Tuesday, 2/20
12 - 1:00 pm

Communication Tips for **the Caregivers**

Tuesday, 1/23
12 - 1:00 pm

FOR FAMILY

CAREGIVERS

Contact Gay Wellman
907-822-5620

Healthy Body/ Healthy **Brain**

Thursday, 1/18
7 - 8:30 pm

ABC Behaviors that **Challenge**

Thursday, 2/8
7 - 8:30 pm

ABC Honoring Connection

Thursday, 3/8
7 - 8:30 pm

* Registration Required



Support Groups around the state

A safe place for caregivers, family and friends of persons with dementia to share experiences and solutions.

Statewide Telephone Support Group

Alzheimer's Resource of Alaska	Caregiver	1st Wednesday 7-8 PM 3rd Wednesday 2-3 PM Dial in 1-877-216-1555, Code 927989	Gay Wellman 822-5620 or (800) 478-1080 x5
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Anchorage

Alzheimer's Resource of Alaska 1750 Abbott Rd.	Caregiver	2nd Thursday	12PM-1:30 PM	Debbie Chulick
	Caregiver	4th Thursday	5:30-7:00 PM	561-3313
	Caregiver	2nd Tuesday	5:30-7:00 PM	Jane Haiar
Chester Park Cooperative 2020 Muldoon Rd.	Caregiver	1st & 3rd Friday	10 -11:30 AM	Kim Jung 561-3313

Eagle River

Holy Spirit Episcopal Church 17545 N. Eagle River Loop Rd.	Caregiver	2nd Thursday	5:00-6:30 PM	Debbie Chulick 561-3313
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Fairbanks

Alzheimer's Resource of Alaska 565 University Ave. Suite 2	Caregiver	2nd Tuesday	5:30-7:00 PM	Joan Adams
		3rd Tuesday	11:30-1:00 PM	452-2277

Homer

Homer Senior Center	Caregiver	2 & 4th Thursdays	2:30-3:30 PM	Pam Hooker 235-7655
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Ketchikan

Ketchikan Senior Center Upper Level	Caregiver	Call for more information		Bernice 225-8080
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Kodiak

Kodiak Senior Center 302 Erskine Ave.	Caregiver	4th Thursday	12:30-1:30 PM	486-6181
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Mat-Su Valley

Alzheimer's Resource of Alaska 10355 E. Palmer-Wasilla Hwy. AK Veterans & Pioneer Home	Caregiver	2nd Wednesday	1-2:30 PM	Kim Jung 561-3313
	Caregiver	First Friday	10:00-11:30 AM	Janice Downing 746-3413

Seward

Seward Senior Center	Caregiver	4th Thursday	1-2 PM	224-5604
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Sitka

Brave Heart Volunteers 120 Katlian Street	Caregiver	Call for more info.		747-4600
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Soldotna

Soldotna Senior Center	Caregiver	2nd & Last Tuesday	1-3 PM	Judy Warren 262-1280
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