

NEGLECT AND ATTENTION

or

***How the cavemen's brain
helped him club the boars!***

**Márcio A. Sotero de Menezes, M.D.
Associate Professor in Neurology and Pediatrics
Children's Hospital and Regional Medical Center
University of Washington**

- ~ 4 year old boy with acute onset of face, arm and leg weakness.
- ER exam L weakness + R gaze preference, L visual field cut? (versus neglect), body turned to the right
- When approached from the left and talk to he would look more confused as if he could not figure out where the voice was coming from.
- Not annoyed by excessive manipulation of the left limbs
- Hypercoagulable work up + for the Prothrombin variant so he was started on 40 mg of Aspirin
- Transferred to the Rehab Service for PT-OT-Speech T.
- After a a few weeks on the Rehab Service he was discharged home with minimal noticeable neglect.

Neuropsychological eval. 5 months after the stroke.

- FS IQ 103 (Verbal > Performance)
- Right hemisphere dysfunction
- Low (73) visual perception scores (DTVMI)
- Visual Attention = 6 (NEPSY)
- Visual Memory = 39 (Differ. Abilities Scale Recognition of Pictures).
- Clear-cut visual field neglect resolved but subtle neglect persisted.

T
1
tse_tra
: 3/10
11/20
S28.8

A CHILDREN'S HOSPITAL 0.0T

003Y M 661
Ac
2003 May
14:50:40.687

Se: 3/2
Im: 10/1
Ax: S21.8

2 x 448
g: 1.0x

512 x 448
Mag: 1.0x

: 11
3500.0
90.0

ET: 11
TR: 3500.0
TE: 90.0

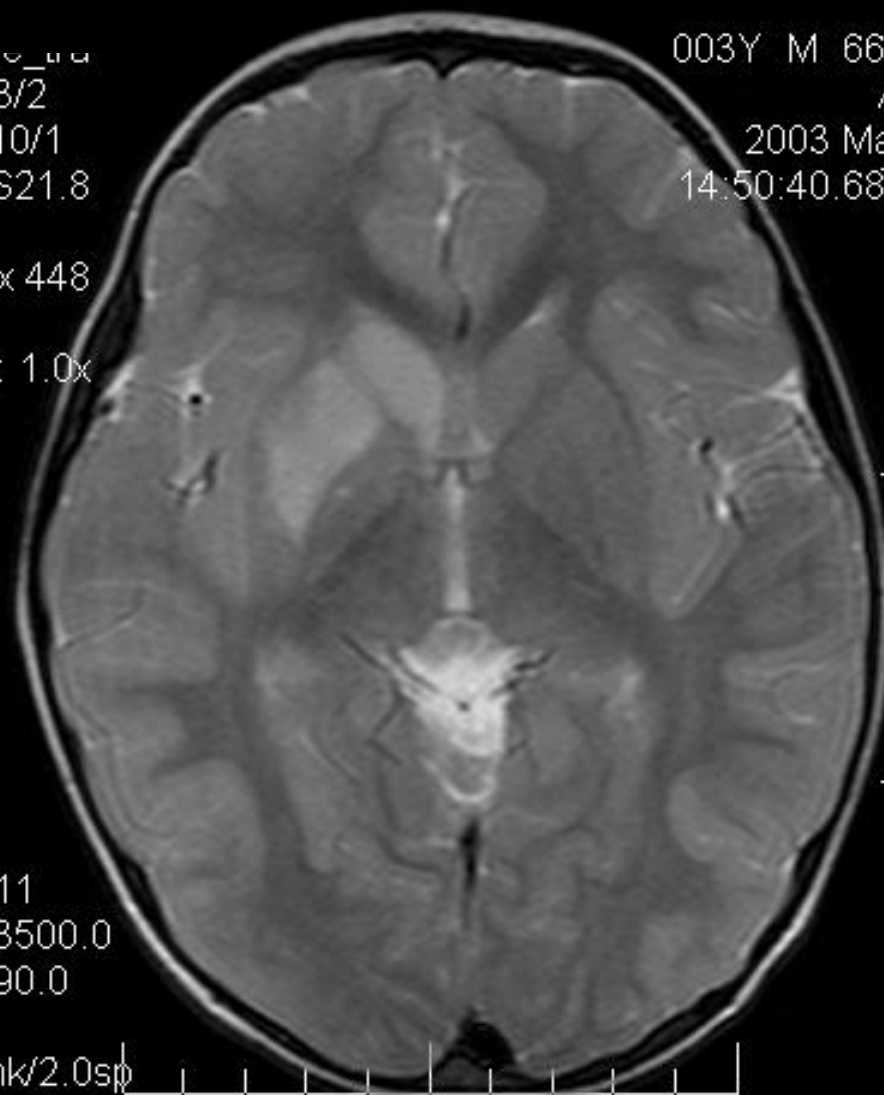
thk/2.0sp
1053 L:551

5.0thk/2.0sp
W:1040 L:544

P DFOV: 17.5 x 20.0

A CHILDREN'S HOSPITAL

003Y M 661
2003 Ma
14:50:40.68



P DFOV: 17.5 x 20.0

_3scan_trace_ADC

an_trace

003Y M

003Y M 661176

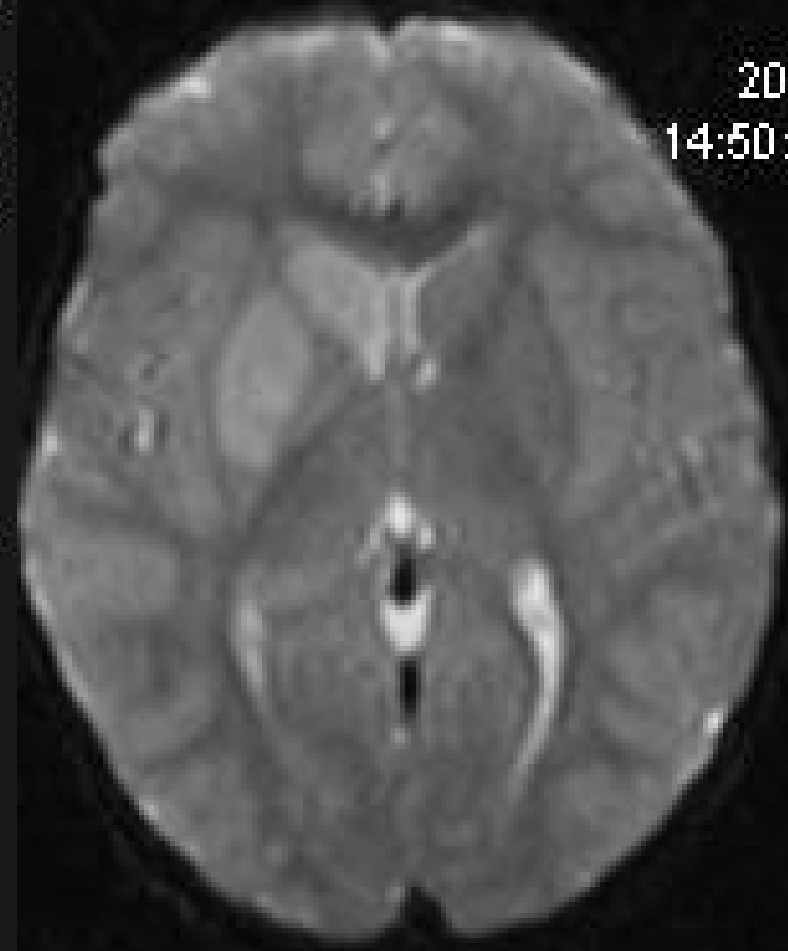
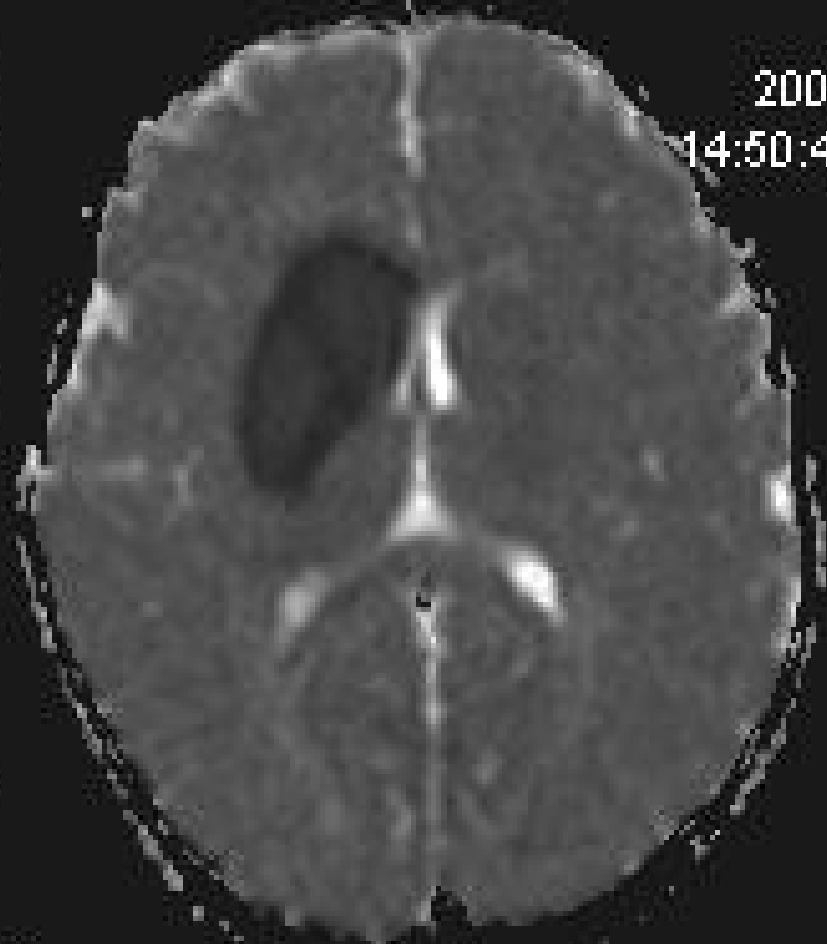
2003 M

Acc:

2003 May 22

14:50:40

14:50:40.687000



Right Hemisphere Deficits

- Neglect (spatial - left side)
- Anosognosia
- **Linguistic Deficits**
- **Literal Interpretations**
- **Difficulty identifying the relevant information**
- **Inability to interpret body-language/facial expressions**
- **Flat affect**
- **Problems with Conversational Rules (turn-talking etc)**
- **Impulsivity**
- **Confabulation (2ary to confusion?)**
- **Visuospatial Deficits - memory, orientation, construct.**
- **Prosopagnosia (inability to recognize familiar faces)**
- **Difficulty with music related tasks**

The History of Neglect

- Before Zingerle = beating about the bush
- Zingerle described neglect as a disorder of spatial representations (Zingerle 1913).
- Babinski -Unilateral asomatognosia (Anton-Babinski Synd.)
- Denny-Brown introduced the notion of "amorphosynthesis," meaning that patients were unable to synthesize contralateral stimuli into coherent percepts (Denny-Brown and Banker 1954).
- Heilman 1970's initiated better explanations and understanding of the "Neglect Network".

2 About a disturbance of attention to self/body/organism in cerebral diseases (spelling?)

1913;34:13-36. In Mark 2003

Lesions leading to clinical neglect

- Right inferior parietal cortex, BA 39-40, banks of the intraparietal sulcus) - Most common
- Dorsolateral and mesial frontal lobe
- Cingulate gyrus
- Thalamus - medial dorsal and medial pulvinar nuclei (n. reticularis?)
- Unilateral intralaminar thalamic nuclei (cat and monkey).
- Basal ganglia - caudate and putamen (dopaminergic nigrostriatal pathways)

NEGLECT AND ATTENTION:

- Neglect is the lack of localized attention to the hemibody or hemispace generally affecting the left side (“spatially biased”).
- Failure to report, respond to, or orient to novel and meaningful stimulus presented to the side opposite to a brain lesion.
- No sensory or motor deficit to explain the findings.

NEGLECT AND ATTENTION:

- Normally attention to a target is directly proportional to its novelty and relevance regardless to its spatial position.
- In cases of neglect the probability of attracting attention is proportional to the “rightness” of the stimulus (inverse to its “leftness”) = Spatial bias.

ATTENTION:

- Attention is a primitive function used by animals and cavemen alike in hunting, grabbing mates by the hair etc...
- More recently (in terms of evolution) questionable uses include paying attention in class etc...

There are two types of Attention :

- ◆ Arousal attention - vigilance
- ◆ Selective

Arousal attention or vigilance

- **Probability of an stimulus to produce a response**
- **Capability of maintaining steady state alertness, wakefulness, arousal and watchfulness**
- **Right pre-frontal (BA 8;9;44;46) and inferior parietal cortex (BA 40).**
- **ARAS including intralaminar thal. and raphe nuclei, l.ceruleus, ventral tegmental area, nucleus basalis.**



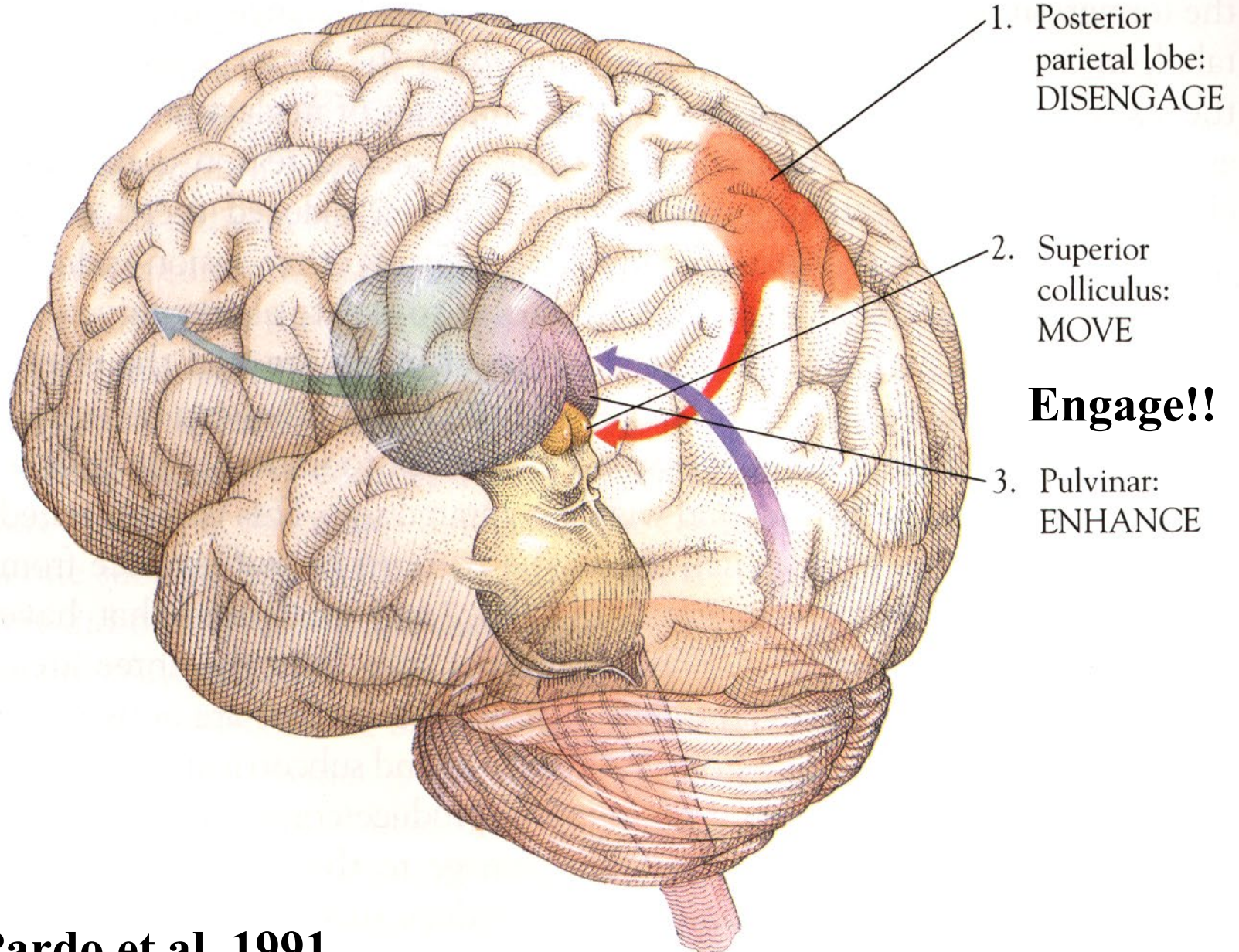
PET during “arousal” tasks

Pardo, Fox and Raichle 1991

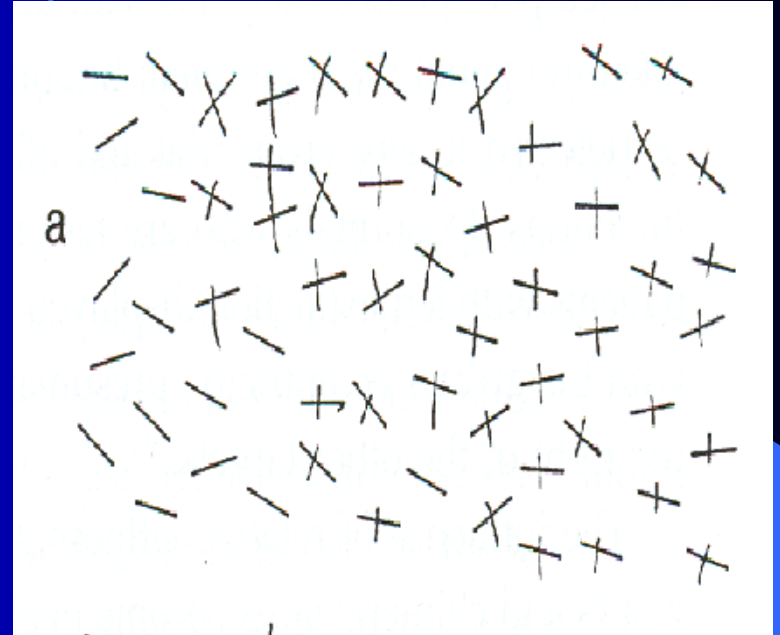
Selective Attention

- **Probability that competing stimuli will be ignored or rejected**
- **Ability to shift the focus attention from one extrapersonal event to the other.**
- **Right pre-frontal, parietal and anterior cingulate cortex, thalamus and midbrain**

Going from the boar to the tiger.



Disengaging does it happen in humans or it is only monkey business?



- Patients with neglect can cancel lines on L
- Patients with neglect tend to do better at erasing tasks than canceling since they do not have to disengage (theoretically) from prior target.

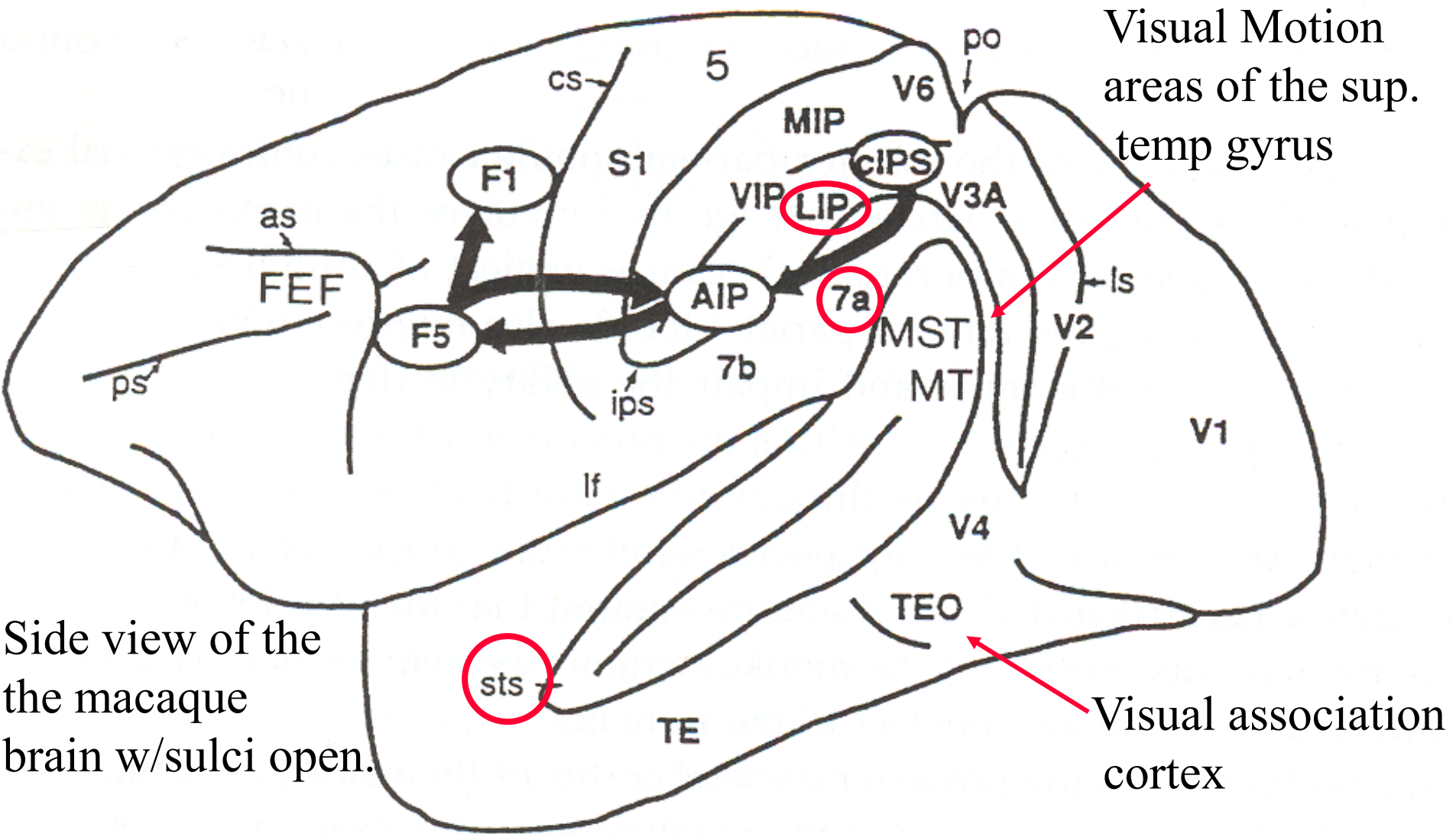
Selective Attention

- The selective attention uses a network that transforms retinocentric information into body-centered spatial frames of reference that allow targeting of stimuli (boars, tigers and other cavemen seeking the food inside of your cave including your spouse, your children and obviously you!).

Attention as awareness of the body and space :

– **Why do we need it?**

- **Body awareness - obvious !**
- **Space awareness (for the cavemen):
To track (and club) that boar
charging towards you.**



Mesulam MM. Principles of Behavioral and Cognitive Neurology. 2nd Edition, Oxford University Press, 2000.

Attention as awareness of the body-space and the parietal lobe:

-How is it done? (at least in monkeys...)

- LIP area (posterior eye field) acquires target (**the boar**) and remembers it in case you have to deviate your eyes for a moment (**the she-boar is going to “bonk” your rear before you club her boyfriend**).
- Other parietal areas (LIP+BA7) will combine retinocentric, proprioceptive (**where is my hand that is holding the club**), vestibular (**which direction am I moving?**), sound direction (**Oh s...! There is also a she-boar!**), environment landmark position (**where is the entrance of the cave?**) to create “world centered” coordinates.

Neuroanatomic Substrates of Attention:

Site

Function

Right frontal lobe; right postero-inferior parietal lobe BA39/40, ARAS, Locus ceruleus

Vigilance -Arousal. Food hungry-not

R posterior parietal specially superior posterior-parietal

**Disengaging attention (see thalamus)
Extrapersonal space- re-mapping external targets (visuo-patial memory).**

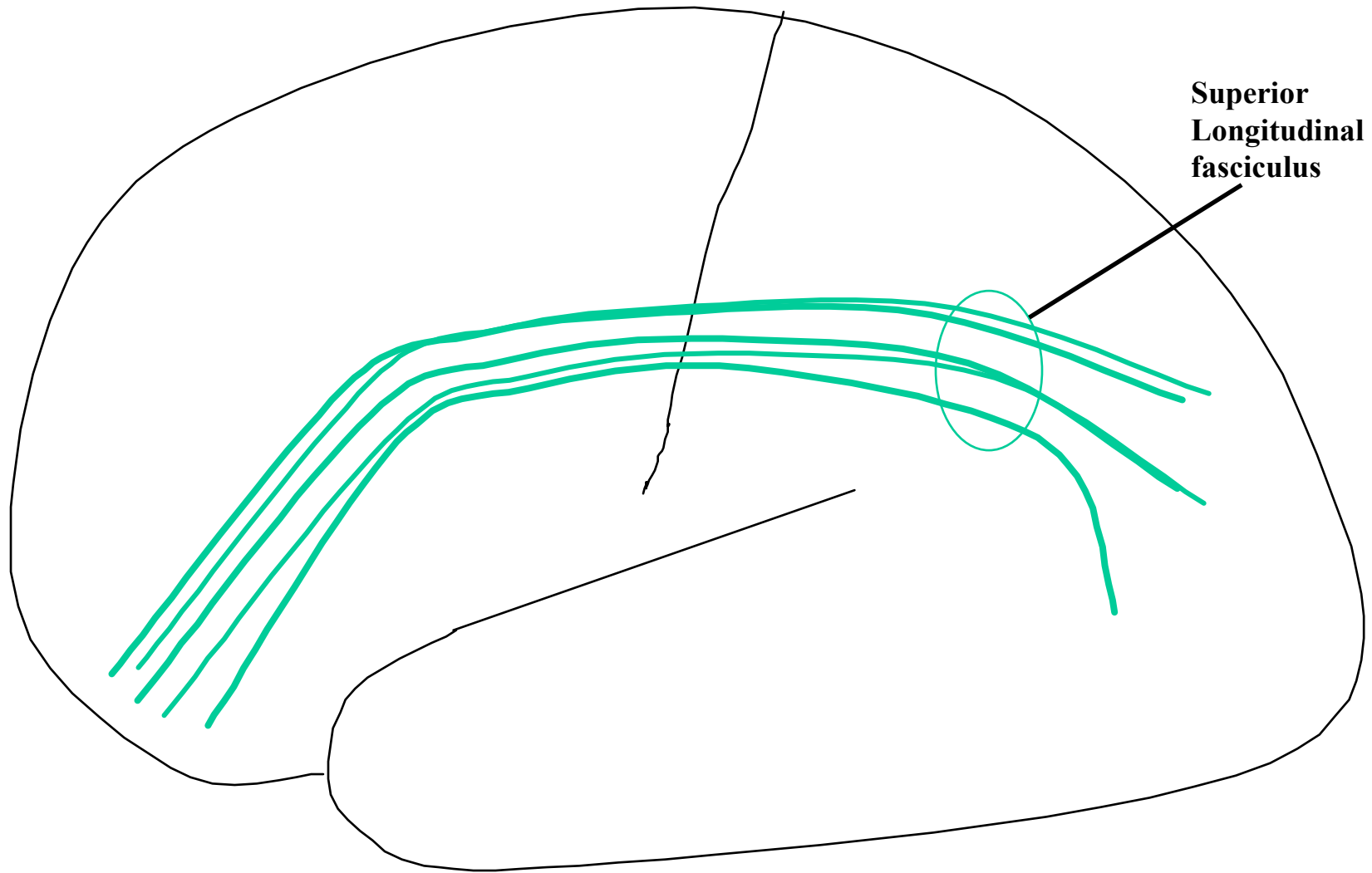
Lateral intraparietal (LIP) area

**Saccade-attention centering target
body awareness**

Anterior Cingulate

**Detection, conscious recognition and identification of the object of attention
the limbic connection (emotion modulating attention)**

Neglect is more common when the lesions involve the Superior longitudinal fasciculus.



Neuroanatomic Substrates of Attention:

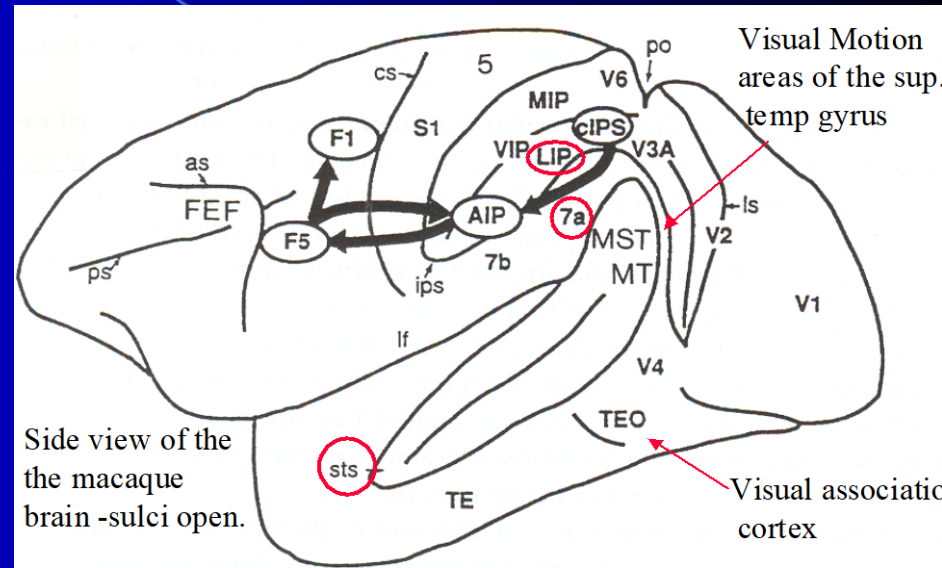
Site	Function
Thalamus - Pulvinar and Medial Dorsal Nuclei	Narrowing the focus, prioritization (relevance) and engaging of attention.
Superior colliculus	Object tracking, “foveating” objects, releasing fixation for before new target, attention shifting
Caudate and Putamen	Overt and covert shifts of attention
Anterior Cingulate, lateral frontal lobe, Wernicke’s area, parietal lobe	Executive attention network

Subcortical Neglect

- Putamen, pulvinar >> caudate

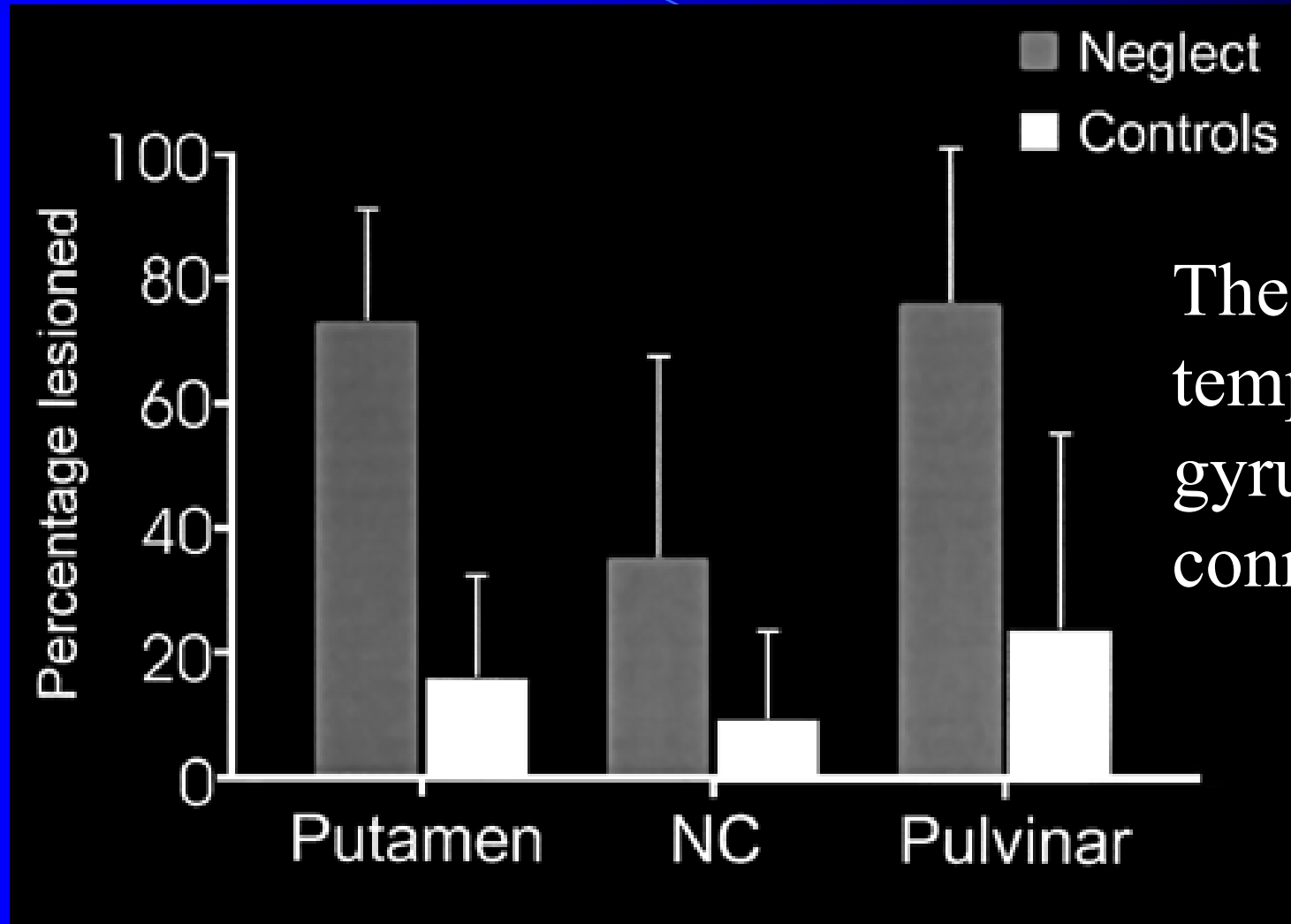
- Connection with STG (visual-motion association cortex)

- Large lesions more likely to cause neglect



Mesulam MM. Principles of Behavioral and Cognitive Neurology. 2nd Edition, Oxford University Press, 2000.

MRI lesion in neglect and controls

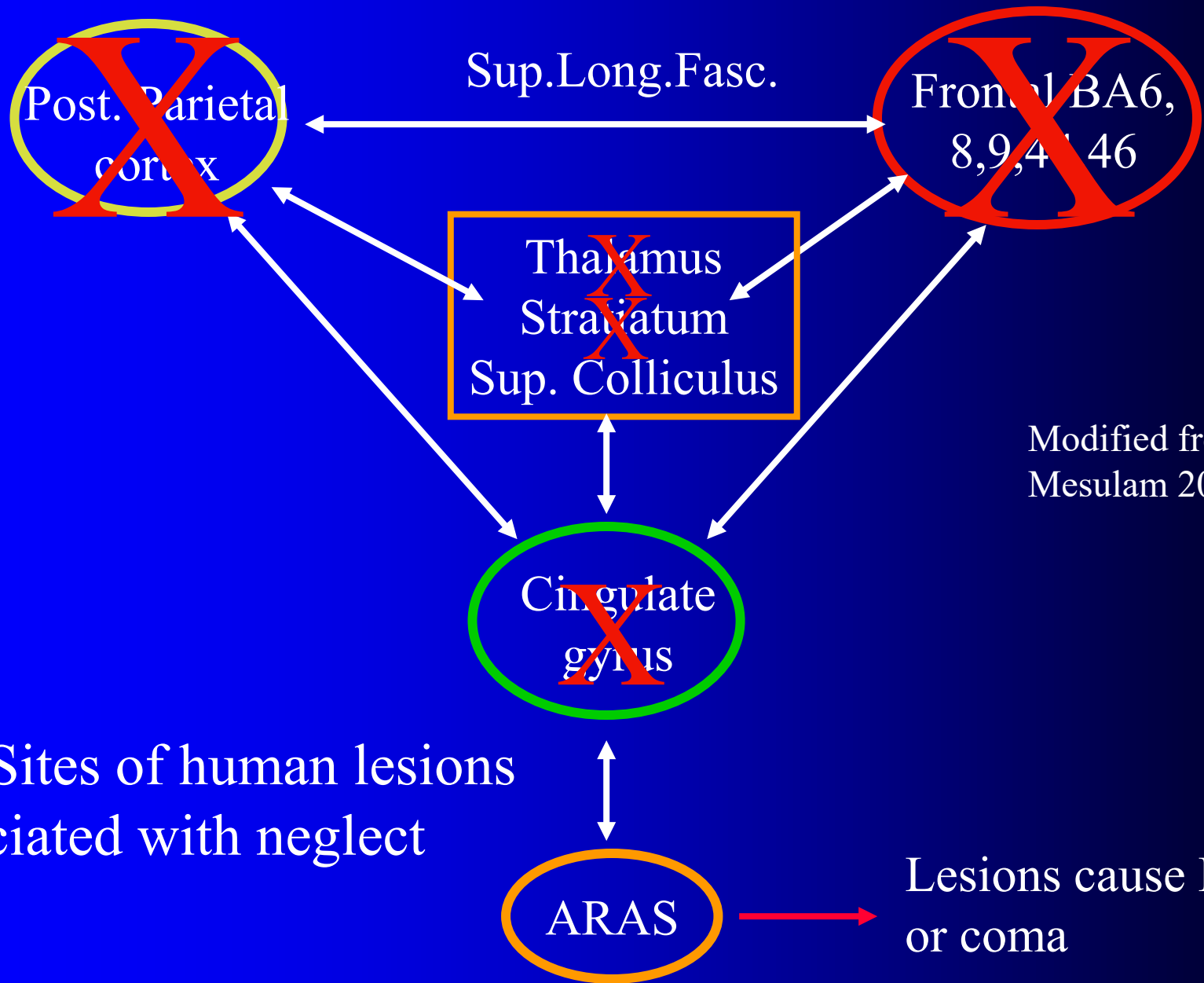


The superior
temporal
gyrus
connection

NEGLECT AND LOCALIZATION:

- Neglect is better thought of as related to a dysfunction of a NETWORK rather than to a lesion in a restricted cortical zone.

“Neglect-related” Circuitry



Modified from MM
Mesulam 2000

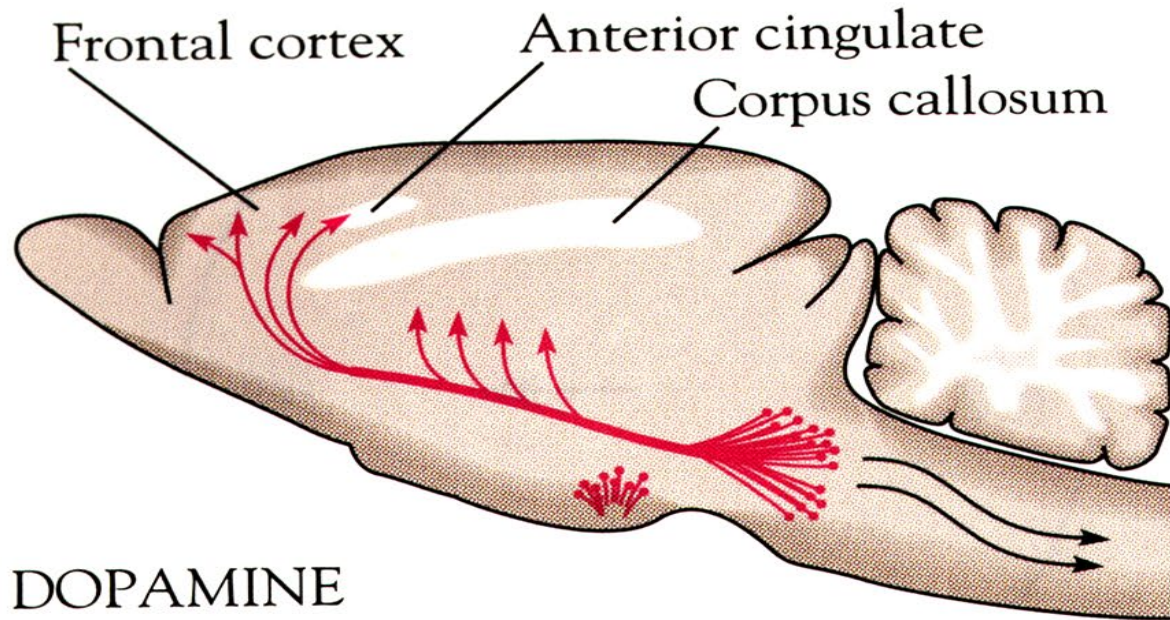
X = Sites of human lesions
associated with neglect

Lesions cause LOC
or coma

Can pharmacological
interventions bias
human attention?

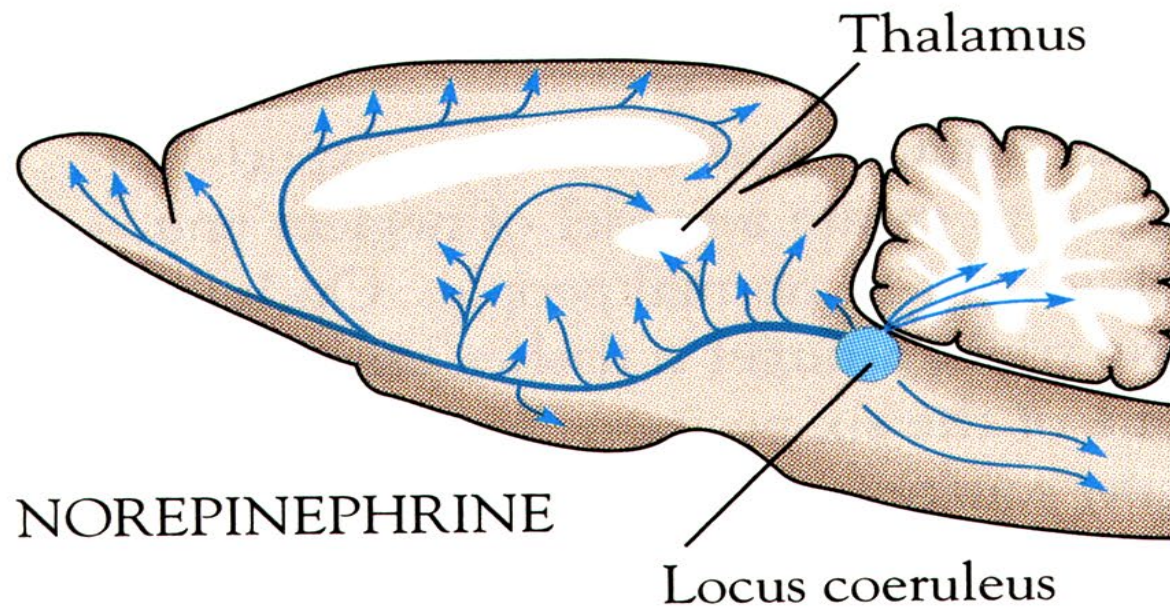
Neuropharmacology, striatal function in neglect :

- Disruption of dopaminergic-nigrostriatal pathways leads to contralateral neglect in cats, rats, monkeys and maybe in humans.
- In humans unilateral Parkinson's (right brain-left hemibody) may cause contralesional neglect.
- DOPAminergic Rx may improve neglect



Localized attention
(move/ control)

Arousal, mood
and other
behavior
modulation



NEGLECT AND RIGHT HEMISPHERE:

- Severe contra-lesional neglect occurs almost exclusively after right hemisphere lesions. Thus neglect is commonly seen on the left side of the body.

Why neglects accompanies mostly right lesions:

- Simplistic explanation:
 - Right hemisphere → awareness of both sides
 - Left hemisphere → awareness of right hemibody

RIGHT HEMISPHERE, ATTENTION AND BODY AWARENESS:

- The right hemisphere appears to be dominant for arousal and spatial attention
- Right brain lesions are associated with greater electroencephalographic slowing than those with left brain.
- Patients with right hemisphere lesions are also have diminished galvanic skin responses when compared to normal controls or individuals with left hemisphere damage (arousal).
- Ipsilateral stimulus reaction time faster w/ L hand.

Other Theories to Explain Neglect

- Attention Vector theory – L hemisphere vector more powerful than the R sided one.
- Premotor intentional deficit (frontal?)
- Disorder of Mental representation:
Patients fail to describe objects/buildings on the left side of a familiar scene based on their mental picture of that view. Map of France, Piazza del Duomo (Milan) experiments.





**Task = Name towns in France using only a mental
a picture of the country**

Types of Neglect I

- **Sensory Neglect = Deficit in Awareness**
 - Visual, tactile, auditory
 - Spatial (right hemisphere)
 - Personal (stimuli in contact with patient)
 - Parietal lesions (Daffner 1990)
- **Representational Neglect**
 - Internal mental images
- **Extinction = Neglect brought up by a competing stimulus in the opposite hemisphere) double simultaneous stimulation.**

Types of Neglect II

- **Motor Neglect = Deficit in Motor Response**
 - Lack of = left sided akinesia (arm/leg)
 - Delayed requiring encouragement = left hypokinesia
 - Decreased amplitude of move/ = left hypometria
 - Right frontal lesions (Heilman & Valenstein 1972)
- **Inability to maintain posture or movements = Motor impersistence**
- **Motor extinction = Moves L limbs on demand except when moving also the right side.**

Neglect = biased attention

When the neglect is severe patient behaves as if one half of the universe has ceased to exist.

MM Mesulam 2000.

Manifestations of Neglect

- First days after stroke lethargic + eyes/head deviated to the right (Vulpian sign)
- Tonic rotation of the trunk to the right side
- Ignoring all manner of input from left;
- Inability to localize sounds from left
- Problems with responding to people and objects on left - looking confused when talked to from the left (Mesulam 2000).

Manifestations of Neglect

- Lack of grooming/shaving, dressing of the right side of the body
- Will not eat food on the left side of the plate
- Inability read or write on the left half of the page
- Decreased arousal (Heilman 1977)
- Poor participation in rehab activities

The Man Who Fell out of Bed. In O. Sacks: *The Man Who Mistook His Wife for a Hat.* Harper Perennial NY, 1970.

...He had come in for some tests, he said. He had no complains, but the neurologists feeling he had a “lazy left leg” thought he should come in.

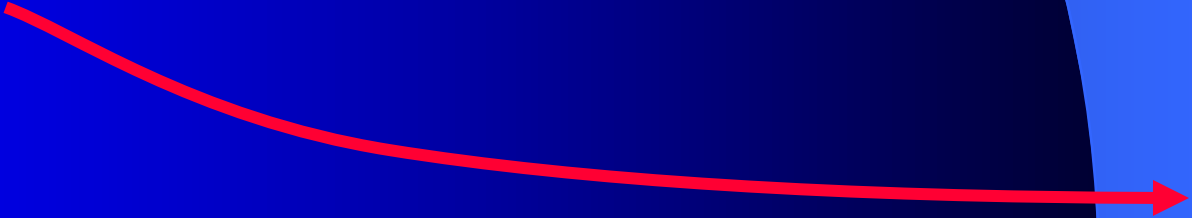
- That same night he woke up and found someone else's severed leg in his bed.

The Man Who Fell out of Bed. In O. Sacks: *The Man Who Mistook His Wife for a Hat.* Harper Perennial NY, 1970.

...Since it was New Year's eve he thought it was sick joke. So he threw "the damn thing" out of the bed...he somehow came after it and then "it" had become attached to him.

Manifestations of Neglect

Body Awareness Related Deficits:

- Bumping into objects on the left hemispace/hemifield.
 - Problems navigating through halls and doorways.
 - Difficulty moving, attending to and recognizing left sided limbs
 - Lack of insight into and awareness of deficits
- 

ANOSOGNOSIA

A = WITHOUT, NO OR LACKING

NOSO(S) = DISEASE

GNOSIA OR GNOSIS = KNOWLEDGE

- A Greek term coined by Babinski before he started scratching people's feet.
- Typically manifests as denial or rationalization of contralateral (left) paralysis.
- Denial may persist even when attention is drawn to the affected limb
- May occur independently from neglect

ANOSOGNOSIA

- Denial of ownership of their contralateral limb a phenomenon known as **somatophrenia**
- Dislike of left side of the body or **misoplegia**.

Other funky manifestations of neglect:

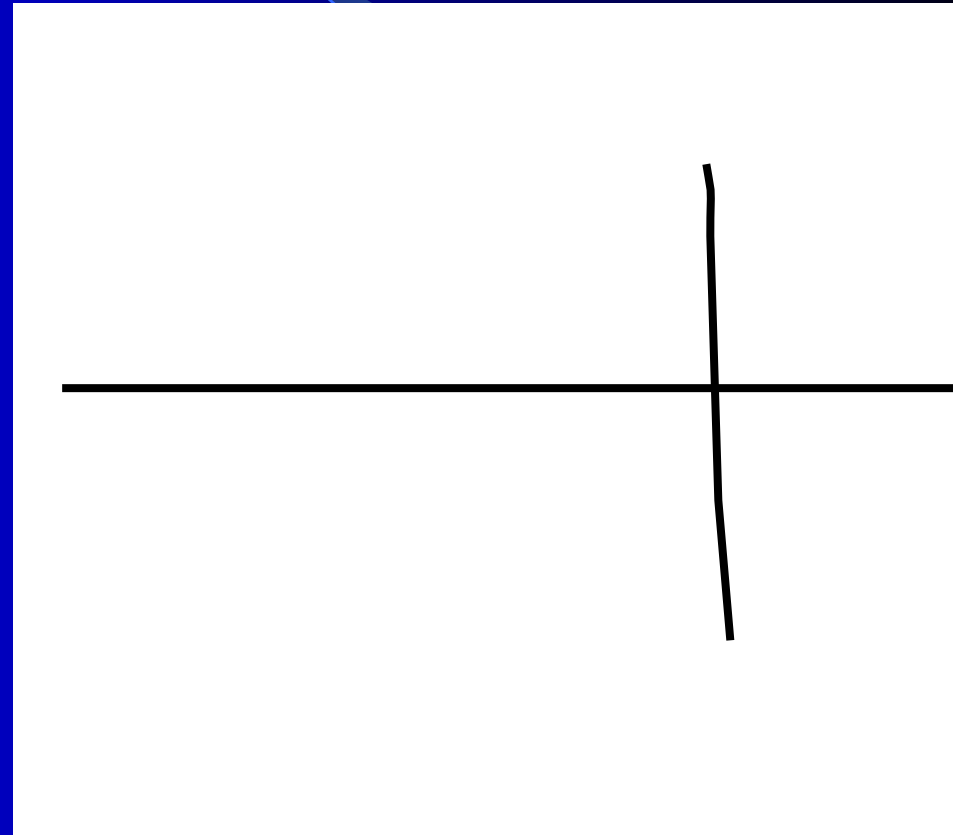
- Anterograde amnesia for objects on the neglected hemifield (duh!)
- Retrograde amnesia for objects on the neglect hemifield (hippocampal connection STS/IPL)

Testing for Neglect

- Line bisection = mark to the R of midline
- Cancellation tasks = missing targets on the L
- Drawing
 - Omission of details on the L
 - Left sided features on the right
- Reading = Starts on middle of line, misses 1/2 word
- DSS extinction (visual, tactile, motoric).

Line bisection task

- Line > 20 cm
- Lines < 5 cm confusing results.
- Avoid time, eye or head movement restriction.
- Larger error if presented on the left field.



Neglect of the left side of a drawing.

Model



Patient's copy



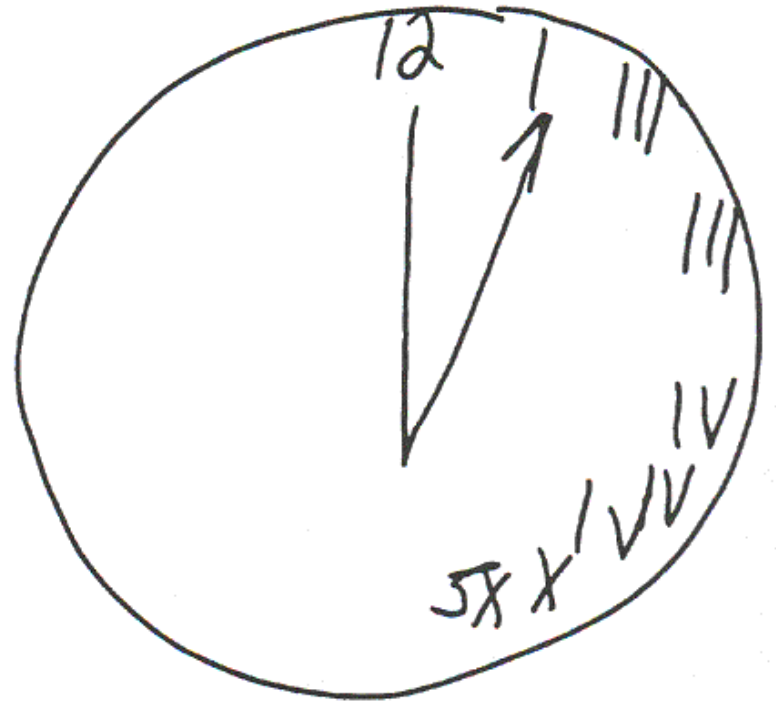
Model

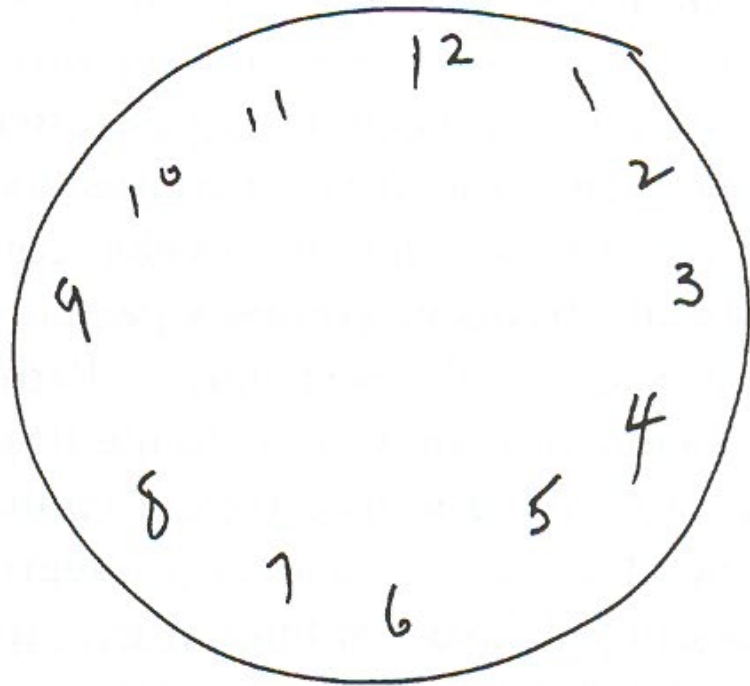
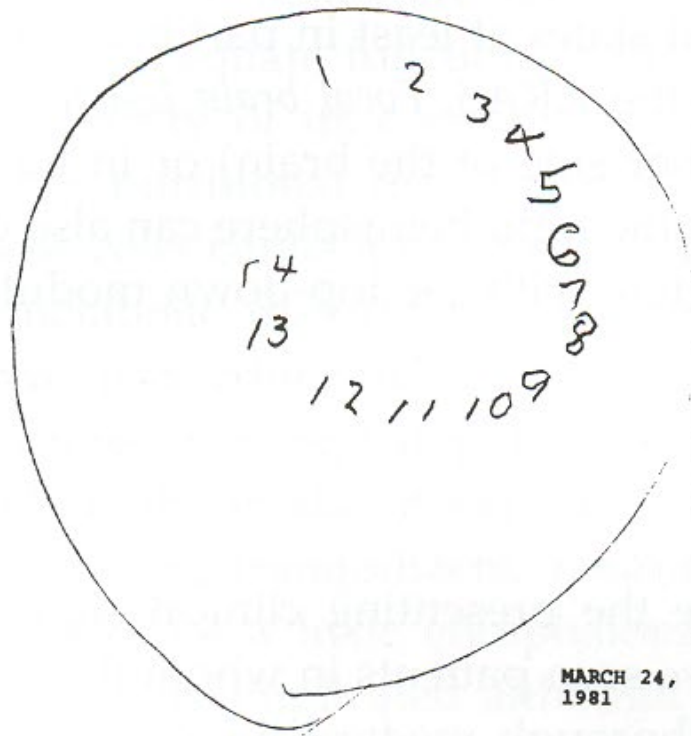
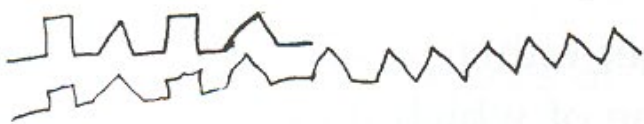


Patient's copy



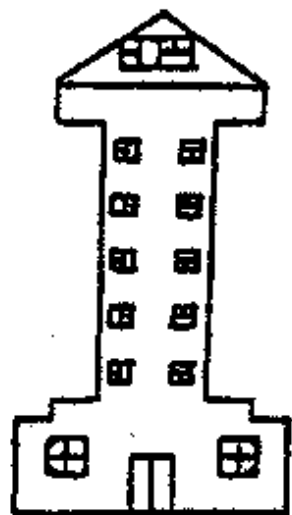
to me but no results were discussed with
me either as to findings or potential
meanings. I am left hanging in the
air with little or no knowledge of
my condition its implications as
to mortality or to safe
methods. This is an extremely
serious omission of good
medical procedures
and does not speak well
for a major medical
institution. I therefore
had serious qualifications
as to both the
administration and medical
competence of this
institution and the
particular section. I
was refused medical
assistance. I strongly
note in fact in
that the resident Miss
Dexelle saw me
briefly and then
left before I could
question her as to



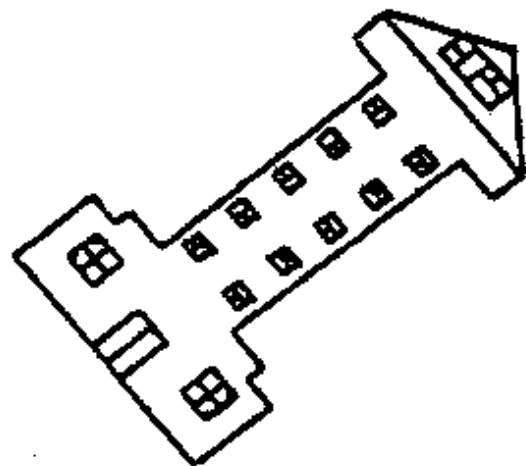


NOVEMBER 3, 1981

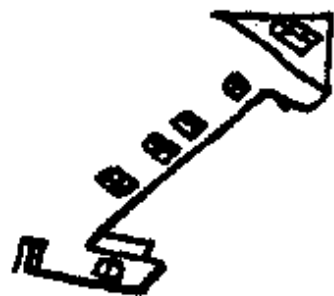
Relative cortical hypoperfusion due to congestive heart failure.



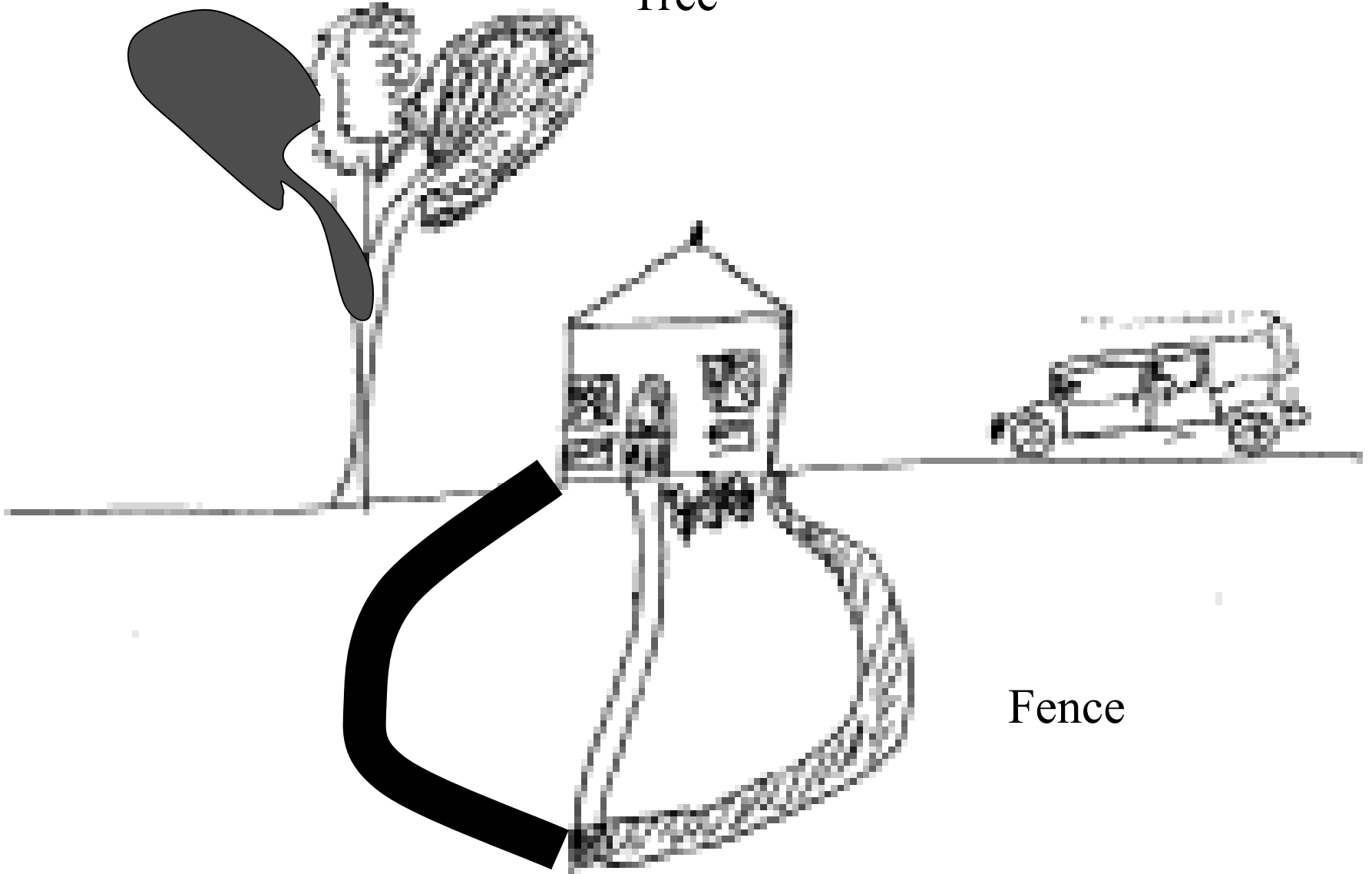
A



B

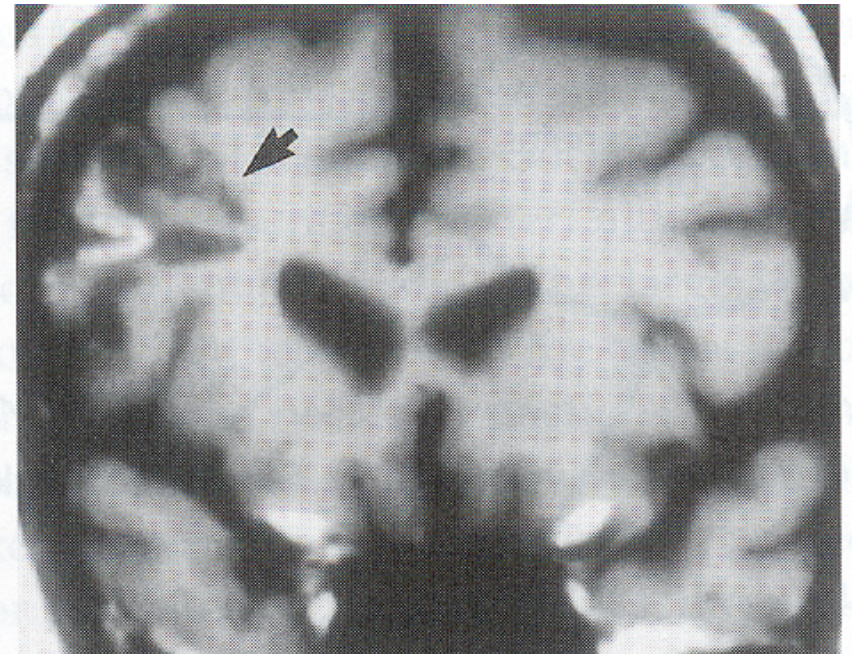
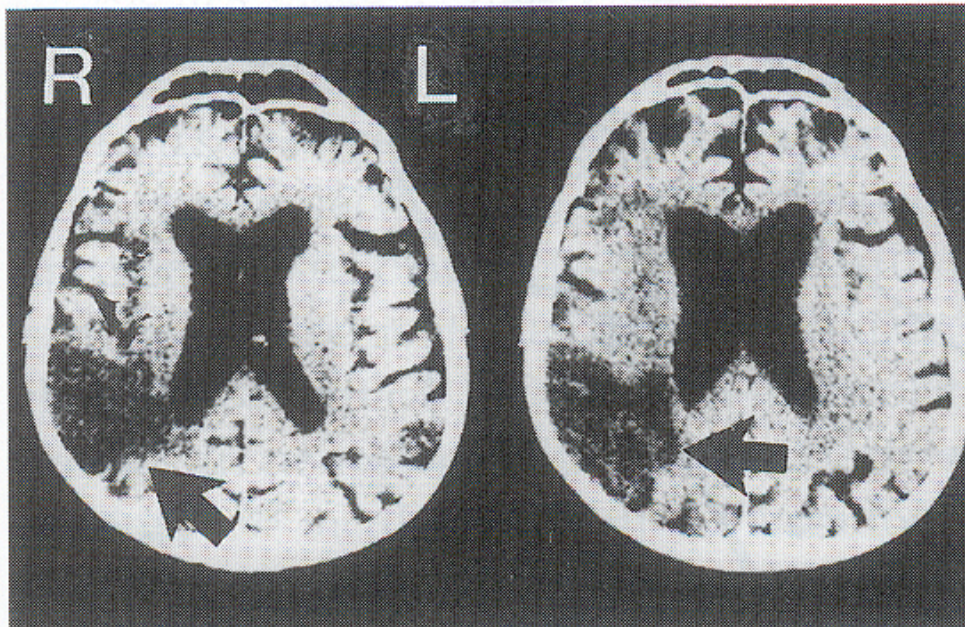
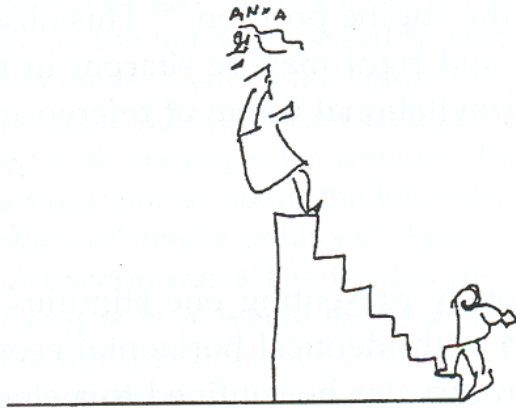
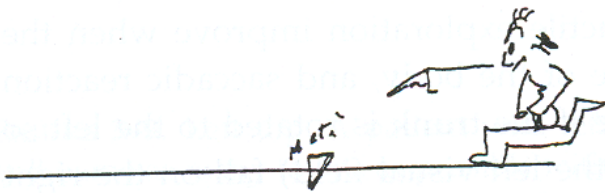


Tree

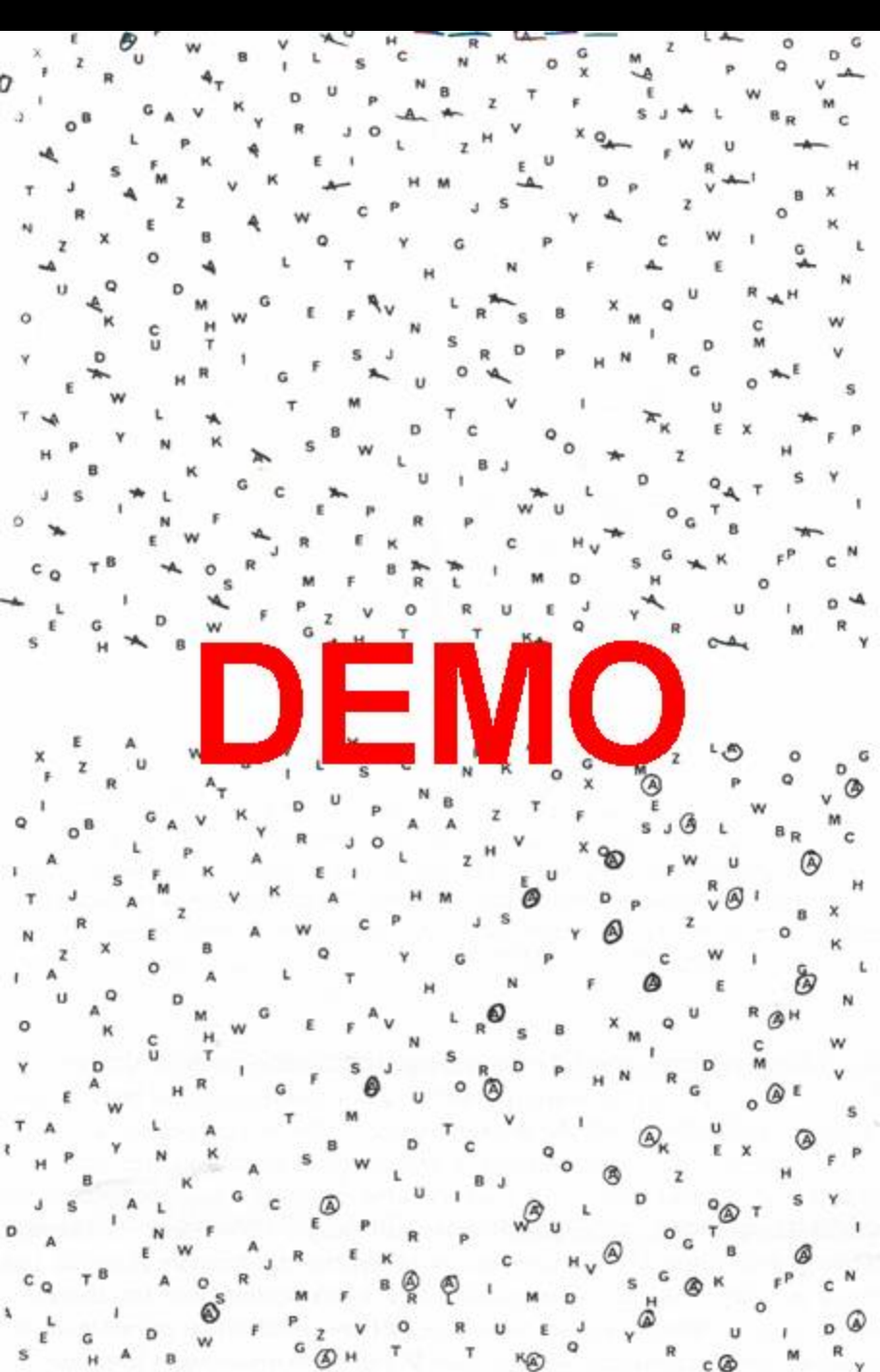


Fence

Dove la sinistra?



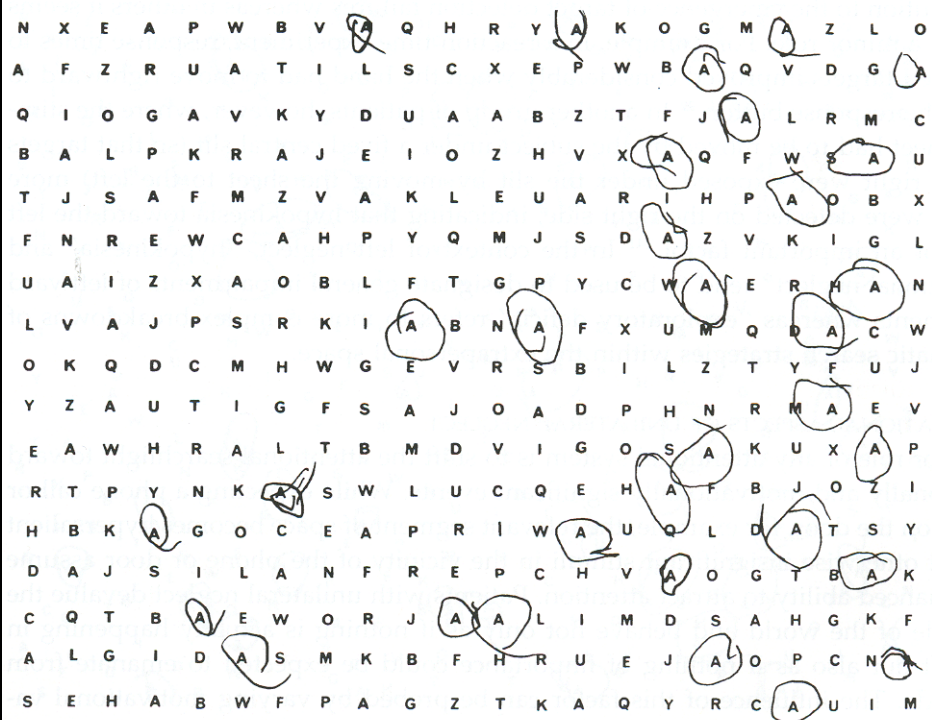
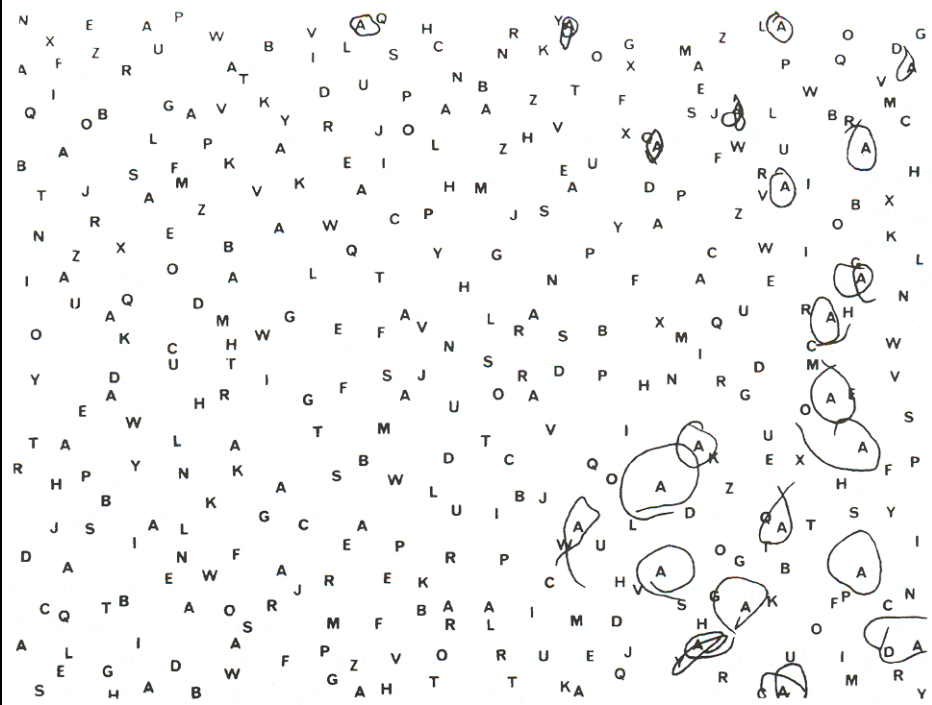
Felini's CVA and Neglect, in Mesulam 2000. Sense of humor always helps!



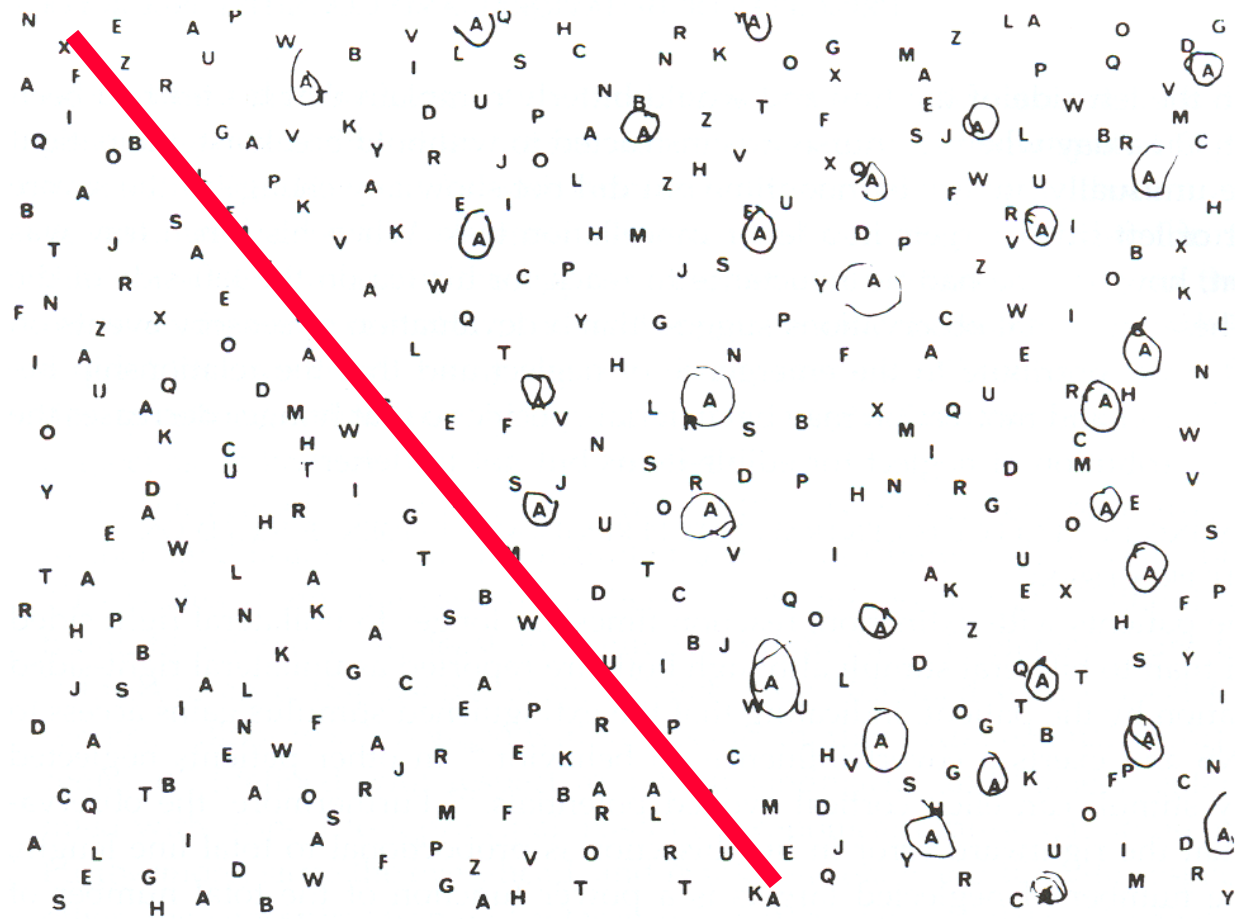
Normal

Letter cancellation
task

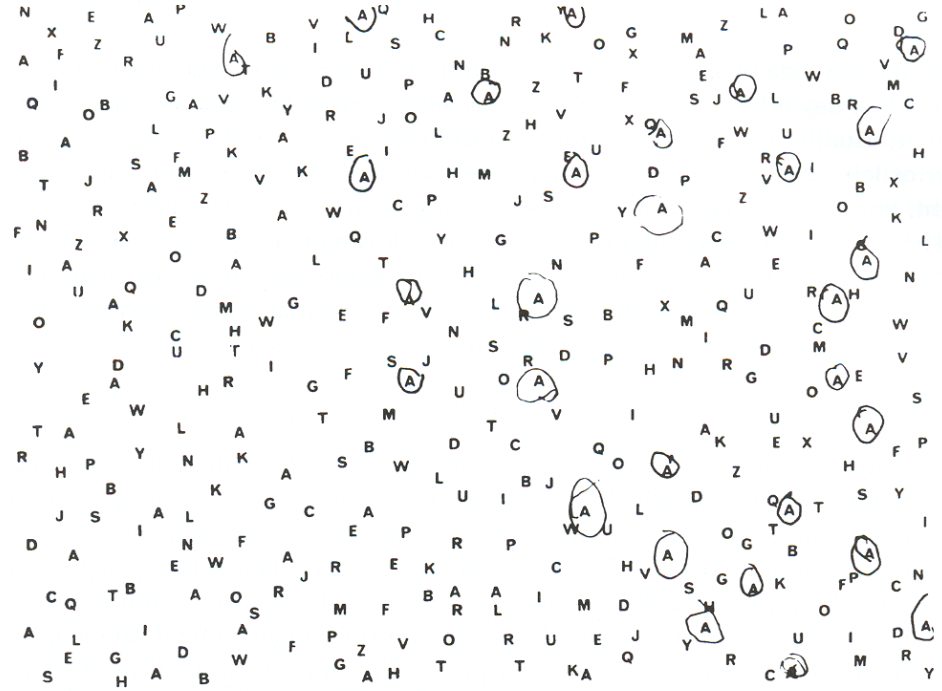
Left neglect



Neglect is less marked when the letters are more organized.

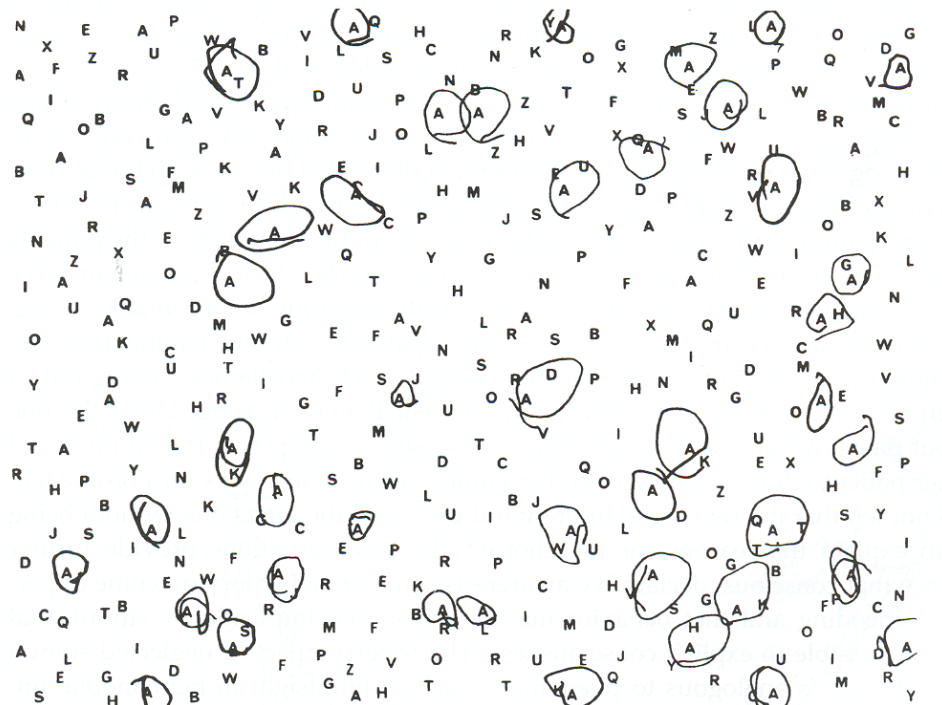


A year later same patient L neglect is improved.
Note worst neglect closer to the body on the neglected hemisphere (L inferior quadrant worse than L superior quadrant).



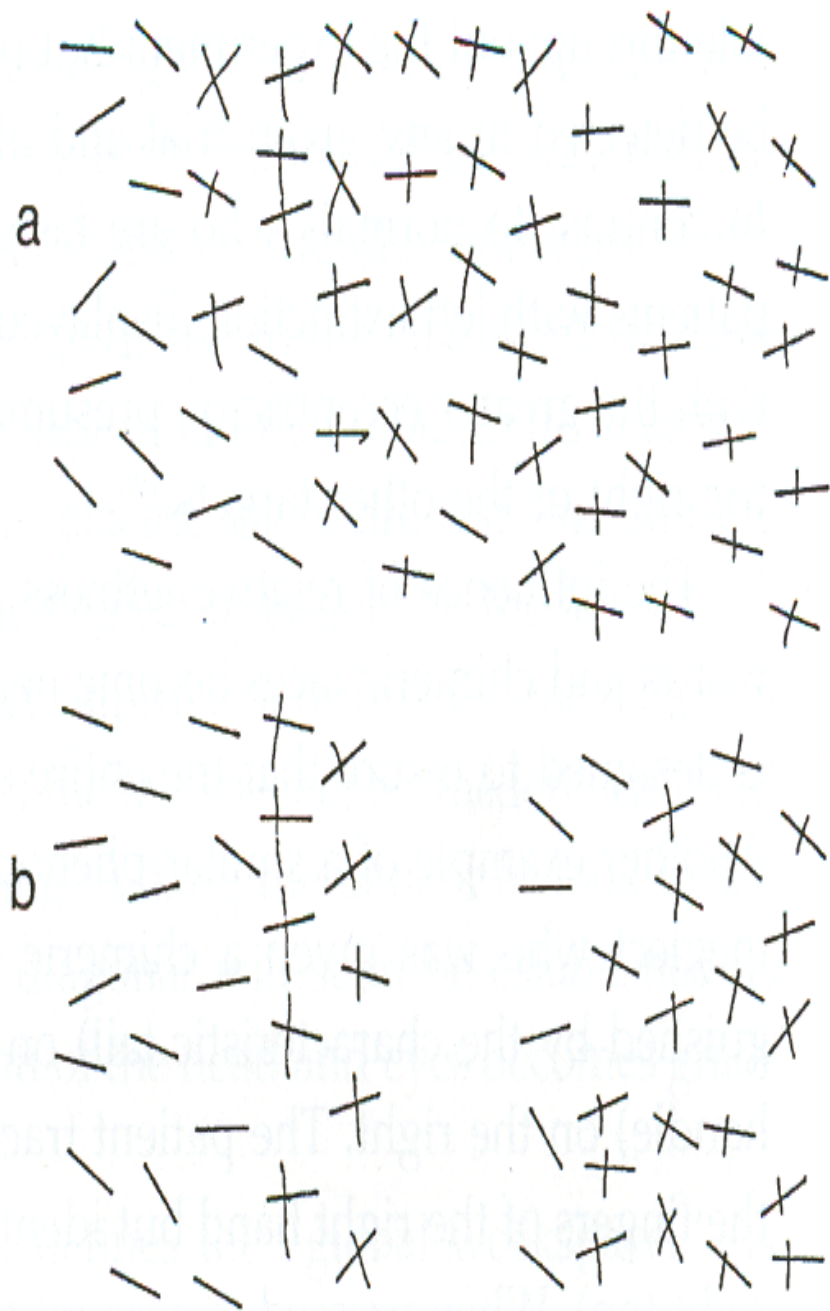
A year latter same patient

L neglect is improved.



Further improvement with stimulus of a penny for each right answer.

Not shown: Back to baseline after a few minutes.



Simple cancellation
test line crossing.

Lines ~ 2 cm.

Criteria:


Missing > 2 lines
on the left field.

Neglect is worst when
test is presented on the
left visual field.

The increasing the sensitivity of cancellation tasks

- Large number of stimuli (>50)
- Distracters (find the A's among A,B,C,D...)
- Variable orientation (crossing lines)
- Presentation of test on the left hemispace/hemifield.

Differential Diagnosis of Neglect

- Hemianopia
 - Bisects the line w/o problems
- Hearing Loss
 - AICA CVA,
 - Sensory-neural hearing loss
- Hemiparesis
- Look for a bigger picture the hemisphere syndrome 

Right Hemisphere Deficit Syndrome

- Attentional Problems (ADHD-like)
- Emotional and interpersonal relationship problems
- Non-verbal communication dysfunction (expressive or receptive)
- Verbal >> Performance IQ
- Visuo-spatial deficits
- Left sided (body) motor or sensory deficits, asymmetrical OKN's, neglect
- Imaging: -Right hemisphere atrophy or lesions, especially on the parietal lobe.

Course of Neglect I

- In spite of an initial dramatic picture, overtime neglect becomes intermittent and/or milder disorder which, may not be recognized unless specialized testing is done (Mark 2003).

Course of Neglect II

- Many patients with neglect recover but most of the data comes from R hemisp. CVA cases:
 - Visual inattention and neglect recovered much more quickly (median 8 weeks to 9 weeks)
 - Slower recovery for more subtle manifestations of neglect, such as extinction (median 19 weeks) and motor impersistence (median 26 weeks).
 - Other CVA symptoms persist longer hemianopia (median 32 weeks) or hemiparesis (median 64 weeks).

Course of Neglect III

- Type and size of lesions are key!
- Hemorrhagic stroke recovers better than ischemic
- Neglect and anosognosia have a significant impact in the patient's recovering predicting longer hospitalization and less independence after a CVA.
- Children have a better prognosis for recovery

Many sources, for review see Voeller 1998 (Peds Neuropsychiatry) and Mark VW. Neglect: in Medlink 2003.

Management of Neglect I

- **Systematic scanning training** of the neglected hemispace (Weinberg 1979).
- **Sensory cueing** (LED's on glasses, sound) Efficacy ?
- **Motor cueing** –Take the R hand to left of the paper or use the left hand.
- **Eye patching** ? R eye patching may be useless but good field patching maybe useful?
- **Prism Adaptation** improves reading and the spatial recall of images from memory ? Usefulness in daily life.
- **Repetitive transcranial magnetic stimulation (rTMS)** at 1 Hz over the left parietal lobe, QOday for 2 weeks, improves performance in pts with L neglect (pen-and-paper tasks).



15

before caloric stimulation



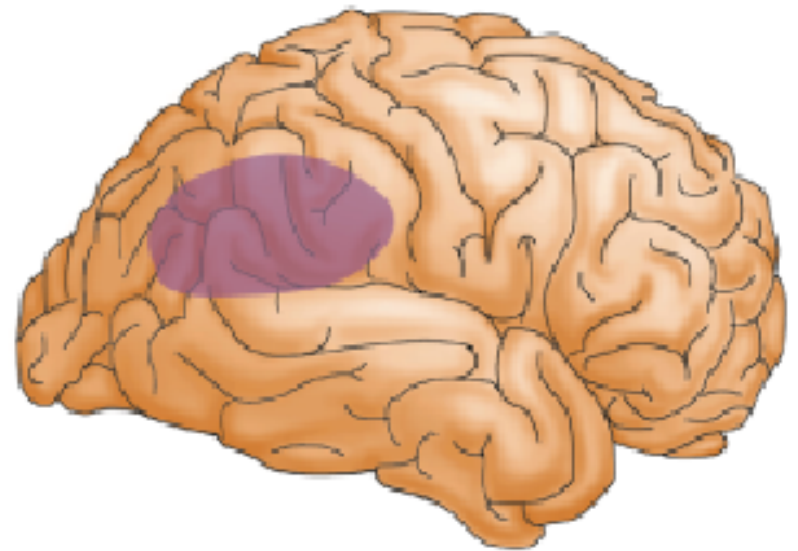
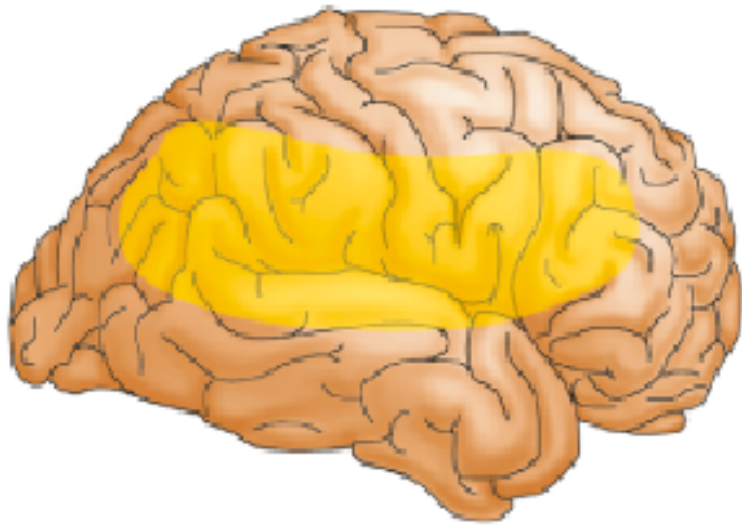
27

after caloric stimulation

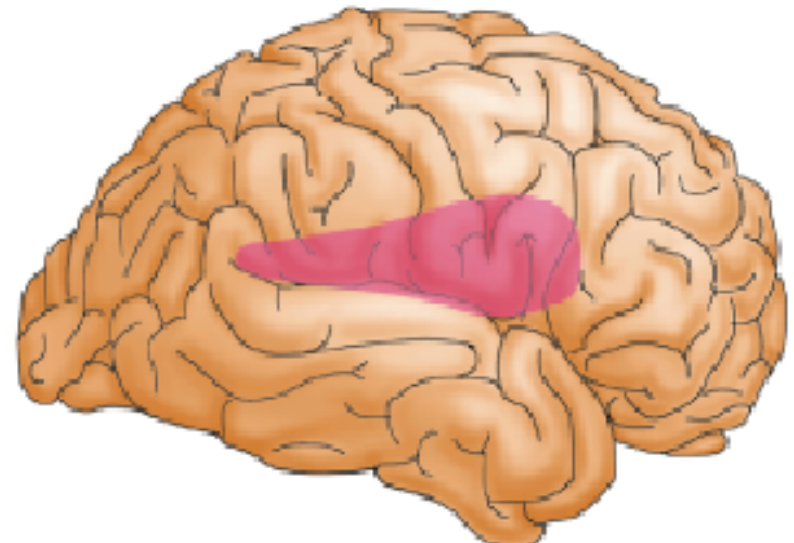
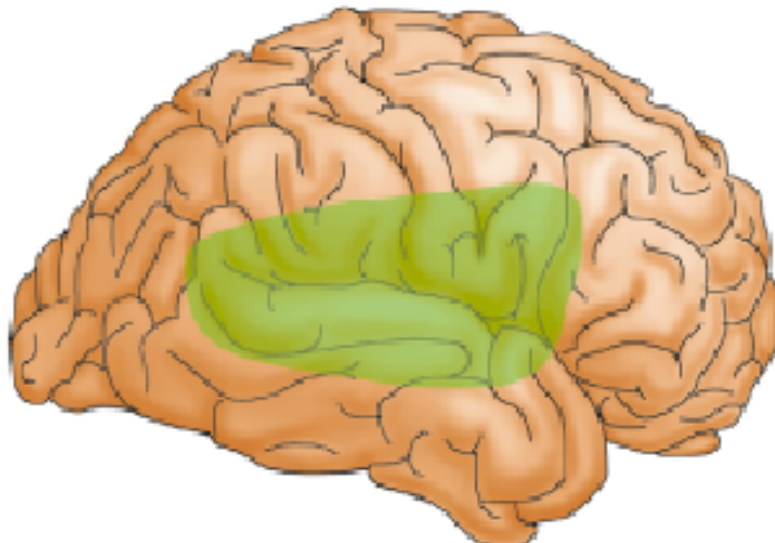
Task = Name towns in France using only a mental a picture of the country before and after caloric stimulation.

Management of Neglect II

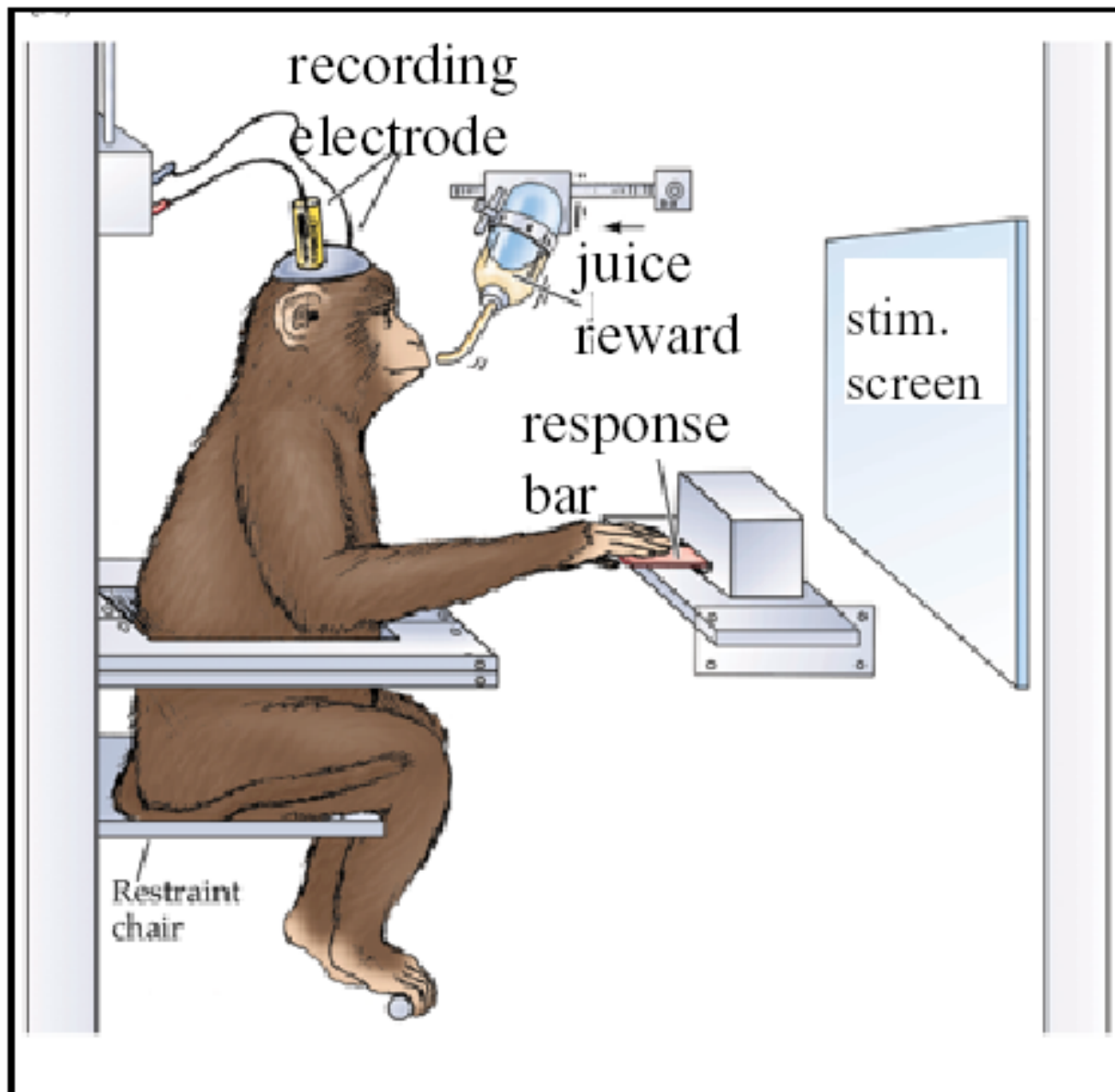
- **Vestibular stimulation:** Injecting cold water into the ear contralateral temporarily ameliorates neglect. Interestingly, it also helps hemiparesis in neglect patients. Transient resolution of somatosensory inattention and anosognosia are not easily explained by the shift in gaze.
- **Transcutaneous electric nerve stimulation (TENS).** Contralateral electric stimulation of the neck has shown variable success.
- **Dopaminergic Rx:** Bromocriptine and Sinemet (L-DOPA +Carbidopa) improved neglect symptoms in 2 small trials.
- Enough! Dai! Chega!Basta! The end



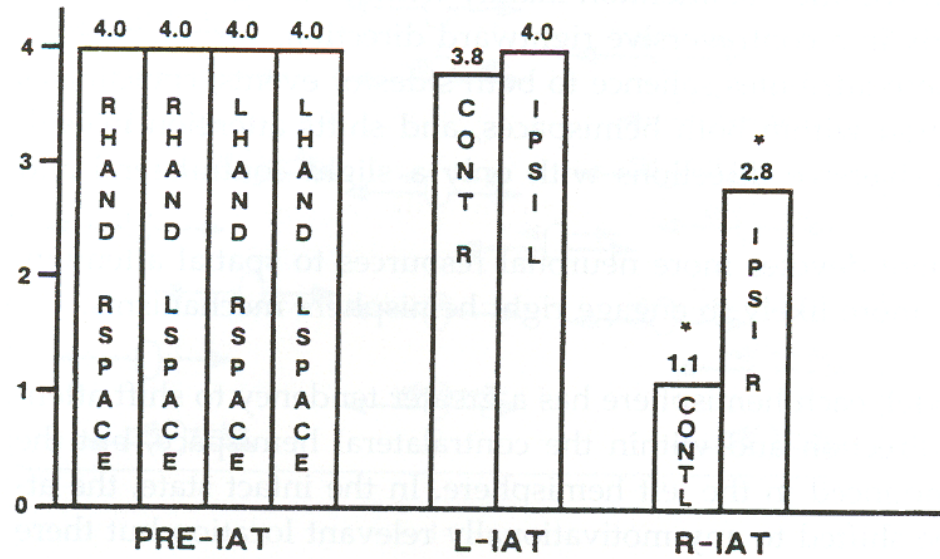
lesions in four patients with neglect syndromes
as determined by brain imaging



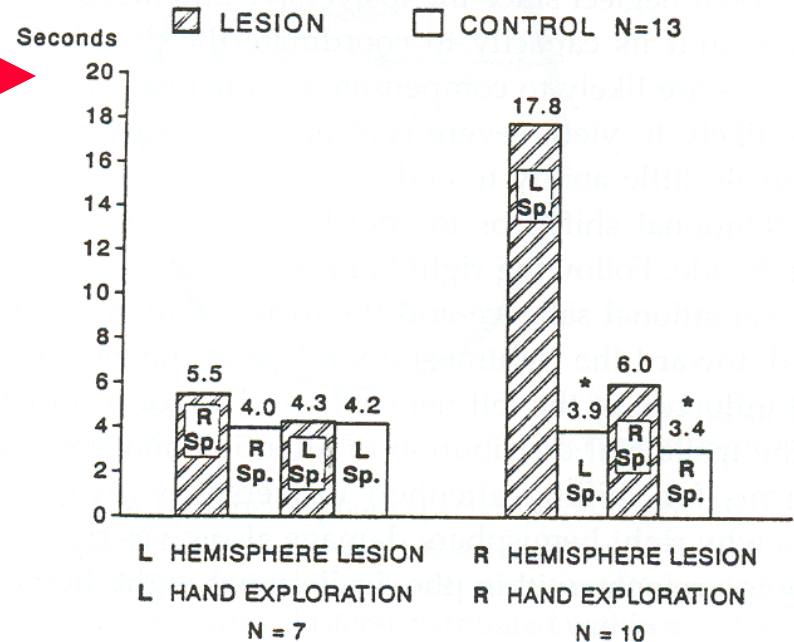
Can we localize in the brain areas related to attention?



INTRACAROTID AMYTAL TEST (IAT)



BLINDFOLDED HEMISPATIAL MANUAL EXPLORATION



4 = Perfect Performance →

Exploration done w/ hand Ipsil. to injection

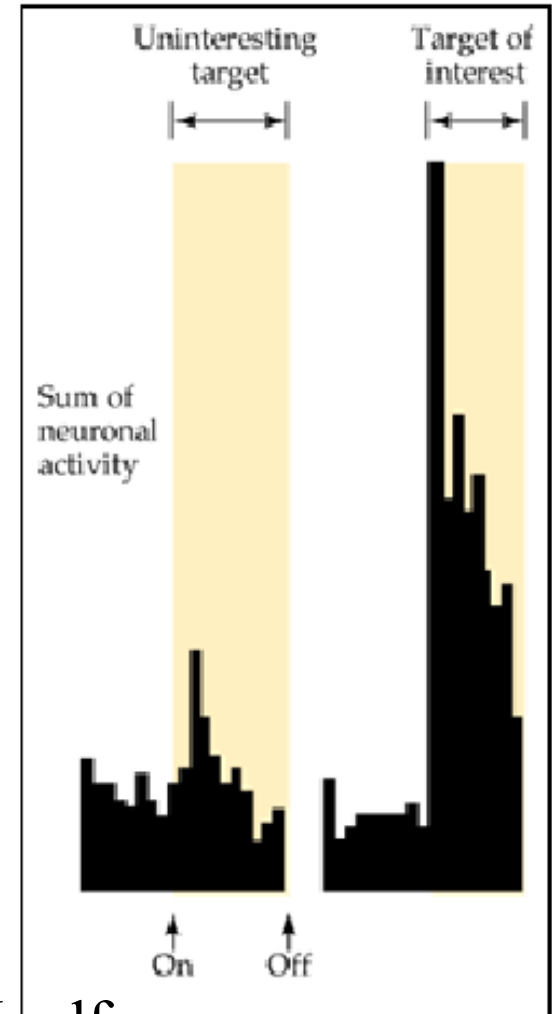
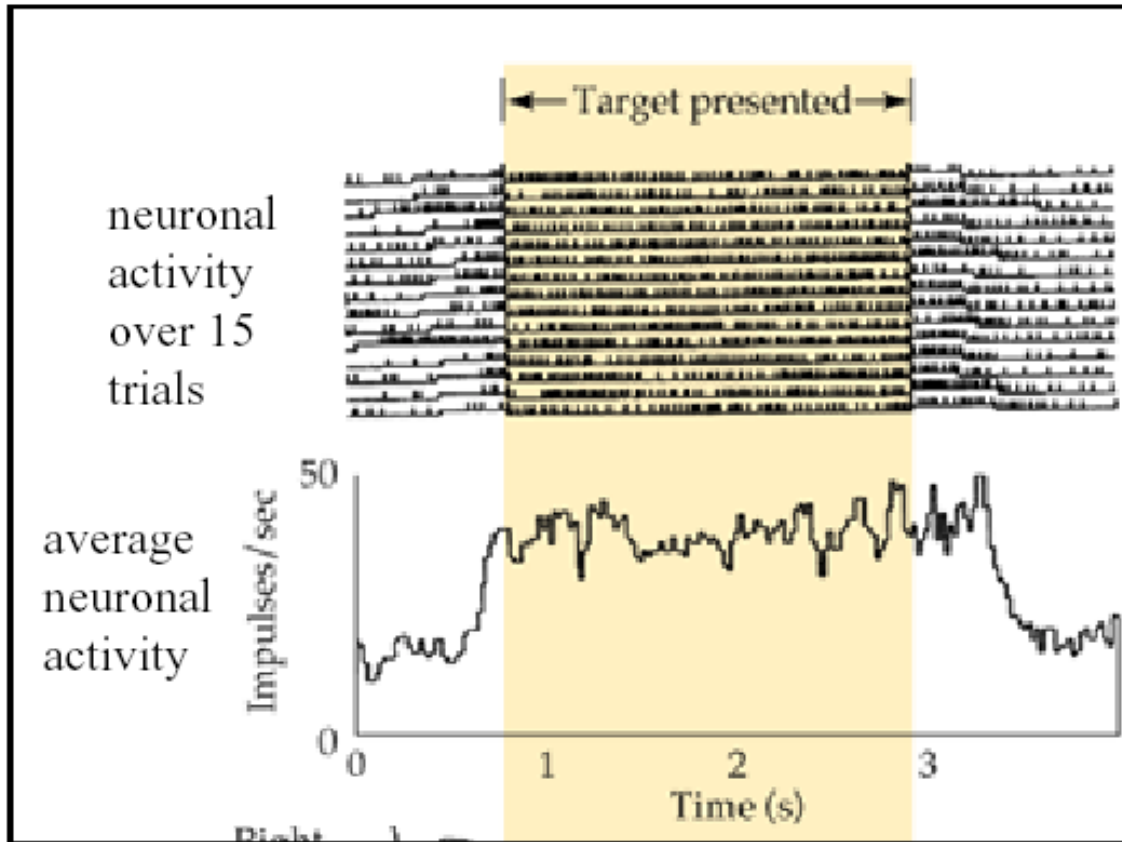
L injection. No deficit

R inj. L >>> R hemispace exploration deficit.

Time for Object Detection →

Both L and R hemispace explorations were slower in patients with L hemisphere lesions (L worst than R)

So, kind of parietal?



Attention as awareness of the body and space II:

- **After you club the she-boar behind you, your eyes quickly find back the male boar charging towards you.**
- **Some LIP information is sound direction based (she boar is behind and to the right - CLUB IT).**
- **LIP and BA 7a neurons fire not only with overt attention shift (attention shift → looks for object and finds it - Where the heck is the boar?) but also with covert ones (cue appears → attention shift -What's between the two big trees? Oh S...! It is boar!).**