

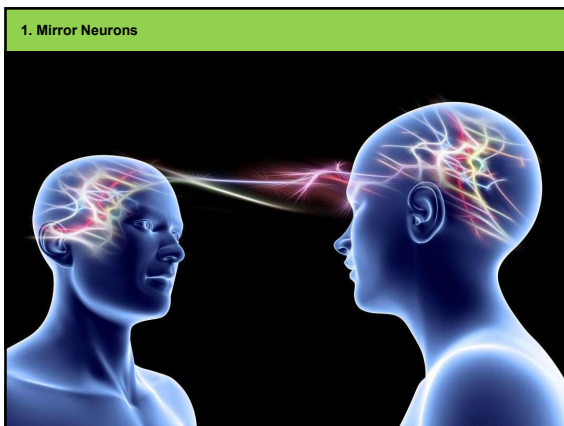
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I predict that mirror neurons will do for psychology what DNA did for biology

Vilayanur S. Ramachandran, 2000

mirror neuron



NIH Public Access
Author Manuscript

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Curr Biol. 2010 April 27; 20(8): 750–756. doi:10.1016/j.cub.2010.02.045.

Single neuron responses in humans during execution and observation of actions

Roy Mukamel^{1,2,3}, Arne D. Ekstrom^{1,4}, Jonas Kaplan^{2,3,5}, Marco Iacoboni^{2,3,6}, and Itzhak Fried^{1,3,6,7}

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⁷Functional Neurosurgery Unit, Tel Aviv Medical Center and Sackler School of Medicine, Tel Aviv University, Tel Aviv 69978, Israel.

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the Neurobiology of Empathy

Neurons that shape civilization



Prefrontal Cortex (PFC)

- Recent phylogenetic development
- Delayed ontogenetic maturation (complete development 20-24 years old).
- Most relevant age-dependent modifications: volumetric involution and WML ("frontal aging hypothesis")

A child with autism - or - an autistic child?

The signs of Autism..

- Inappropriate playing with toys
- Hyperactivity or inattentiveness
- Hyperactive or impulsive
- Hyperactive or impulsive
- Hyperactive or impulsive
- Hyperactive or impulsive
- Hyperactive or impulsive
- Hyperactive or impulsive

The reality of Autism..

- Playing with toys in ways that don't make sense to others
- Preference for solitary play
- Preference for solitary play
- Preference for solitary play
- Preference for solitary play
- Preference for solitary play
- Preference for solitary play
- Preference for solitary play

DETOUR

Living Amongst Autists

Polar PFC: metacognition (putting oneself into another's shoes)

Theory of Mind (ToM), empathy, humor

The frontal lobes are necessary for 'theory of mind'

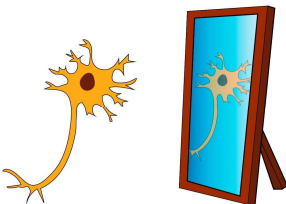
Neural correlates of feeling sympathy

Jean Decety^{a,b,*}, Thierry Chaminade^{a,b}

AUTISM SPECTRUM DISORDER

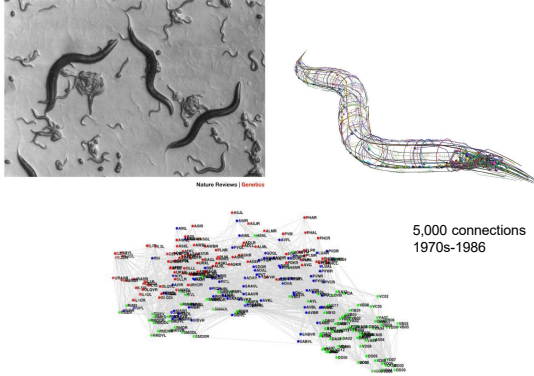
HIGH-FUNCTIONING AUTISM	AUTISM	SEVERE AUTISM
LEVEL 1	LEVEL 2	LEVEL 3
Needs support	Needs substantial support	Needs very substantial support
Patient's social and communication skills and repetitive behaviors are only noticeable without support.	Patient's social and communication skills and repetitive behaviors are still obvious to the casual observer, even with support in place.	Patient's social and communication skills and repetitive behaviors severely impair daily life.

1. Mirror Neurons



TAKE HOME MESSAGE:
 – Brain cells that “reflect” the actions of others –

Caenorhabditis elegans



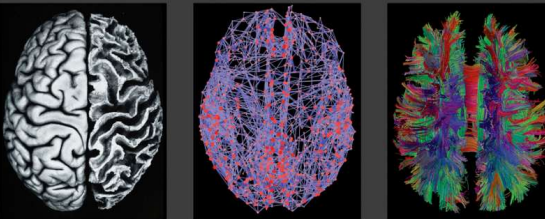
5,000 connections
1970s-1986

2. The Connectome

‘You are your connectome’
 Sebastian Seung, 2011



The Human Connectome

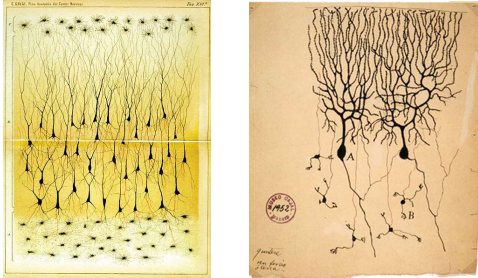


Anatomy
 Klingler's method for fiber tract dissection uses freezing of brain matter to spread nerve fibers apart. Afterwards, tissue is carefully scratched away to reveal a relief-like surface in which the desired nerve tracts are naturally surrounded by their anatomical brain areas.

Connectome
 Shown are the connections of brain regions together with “hubs” that connect signals among different brain areas and a central “core” or backbone of connections, which relays commands for our thoughts and behaviors.

Neuronal Pathways
 A new MRI technique called diffusion spectrum imaging (DSI) analyzes how water molecules move along nerve fibers. DSI can show a brain's major neuron pathways and will help neurologists relate structure to function.

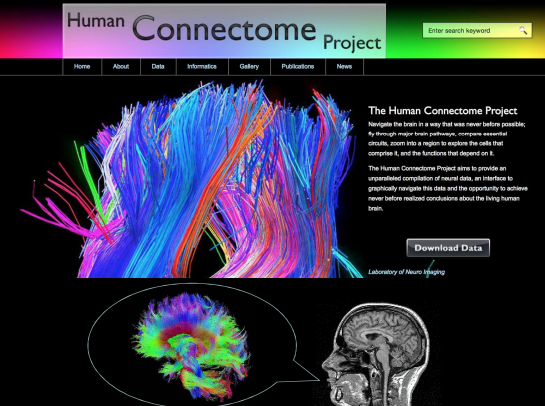
Syncytium or Network... or both?



Human Connectome Project

Home About Data Informatics Gallery Publications News

Enter search keyword



The Human Connectome Project
 Navigates the brain in a way that was never before possible. By tracing major brain pathways, compare essential details across brain regions to explore the cells that comprise it, and the functions that depend on it.



The Human Connectome Project aims to provide an unparalleled compilation of neural data, an interface to intelligently organize the data and the opportunity to achieve never before realized conclusions about the living human brain.

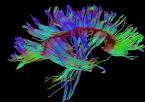
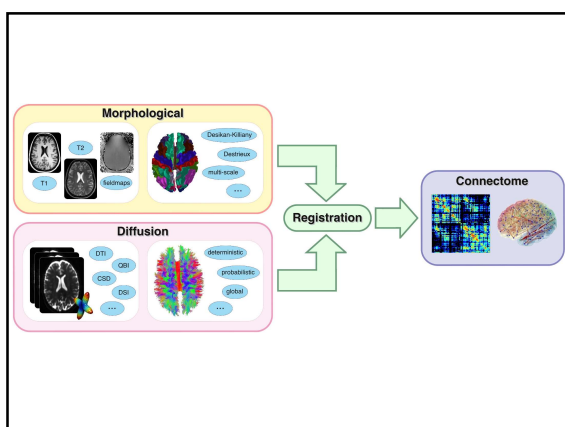
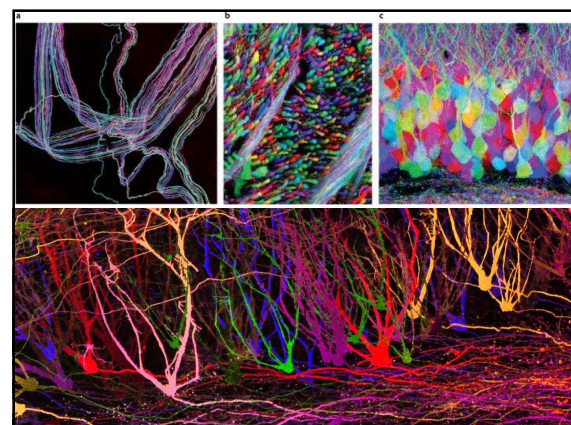
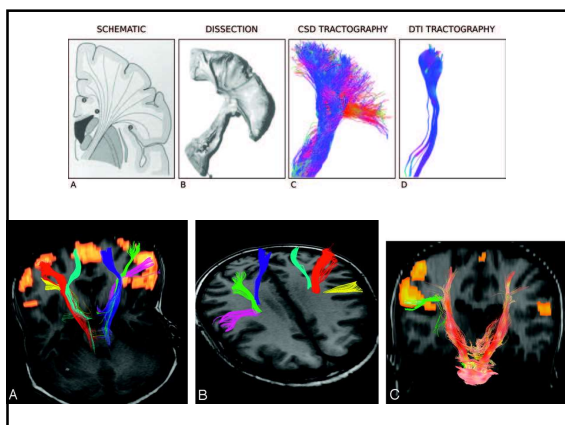
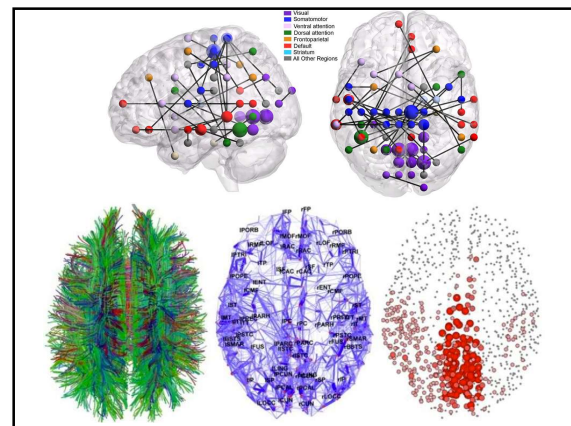
Download Data

Laboratory of Neural Imaging

Diffusion Tensor Imaging of the Brain - DTI -

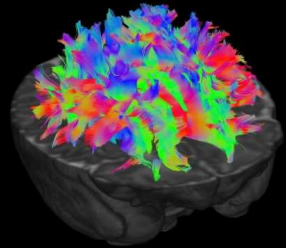
Diffusion in brain tissue

- Differentiate between tissues based on the diffusion (random motion) of water molecules within them
- Gray matter: Diffusion is unrestricted \Rightarrow isotropic 
- White matter: Diffusion is restricted \Rightarrow anisotropic 

2. The Connectome

**TAKE HOME MESSAGE:
- A COMPLETE WIRING
DIAGRAM OF THE BRAIN -**




3. Embodied cognition

Traditionally, the brain is thought of as the master controller – generating thoughts and actions by converting abstract representations of the world into commands for the body.

According to a new theory, however, thoughts and behaviours are not produced by the brain alone, but are the result of dynamic interactions between the brain, the body and the environment.


Costandi. 50 Human Brain Ideas You Really Need to Know.



THE EXTENDED MIND THEORY (EMT)

The extended mind
ANDY CLARK & DAVID CHALMERS¹

'Where does the mind stop and the rest of the world begin?'




'Bodily states and action underlie cognition.'
American cognitive scientist Lawrence Barsalou, 2008

1. Introduction
What does the mind stop and the rest of the world begin? The question invites two standard replies. Some accept the boundaries of skin and skull, and say that what is outside the body is outside the mind. Others are impressed by arguments suggesting that the meaning of our words 'rests out in the world', and hold that our utterances about meaning connect us into an externalist about mind. We propose to pursue a third position. We advocate a very different sort of externalism: an actual externalism, based on the active role of the environment in driving cognitive processes.
2. Extended cognition
Consider three cases of human problem-solving:
(1) A person sits in front of a computer screen which displays images of various two-dimensional geometric shapes and is asked to answer questions concerning the potential fit of such shapes into deformed 'sockets'. To assist fit, the person must mentally rotate the shapes to align them with the sockets.
(2) A person sits in front of a similar computer screen, but this time can choose either to physically rotate the image on the screen, by pressing a rotate button, or to mentally rotate the image as before. We can also suppose, not unrealistically, that some speed advantage accrues to the physical rotation operation.
(3) Sometime in the not-distant future, a person sits in front of a similar computer screen. This agent, however, has the benefit of a neural implant which can perform the rotation operation as fast as the computer in the previous example. The agent must still choose which mental resource to use: the implant or the good old-fashioned neural resource, as each resource makes different demands on attention and other concurrent brain activity. How much cognitive is present in these cases? We suggest that all three cases are similar. Case (1) with the mental implant seems clearly to be one par with case (1). And case (2) with the rotate button displays the same sort of computational structure as case (1), distributed across agent and computer instead of internalized within the agent. If the rotation in case (1) is cognitive, by what right do we count case (2) as fundamentally different? We cannot simply point to the distributed boundary as justification, since
¹ Authors are listed in order of degree of belief in the central thesis.
Received 10 January 1998; revised 14 July 1998; accepted 10 October 1998

'The body ... serves to impress notions of external objects ... and to recall and connect them interiorly ... [it] is indispensable for thinking.'
Immanuel Kant, 1755

Embodied Cog Examples

- Hill looks steeper wearing a backpack
- Holding a warm drink, people rate others as more warm and friendly than w/cold drink
- Faster to respond 'yes' when pushing lever, faster to respond 'no' when pulling it
- Right handed people view things more positively on the right side and vice versa
- More likely to recall positive experiences when moving marbles up into box than when moving them down



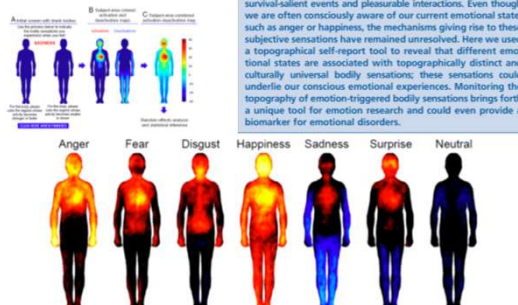
Bodily maps of emotions

Lauri Nummenmaa^{1,2,3}, Enrico Gleason⁴, Riitta Hari^{1,2}, and Jari K. Hietanen¹

¹Department of Biomedical Engineering and Computational Science and ²Brain Research Unit, U.S. Lappeenranta University of Applied Sciences, Lappeenranta, Finland; ³Turku PET Centre, University of Turku, FI-20521 Turku, Finland; and ⁴Human Information Processing Laboratory, School of Social Sciences and Humanities, University of Tampere, FI-33014 Tampere, Finland


Contributed by Riitta Hari, November 21, 2013; accepted for review June 11, 2014.

Emotions coordinate our behavior and physiological states during survival-salient events and pleasurable interactions. Even though we are often consciously aware of our current emotional state, such as anger or happiness, the mechanisms giving rise to these subjective sensations have remained unresolved. Here we used a topographical self-report tool to reveal that different emotional states are associated with topographically distinct and culturally universal bodily sensations; these sensations could underlie our conscious emotional experiences. Monitoring the topography of emotion-triggered bodily sensations brings forth a unique tool for emotion research and could even provide a biomarker for emotional disorders.



3. Embodied cognition

**TAKE HOME MESSAGE:
– THE MIND IS A
PRODUCT OF BRAIN,
BODY AND OUTSIDE
WORLD INTERACTIONS –**




4. Bodily awareness

Who am I, and how did I come to be who I am?


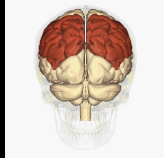
Self-identity is a complex phenomenon that consists of multiple components, including personality, memory and sexual and national identity.

At the core of the self is something that most of us take for granted – the body, and our awareness of it.




'Body am I entirely, and nothing more; and soul is only the name of something about the body.'
Friedrich Nietzsche, 1883

Parietal Lobe





A portrait of Henry Head, the pioneering English neurologist who first defined and used the term "body schema".



Body Schema Disturbance



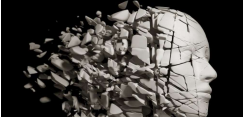
- Finger Agnosia**
patients cannot identify their own fingers or those of another person.
- Right-Left Disorientation**
Lesions of the left parietal lobe commonly result in right-left disorientation.
- Assessment**
Autopagnosia
Have patient point to own body parts and those on others.
- Finger Agnosia**
Have patient close their eyes and indicate which of their fingers has just been touched.



Bodily awareness

Body ownership


Agency and free will

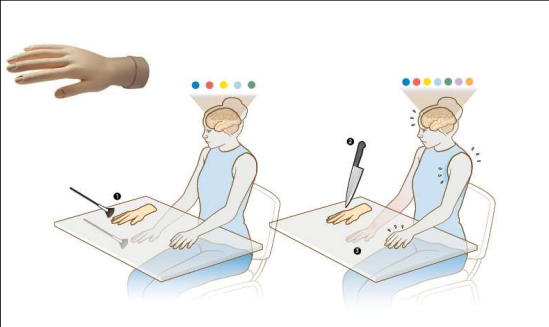
Somatoparaphrenia

- When an individual denies ownership of a limb, or part of their body
- Sometimes believes that the limb belongs to someone else
- Related to body integrity identity disorder (BIID)
- May cause the person to desire amputation


DETOUR
→



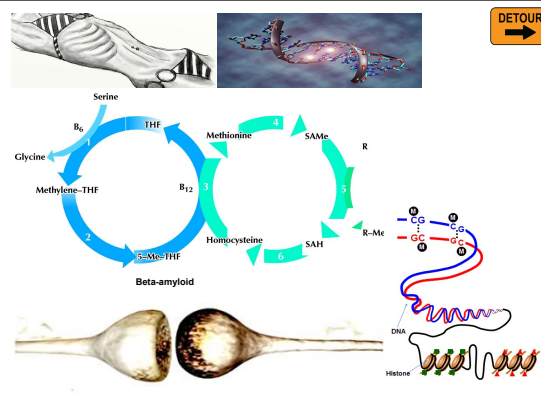
Anorexia Nervosa



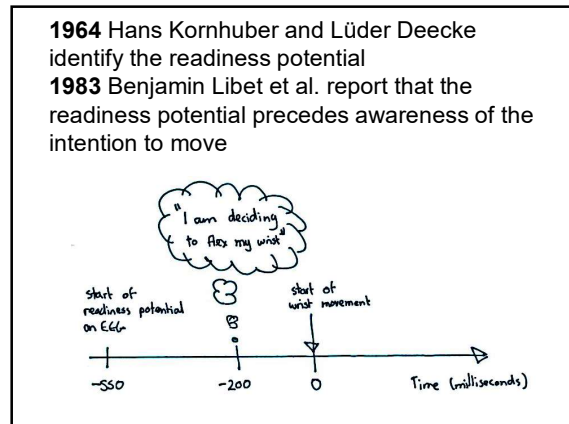
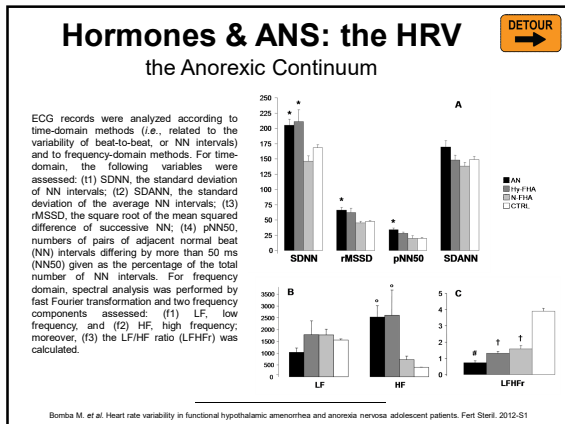
1998 Matthew Botvinick and Jonathan Cohen describe the rubber hand illusion



DETOUR
→



The diagram illustrates the methionine cycle, a metabolic pathway involving Serine, Methionine, SAMe, Homocysteine, Methylene-THF, THF, and Glycine. It also shows the conversion of Homocysteine to SAMe and the role of B12 and B6. The cycle is linked to the production of Beta-amyloid, which is associated with neurodegeneration. The diagram also shows the structure of DNA and Histone.



4. Bodily awareness

TAKE HOME MESSAGE:
– AWARENESS OF THE BODY IS CRITICAL TO THE SENSE OF SELF –

2007 Patrick Haggard et al. discover the brain's veto power
2008 Researchers predict choices from brain activity up to 10 seconds before actions
2010 Study shows readiness potential can be detected regardless of which decision is made
2011 Neurosurgeons identify motor cortical neurons that are activated up to 1.5 seconds before the will to act

Free Will vs. Free Wont

Brain signal: -0.3 sec
 Desire to move: -0.2 sec
 Voluntary Movement: 0
 Veto power: -0.3 to -0.2 sec
 Half a second

'We feel we choose, but we don't.'
 Patrick Haggard, 2011

Loeb (1983)

5. Free will

Do not dream about things you can not reach yourself; your highest achievement is freedom, it can not make you beautiful, rich, strong or happy in the eyes of the world, but can set you free

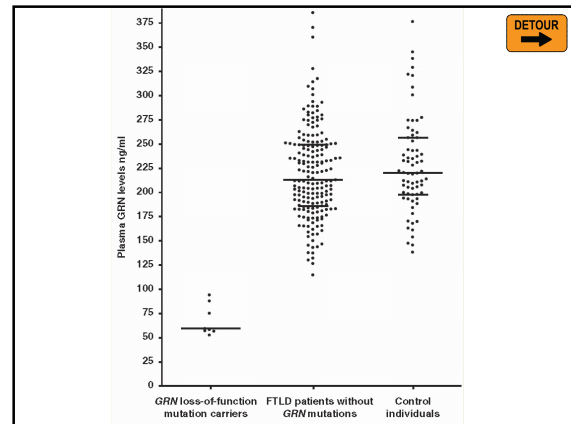
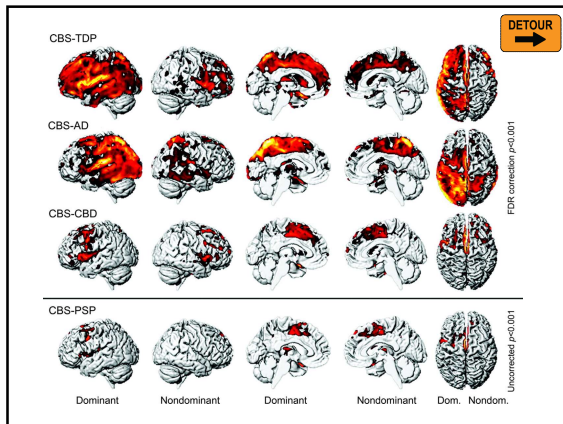
– René Descartes –

There are several causes related with the distinct subtypes of alien hand syndrome that appear to be associated with specific distributions of associated brain injury.

They are :-

- Damage to Corpus callosum
- Unilateral or bilateral injury to brain's frontal lobe
- Damage to the posterolateral parietal lobe and/or the occipital lobe of the brain

Stanley Kubrick 1964 *Dr Strangelove*



Progranulin Leu271LeufsX10 is one of the most common FTD and CBS associated mutations worldwide

Janina Benussi^{1,2}, Roberta Ghidoni^{1,2,3,4,5}, Eleonora Pegonini¹, Davide V. Moretti¹, Ottavio Zanetti^{1,2}, Giuliano Binetti^{1,6*}

ABSTRACT

Mutations in the progranulin gene (*PGRN*) are a major cause of frontotemporal lobar degeneration (FTLD). Herein we estimated the contribution of the *PGRN* Leu271LeufsX10 mutation to FTLD and related disorders in the Brescia cohort. The *PGRN* Leu271LeufsX10 mutation was found in 21% of corticobasal syndrome (CBS), 20% of frontotemporal dementia with motor neuron disease (FTD-MND), 15% of behavioral variant frontotemporal dementia (FTD), 9.5% of primary progressive aphasia (PPA), 2% dementia with Lewy bodies and 0% of progressive supranuclear palsy and multiple system atrophy cases. The prevalence strongly increased in familial forms (75% CBS, 50% FTD-MND, 27% FTD, 18% PPA); in our cohort this mutation is a major disease determinant for FTLD-related disorders with a prominent motor component. *MAPP* haplotype was demonstrated to be a disease modifier in *PGRN* Leu271LeufsX10 carriers; in H1H2 subjects the disease onset was earlier than in H2H2 individuals. Sequencing of the whole *PGRN* gene disclosed a previously described mutation (c.27>C, Met1X) and three novel ones (c.709>3; c.1011 delG, His340TufsX21; c.1021C>T, Gin341X) in single families. In the Brescia cohort, while *MAPP* mutations have low prevalence, mutations in *PGRN* were shown in 28% of familial FTLD and 75% of familial CBS cases. The *PGRN* Leu271LeufsX10 mutation becomes one of the most common mutations worldwide, since it was identified in 38 patients belonging to 27 unrelated families.

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*DETOUR

Progranulin Resolves Inflammation

Wei Tang,^{1,2*} Yi Lu,^{1,2,3*} Qing-Yan Tian,^{1,4} Yan Zhang,¹ Feng-Jin Guo,¹ Guang-Yi Liu,¹ Nabeek Mazaffar Syed,¹ Yangjie Lai,¹ Edward Alan Liu,¹ Li Kong,¹ Jeffrey Su,¹ Fangfang Yin,¹ Ai-Hao Ding,¹ Alexandra Zarin-Zhrov,¹ Michael L. Dustin,³ Jian Yao,¹ Joseph Craft,¹ Zhihan Yin,¹ Jian Q. Feng,² Steven B. Abramson,² Xia-Ping Yu,¹ Chuan-Ju Liu^{1,5,6*}

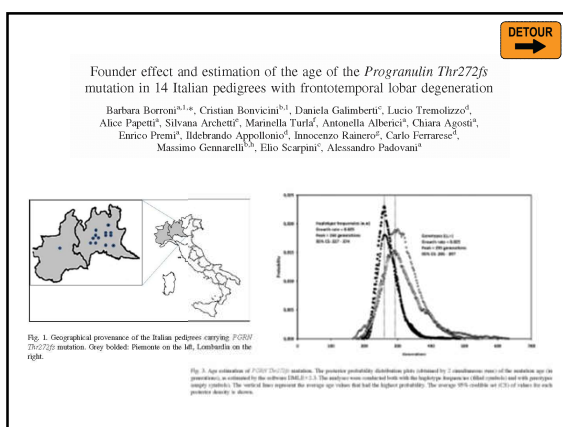
The Growth Factor Progranulin Binds to TNF Receptors and Is Therapeutic Against Inflammatory Arthritis in Mice

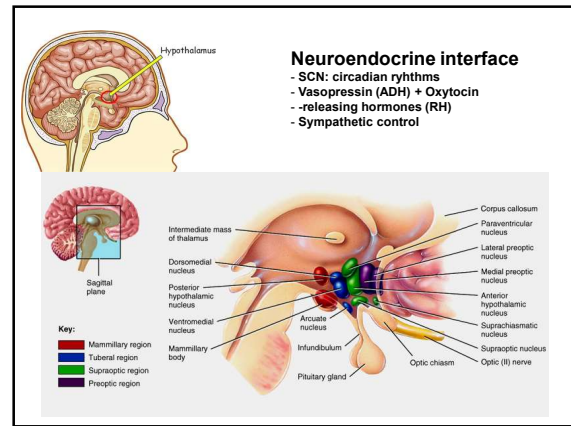
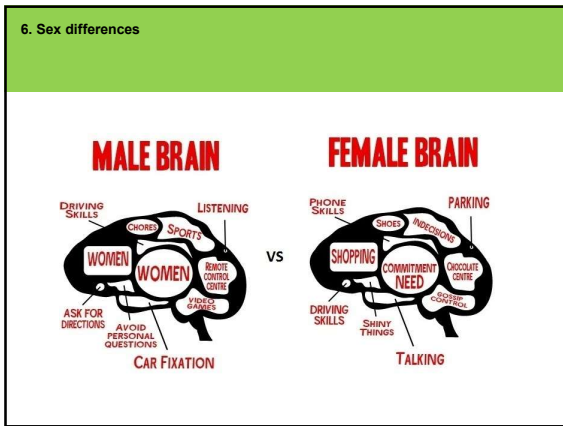
Loss of function mutations in the progranulin gene are related to pro-inflammatory cytokine dysregulation in frontotemporal lobar degeneration patients

Paola Bossi,¹ Francesca Salvi,¹ Antonella Alberti,¹ Silvana Archetti,¹ Giuseppe Bellodi,¹ Daniela Galimberti,¹ Elio Scarpini,¹ Gianfranco Spalloni,¹ Carlo Colognori,¹ Alessandro Padovani,¹ and Barbara Bonini¹

Journal of Neuroinflammation 2011, **8**:65

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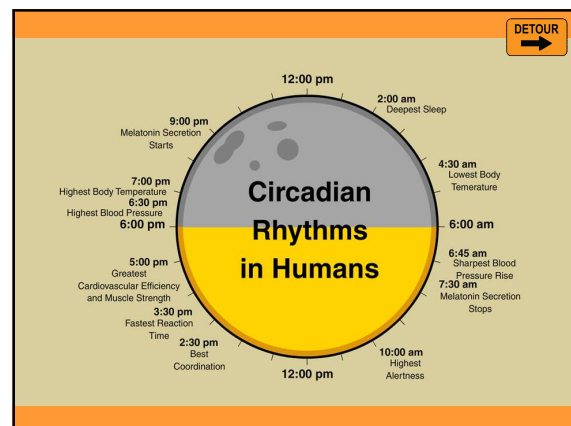
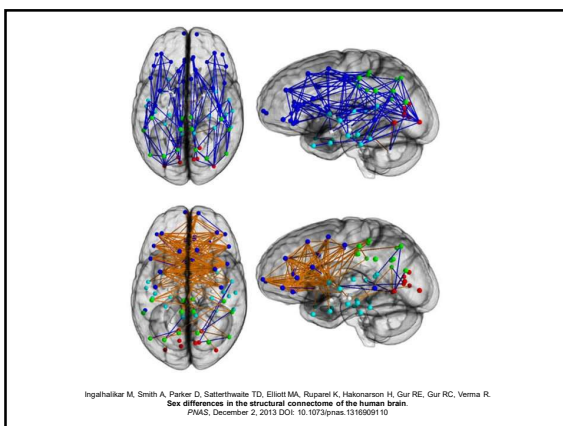
*The Brain—is wider than the Sky—
For—put them side by side—
The one the other will contain
With ease—and You—beside—
The Brain is deeper than the sea—
For—hold them—Blue to Blue—
The one the other will absorb—
As Sponges—Buckets—do—
The Brain is just the weight of God—
For—Heft them—Pound for Pound—
And they will differ—if they do—
As Syllable from Sound
—Emily Dickinson*

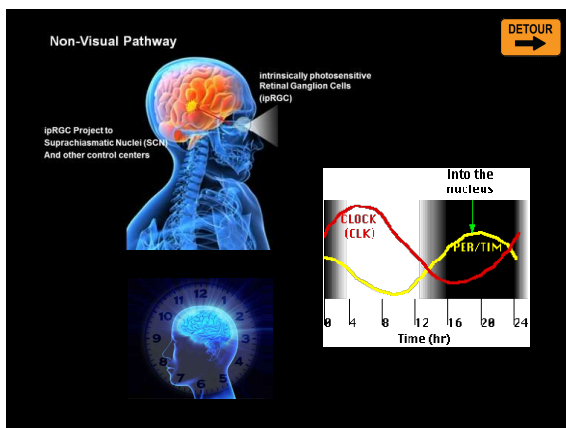
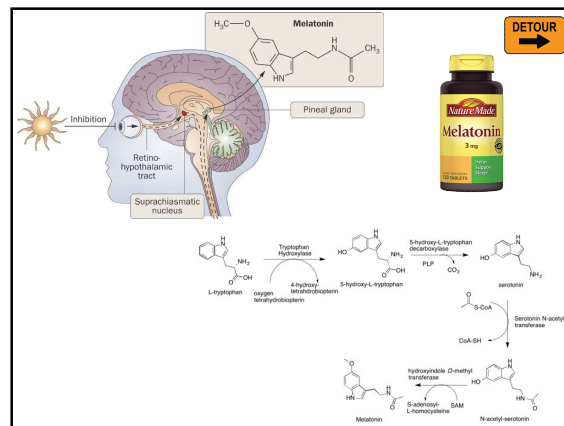
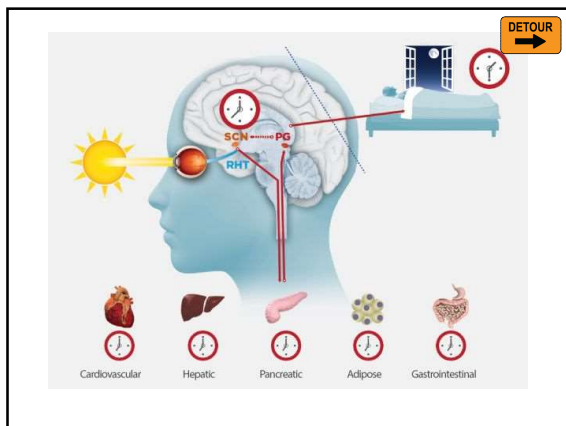
Brain of male

Brain of female

the "cuddle hormone"

Studies have looked at oxytocin's role in various behaviors, including orgasm, social recognition, pair bonding, anxiety, and maternal behaviors.



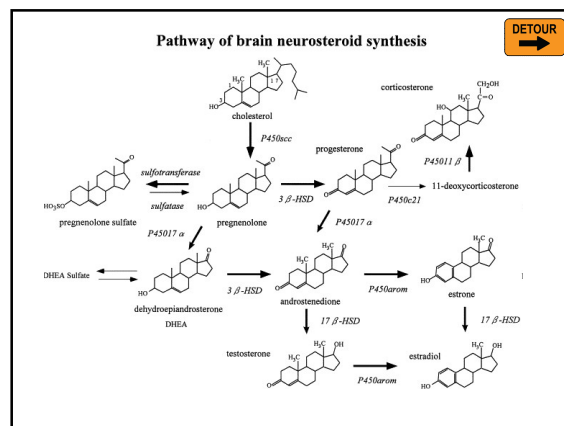
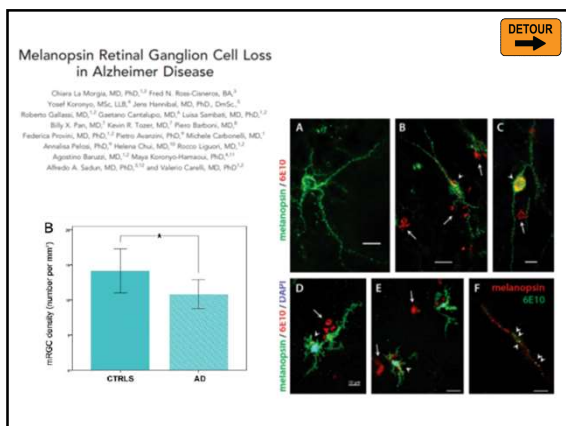


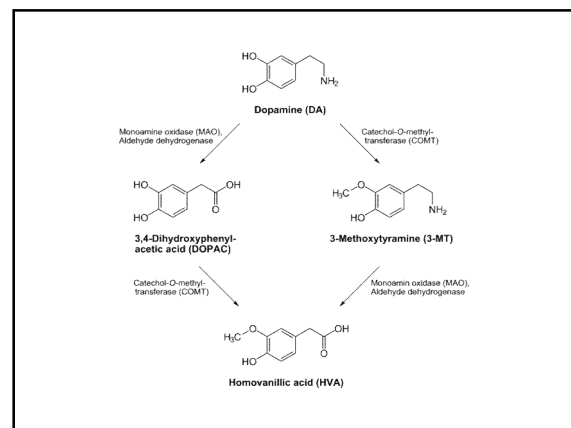
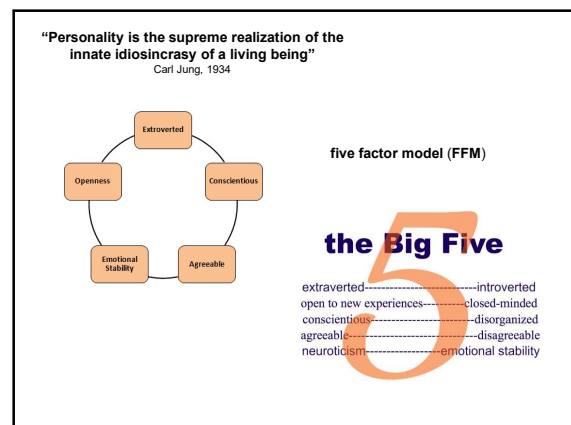
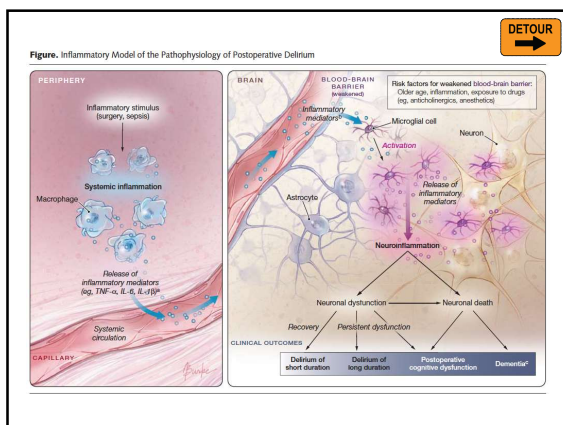
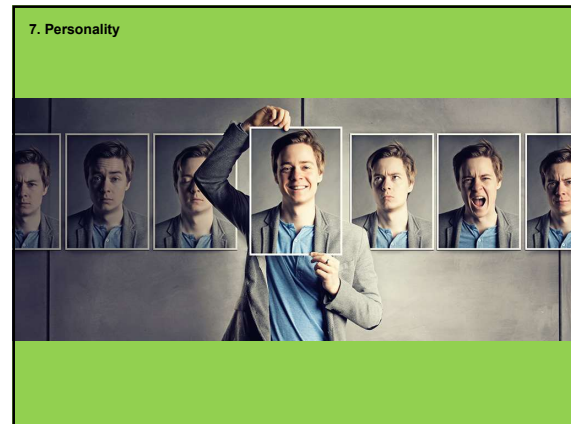
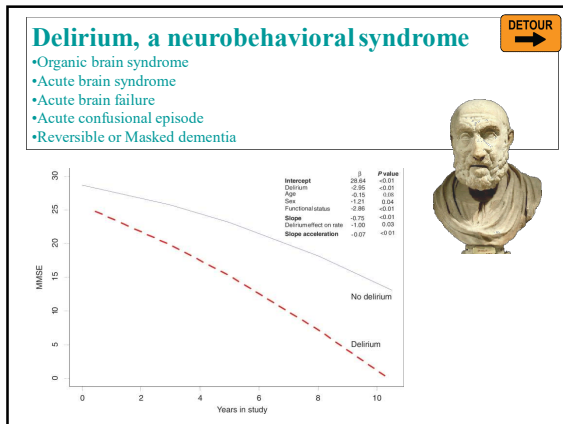
Depression

History Of SSRI's

- SSRI's were introduced in 1987
- The first was Fluoxetine (Prozac; Eli Lilly & Company) FDA approved 1987
- Sertraline (Zoloft; Pfizer, Inc) FDA approved 1991
- Paroxetine (Paxil; GlaxoSmithKline) FDA approved 1992
- Citalopram (Celexa; Forest Pharmaceuticals) FDA approved 2000
- Escitalopram (Lexapro; Forest Pharmaceuticals) FDA approved 2002


DETOUR →








The Role of the Catechol-O-Methyltransferase (COMT) Gene in Personality and Related Psychopathological Disorders
 Montag et al. CNS Neurol Disord Drug Targets. 2015

SNP Val158Met

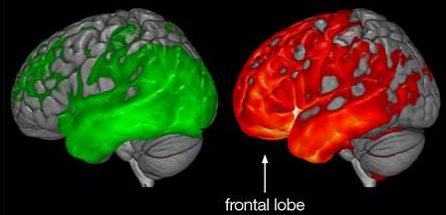
Target Cards: 

Sorted Cards: 

Card to be sorted: 



Alzheimer's Disease **Frontotemporal Dementia**




frontal lobe

DETOUR →

Neuroanatomy of the self

Evidence from patients with frontotemporal dementia
 B. L. Miller, MD, W. W. Seeley, MD, P. Mychack, PhD, H. J. Rosen, MD, Ismael Mena, MD and K. Boone, PhD
Neurology, 2001



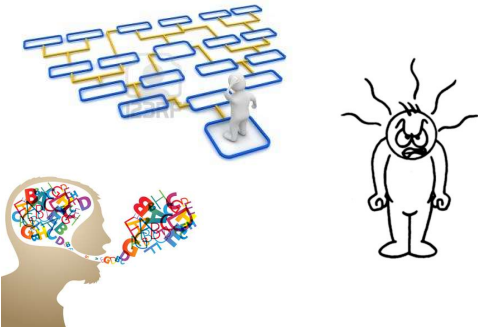
Methods: Seventy-two consecutive FTD patients were evaluated with neuropsychiatric, neuropsychologic, and behavioral measures. Patients were imaged with MRI and SPECT. Charts were reviewed by a social psychologist to determine patients who exhibited a dramatic change in their self as defined by changes in political, social, or religious values. The brain areas with the most severe atrophy or hypoperfusion on neuroimaging were noted.

Results: Seven of 72 patients exhibited a dramatic change in self. In six of the seven, the selective dysfunction involved the nondominant frontal region. In contrast, only one of the other 65 patients without selective nondominant frontal dysfunction showed a change in self.

Conclusions: FTD patients with asymmetric loss of function in the nondominant frontal lobe often exhibit a diminished maintenance of previously learned self-concepts despite intact memory and language. Normal nondominant frontal function is important for the maintenance of the self.

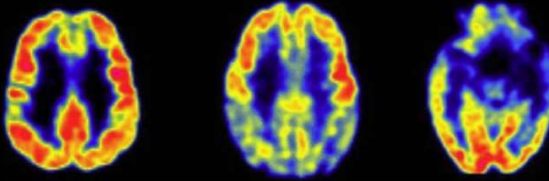
DETOUR →

FTLD
 (Frontotemporal Lobar Degeneration)



DETOUR →

"Dementia That's Neither Alzheimer's Nor Easy"



Normal Alzheimer's FTD

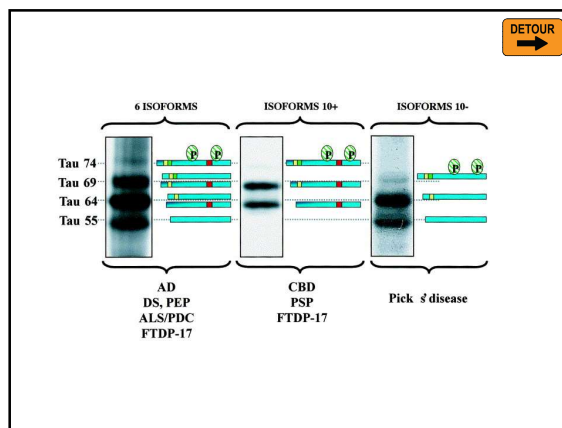
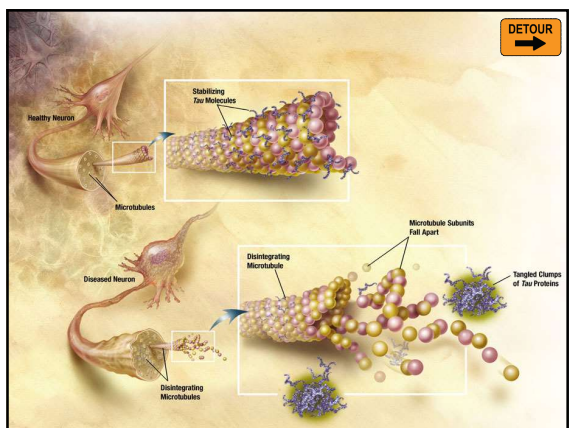
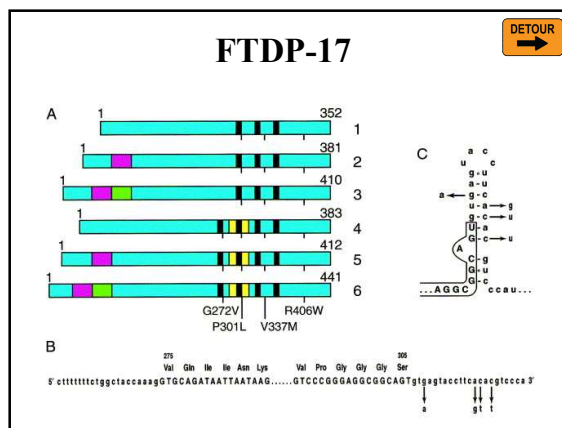
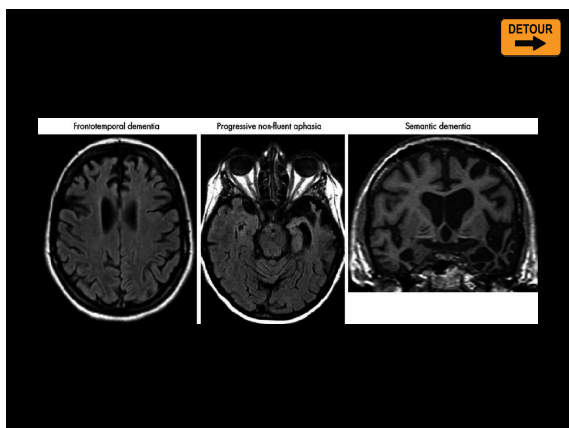
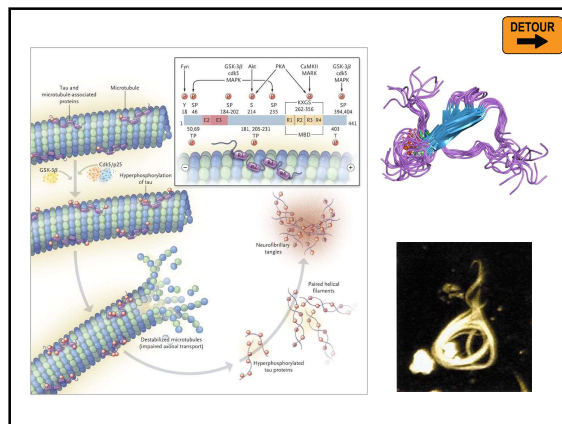
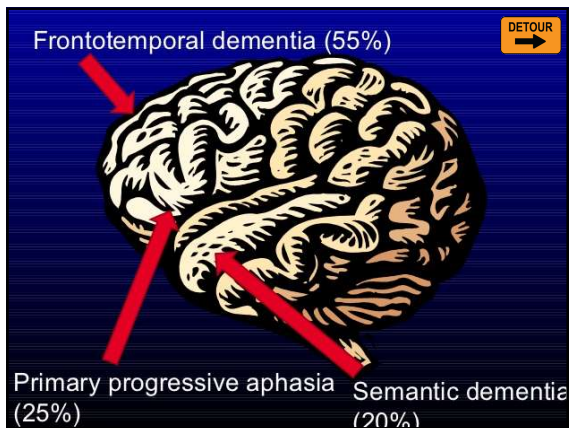
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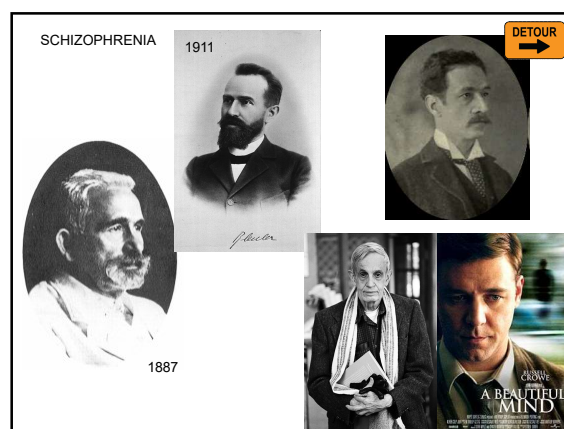
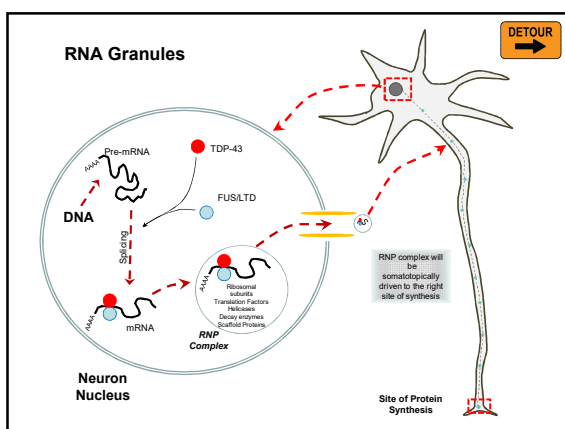
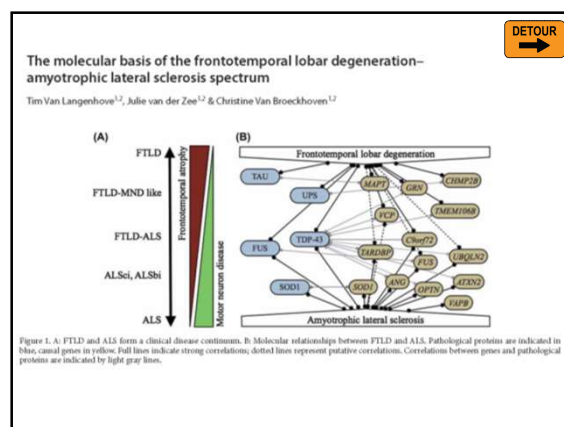
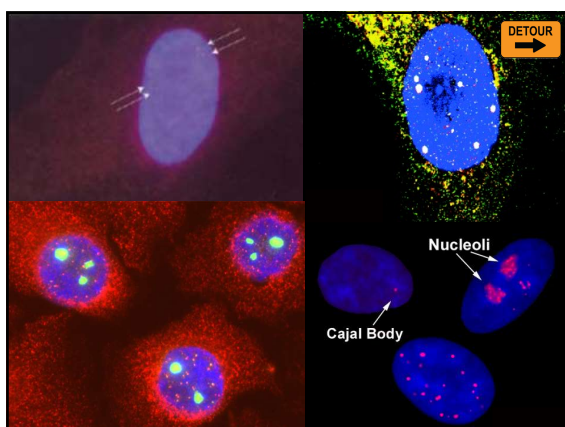
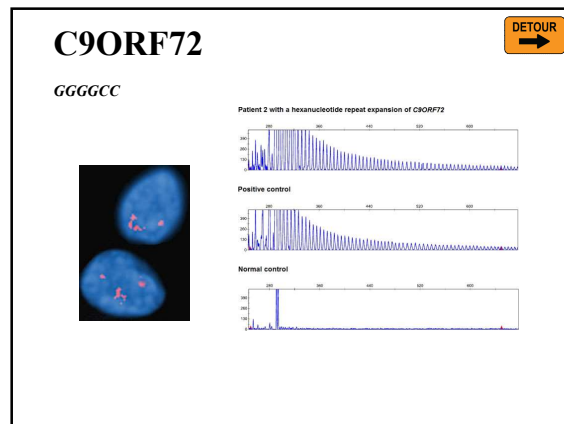
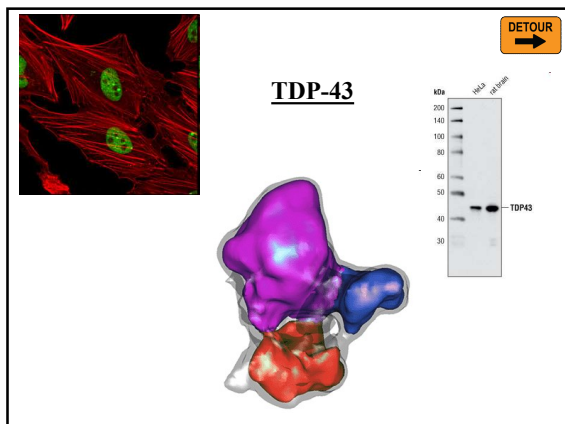
Frontotemporal dementia subtypes

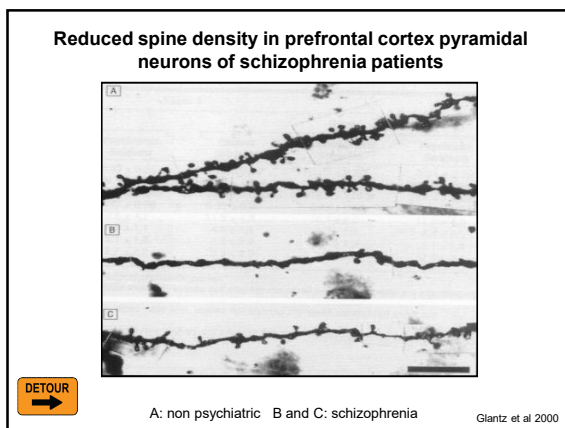
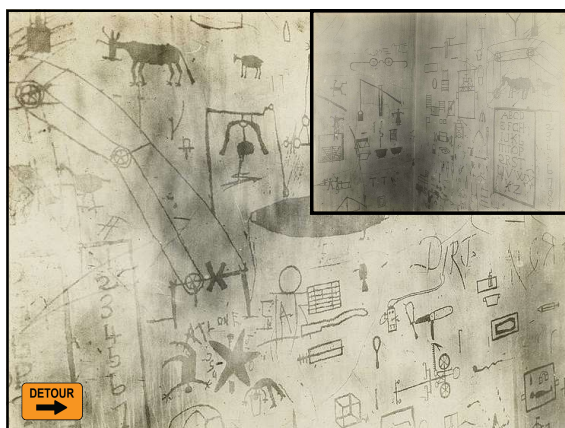
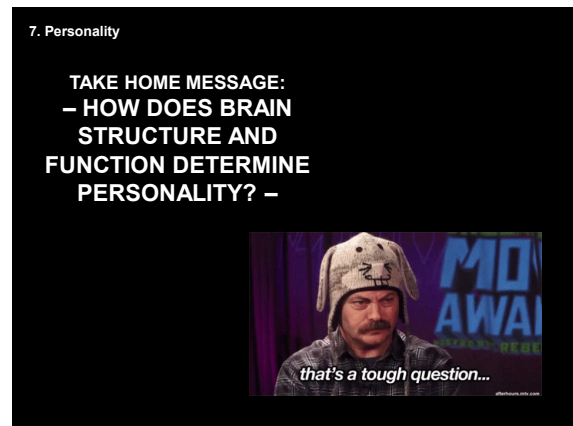
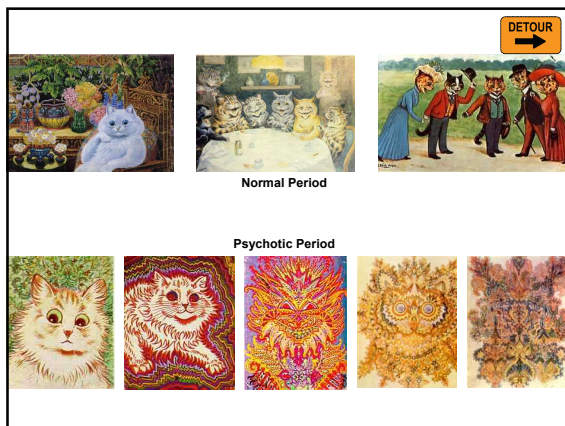
- **Behavior variant (bvFTD)**
- Semantic dementia (SD)
- Progressive nonfluent aphasia (PNFA)
- Progressive Supranuclear Palsy (PSP)
- Corticobasal degeneration (CBD)
- FTD with motor neuron disease (FTD-MND)
- ALS/CTE (Chronic Traumatic Encephalopathy)

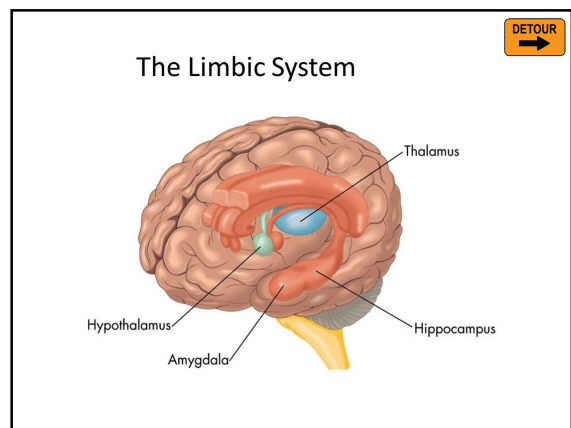
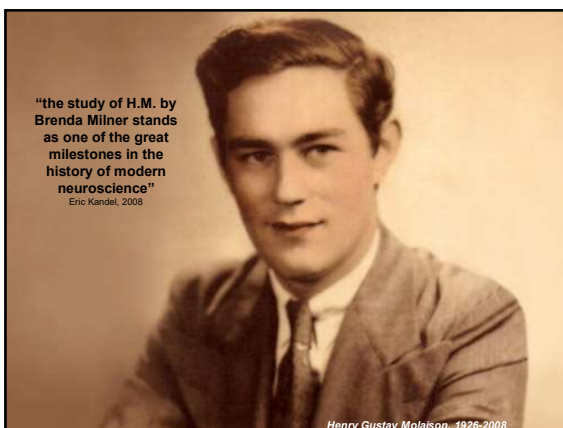
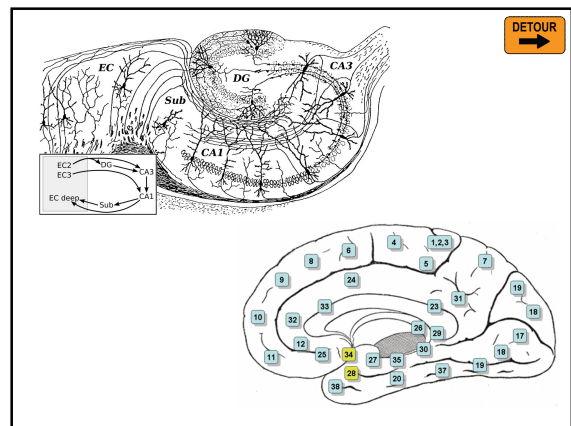
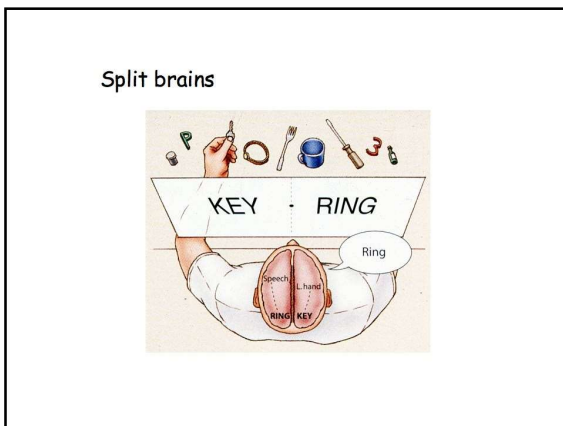
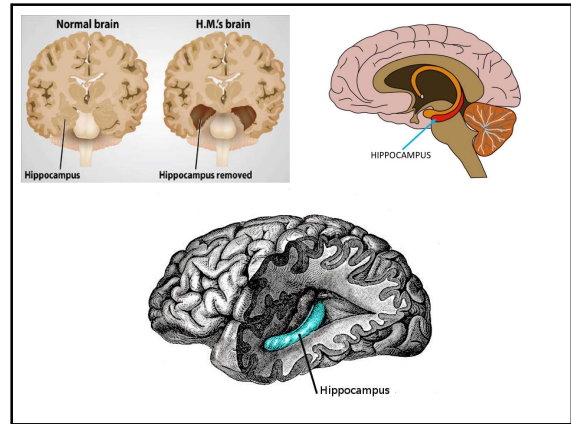
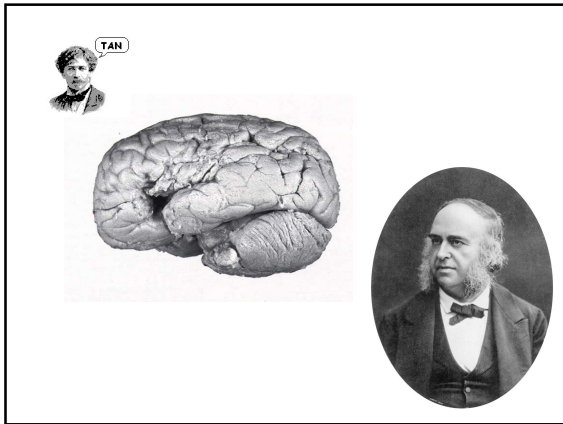
Boxer AL, Miller BL. Clinical features of frontotemporal dementia. *Alzheimer Dis Assoc Disord.* 2005;19 S1:S3-6

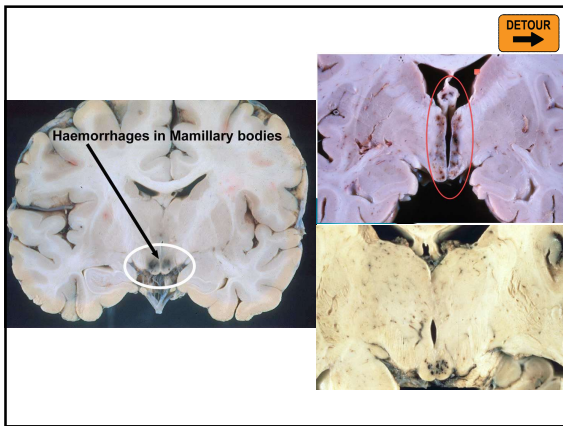
DETOUR →











Wernicke's Encephalopathy

TRIAD

- 1 – **Confusion (90%)**
- 2 – **Ataxia (87%)**
- 3 – **Ophtalmoplegia (96%)**

Korsakoff's Syndrome

- Characterized by amnesia, creation of new memories, apathy
- Both of these diseases are caused by vitamin B1 (thiamine) deficiencies, simultaneous occurrence makes wernicke-korsakoff disorder

Wernicke's Encephalopathy

- Reduced B1
- Beri-beri, Korsakoff
- 1881 case series
- 1930 role of B1

(Tarnowskie Góry, 15-05-1848 – Grafenroda, 15-06-1905)

Aneurin, (1926)

Cc1nc(N)c2nc(C)nc2n1CO

BRAIN BREW

BEC, Blood Ethanol Concentration

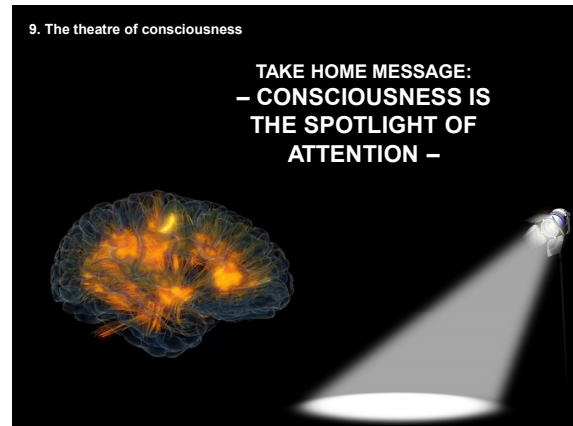
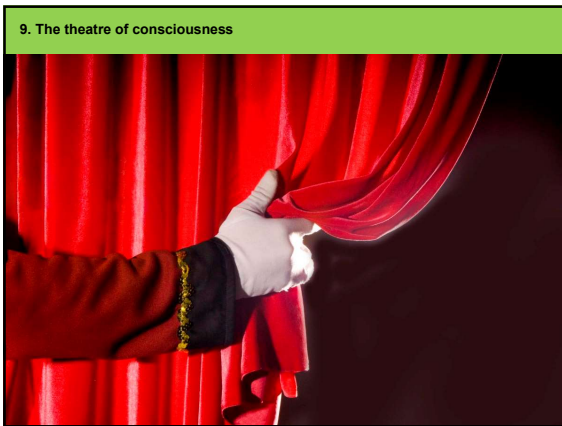
50-150 mg/dL (0.5-1.5 g/L): euphoria, reduced concentration

150-250: ataxia and sleepiness

>400: coma, respiratory failure, death

8. Brain-damaged patients

**TAKE HOME MESSAGE:
– CASE STUDIES PROVIDE VALUABLE INSIGHTS INTO BRAIN FUNCTION –**



“We experience ourselves and the world as a constant flow of thoughts and sensations, but how the brain generates this stream of consciousness is a mystery. According to one influential theory, consciousness is like a theatre...”
Costandi M.

Working Memory

- operates over a few seconds
- temporary storage
- manipulates information
- focuses attention



Global Workspace Theory

- Bernard Baars (1988; Baars et al., 1998) argues that the function of consciousness is to broadcast information to separate functional modules through-out the brain.
- His ‘global workspace’ is a central processor that contains the contents of consciousness.
- The Workspace functions as a cognitive “blackboard”.

A Life Changed Forever

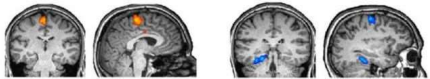
- Due to the potassium deficiency, Terri had tremendous brain damage. This brain damage was permanent and made Terri go into a vegetative state for the last fifteen years of her life. Doctors said that there was no chance that she would return to normal someday, and the controversy to keep her on life support would begin...

THE DIFFERENCES

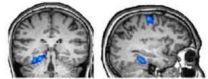
How vegetative state differs from coma & brain death

Vegetative state	Coma	Brain death
A patient in a vegetative state has slightly more brain functions than a person in a deep coma, and may open eyes or even make sounds, while remaining unresponsive to instructions	A coma is a deep state of unconsciousness in which patients are alive but unable to move or respond to the external surroundings. A patient in coma may slip into a vegetative state	A brain dead patient is dead. Brain death is linked to the irreversible loss of the brain stem, a key region of the brain responsible for the capacity for consciousness and the capacity for breathing. It is irreversible

« HEALTHY SUBJECT »

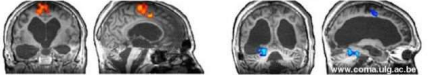



Answers « YES »





Answers « NO »

« VEGETATIVE STATE »





10. Consciousness disorders

**TAKE HOME MESSAGE:
– AWARENESS IS IMPAIRED IN
CONSCIOUSNESS DISORDERS –**

