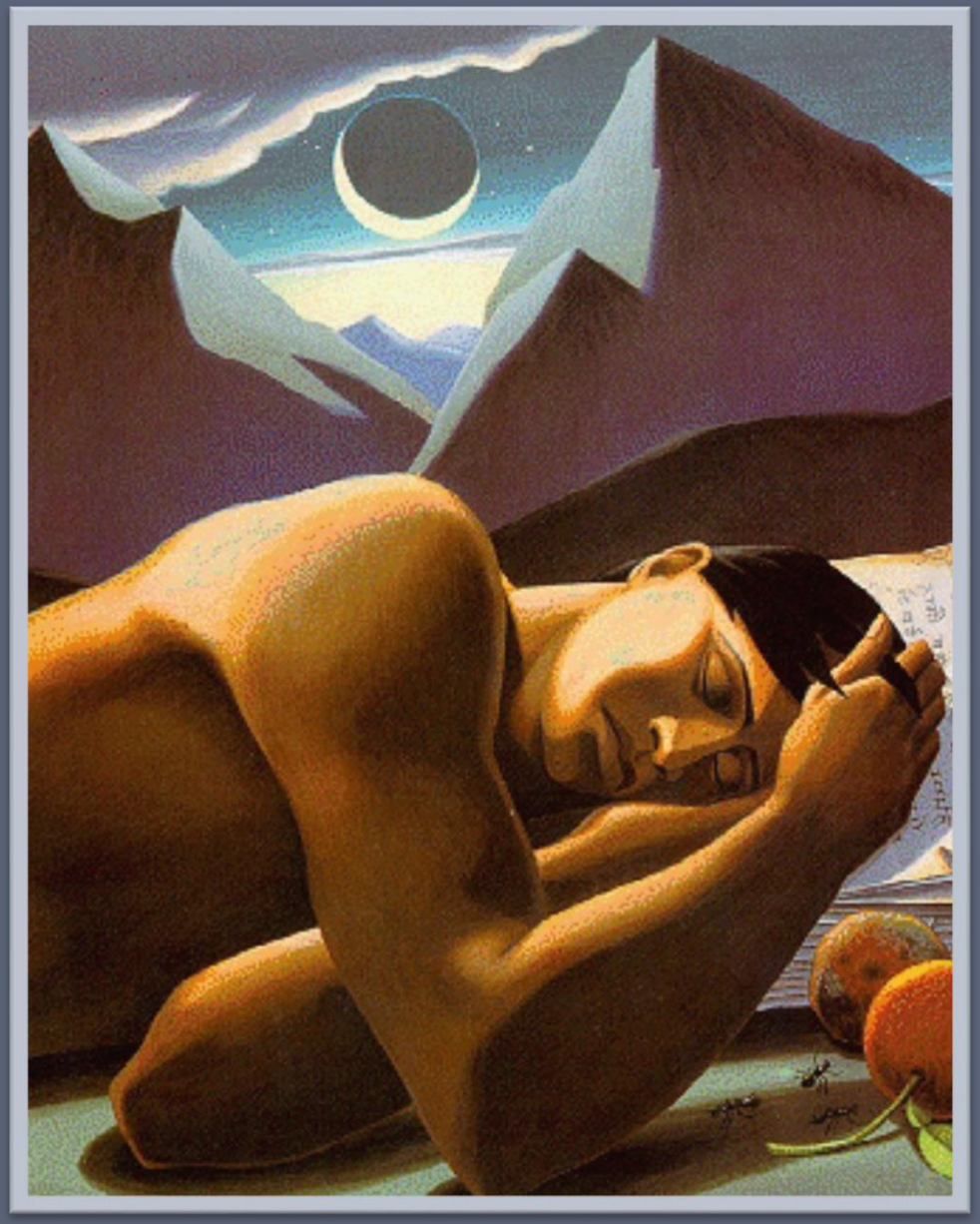
Alzheimer's Disease

A mind in darkness awaiting the drink of a gentle color.

Mary ET Boyle, Ph. D.
Department of Cognitive Science
UCSD

Gabriel García Márquez



One Hundred Years of Solitude

Alois Alzheimer

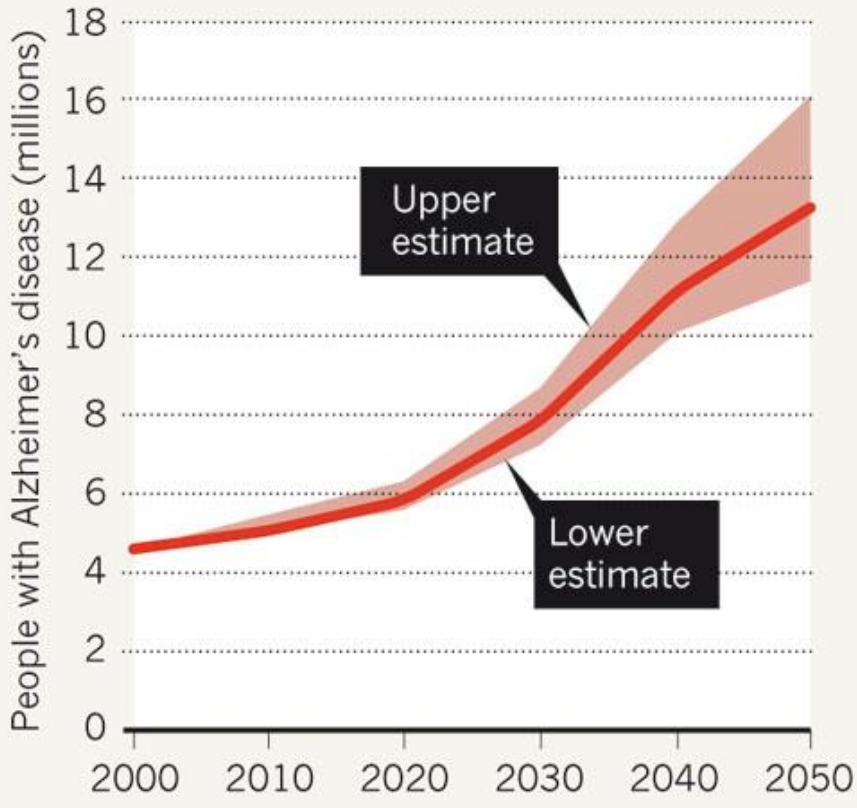
- Case of Auguste D., 50 year old woman in Germany - 1906
- Her disruptive behavior prompted her husband to see Dr. Alzheimer.

insight: dementia is physical

- Alzheimer examined Auguste D.’s brain.
- Discovered plaques and tangles.
- At the time it was thought that dementia was normal aging.

DEGENERATION GENERATION

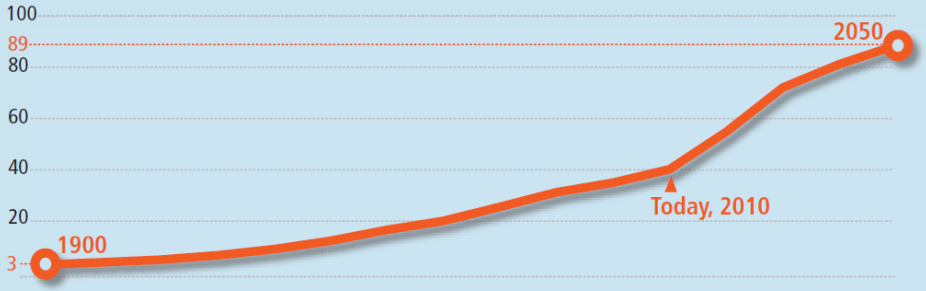
The prevalence of Alzheimer's disease is expected to rise sharply in the United States as its population ages.



L. E. Hebert et aL. Arch. Neurol. 69, 670–671 (2012)

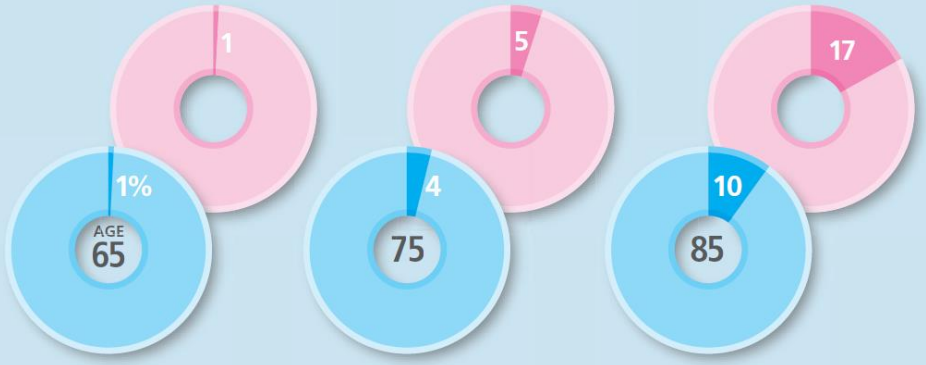
THE POPULATION IS AGING …

Millions of people aged 65 and older, living in the U.S.



… AND AGE IS THE BIGGEST RISK FACTOR FOR ALZHEIMER'S …

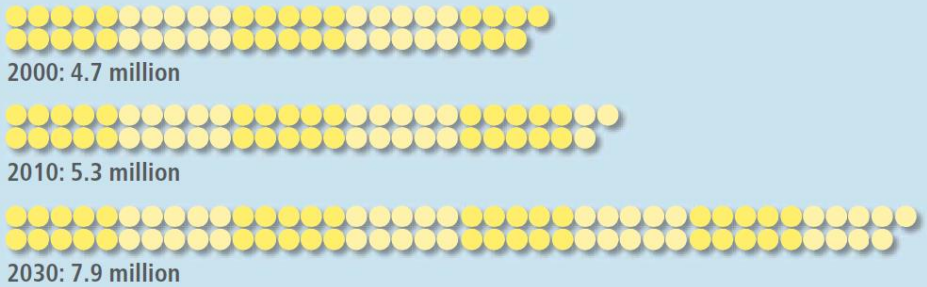
Risk of developing Alzheimer's at a given age over the next 10 years, for males and females.



… SO THE NUMBER OF CASES IS GROWING

Numbers of people diagnosed with Alzheimer's will increase by nearly 50 percent during the next 20 years.

1 dot represents 100,000 people diagnosed with Alzheimer's.



Scientific American (June 2010) *Alzheimer's:* **Forestalling the Darkness**

EARLY ONSET:

Memories begin failing in one's 40s, occasionally as early as 32.

By 47, on average, full-blown Alzheimer's develops.

New York Times, The Vanishing Mind 2010

THE VANISHING MIND

Alzheimer's Stalks a Colombian Family

The New York Times

YARUMAL, Colombia — Tucked away on a steep street in this rough-hewn mountain town, an old woman found herself diapering her middle-age children.

At frighteningly young ages, in their 40s, four of Laura Cuartas's children began forgetting and falling apart, assaulted by what people here have long called La Bobera, the foolishness. It is a condition attributed, in hushed rumors, to everything from touching a mysterious tree to the revenge of a wronged priest.

It is Alzheimer's disease, and at 82, Mrs. Cuartas, her gray raisin of a face grave, takes care of three of her afflicted children.

One son, Darío, 55, babbles incoherently, shreds his socks and diapers, and squirms so vigorously he is sometimes tied to a chair with baggy blue shorts.

A daughter, María Elsy, 61, a nurse who at 48 started forgetting patients' medications, and whose rages made her attack a sister who bathed her, is a human shell, mute, fed by nose tube.

Another son, Oderis, 50, denies that his memory is dying, that he remembers to buy only one thing at a time: milk, not milk and plantains. If he gets Alzheimer's, he says, he will poison himself.

"To see your children like this ... ," Mrs. Cuartas said. "It's horrible, horrible. I wouldn't wish this on a rabid dog. It is the most terrifying illness on the face of the earth."

For generations, the illness has tormented these and thousands of others among a sprawling group of relatives: the world's largest family to experience Alzheimer's disease. Now, the Colombian clan is center stage in a potentially groundbreaking assault on Alzheimer's, a plan to see if giving treatment before dementia starts can lead to preventing Alzheimer's altogether.

Most family members come from one Andes region, Antioquia. Geography, and Basque ancestry, have isolated people here, who call themselves paisas, countrymen. Over three centuries, many in this clan of 5,000 people have inherited a single genetic mutation guaranteeing that they will develop Alzheimer's.

Large families, and intermarriage, have accelerated the spread. Mrs. Cuartas's fourth debilitated child, in Medellín, Carlos Alberto Villegas, a former livestock trader and guitar serenade her now often fed by baby bottle, married a distant cousin. His mother-in-law is an addled ghost; three of his wife's 11 siblings, so far, are developing dementia.

With Alzheimer's in both parents' families, Mr. Villegas's three children could face extraordinary risk. One, Natalia, 22, asks: "How long have I got, till I'm 35? There's no way out."

Memories begin failing in one's 40s, occasionally as early as 32. By 47, on average, full-blown Alzheimer's develops.

Their form of Alzheimer's, early-onset, was once considered too different to provide clues about far more common late-onset Alzheimer's, which has unknown causes and primarily affects people over 65.

But it turns out that both forms produce nearly identical brain changes and symptoms. Now, scientists will test as-yet-unproven treatments on Colombians genetically destined for Alzheimer's but not yet showing symptoms. They will give a to-be-determined drug or vaccine and see if it prevents memory loss or brain atrophy. If their disease can be halted, that could generate treatments to protect millions worldwide from common Alzheimer's.

Devising an Early Attack

Alzheimer's has repeatedly resisted attempts to treat it. Current drugs, for people who are already impaired, show little benefit. Now scientists want to attack earlier. New findings show "the brain is badly damaged by the time they have dementia," said Dr. John C. Morris, an Alzheimer's researcher at Washington University in St. Louis. "Perhaps the reason our therapies have been ineffective or mostly ineffective is that we're administering them too late."

With Alzheimer's afflicting 5-3 million Americans and 30 million people worldwide, numbers that some predict will double or triple by 2050, "we can't wait to try to do prevention until we are absolutely certain what causes" the disease, said Neil Buckholtz, chief of dementias of aging at the National Institute on Aging. "This public health emergency," he said, is "just going to get out of control if we don't do something."

But preventive research is difficult. Participants should be people guaranteed, or highly likely, to develop dementia, and with common Alzheimer's identifying such people is challenging because the disease's cause is

Over three centuries, many in this lineage of 5,000 people have inherited a single genetic mutation guaranteeing that they will develop Alzheimer's.

New York Times, The Vanishing Mind 2010

A Clouded Inheritance

A group of 25 families in Colombia has inherited a genetic mutation from common ancestors, making members prone to early-onset Alzheimer's.

At right, Alzheimer's cases among the founding members of the clan and some of their early descendants, who number in the thousands today.

KEY

- *No Alzheimer's*
- *Suspected cases*
- *Known cases*

Javier San Pedro Gómez
Lived into his 70s

María Luisa Chavarriaga Mejía
Suspected carrier of the Paisa mutation

Born circa 1745

Mauricio
Common ancestor of Carlos Alberto and Blanca Nelly

1770

1790

1810

1850

1890

1910

PAISA MUTATION
The inherited disease is caused by a mutation of the presenilin 1 gene on chromosome 14.

Note: the chart has been simplified and does not show all children or descendants.

TODAY Carlos Alberto Villegas, his wife and their siblings descend from a common ancestor, circled above, who had the Paisa mutation.

Carlos Alberto, 53. *Onset of memory problems at 41.*

María Elsy, 61 (his sister) *48 at onset.*

Darío, 55 (his brother) *47 at onset.*

Oderis, 50 (his brother) *46 at onset.*

Blanca Nelly, 41 (his wife) *Currently no symptoms.*

William, 48 (her brother) *45 at onset.*

Gladys, 36 (her sister) *Too afraid to have childen.*

Liliana, 29 (her sister) *Terrified of any memory lapse.*

Two sisters show early symptoms but deny it.

Source: University of Antioquia

New York Times, The Vanishing Mind 2010

THE NEW YORK TIMES

The New York Times

Health

The Vanishing Mind

In the mountains of northwest Colombia, many members of a sprawling extended family suffer from a genetic mutation that makes them begin to forget in their early 40s. | Related Article

New York Times, The Vanishing Mind 2010

eFAD	• Early onset familial Alzheimer disease
family	• Dominant genetic trait • One parent had eFAD • Siblings: 50%
same, (mostly)	• eFAD and late-onset AD is essentially the same disease

60 years

early onset

late onset

95%

genetic

sporadic

eFAD	late onset familial
EOAD sporadic	late onset sporadic

Early-Onset Alzheimer Disease in Families With Late-Onset Alzheimer Disease

A Potential Important Subtype of Familial Alzheimer Disease

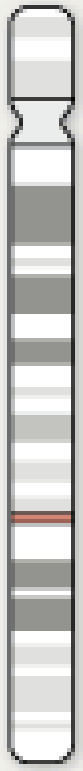
Kiri L. Brichell, MBChB; Ellen J. Steinbart, RN, MA; Malia Rumbaugh, MS, CGC; Haydeh Payami, PhD; Gerard D. Schellenberg, PhD; Vivianna Van Deerlin, MD, PhD; Wuxing Yuan, MS; Thomas D. Bird, MD

autosomal dominant forms (eFAD)

amyloid precursor protein (APP) Chromosome 21	presenilin-1 (PS1) Chromosome 14	presenilin-2 (PS2) Chromosome 1

Accounts for most eFAD

Members of 25 extended families, with 5,000 members, develop early-onset Alzheimer's, usually before the age of 50, if they harbor an aberrant version of a particular gene.



PAISA MUTATION
The inherited disease is caused by a mutation of the presenilin 1 gene on chromosome 14.

New York Times, The Vanishing Mind 2010

12 to 15 fold increase risk for AD

Not autosomal dominant (ApoE) ApoE4	ApoE4 is thought to lower the age of onset by a decade

lessons	• eFAD • Test drugs before symptoms
drugs	• Many recent drug candidates have failed in trials. • Perhaps because the drugs were given too late.
memory	• When a person loses their memory – it is too late. • The disease has been present for a long time by the time there are symptoms.
lifestyle	• Preventative or delay strategies.

Francisco Lopera

Scientific American (June 2010)
Alzheimer's: **Forestalling the Darkness**

Treatment plan eFAD

Delay or stop Assessing treatment by tracking AD specific biomarkers.	Administered 7 years before average age of diagnosis	Alzheimer's Prevention Initiative

Amyloid accretion

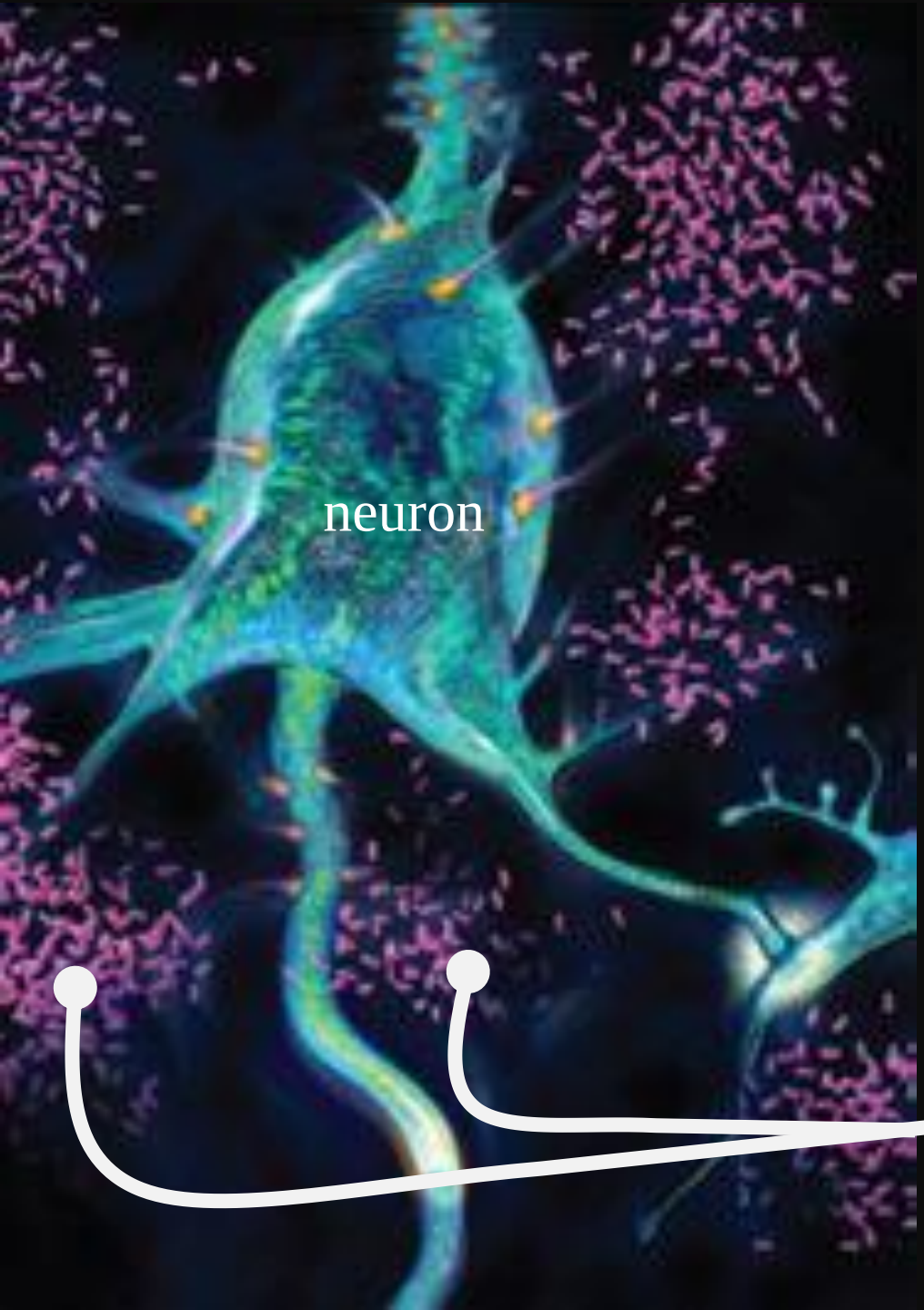
- 5 – 20 years before diagnosis of Alzheimer's dementia
- damages synapses

Tau buildup

- 1 – 5 years before diagnosis
- Tau protein detaches from the microtubules.

Brain shinkage

- 1 – 3 years before diagnosis
- Cell death shrinks the brain.



Amyloid Accretion
5–20 years before diagnosis of Alzheimer's dementia

Scientific American (June 2010)
Alzheimer's: **Forestalling the Darkness**

Scientific American (June 2010)
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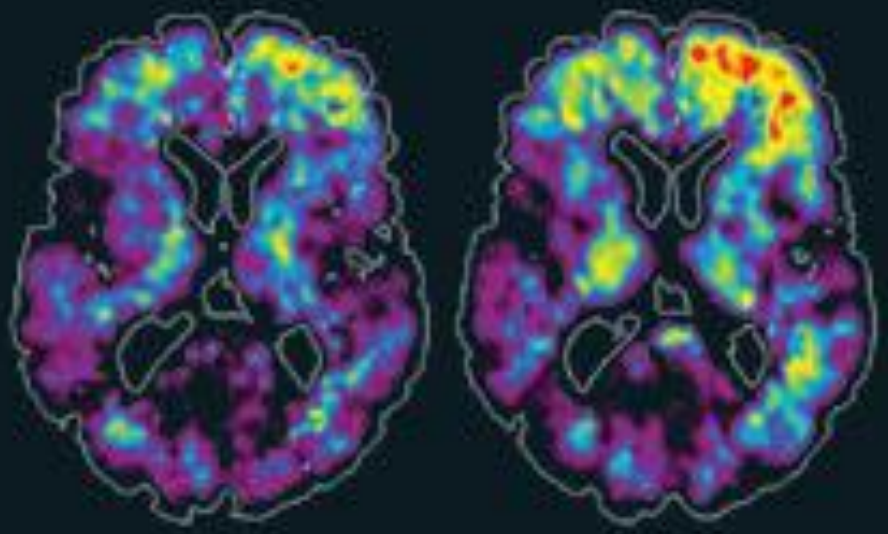
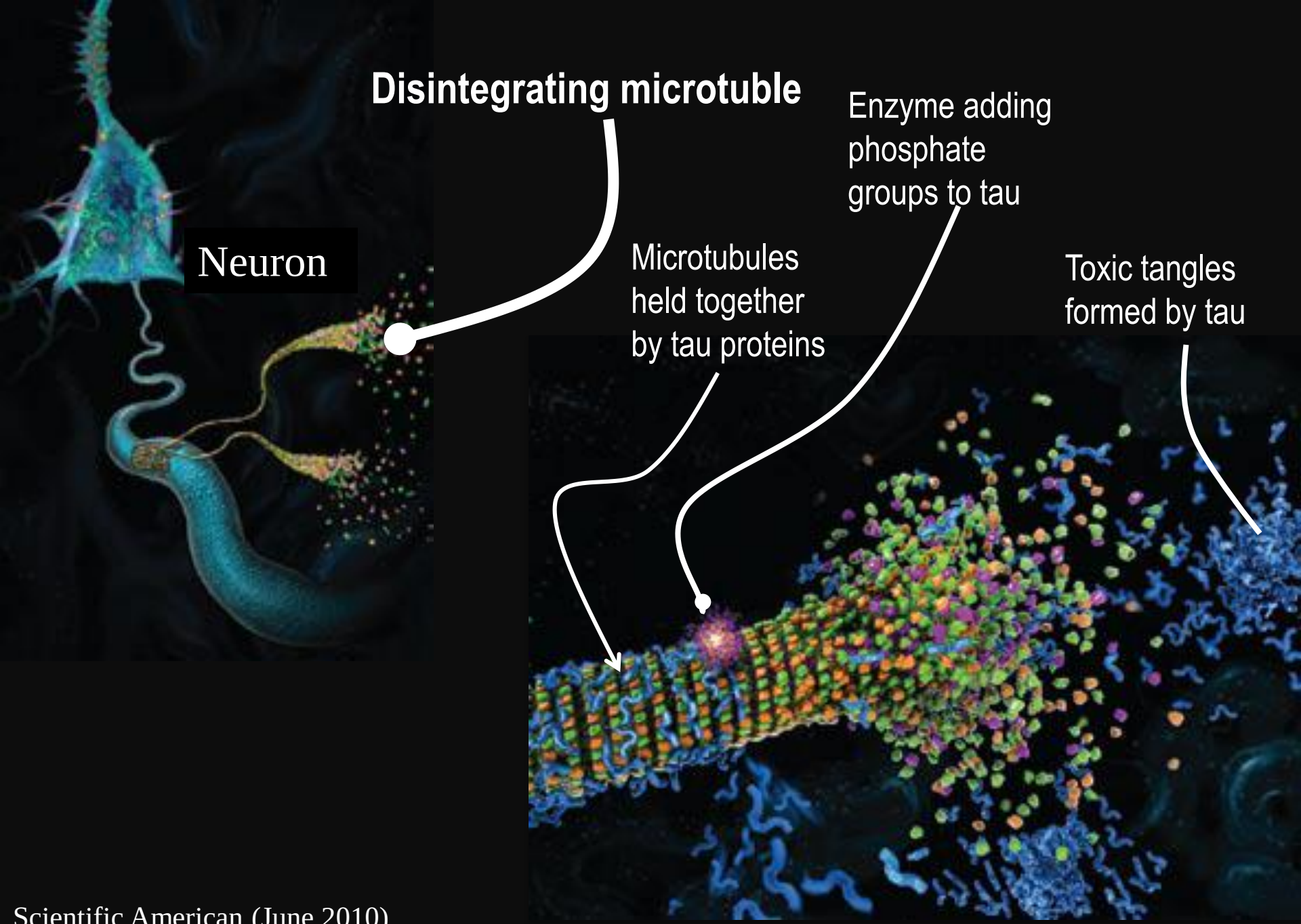
Baseline 24 months



PET scans show increasing retention in the brain's frontal lobes of the amyloid-beta tracer Pittsburg imaging compound-B (PIB) over the course of two years in a 74-year-old, even while the subject remained cognitively normal.

Scientific American (June 2010)
Alzheimer's: **Forestalling the Darkness**



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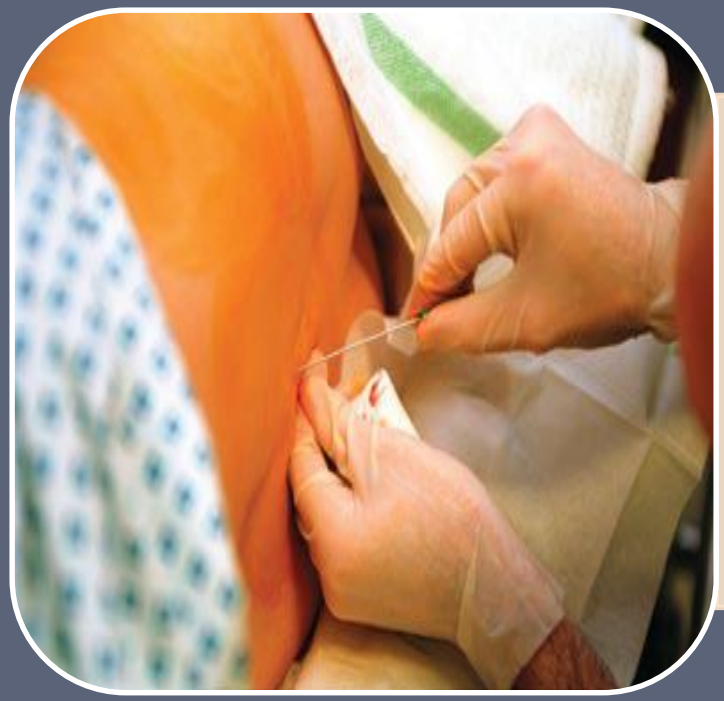
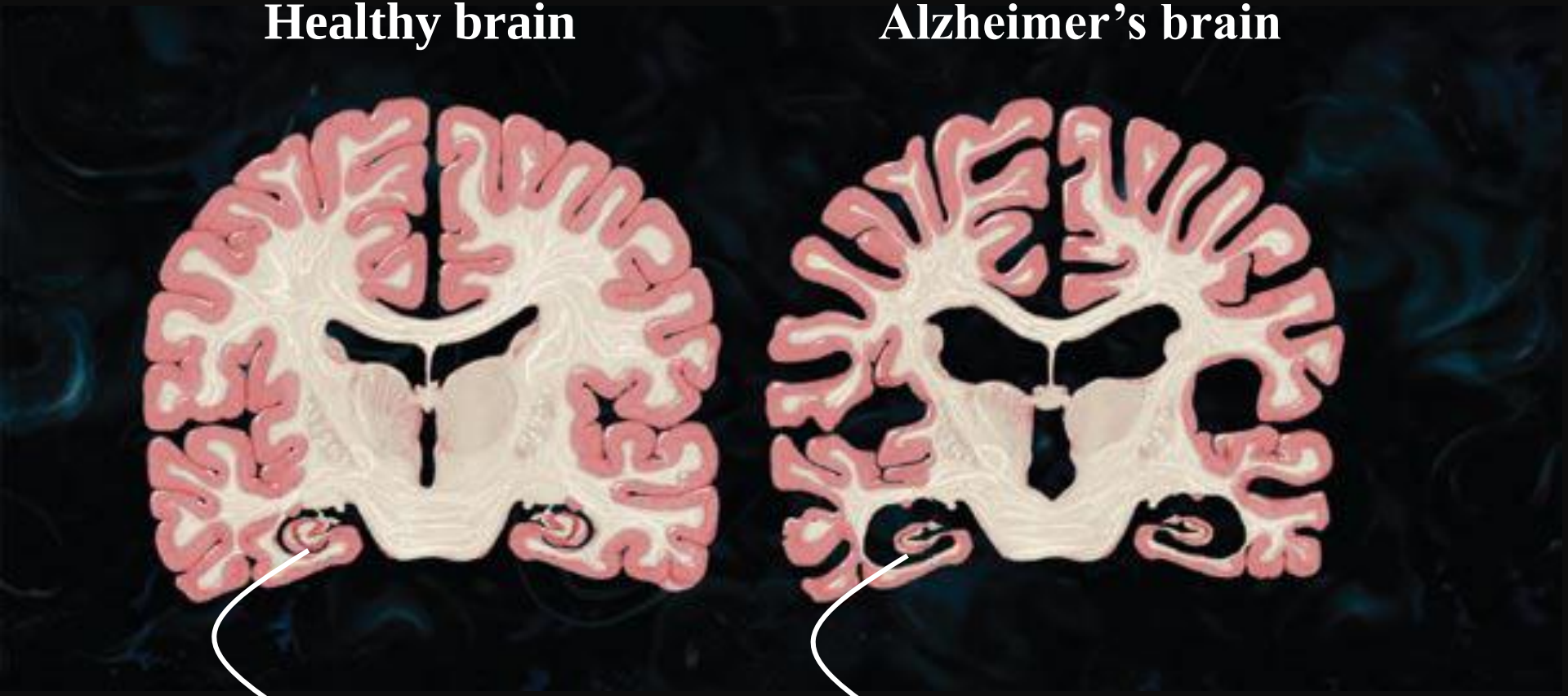


- Spinal tap
- Measures levels of tau protein



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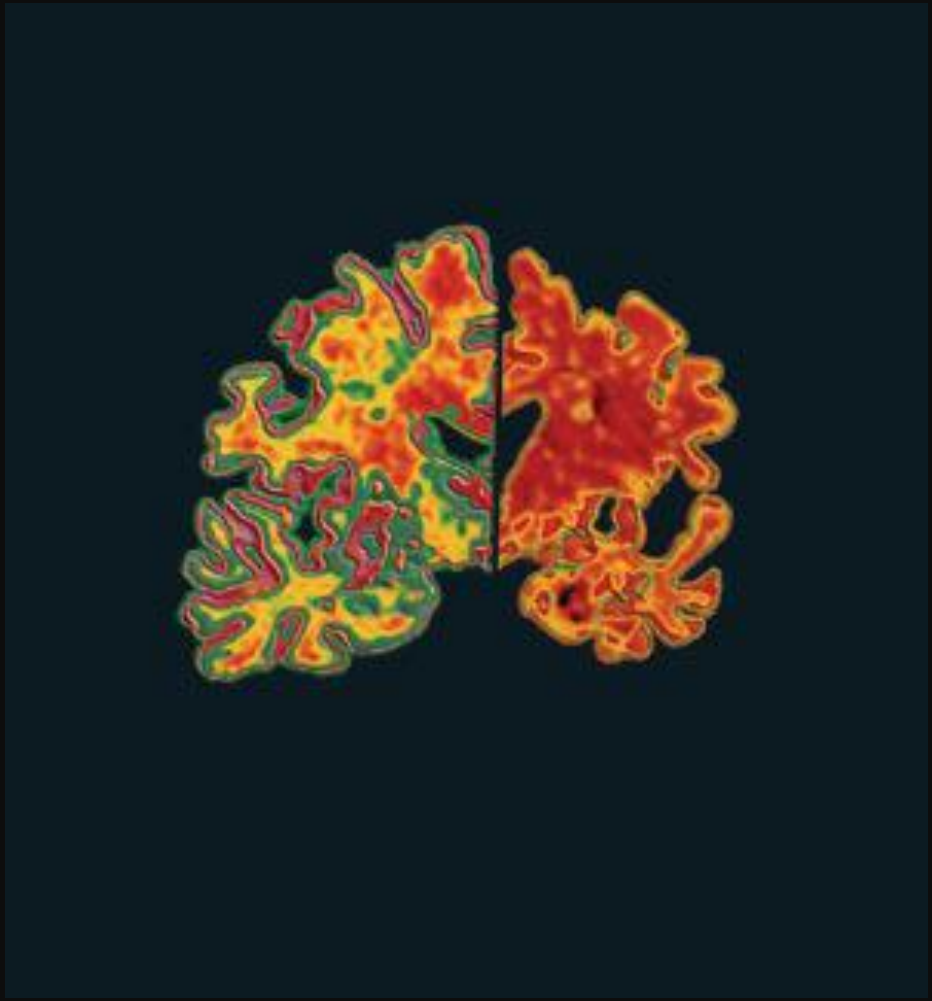


Computer graphic of slices through a normal brain and an Alzheimer's brain, derived from volumetric magnetic resonance imaging, shows considerable shrinkage (*right) from* degeneration and death of nerve cells.

Scientific American (June 2010)
Alzheimer's: **Forestalling the Darkness**

data biomarker

correlate with Cognitive Improvement

Does changing amyloid beta levels really improve cognition?

One needs to apply a cognitive test along with a biomarker measure in order to make sure that the treatments are helping.

Inhibitors of enzymes that produce amyloid-beta

Enzymes are involved in precursor steps

Vaccines/Antibodies

Vaccines induce the body to produce antibodies that bind to amyloid and clear them from the brain.

Amyloid-beta aggregation blockers

Agents that prevent amyloid fragments from clumping could prevent damage to neurons

Anti-tau compounds

Blocking production of the toxic form of the tau protein

Or

Impeding its aggregation into tangles

Review TRENDS in Neurosciences Vol.24 No.4 April 2001

Targeting small Aβ oligomers: the solution to an Alzheimer's disease conundrum?

William L. Klein, Grant A. Krafft and Caleb E. Finch

Amyloid β (Aβ) is a small self-aggregating peptide produced at low levels by normal brain metabolism. In Alzheimer's disease (AD), self-aggregation of Aβ becomes rampant, manifested most strikingly as the amyloid fibrils of senile plaques. Because fibrils can kill neurons in culture, it has been argued that fibrils initiate the neurodegenerative cascades of AD. An emerging and different view, however, is that fibrils are not the only toxic form of Aβ, and perhaps not the neurotoxin that is most relevant to AD: small oligomers and protofibrils also have potent neurological activity. Immuno-neutralization of soluble Aβ-derived toxins might be the key to optimizing AD vaccines that are now on the horizon.

Klein, W. L. et al (2001), TINS, Vol.24 No.4

Atomic force microscopy of amyloid-β_{1-42} forms.

Aβ-derived diffusible ligands

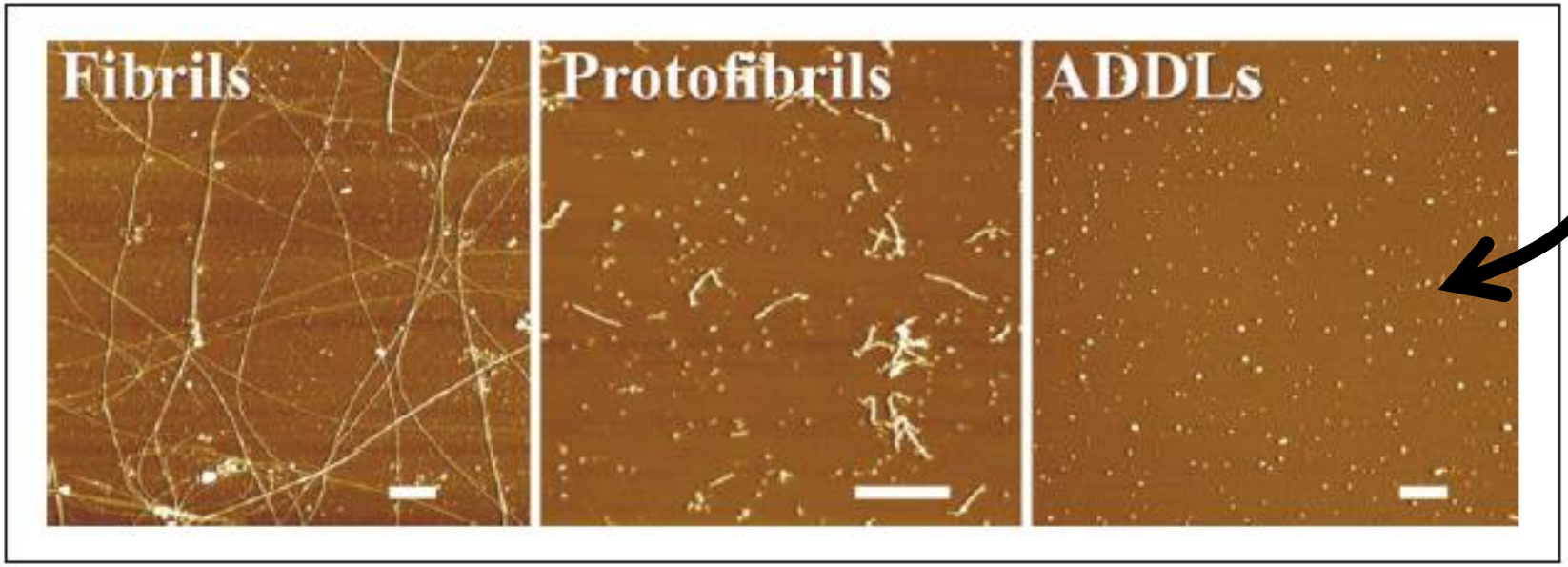
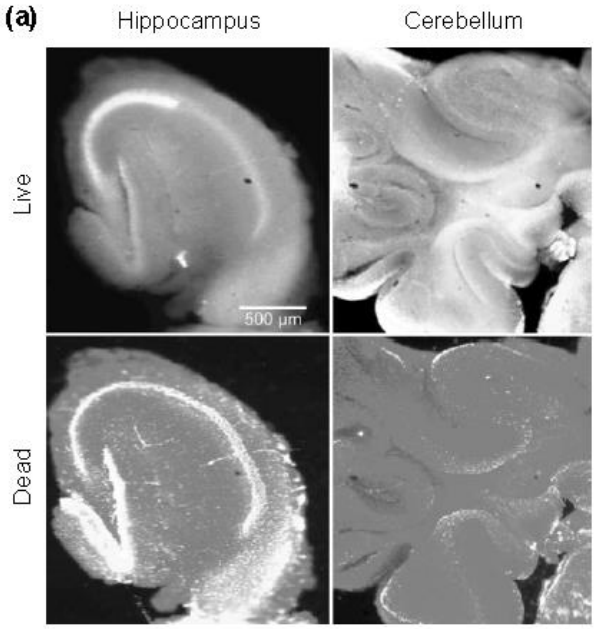


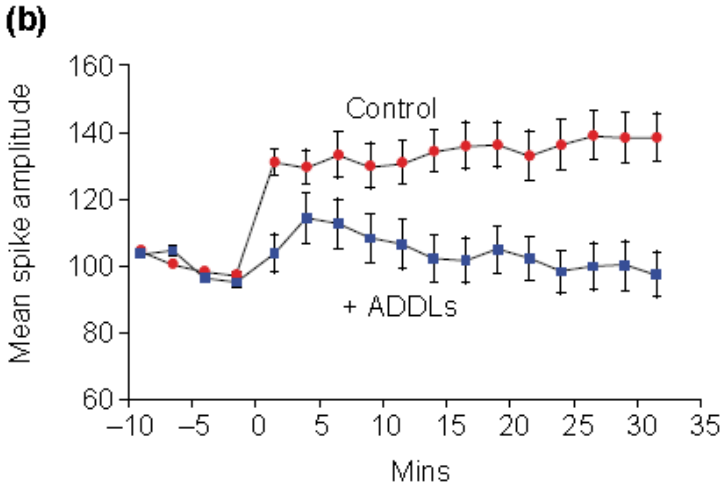
Fig. 1. Different assembled states of amyloid β_{1-42} ($A\beta_{1-42}$). The assembled forms obtained from incubation of synthetic $A\beta_{1-42}$ are highly sensitive to preparation and incubation[10]. Widely differing proportions of insoluble fibrils, soluble protofibrils (PFs) and oligomers are revealed by atomic force microscopy[11]. Typical PF and fibril preparations contain varying levels of small globular molecules, putatively $A\beta_{1-42}$ oligomers; Aβ-derived diffusible ligand (ADDL) preparations initiated from monomeric dimethyl sulphoxide stock solutions are fibril- and PF-free, and (uniquely) comprise oligomers. Scale bar, 200 nm. Fibril, PF and ADDL preparations all show neurotoxicity *in vitro*. Courtesy of Brett Chromy and Blaine Stine.

Klein, W. L. et al (2001), TINS, Vol.24 No.4



(a) ADDLs are potent neurotoxins that slowly kill hippocampal neurons in mature brain slice preparations. With the live–dead dual fluorescence assay, **ADDLs selectively induce death in hippocampal CA1 neurons**, whereas a subpopulation of CA3 neurons and cerebellar neurons are resistant.

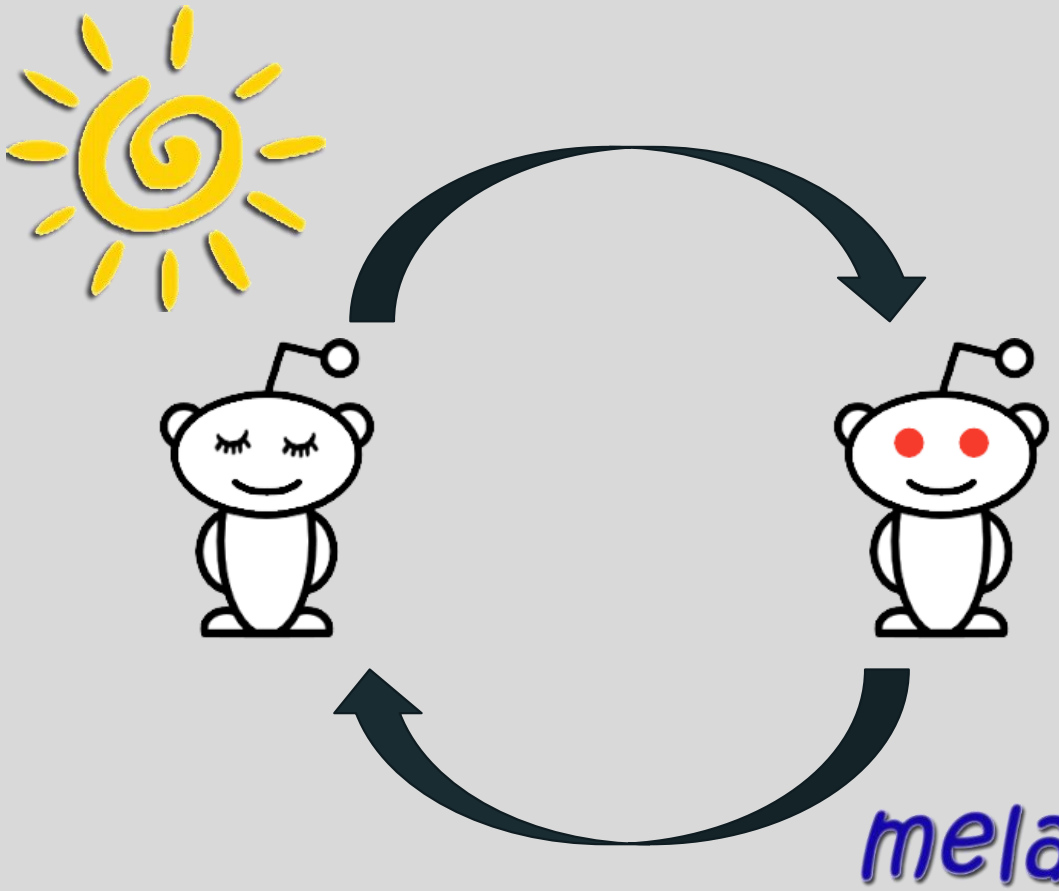
(b) ADDLs block LTP in hippocampal slice within 1 hr. In vivo stereotaxic injections give similar results. As seen here, ADDLs do not block pre-tetanic population spikes, nor do they inhibit EPSPs or LTD



Klein, W. L. et al (2001), TINS, Vol.24 No.4

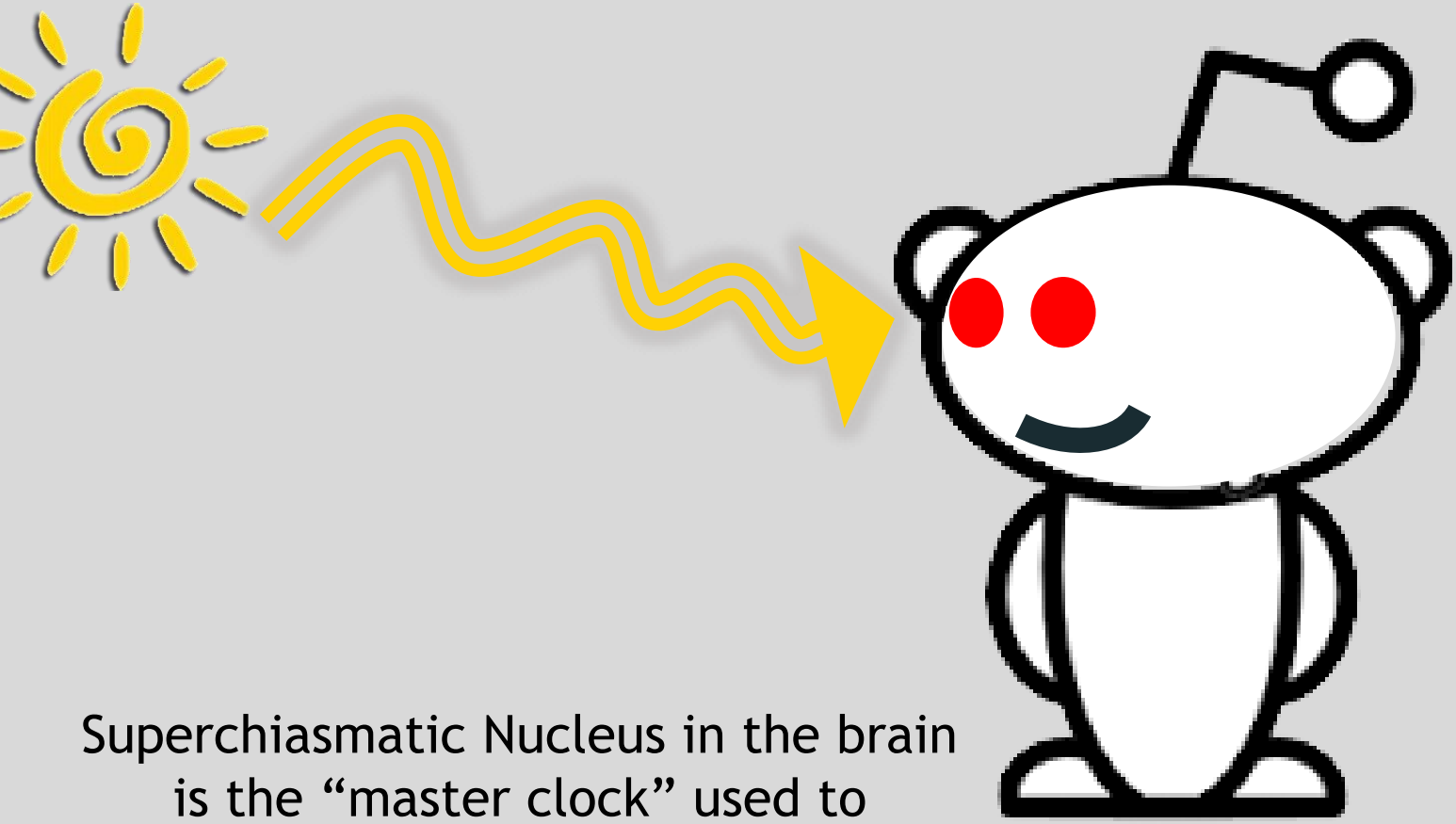
What Causes Alzheimer's?

- Scientists are still not certain.
- Age and family history have been identified as potential risk factors.
- Researchers are exploring the role of genetics.
- Diabetes?
- Sleep problems?

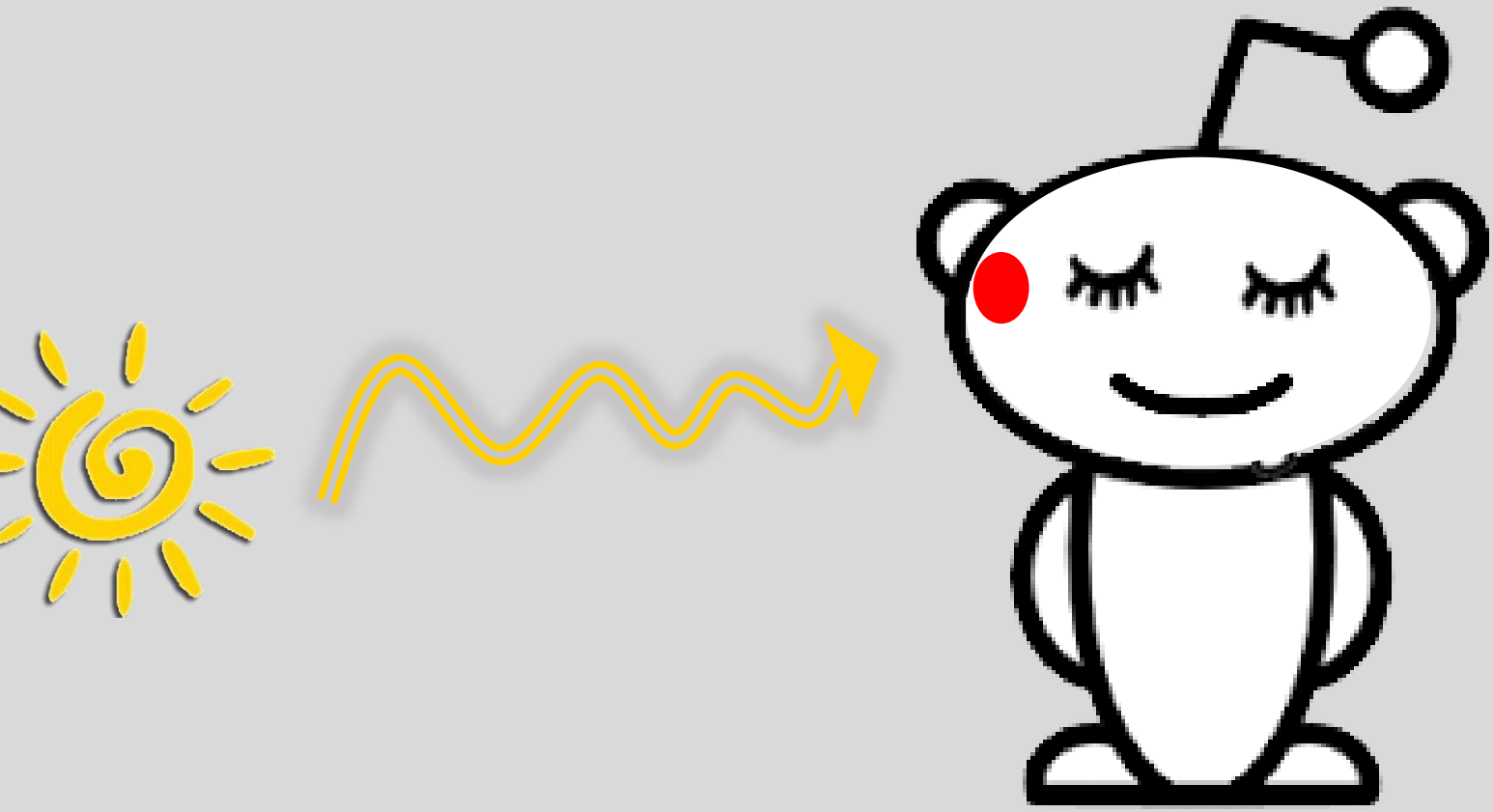


Light & Melatonin are the two most influential external cues that synchronize the circadian rhythm

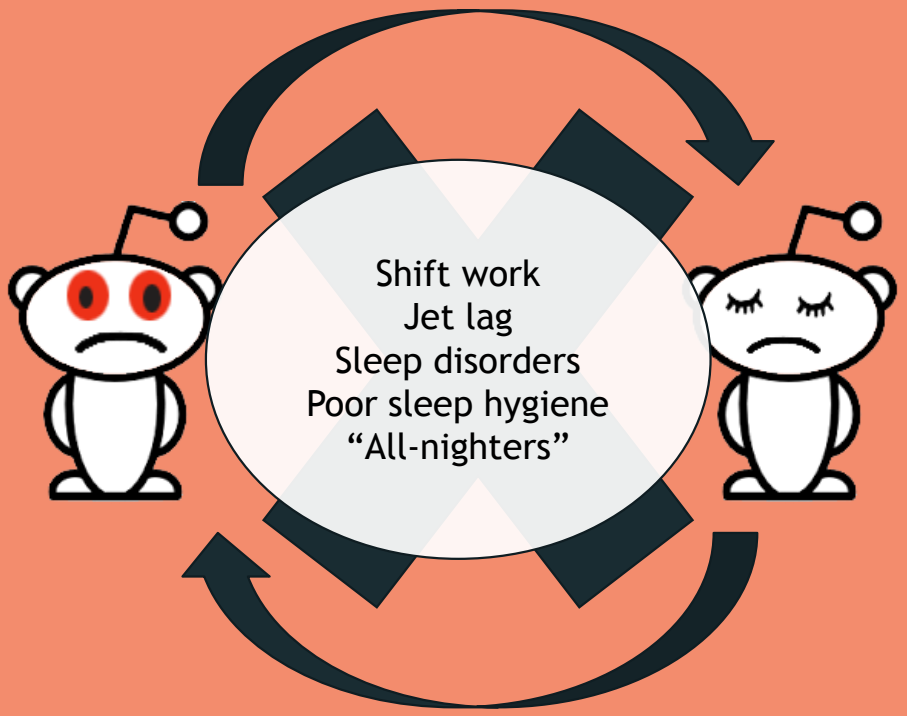
Sleep wake cycle is regulated by the circadian system.



Superchiasmatic Nucleus in the brain is the “master clock” used to coordinate and synchronize most of the body clocks in the periphery.



melatonin



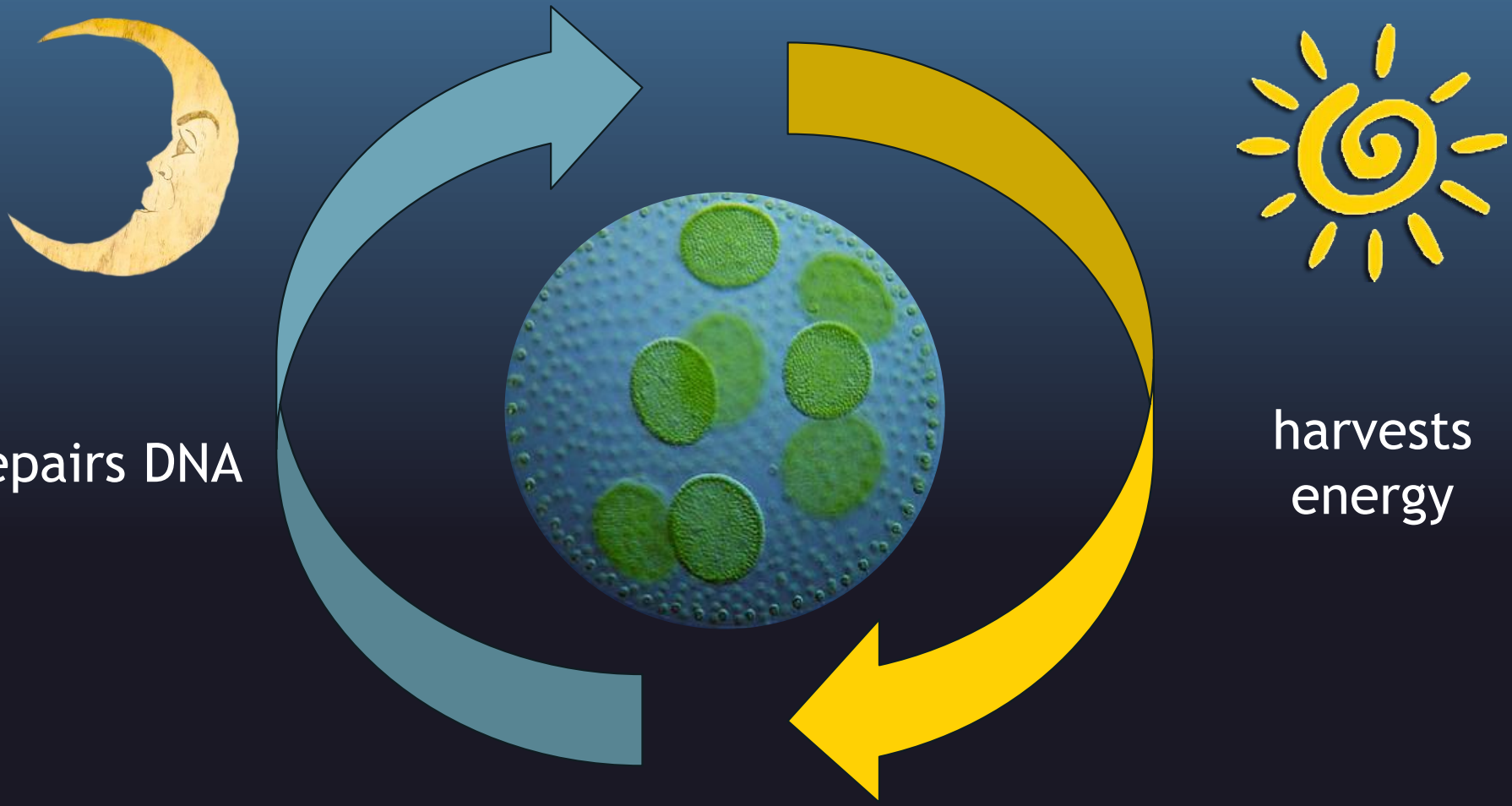
metabolic disruption

weight gain, obesity

impaired immunity

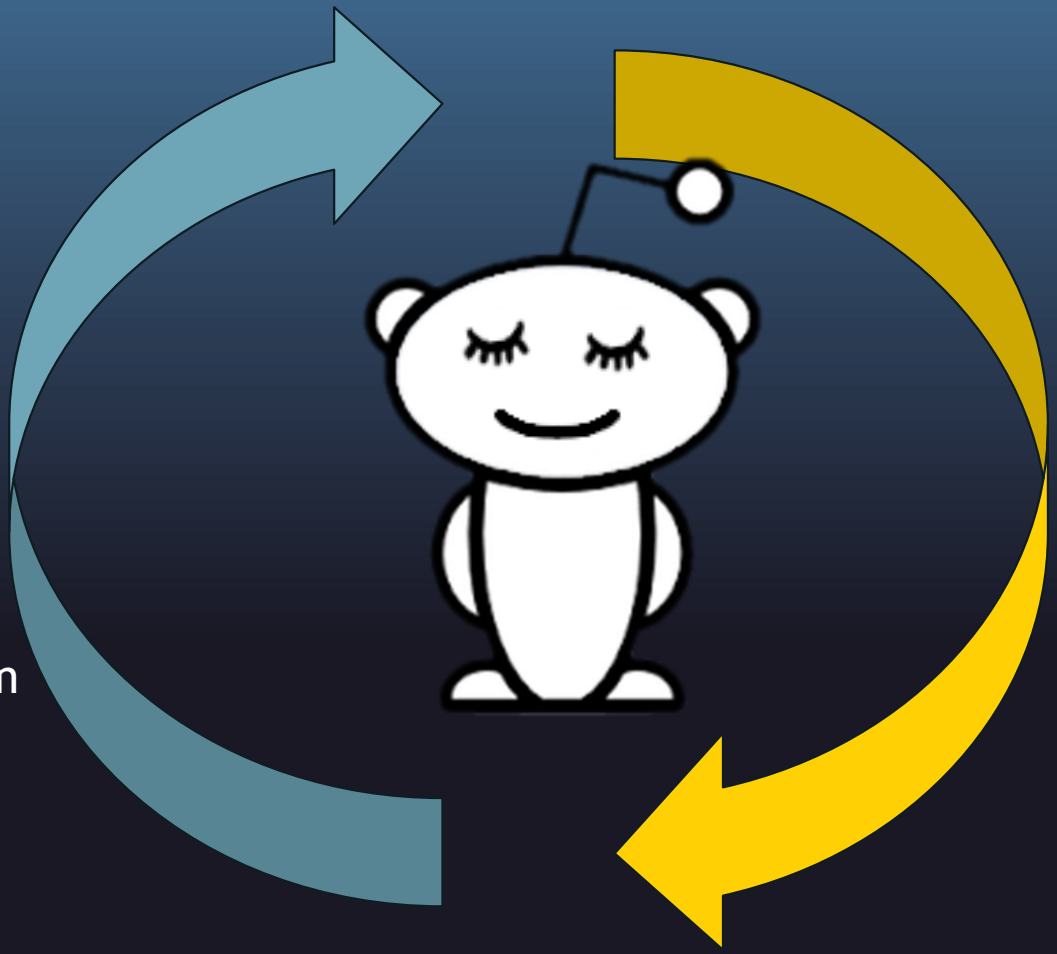
cognitive malfunction

If the sleep wake cycle is disrupted it can cause metabolic dysregulation



Cyanobacteria is a photoautotropic organism that has a self-sustained circadian rhythm

- Fasting
- Release of hormones
- Immune system activity
- Resting



Eating

Exercising

Thinking

Working

Our metabolic clocks are based on the diurnal rhythm – it is in our genes.

Shift workers are more prone to developing metabolic disorders

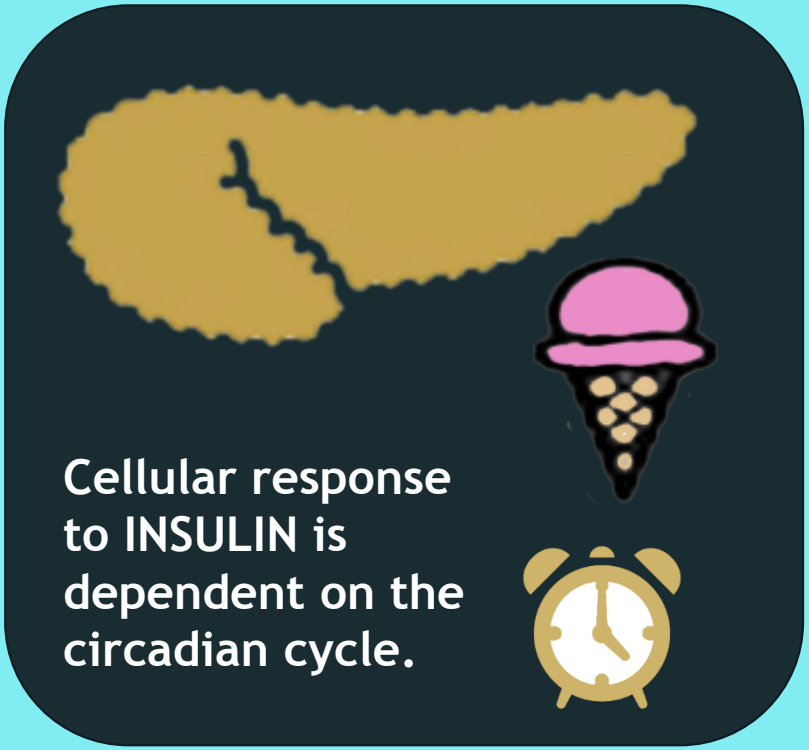
40% more likely to have: cardiovascular disease

Higher incidence of Diabetes Type II

Higher risk of cancer – melatonin disruption

Puttonen S, Härmä M, Hublin C.Scand J Work Environ Health. 2010 Mar; 36(2):96-108. Epub 2010 Jan 20.
The Health Survey for England (2013);
Davis S, Mirick DK.Cancer Causes Control. 2006 May; 17(4):539-45.

SCN is not the only clock in the body



Time of eating has a huge effect on the liver and insulin efficacy

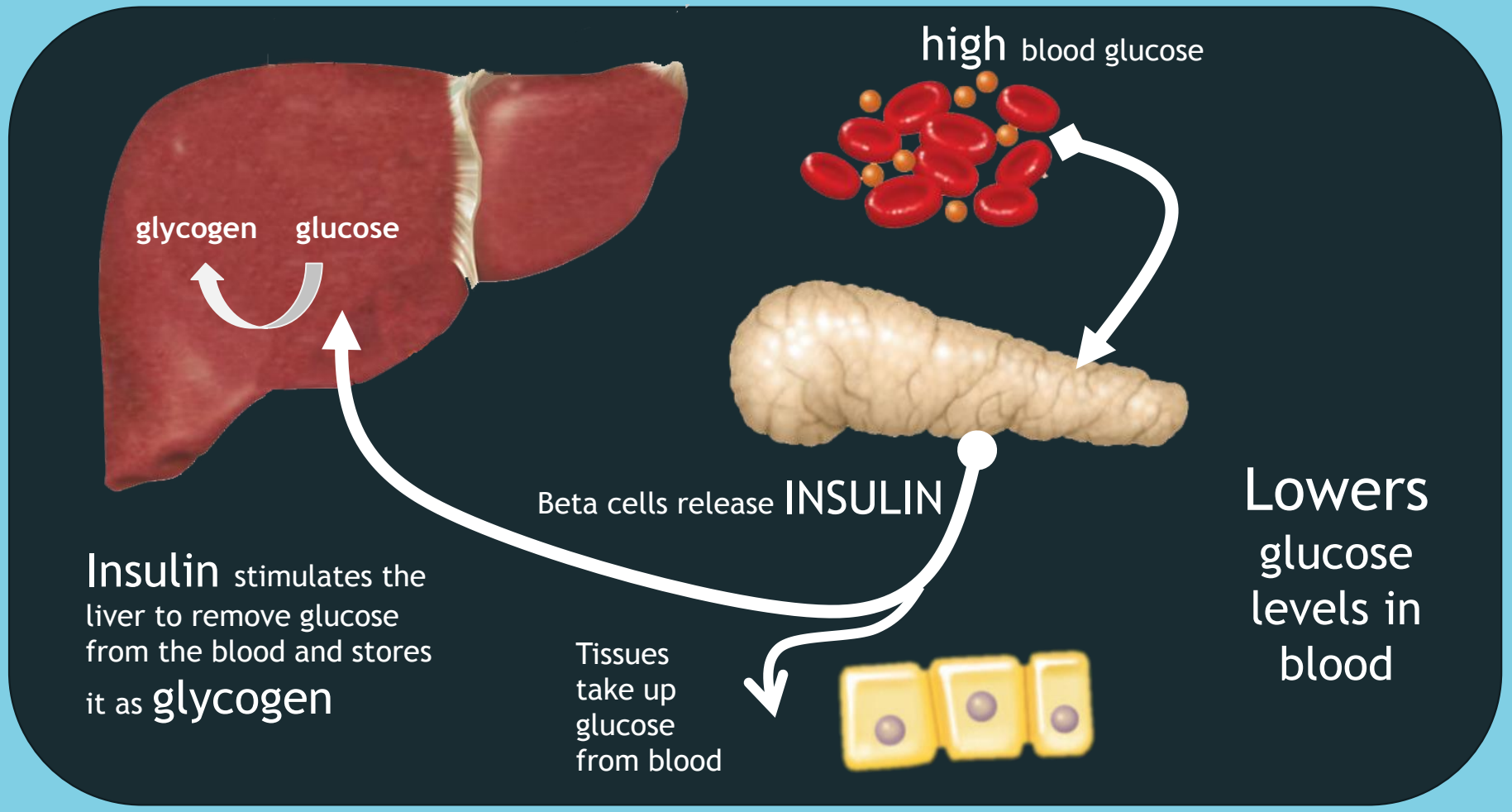


Figure adapted from Kaidanovich-Beilin, O. et al 20

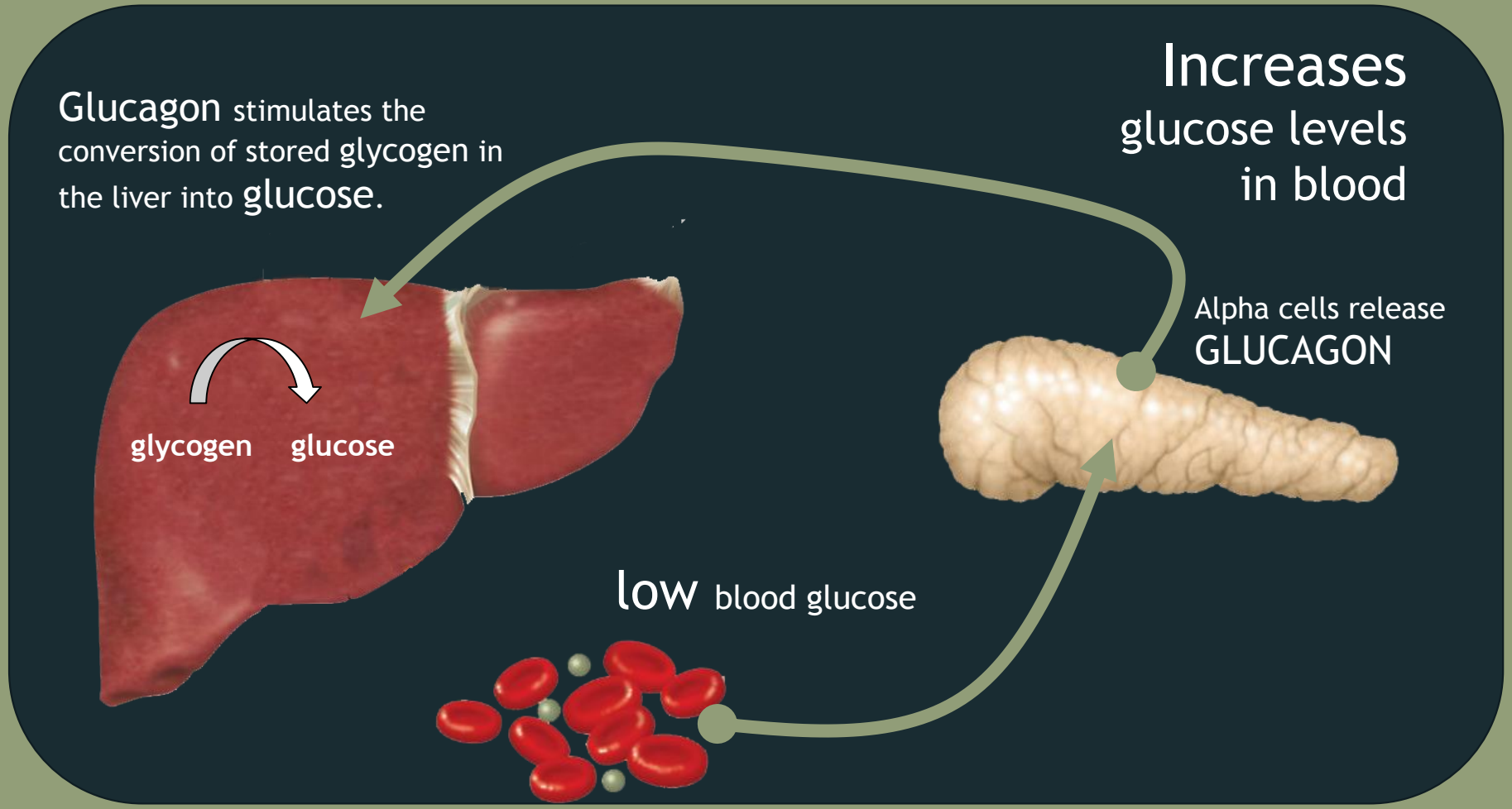
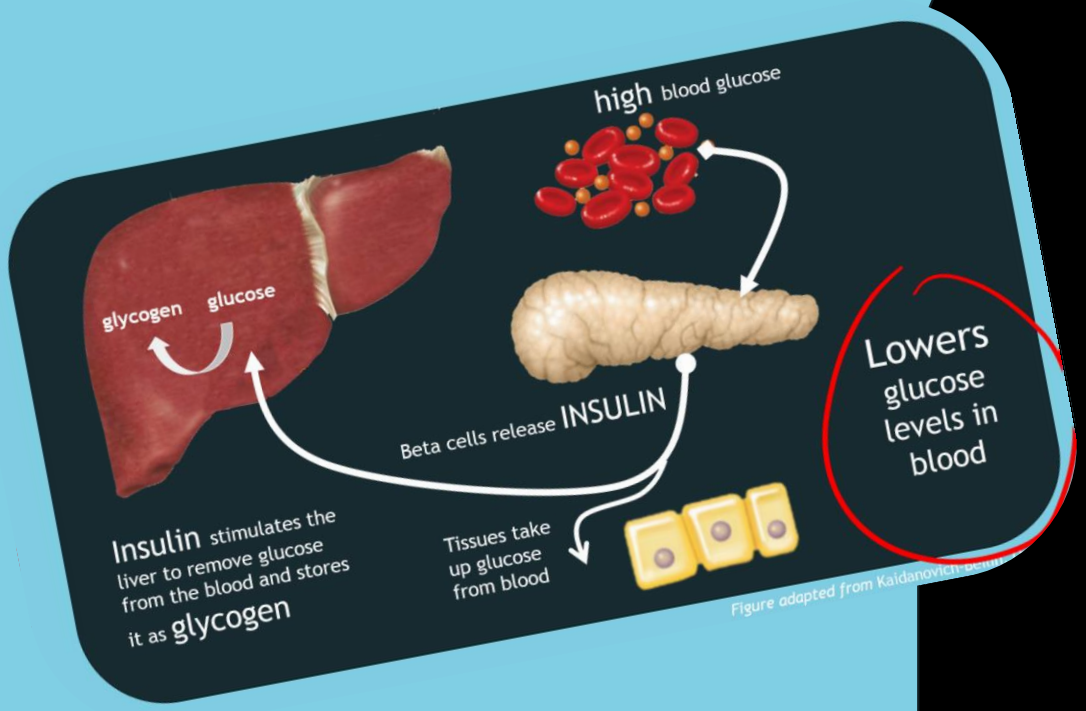


Figure adapted from Kaidanovich-Beilin, O. et al 2012

Insulin-sensitivity is dependent on the peripheral clock in muscle cells.

Glucose uptake in muscle is dependent on the circadian rhythm.



Insulin activates insulin receptors in the brain → affects feeding behaviors, reward, body metabolism, normal emotion & cognitive behaviors.

insulin receptors are found throughout the brain – cortex, midbrain and hypothalamus.

The risk of developing Alzheimer's disease is increased by 50 percent in people with diabetes.

Craft, S. Nat. Rev. Neurol. 8, 360–362 (2012);

Diabetes is a risk factor for dementia

J Neural Transm (1989) 75: 227–232

Journal of Neural Transmission

Cerebral excess release of neurotransmitter amino acids subsequent to reduced cerebral glucose metabolism in early-onset dementia of Alzheimer type

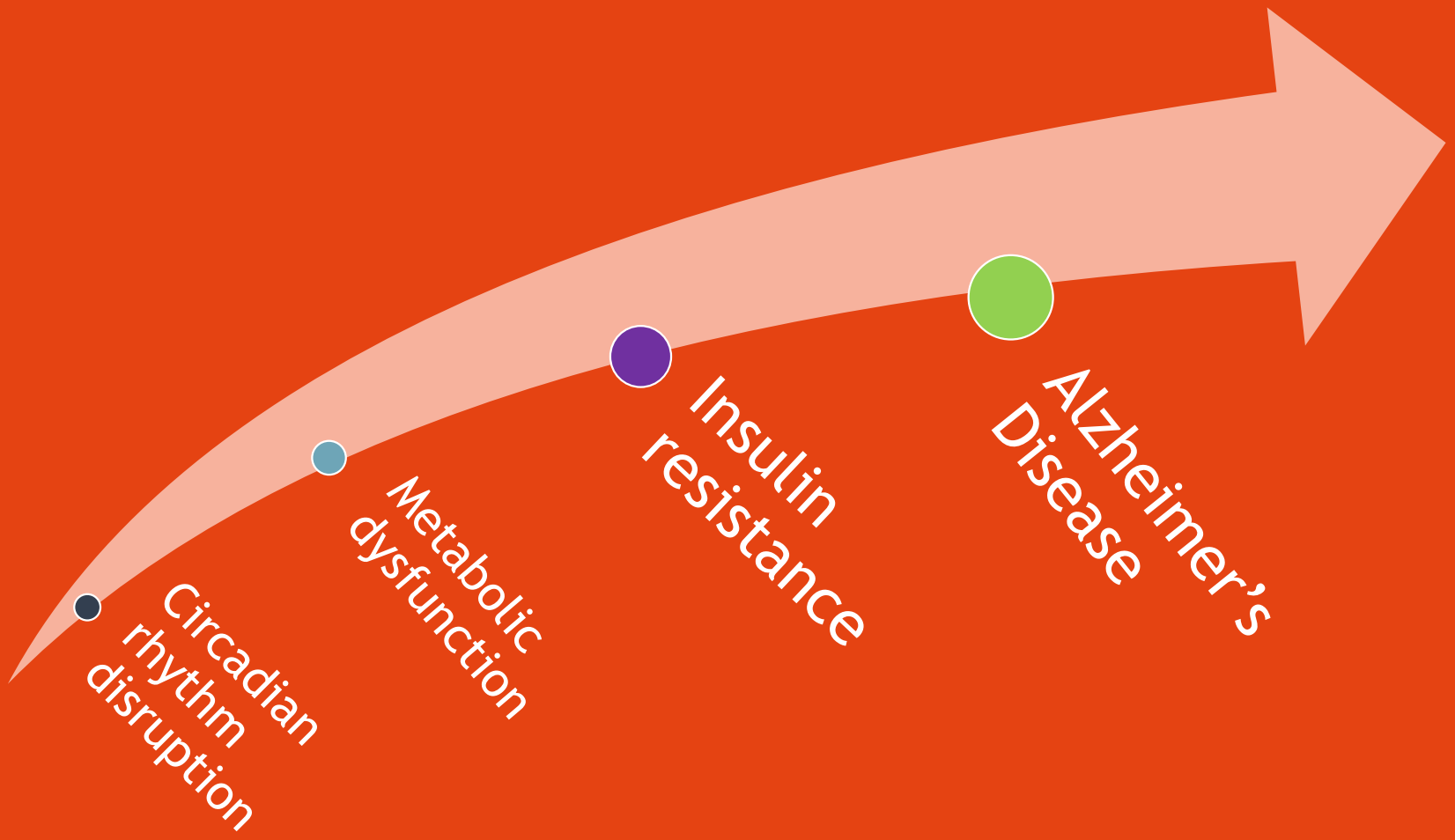
Short Note

S. Hoyer and **R. Nitsch**

Department of Pathochemistry and General Neurochemistry, University of Heidelberg, Heidelberg, Federal Republic of Germany

Accepted November 2, 1988

Summary. A massive cerebral release of amino acids and ammonia was found in early-onset dementia of Alzheimer type. Aspartate and glycine were liberated in high concentrations, whereas glutamate remained rather unchanged. This excess cerebral protein catabolism is due to a 44% reduction in cerebral glucose metabolism. Whereas glutamate and other glucoplastic amino acids may substitute glucose, elevated aspartate may contribute to neuronal damage. The results are discussed with respect to a possible neuronal insulin/insulin receptor deficiency.



Talbot, K. et al. J. Clin. Invest. 122, 1316–1338 (2012).

What's insulin got to do with it?

It is not just in the pancreas!

insulin	• Hormone helps store sugar and fat for energy – produced in pancreas.
Type 1 diabetes	• When body cannot produce enough insulin
Type 2 diabetes	• When body has inadequate insulin response
Type 3 diabetes?	• Neurodegenerative diseases? Alzheimer's, Parkinson's & Huntington's

Insulin receptors in the brain!

insulin

- Learning and memory
- Snort insulin → better recall
- Memory tasks → increases insulin levels

Suzanne de la Monte @ Brown University

- Does insulin have a part in Alzheimer's disease?
- Postmortem study – compare insulin receptors in AD and healthy control brains.

healthy brains had more insulin…

- Healthy brains had on average 4x higher insulin levels and 10x as many insulin receptors in the learning and memory regions of the brain

diabetics are…

- 2x more likely to develop AD
- 7x more likely to develop Huntington's disease
- 50% of Parkinson's patients have glucose metabolism dysfunction.

AD and T2D share:

- Demographic profiles
- Risk factors
- Clinical features
- biochemical features

Type 2 Diabetes – metabolic disorder

> 30 years of age

7% global population

Characterized by a relative insulin deficiency

Risk factors –high blood glucose, obesity, vascular disease, insulin resistance

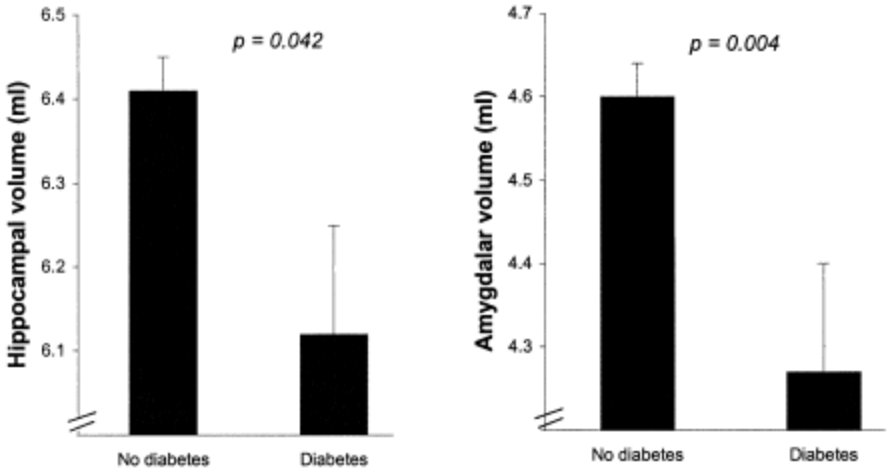
All of these factors, individually and collectively, increase the risk of AD and vascular dementia

Type 2 diabetes and atrophy of medial temporal lobe structures on brain MRI

T. den Heijer[1,2], S. E. Vermeer[1,2], E. J. van Dijk[1,2], N. D. Prins[1,2], P. J. Koudstaal[1,2], A. Hofman[1], M. M. B. Breteler[1]

[1] Department of Epidemiology and Biostatistics, Erasmus Medical Center, Rotterdam, The Netherlands
[2] Department of Neurology, Erasmus Medical Center, Rotterdam, The Netherlands

Diabetologia (2003) 46:1604–1610
DOI 10.1007/s00125-003-1235-0



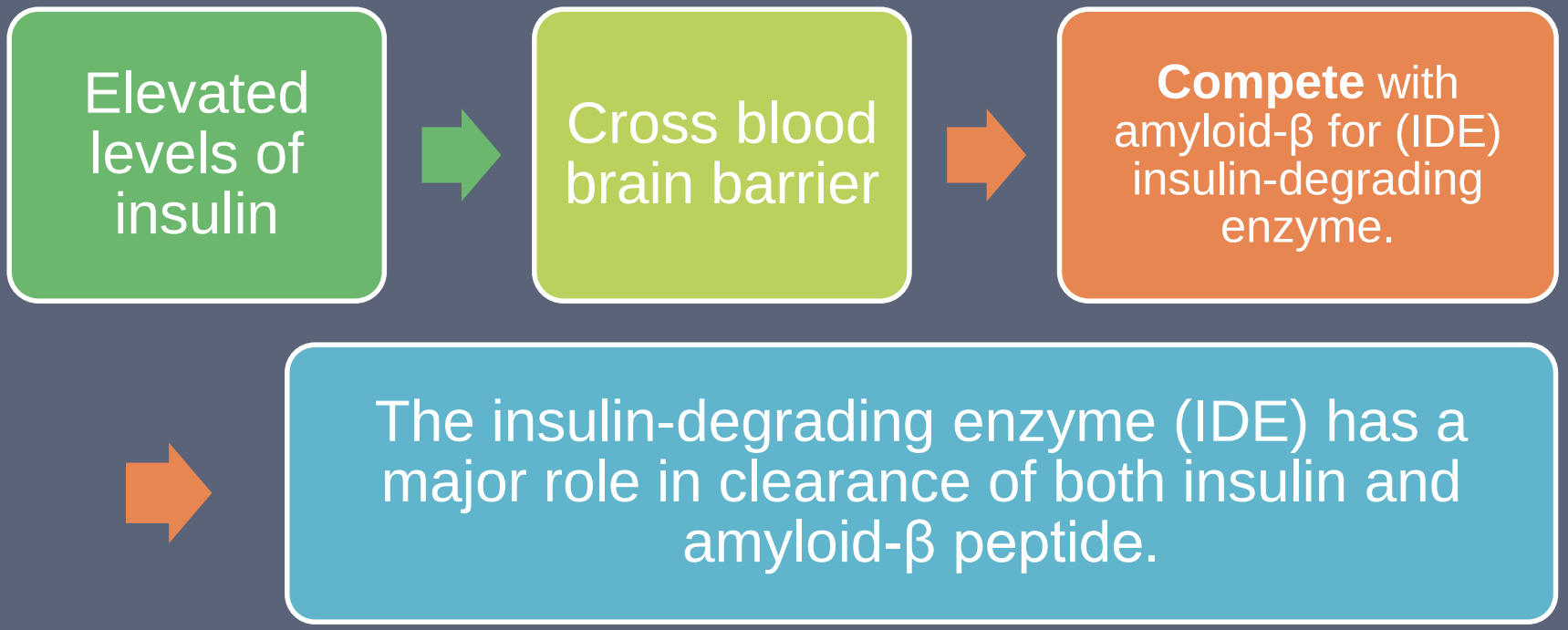
We observed that people with Type 2 diabetes had more hippocampal and amygdalar atrophy on MRI than people without diabetes. Moreover, in persons without diabetes mellitus, insulin resistance was associated to amygdalar atrophy on MRI. The presence of atherosclerosis or cerebrovascular disease did not explain the associations.

The strengths of our study are its population-based design and the large sample with volumetric MRI. The prevalence of diabetes mellitus in our study was comparable to another Dutch population study [27], leading to a moderate number of people with diabetes mellitus studied in the sample. However, the associa-

Fig. 2. Hippocampal volumes and amygdalar volumes (+standard error) on brain MRI in participants with diabetes (n=41) and without diabetes (n=465). Volumes are adjusted for age and sex and normalised to average head size

T. den Heijer, et al (2003)

Functional relationship between AD and type-2 diabetes (T2D)



Medical Hypotheses (2004) 62, 689–700

ELSEVIER

medical hypotheses

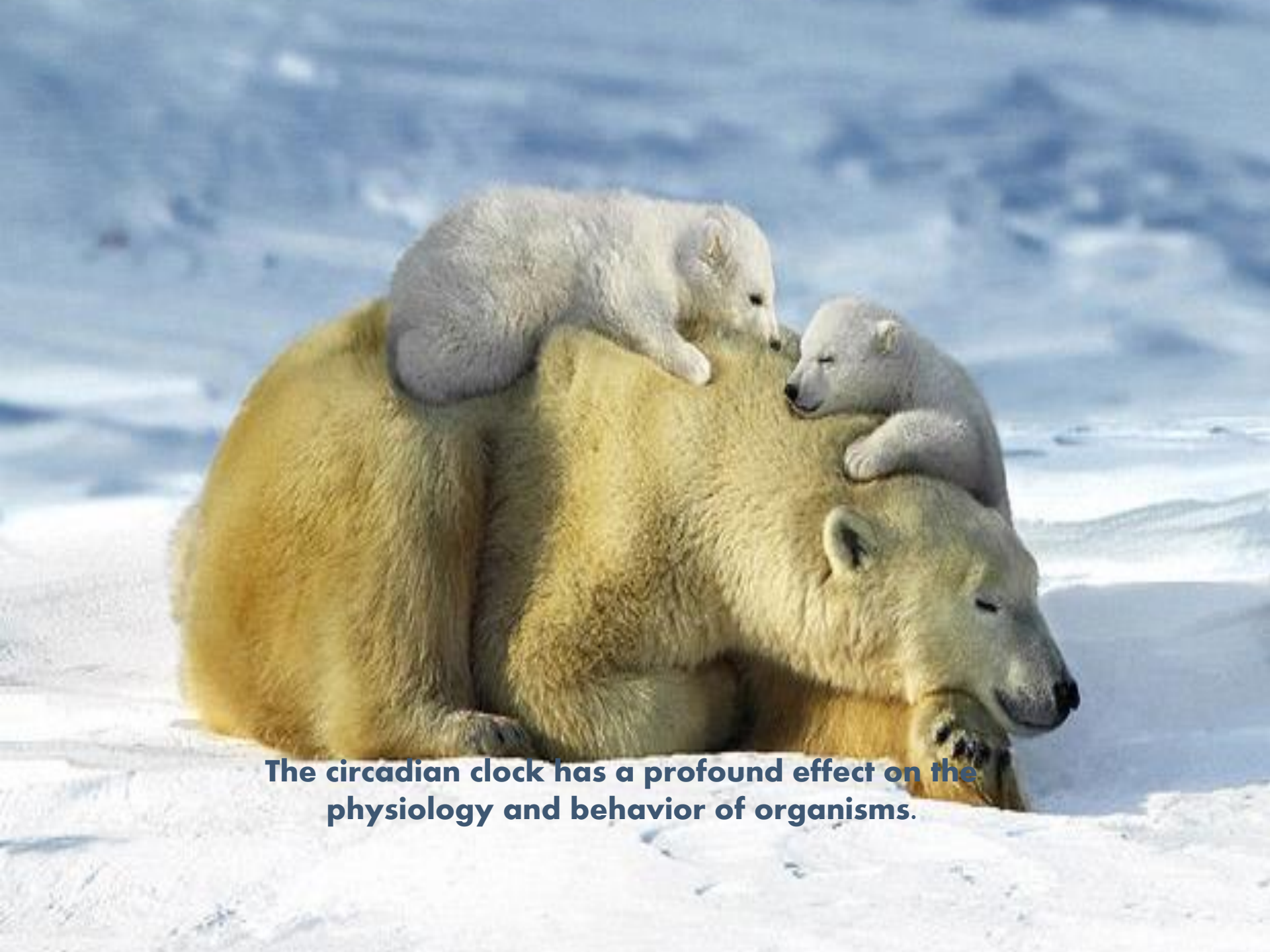
http://intl.elsevierhealth.com/journals/mehy

High carbohydrate diets and Alzheimer's disease

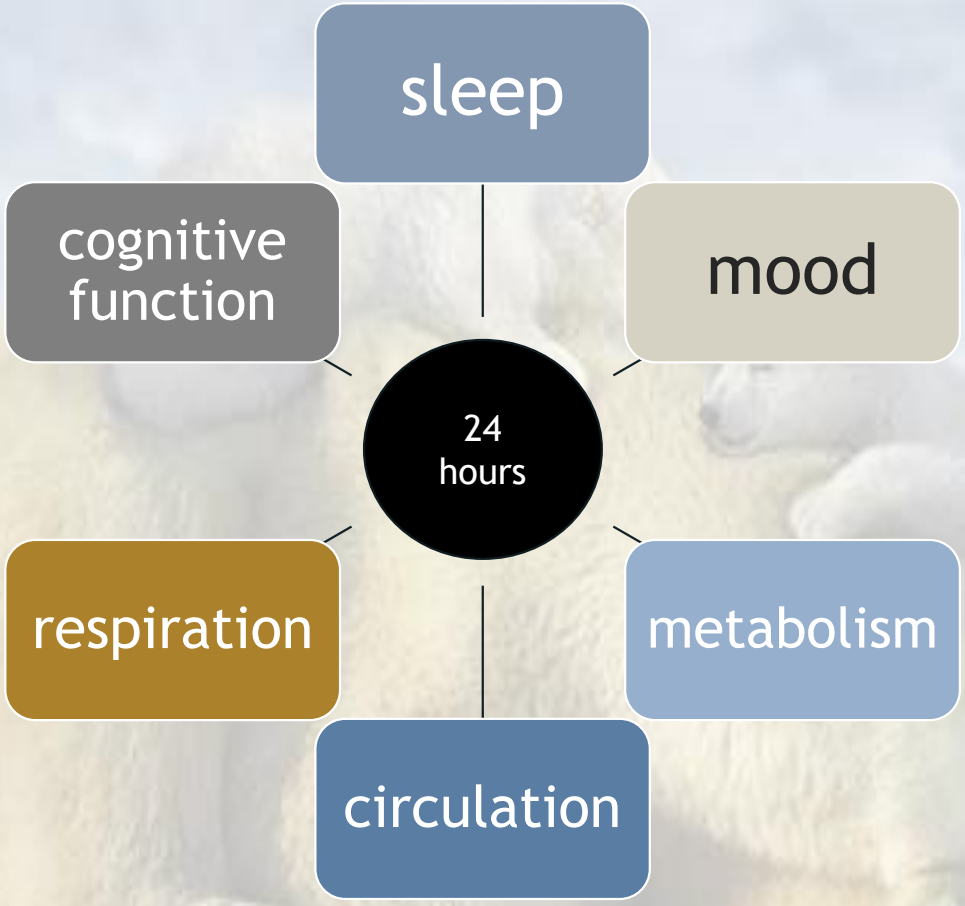
Samuel T. Henderson*

High carbohydrate intake worsens cognitive performance and behavior in patients with Alzheimer's disease.

Henderson, 2004



The circadian clock has a profound effect on the physiology and behavior of organisms.

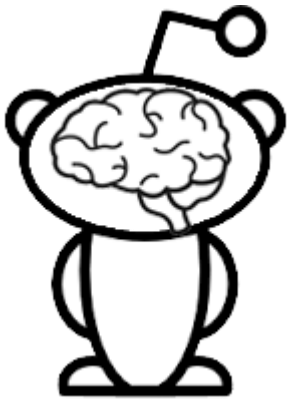


The circadian clock has a profound effect on the physiology and behavior of organisms.

A Single Night of Partial Sleep Deprivation Induces Insulin Resistance in Multiple Metabolic Pathways in Healthy Subjects

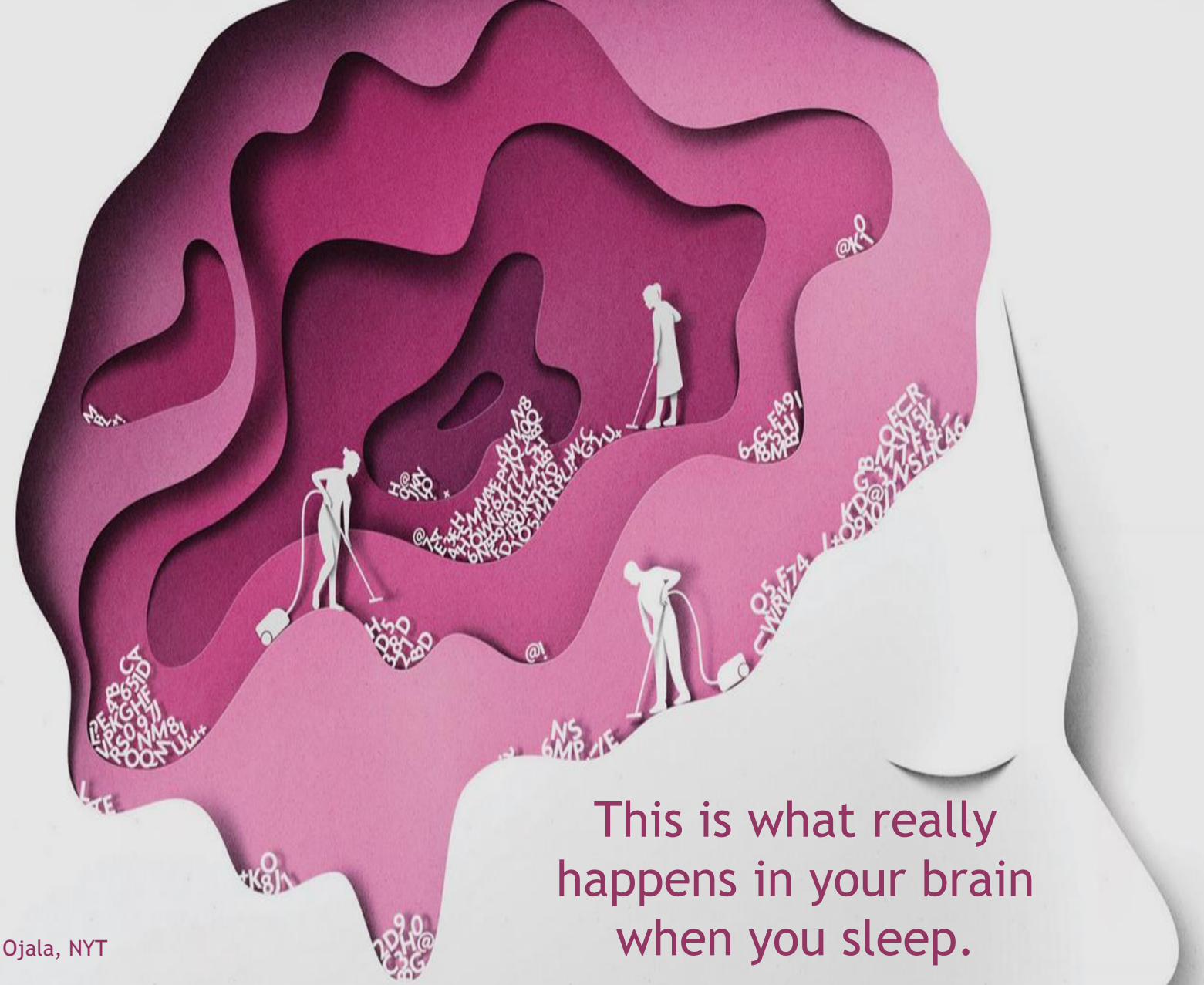
Esther Donga, Marieke van Dijk, J. Gert van Dijk, Nienke R. Biermasz, Gert-Jan Lammers, Klaas W. van Kralingen, Eleonara P. M. Corssmit, and Johannes A. Romijn

Departments of Endocrinology and Metabolic Diseases (E.D., M.v.D., N.R.B., E.P.M.C., J.A.R.), Neurology (J.G.v.D., G.-J.L.), and Pulmonology (K.W.v.K.), Leiden University Medical Center, 2300 RC Leiden, The Netherlands



the effect of a single night of partial sleep on insulin sensitivity

Donga, E., et al. (2010) J Clin Endocrinol Metab 95: 2963-2968



This is what really happens in your brain when you sleep.

Figure: Eiko Ojala, NYT

Nedergaard Lab

Principal Investigator

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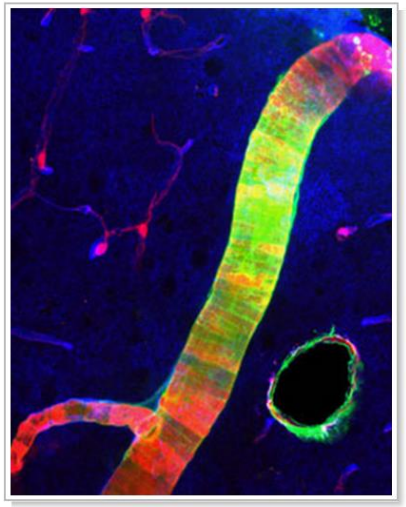
Glymphatic System

Throughout most of the body, a complex system of lymphatic vessels is responsible for cleansing the tissues of potentially harmful metabolic waste products, accumulations of soluble proteins and excess interstitial fluid. But astonishingly, the body's most sensitive tissue –the central nervous system – lacks a lymphatic vasculature. What then accounts for the efficient waste clearance that must occur in order for the neural tissue of our brains to function properly?



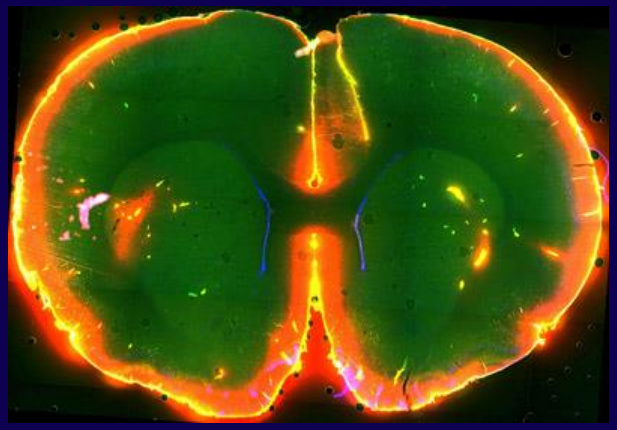
Large (green) and small (red) tracers tagged to soluble proteins in the paravascular cerebrospinal fluid.

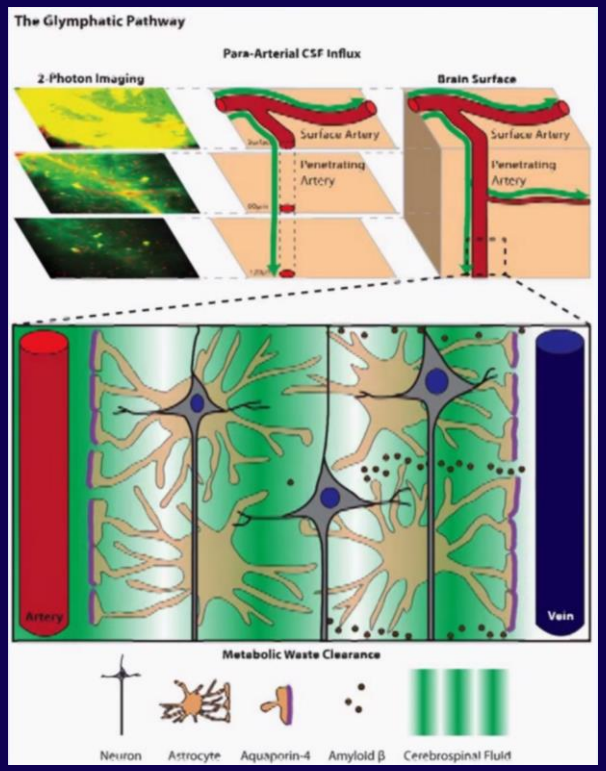
This question has puzzled scientists for centuries. Our group believes that understanding how this process functions in the healthy nervous system holds the key to developing treatment options for a wide variety of neurological diseases, especially those characterized by the improper accumulation of misfolded proteins. The breakdown of the brain's innate clearance system may in fact underlie the pathogenesis of neurodegenerative disorders such as Alzheimer's, Parkinson's, and Huntington's disease, in addition to ALS and chronic traumatic encephalopathy. Past efforts to explain how the brain cleanses parenchymal tissue have suggested that solute and fluid exchange occurs between the interstitial fluid and the cerebrospinal fluid, and that this exchange is driven by diffusion. Yet as many have noted, the distances for diffusion in the brain are too great to explain the highly regulated interstitial environment.

Sleep Drives Metabolite Clearance from the Adult Brain

Lulu Xie,[1,*] Hongyi Kang,[1,*] Qiwu Xu,[1] Michael J. Chen,[1] Yonghong Liao,[1] Meenakshisundaram Thiyagarajan,[1] John O'Donnell,[1] Daniel J. Christensen,[1] Charles Nicholson,[2] Jeffrey J. Iliff,[1] Takahiro Takano,[1] Rashid Deane,[1] Maiken Nedergaard[1,†]

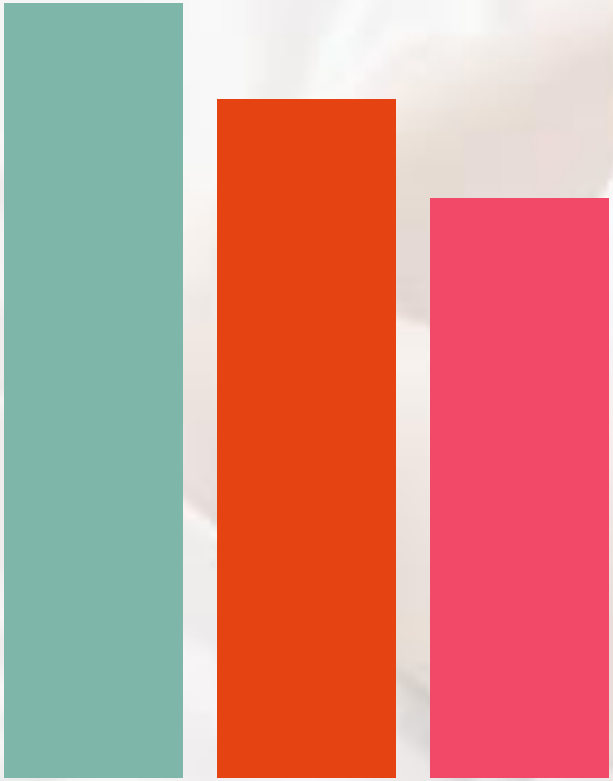
The conservation of sleep across all animal species suggests that sleep serves a vital function. We here report that sleep has a critical function in ensuring metabolic homeostasis. Using real-time assessments of tetramethylammonium diffusion and two-photon imaging in live mice, we show that natural sleep or anesthesia are associated with a 60% increase in the interstitial space, resulting in a striking increase in convective exchange of cerebrospinal fluid with interstitia fluid. In turn, convective fluxes of interstitial fluid increased the rate of β-amyloid clearance during sleep. Thus, the restorative function of sleep may be a consequence of the enhanced removal of potentially neurotoxic waste products that accumulate in the awake central nervous





https://www.youtube.com/watch?v=ci5NMscKJws

Average Number of Hours of Sleep per Night



Are you getting enough sleep?

Kripke, D et al (1979) Arch Gen Psychiatry;
Gallup Organization (1995), Sleep in America;
National Center for Health Statistics (1984 & 2004) Morb Mortal Wkly Rep 2005

What would happen if you got one more hour of sleep?

How much can an extra hour's sleep change you'

9 October 2013 Last updated at 04:24 ET

9 October 2013 Last updated at 04:24 ET

The average Briton gets six-and-a-half hours' sleep a night, according to the Sleep Council. Michael Mosley took part in an unusual experiment to see if this is enough.

It has been known for some time that the amount of sleep people get has, on average, declined over the years.

This has happened for a whole range of reasons, not least because we live in a culture where people are encouraged to think of sleep as a luxury - something you can easily cut back on. After all, that's what caffeine is for - to jolt you back into life. But while the average amount of sleep we are getting has fallen, rates of obesity and diabetes have soared. Could the two be connected?

We wanted to see what the effect would be of increasing average sleep by just one hour. So we asked seven volunteers, who normally sleep anywhere between six and nine hours, to be studied at the University of Surrey's Sleep Research Centre.

The volunteers were randomly allocated to two groups. One group was asked to sleep for six-and-a-half hours a night, the other got seven-and-a-half hours. After a week the researchers took blood tests and the volunteers were asked to switch sleep patterns. The group that had been sleeping six-and-a-half hours got an extra hour, the other group slept an hour less.

While we were waiting to see what effec this would have, I went to the John Radcliffe hospital in Oxford to learn more about wha actually happens when we sleep.

In the Sleep Centre, they fitted me up wit a portable electro-encephalograph,

THINKSTOCK

Go to this website
and read the article.

http://www.bbc.com/news/magazine-24444634