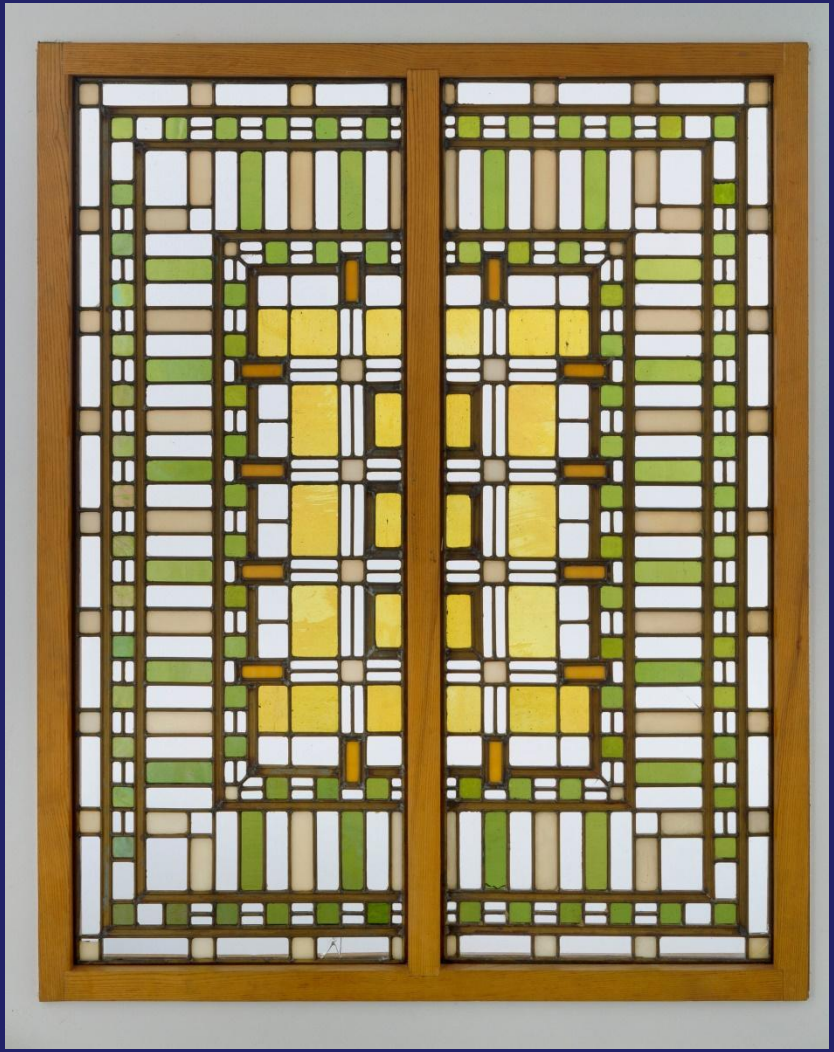
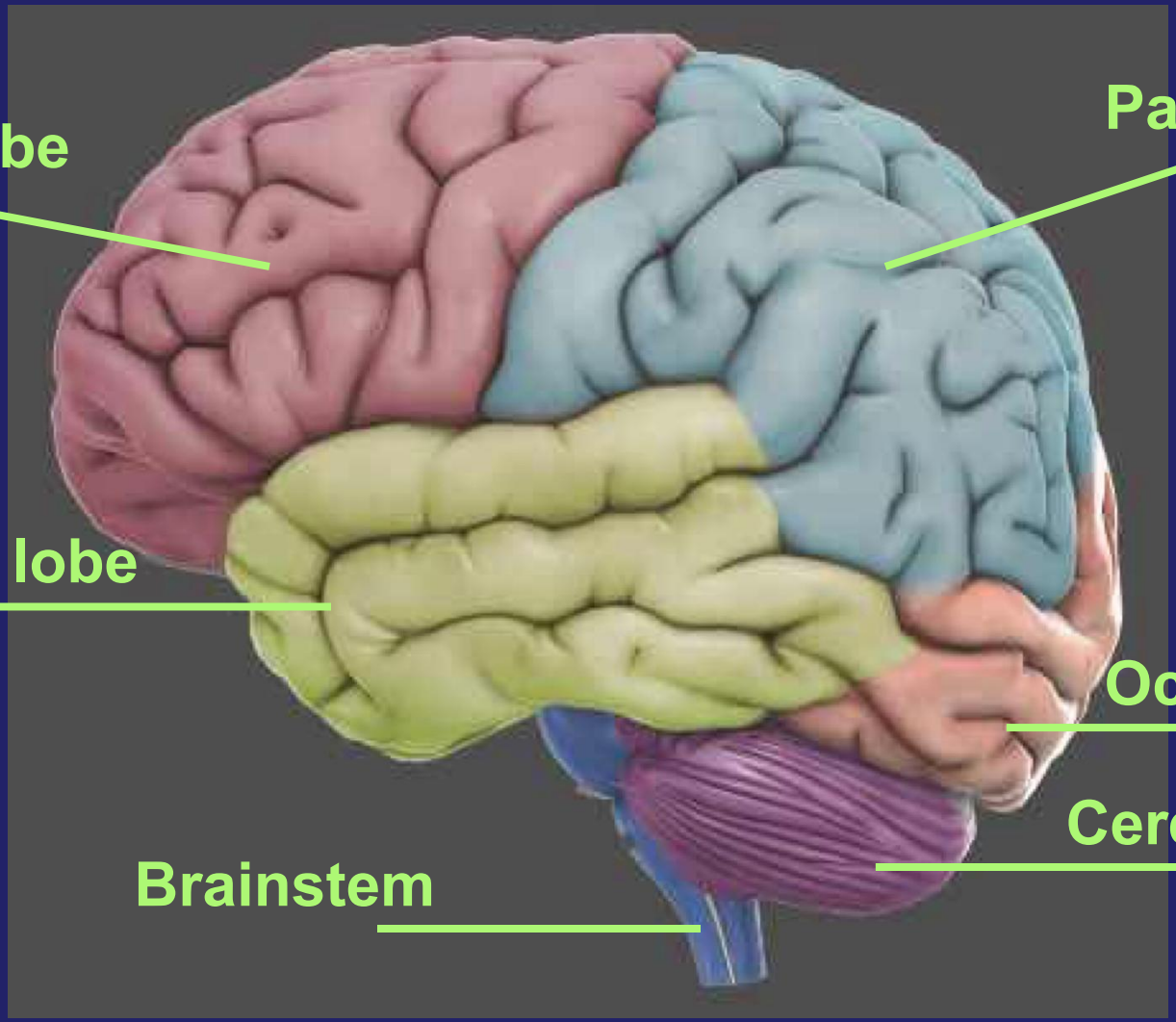
Neurologic Neglect



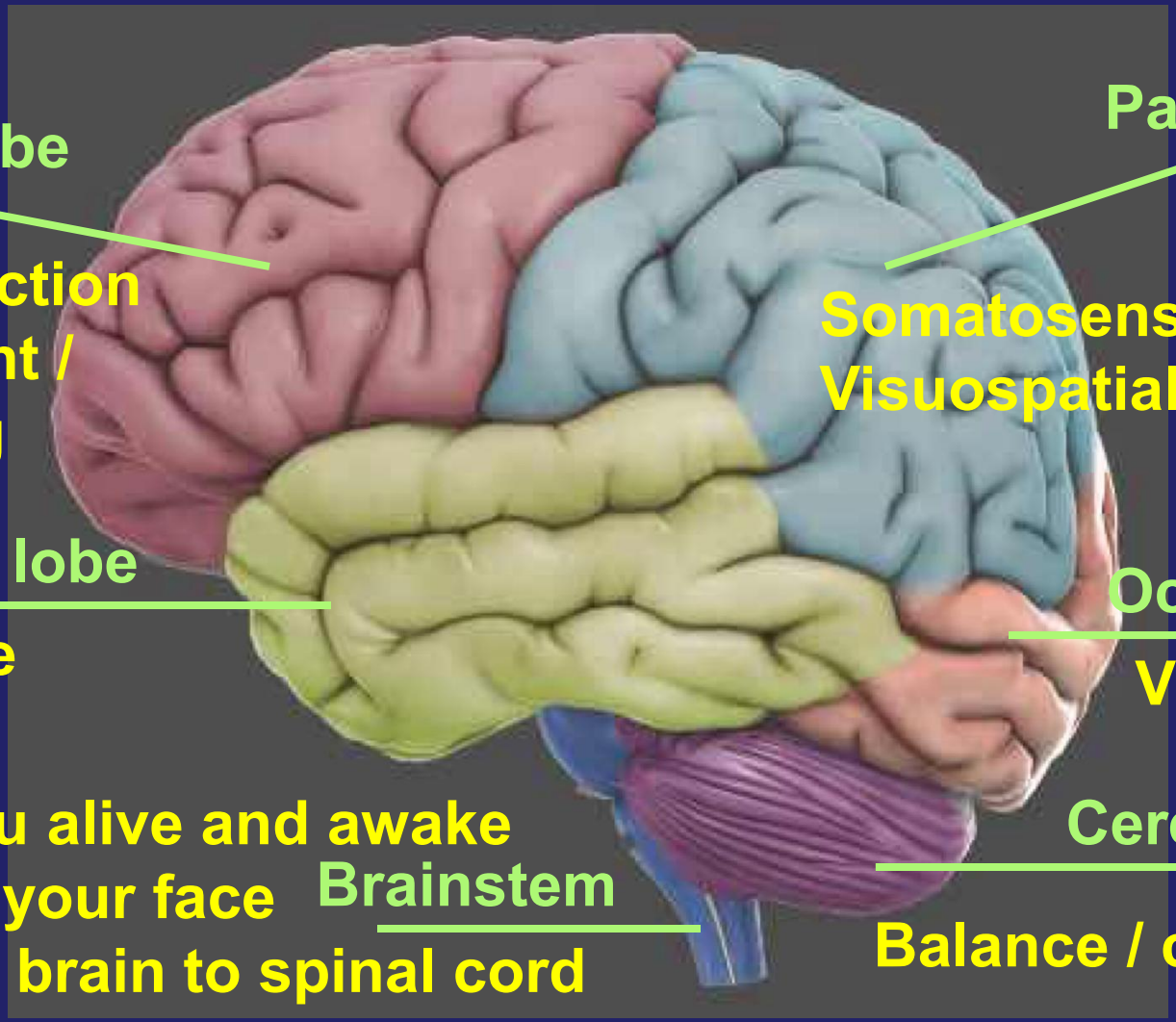
Joanne Alonso Byars, MD

June 19, 2014

- Before we start on neglect, a quick review of neuroanatomy…



- What do these brain regions do?
  (simple version)



Frontal lobe

Motor function
Judgement / reasoning

Parietal lobe

Somatosensory function
Visuospatial function

Temporal lobe

Language
Memory

Occipital lobe

Vision

Keeps you alive and awake
Operates your face
Connects brain to spinal cord

Brainstem

Cerebellum

Balance / coordination

- What is neglect?
  - Failure to report, respond, or orient to meaningful or novel stimuli presented in a portion of space
    - Usually the left
  - In spite of adequate elementary motor and sensory function
- Frequently (but not always) associated features
  - Anosognosia
    - Lack of awareness of deficits
  - Anosodiaphoria
    - Lack of concern about deficits

- Differential diagnosis of neglect: neglect vs deficit in elementary sensorimotor function
  - Visual hemispatial neglect
    - Hemianopia
  - Tactile hemispatial neglect
    - Hemianesthesia
  - Auditory hemispatial neglect
    - Ear/CN VIII lesion
    - Cortical lesions do NOT cause unilateral hearing loss
      - Can use imaging, evoked potentials to distinguish
  - Motor neglect
    - Hemiparesis, ataxia, clumsiness

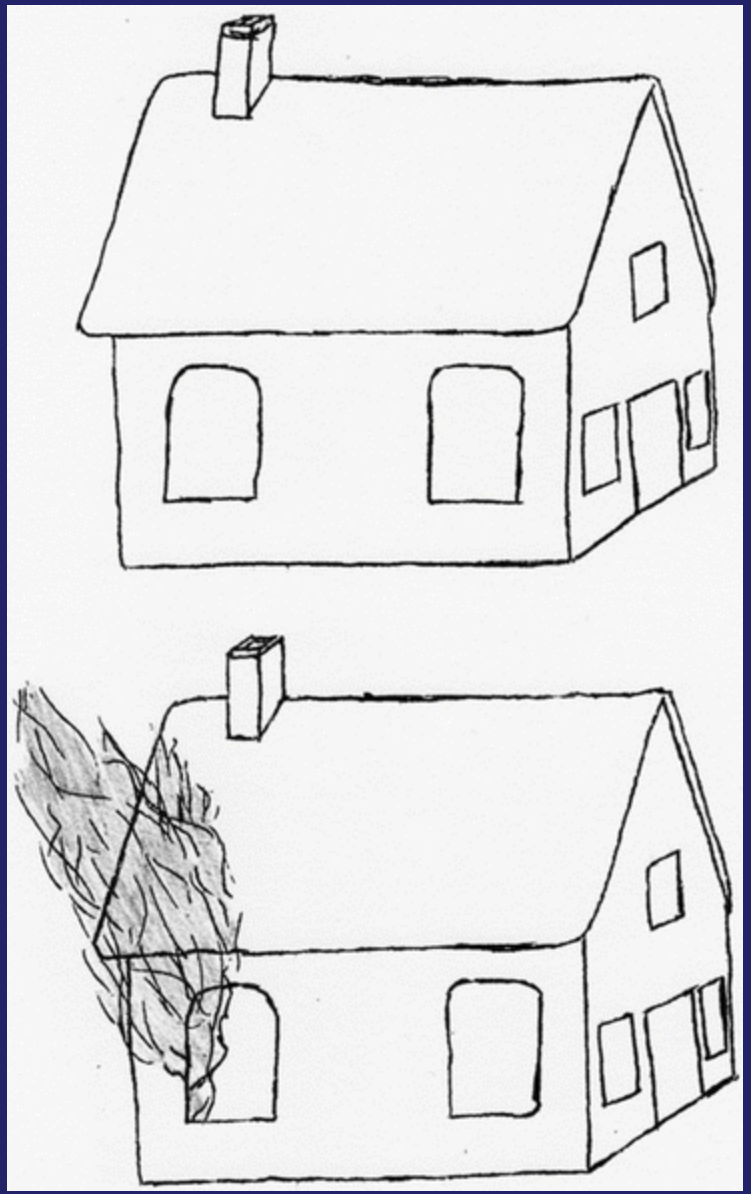
- Prevalence of neglect
  - Likely 40% or greater in R hemisphere stroke (estimates vary widely)
- Neglect often underrecognized and underdiagnosed
  - Can result in underestimation of deficits, lack of appropriate interventions, and poor rehab participation

- Patients with neglect often improve with time, but recovery frequently not complete
  - Greatest recovery in 1st month
  - Even with spontaneous recovery, patients can experience impaired participation in rehab in the important early post-stroke period

- Why do we care about neglect?
  - Leads to worse outcomes
    - Neglect = deficit with worst prognosis for independent living (worse than global aphasia)
  - Impairs participation in rehabilitation therapies
  - Safety concerns
  - Distress to families/caregivers (often moreso than patients)
- We can’t neglect neglect!

- Why should psychiatrists care about neglect?
  - Can result in strange-seeming behaviors that could potentially lead to psychiatric consultation
  - Interesting window into the brain and its functions
    - Raises questions about how we recognize and interact with our environment
    - Blurs the boundary between conscious/unconscious knowledge and behaviors
    - Shows us how much we DON'T know about how the brain works

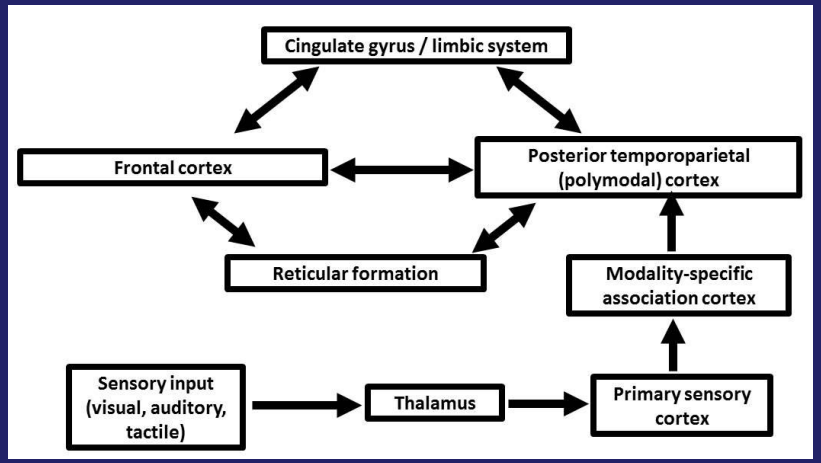
- Which house would you rather live in?



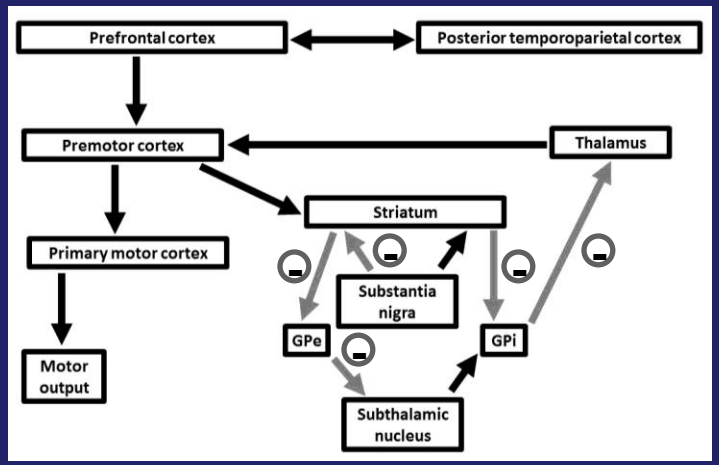
- Famous neglect case study:
  - Patient with L hemineglect
  - INSISTED the houses were exactly the same
  - BUT: she always picked the top house to live in
  - Conscious vs unconscious knowledge?
  - (Another study in neglect did not replicate this finding)

- Causes of neglect
  - Most commonly occurs post-stroke, but can occur from any process that impairs brain structure/function
    - TBI
    - Mass
    - Complicated migraine
    - Post-ictal state
    - Neurodegenerative dementia

- Localizing the lesion in neglect
  - Classically associated with nondominant (usually right) temporoparietal lesion
  - However, many brain regions combine to allow attention and intention; damage to any one of these regions or their connections can produce neglect



Attentional systems



Intentional systems

- Localizing the lesion in neglect
  - Attentional (sensory) neglect:
    - Temporoparietal lobe lesion (generally)
  - Intentional (motor) neglect:
    - Frontal lobe lesion (generally)
  - Both systems needed for successful interaction with environment

Localizing the lesion in neglect

- Neglect more common and severe with right than left hemisphere lesions
- L-sided neglect far more common than R-sided neglect, but R hemineglect does exist

- Reason for asymmetry in neglect
  - L hemisphere attends primarily to R side / R-ward direction
    - But R hemisphere can attend to both sides / both directions
  - L hemisphere can prepare for R-sided or R-ward actions
    - But R hemisphere can prepare for actions to both sides / both directions

- Neglect comes in many forms
  - Prototypical form is:
    - Left-sided
    - Visuospatial (looking at things)
    - Egocentric (body-referenced)
    - Attentional (noticing things)
  - But many other presentations exist
  - Most of the literature focuses on left-sided visuospatial egocentric attentional neglect

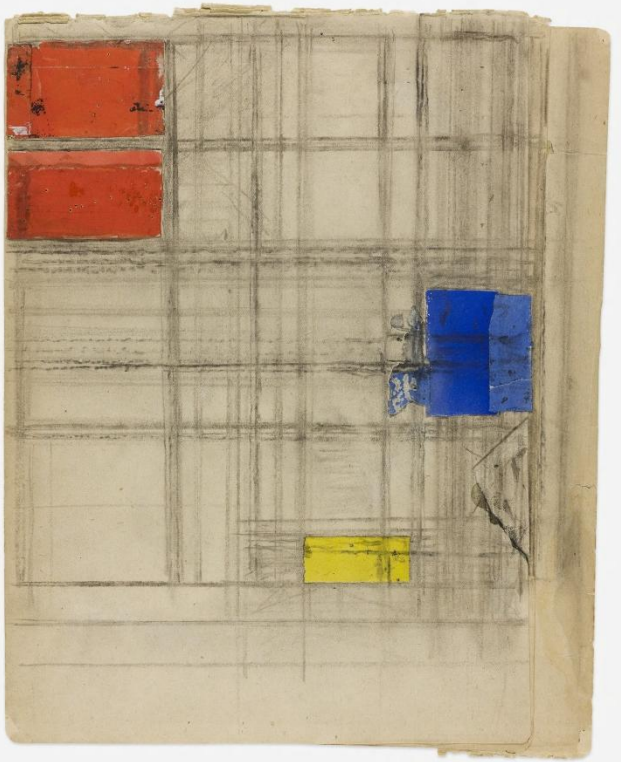
Forms of Neglect

		Modes of involvement					
Dimensions of neglect	Input/output	Afferent: attentional (sensory) neglect			Efferent: intentional (motor) neglect		
	Sensorimotor modality	Visual	Auditory	Tactile	Limb movement		Eye gaze
	Domain	Spatial		Personal		Representational	
	Temporal distribution	Occurs with single unilateral stimulus / movement			Only occurs with bilateral simultaneous stimuli / movements		
	Spatial distribution	Frame of reference			Location		
		Body-centered	Environment-centered	Object-centered	Horizontal (left vs right; ipsilesional vs contra-lesional)	Vertical (up vs down)	Radial (proximal vs distal)

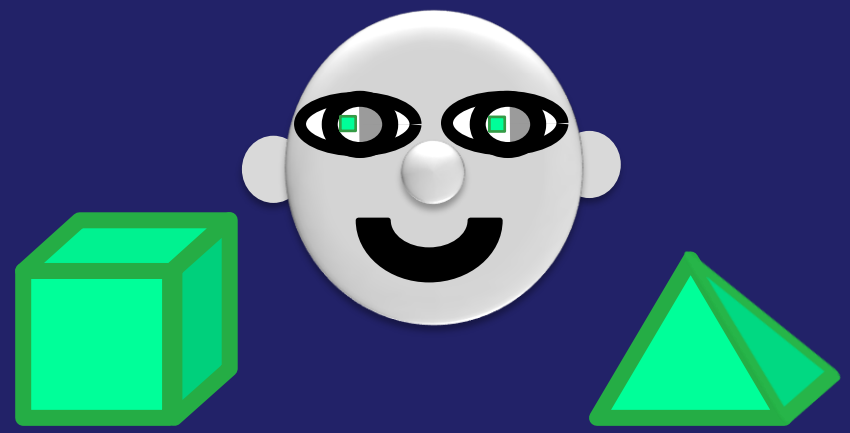
- Extinction
  - Less severe form of neglect, but can still cause problems
  - Patient can detect single stimuli presented separately in right and left hemispace
  - When stimuli presented simultaneously in right and left hemispace, patient only detects ipsilesional stimulus

- Extinction example
  - Examiner touches patient on right hand
    - Patient reports a touch on the right hand
  - Examiner touches patient on the left hand
    - Patient reports a touch on the left hand
  - Examiner touches patient on the right hand and the left hand at the same time
    - Patient reports a touch only on the right hand

- Spectrum of severity
  - Severe neglect often grossly obvious: patient doesn't respond to examiner in left hemispace, etc
  - Less severe neglect may require specific bedside tests to uncover
    - But still disabling, so important to recognize
- Testing:
  - Line bisection, target cancellation, picture copying and others

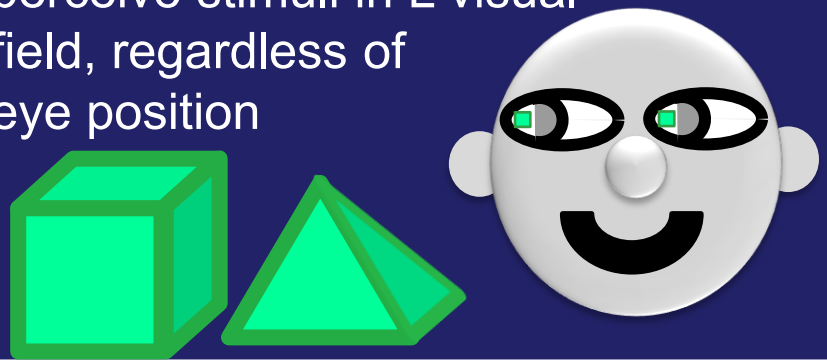


- Visual hemispatial neglect vs hemianopia

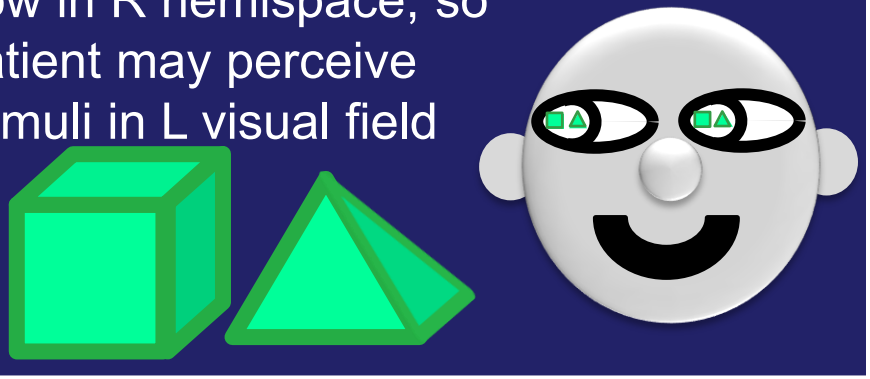


Hemianopia or hemineglect?

Hemianopia: Patient cannot perceive stimuli in L visual field, regardless of eye position



Hemineglect: Both R and L visual field now in R hemispace, so patient may perceive stimuli in L visual field

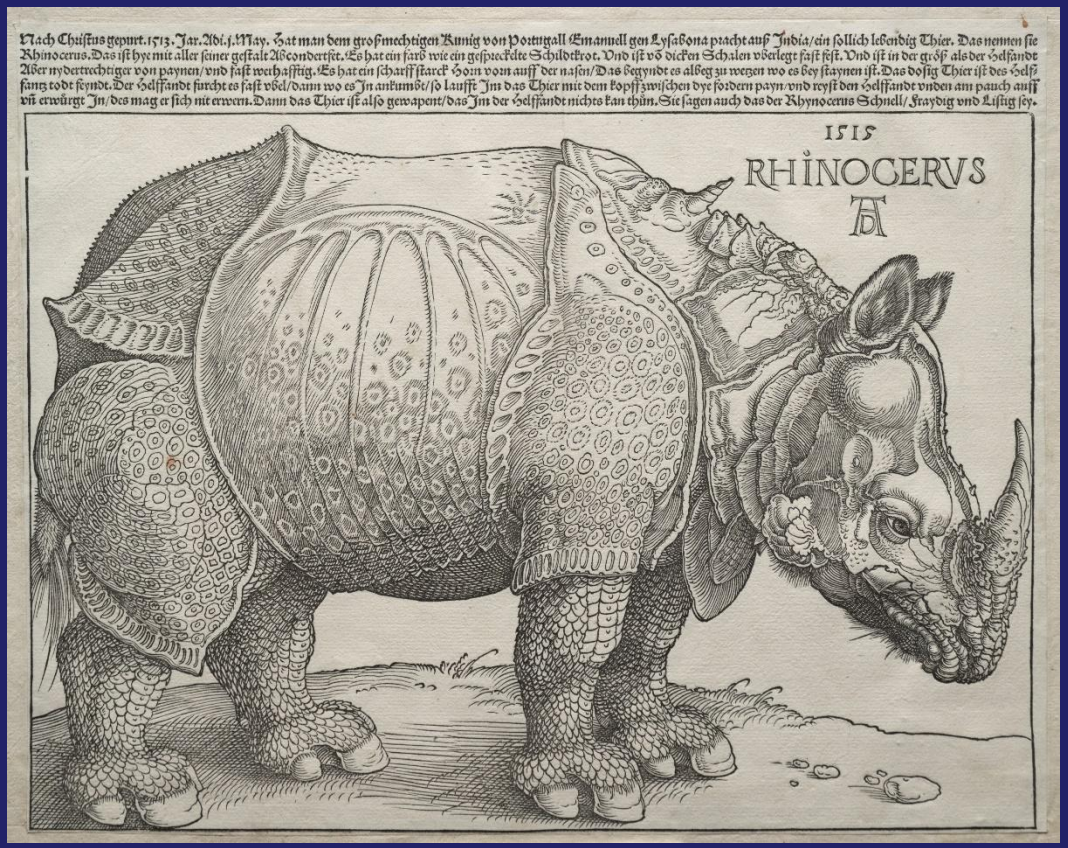


- Tactile hemispatial neglect vs hemianesthesia
  - Move patient's left hand from left to right hemispace
    - If patient now detects tactile stimuli on L hand = neglect
    - Maneuver will not help hemianesthesia (nor all cases of neglect)
  - Cold calorics to left ear can transiently reverse tactile neglect but not hemianesthesia
  - Imaging to localize lesion

- Auditory hemispatial neglect vs unilateral hearing loss
  - Imaging to localize lesion
  - Auditory evoked potentials to distinguish deafferentation from inattention

- Motor (intentional) neglect vs elementary motor deficit
  - Move patient's left hand from left hemispace to right hemispace
    - If movement deficit resolves = neglect
    - Maneuver will not help primary motor deficits (nor all cases of neglect)
  - Patients with hemiparesis often look like they are trying to move limbs; patients with neglect frequently do not seem to attempt movement
  - Imaging to localize lesion to CST or elsewhere

Attentional (sensory) neglect

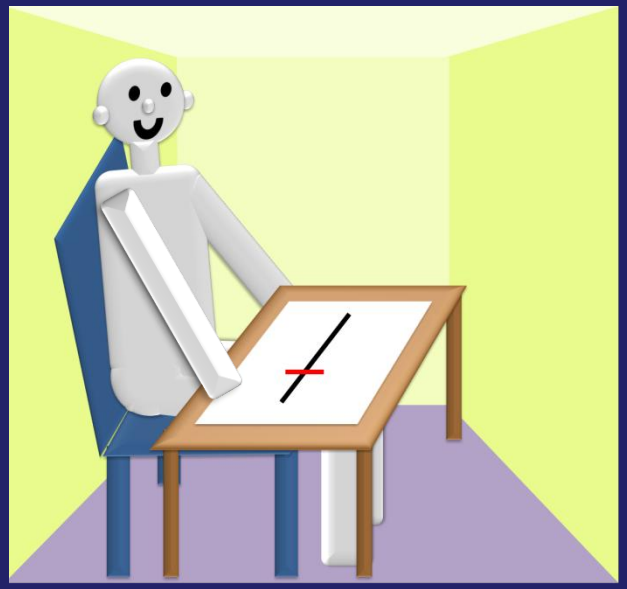


- Simple bedside screening for sensory neglect
  - Visual neglect
    - Line bisection
      - Longer lines more sensitive
    - Target cancellation
    - Drawing / copying
    - Each test assesses different aspect of neglect—patients may show impairment on one but not others

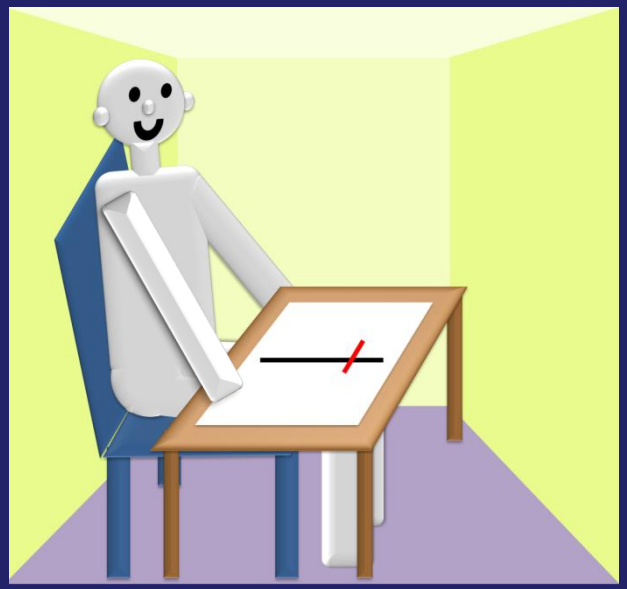
- Tactile neglect
  - Have patient close eyes and lightly touch patient on L and R extremities; patient tells you when he/she detects stimulus
- Auditory neglect
  - Have patient close eyes and rub fingers near L and R ears; patient tells you when he/she detects stimulus

- Forms of neglect
  - Spatial distribution: location
    - Horizontal
      - Neglect usually left, right neglect does exist
    - Vertical
    - Radial
    - Combinations of these
    - Very rare forms, like quadrantanopic
  - Horizontal neglect most common, but should check for neglect in other location distributions

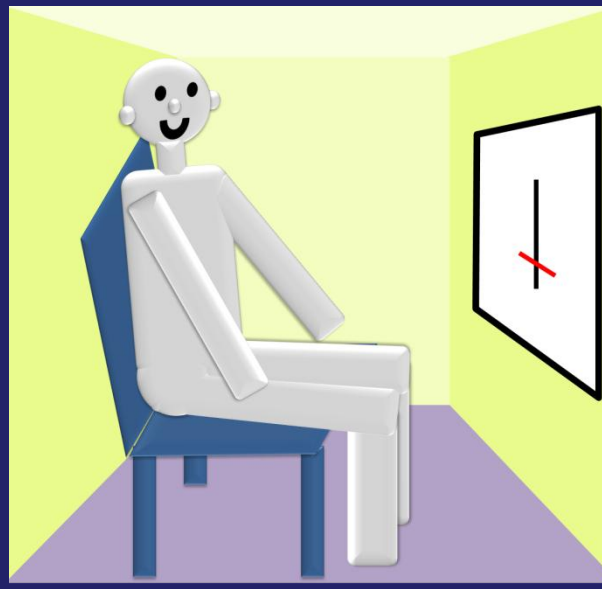
Spatial distribution of neglect: location



Horizontal neglect



Radial neglect



Vertical neglect

- **Testing by line bisection**
  - Things we attend to appear larger than things we don't attend to
  - Neglected half of line appears shorter than non-neglected half, so patients perceive midpoint closer to the non-neglected side
  - Or, patients may fail to disengage from right half of line

Spatial distribution: frame of reference

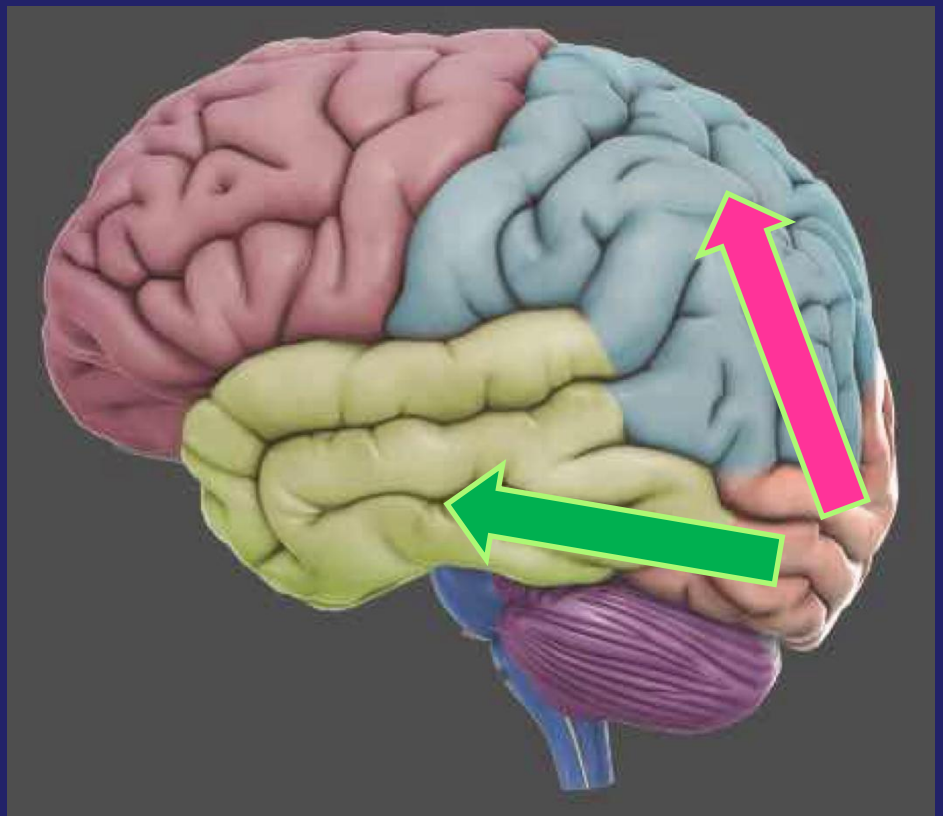
- Egocentric
- Allocentric
- Environment-centered

- Egocentric vs allocentric
  - Patient may neglect the left—but left of what?

- Neglect of things in the left side of the environment, regardless of patient's body axis position
  - Environment-centered neglect
    - Less clear lesion location pattern
    - Less well-characterized
- Egocentric vs allocentric neglect better studied

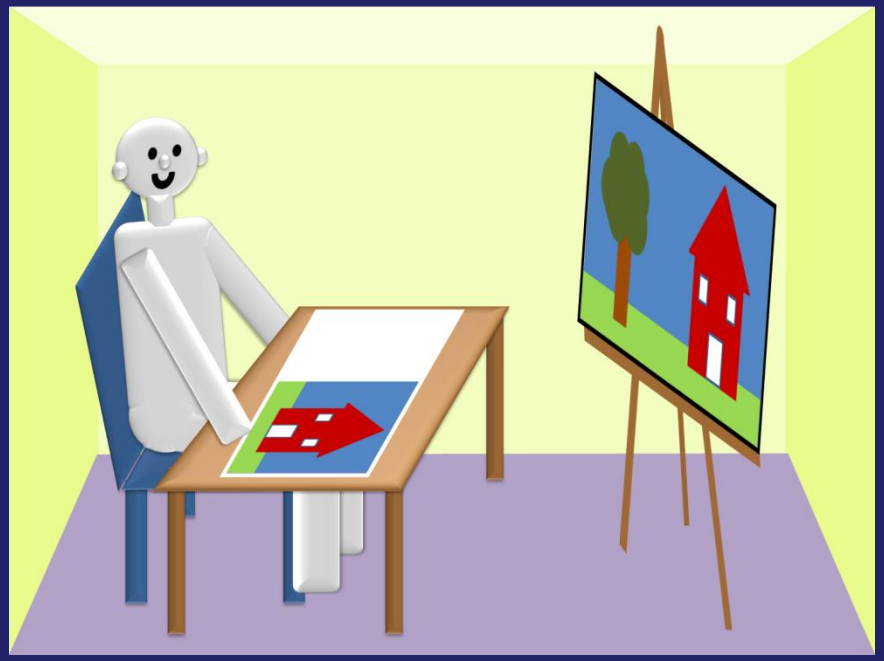
- Neglect of things in patient's left hemispace = egocentric
  - Dorsal (parietooccipital) stream lesion
- Neglect of left side of objects, regardless of whether in patient's right or left hemispace = allocentric
  - Ventral (temporooccipital) stream lesion

- “Where” pathway and “What” pathway
  - Occipitoparietal pathway (dorsal stream)
    - Tells you WHERE something is
  - Occipitotemporal pathway (ventral stream)
    - Tells you WHAT something is



- We need both the WHAT and the WHERE pathway to function safely and effectively in the world
  - You're walking down the street and see something
    - Is it a bird or a car?
    - Is it stopped and stationary, or is it headed quickly towards you?

Egocentric vs allocentric neglect: drawing task

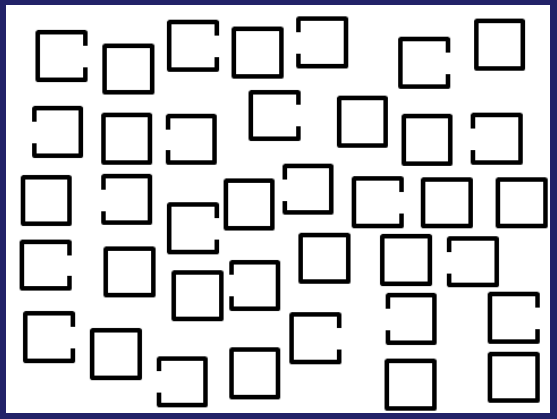


Egocentric neglect (body-centered)

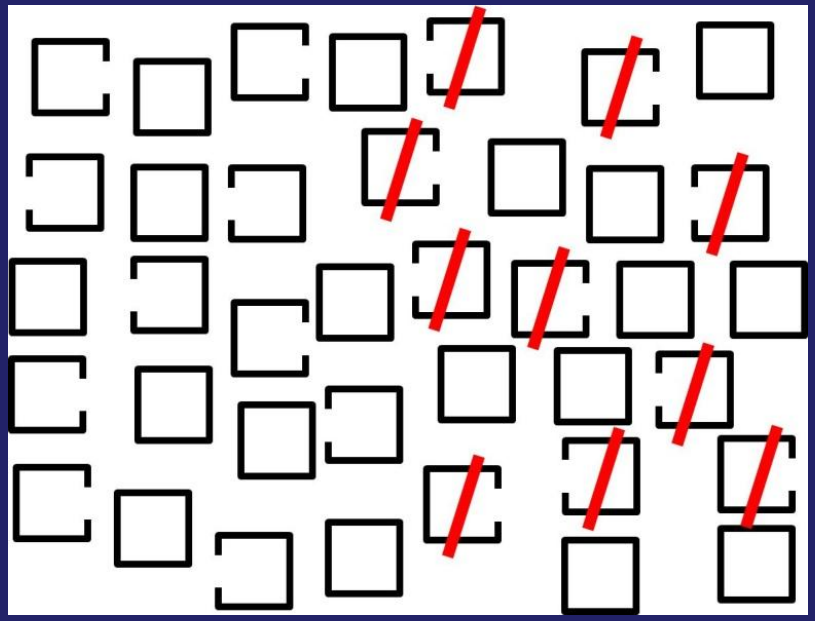
Allocentric neglect (object-centered)

Egocentric vs allocentric neglect: cancellation task

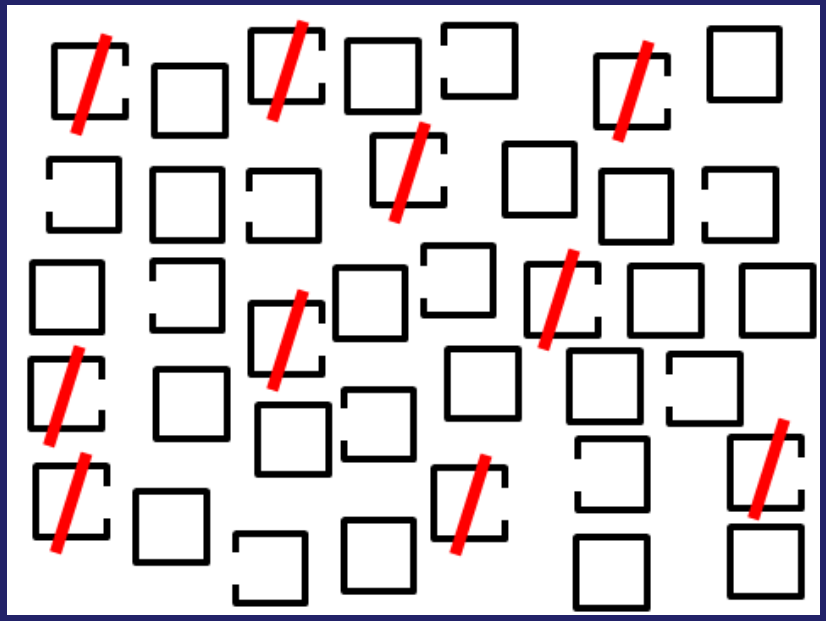
Target stimulus
"Cross out all the open squares"



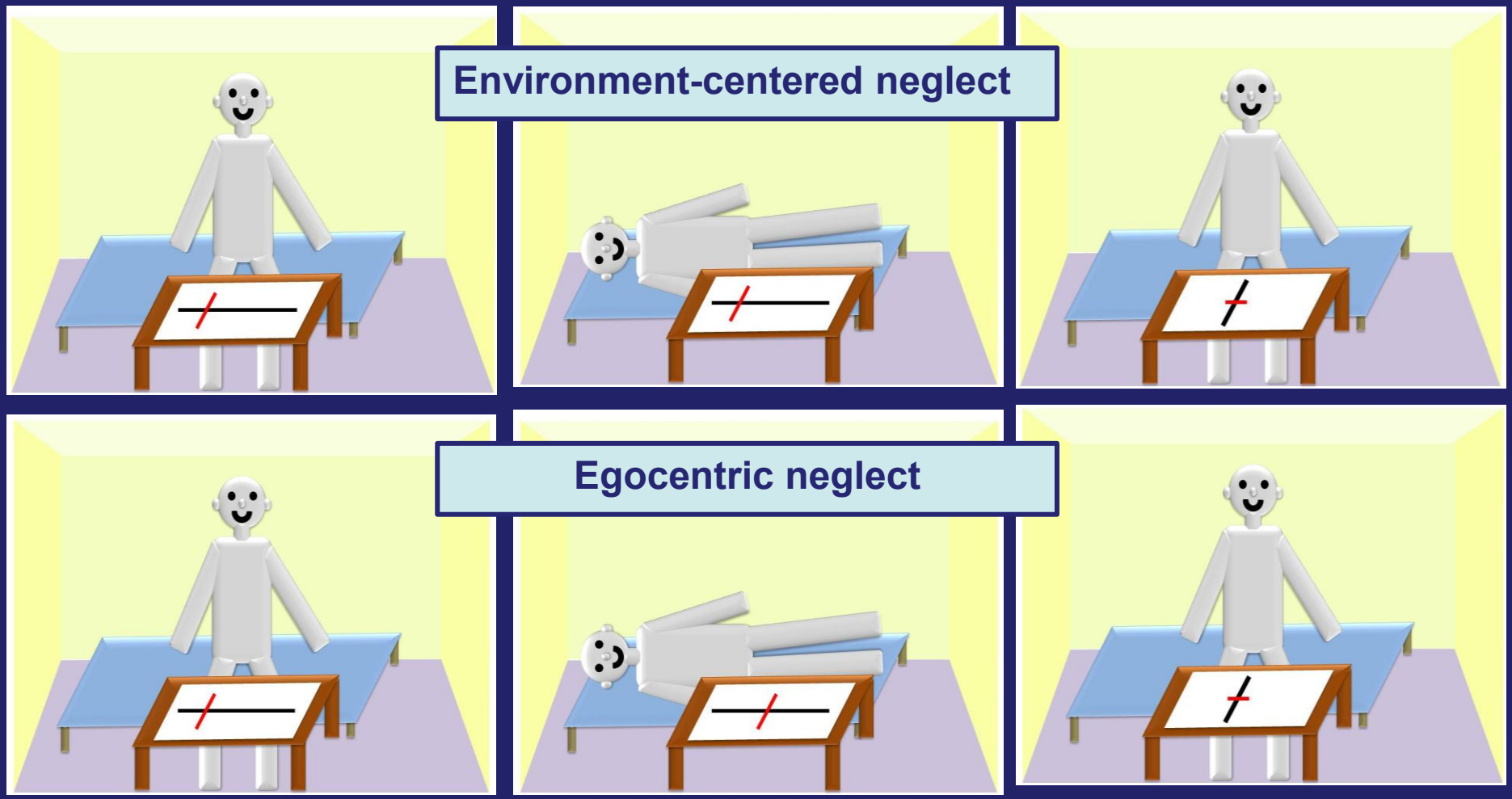
Egocentric neglect



Allocentric neglect



- Egocentric vs environment-centered neglect: line bisection task

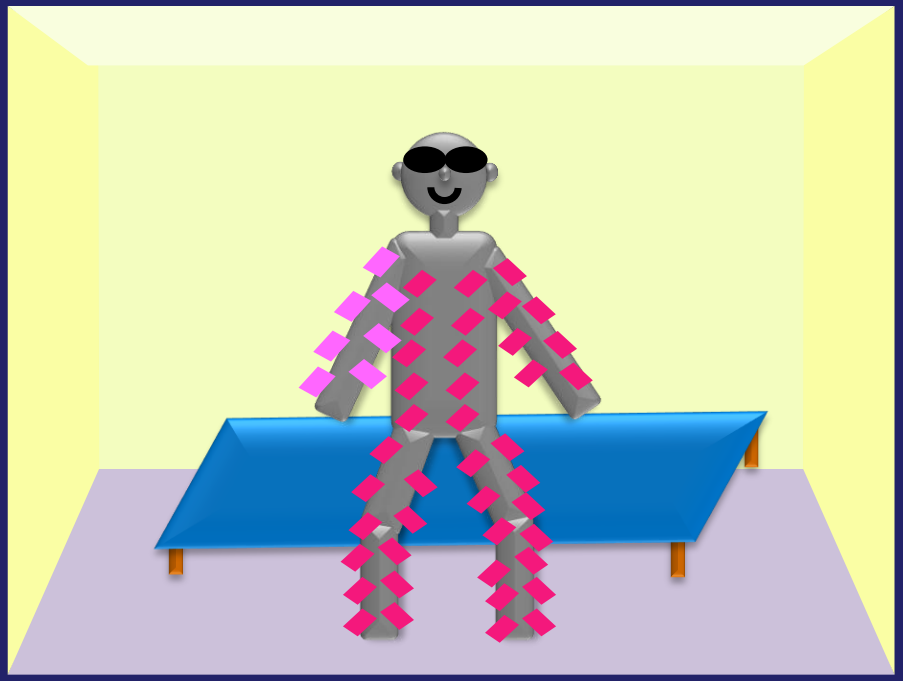


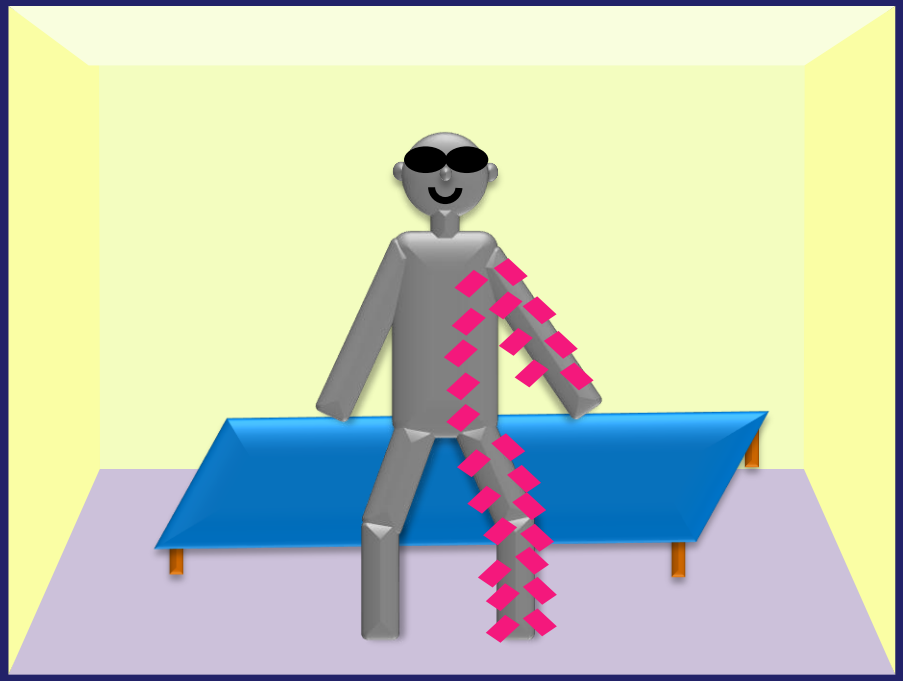
- Forms of neglect
  - Domain
    - Spatial
    - Personal
    - Representational (conceptual)

- Personal neglect
  - Neglect of one side of body
  - May represent damage to mental representation of the body
  - May present with failure to dress or groom left side of body

- Can involve allesthesia and/or allokinesia
  - Allesthesia = when touched on L, think touch was on R
  - Allokinesia = when asked to move L limb, move R instead
- Often associated with anosognosia (failure to realize your own body parts belong to you)

- Personal neglect
  - “Take off all the post-it notes on your body.”



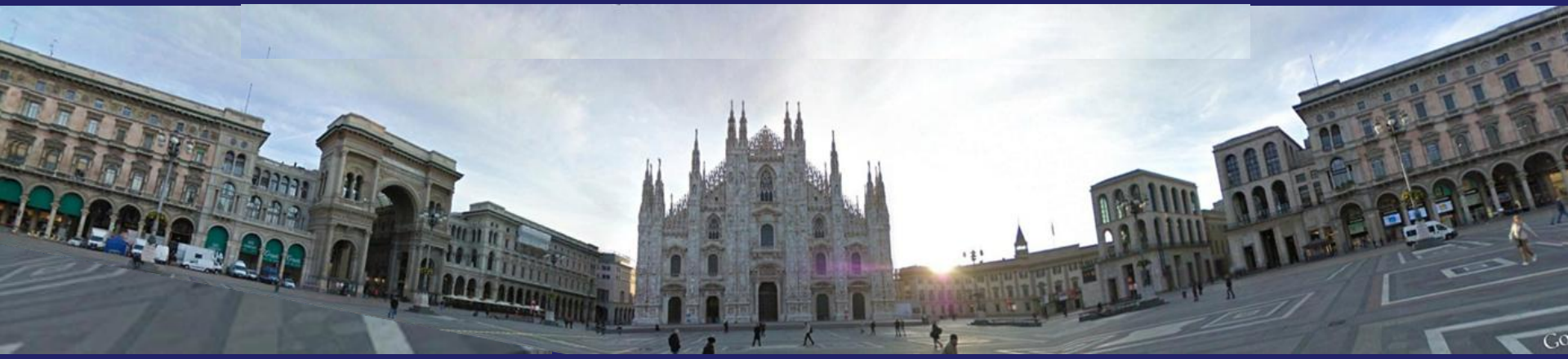


Only put stickies on RUE if LUE is NOT hemiplegic

- Representational neglect
  - Neglect of one side of mental images
  - The case of the neglect patients from Milan
    - Bisiach and Luzzatti (1978) asked the patients to imagine they were standing on the steps of the Duomo, and to describe what they saw in the Piazza
    - Then asked them to imagine they were standing on the opposite side of the Piazza, and to again describe what they saw
  - May occur with posterior temporal-inferior parietal lesions
    - Impair retroactivation of sensory association areas

Piazza del Duomo, Milan

View of the Piazza while standing on the steps of the Duomo



View of the Piazza from the other side: looking at the Duomo

Images from Google Earth

View of the Piazza while standing on the steps of the Duomo

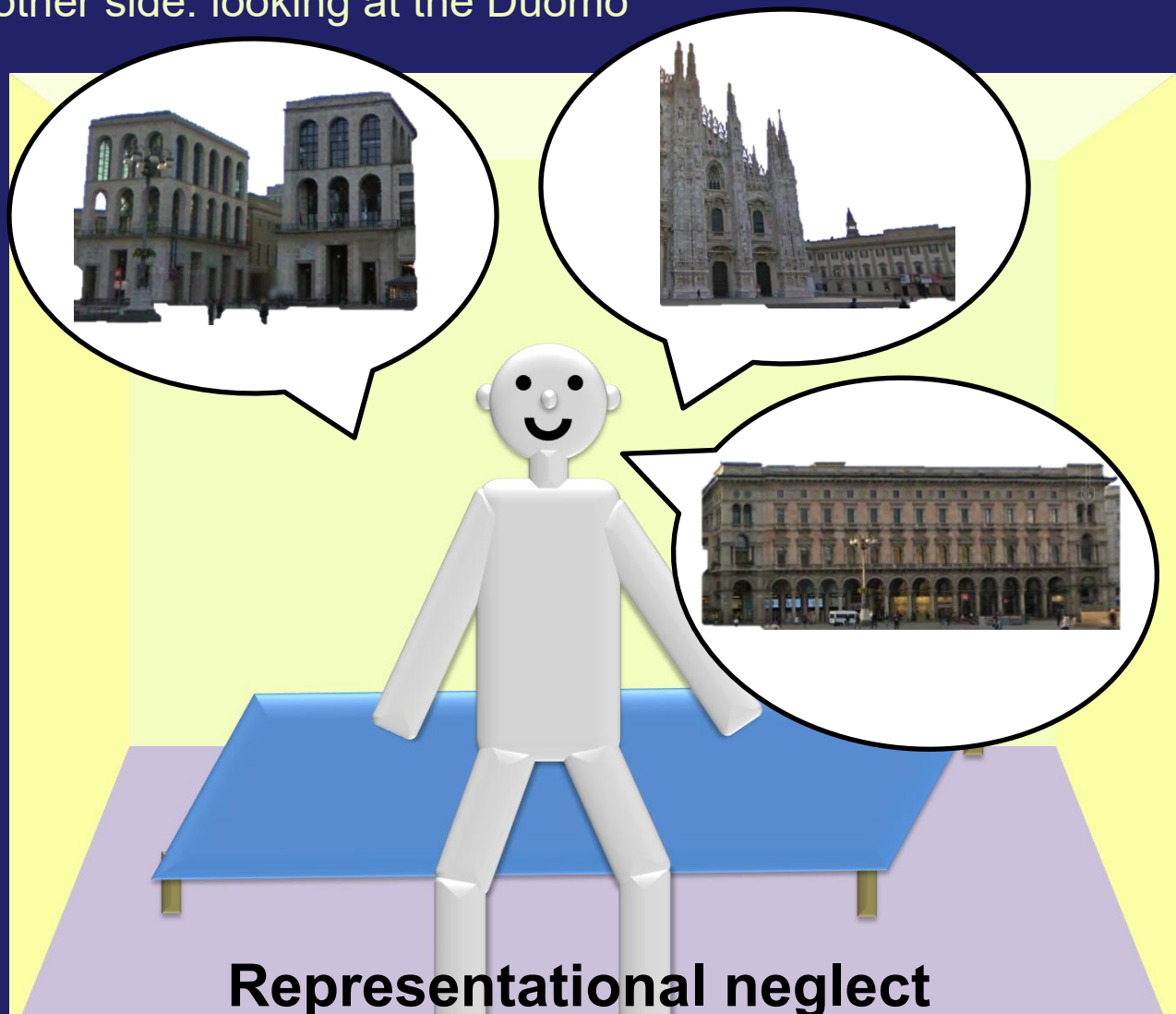
"What do you see standing on the steps of the Duomo?"

Images from Google Earth

Representational neglect

View of the Piazza from the other side: looking at the Duomo

"What do you see if you're standing on the other side of the Piazza, looking at the Duomo?"



Images from Google Earth

Representational neglect

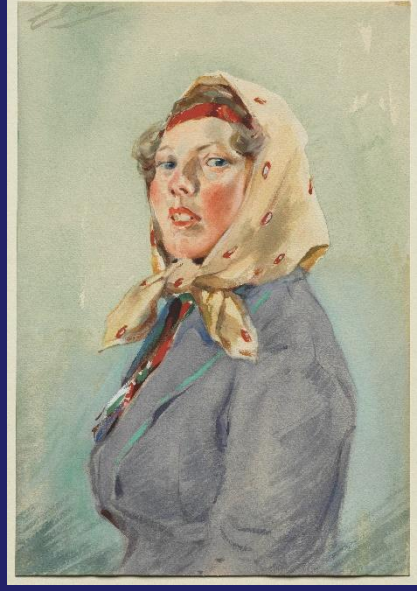
Intentional (motor) neglect

- Forms of motor (intentional) neglect
  - Limb akinesia
    - Patient doesn’t move left limbs
  - Hemispatial akinesia
    - Patient cannot move left limbs when on left side of body
    - Can use the left limb when brought to right side of body

- Forms of motor (intentional) neglect
  - Directional akinesia
    - Patients cannot move either arm, leg, or eye, or their head in the left direction
    - Can also manifest as deviation of eyes, limbs, or head to the right at rest; even if can voluntarily move in either direction
      - “Gaze palsy” is misnomer, as not deficit in oculomotor system

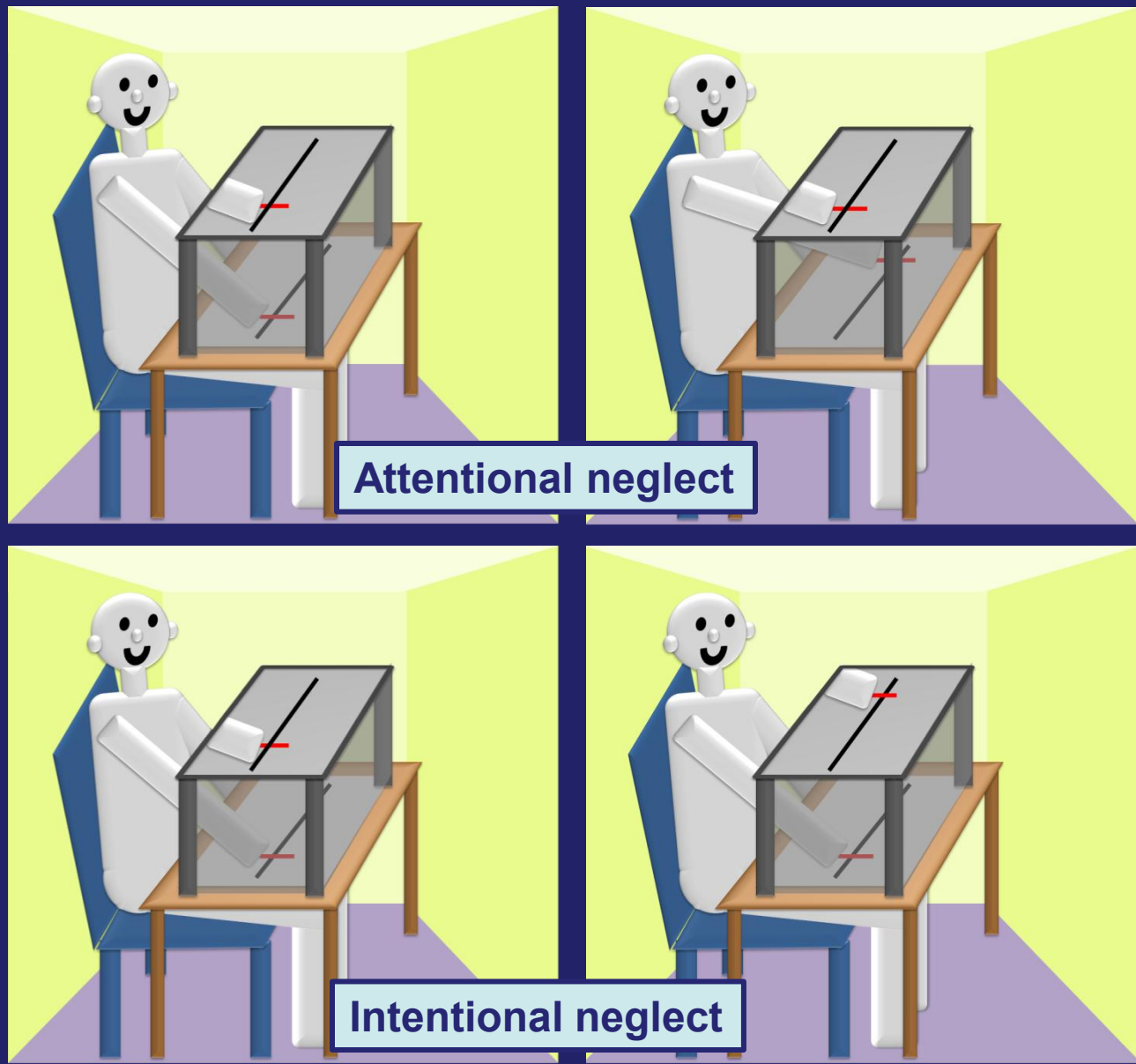
- Mild forms of intentional neglect:
  - Hypokinetic neglect
    - Delay in moving L-sided body parts
  - Hypometric neglect
    - L-sided body part movements are abnormally small
  - Motor impersistence
    - Inability to sustain movements/hold postures with L-sided body parts
  - Assessed by comparison with R-sided body parts/movements

- Motor extinction
  - Limbs move normally on both sides when executing single movements
  - When asked to move limbs on both sides simultaneously, patient only moves right limb
  - Can also occur as extinction hypokinesia
    - Limbs on both sides can move simultaneously, but left limb moves more slowly right limb
    - Left limb moves more slowly when also moving right limb then when moving alone



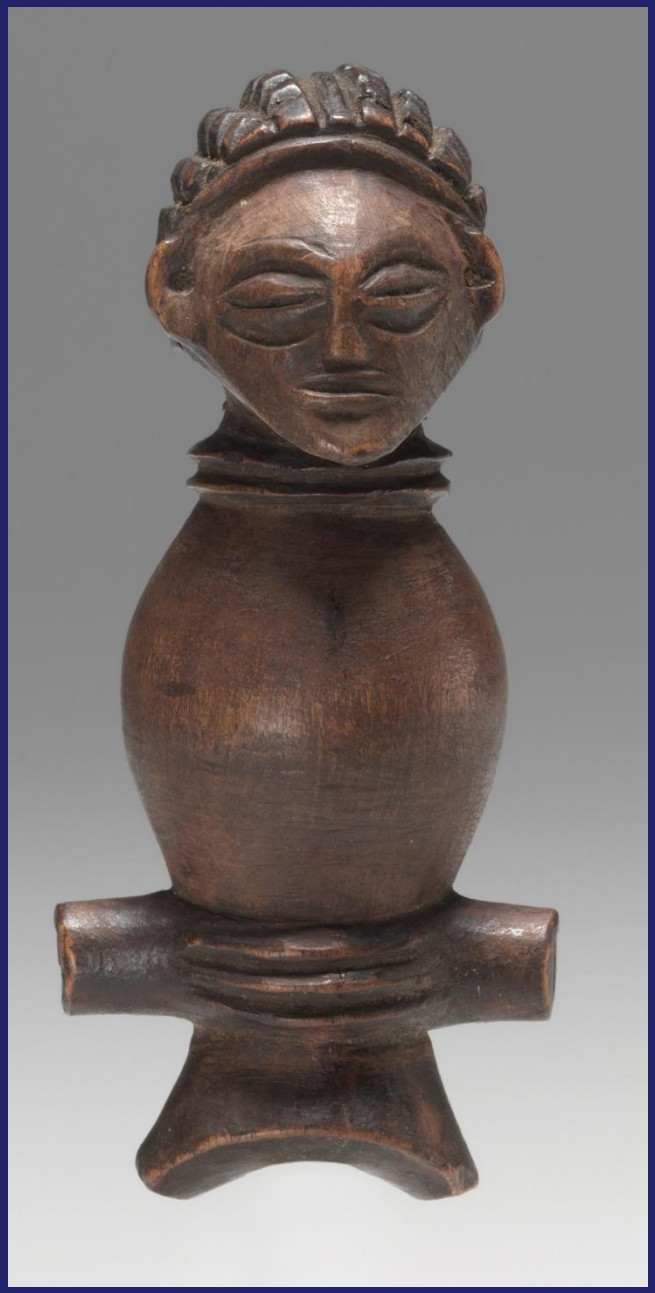
- Distinguishing attentional and intentional hemispatial neglect
  - If a patient fails to reach into L hemispace to perform a task, is it because the patient does not attend to L hemispace or does not act towards L hemispace?
  - Can reverse sensory feedback (with mirrors or video images) to dissociate direction of attention and direction of action, to see which is impaired

- Reversed feedback reverses direction of neglect = attentional
- Reversed feedback does not change direction of neglect = intentional



Treatment of neglect

- Treatment of neglect
  - Recognize presence of neglect
  - Evaluate underlying cause and treat that (if possible)
    - tPA, secondary stroke prophylaxis
    - Potentially reversible causes (seizures, migraines)
  - Rehabilitation therapies targeting neglect



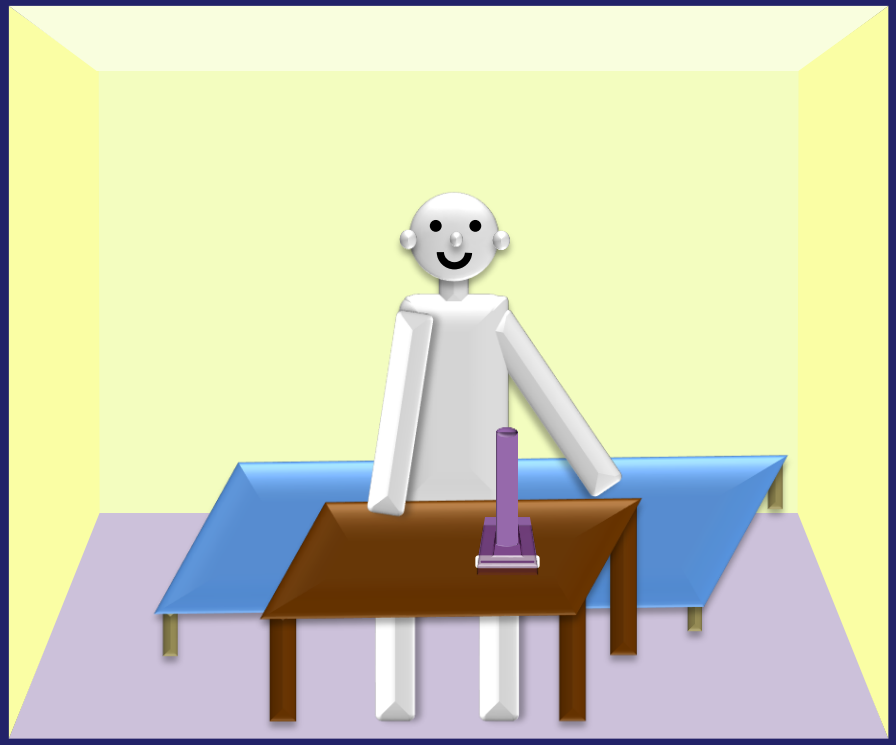
- Maintain safety—even mild neglect poses serious hazards
  - No driving
  - Careful with steps, obstacles, etc in neglected space
  - Keep in mind anosognosia for deficits

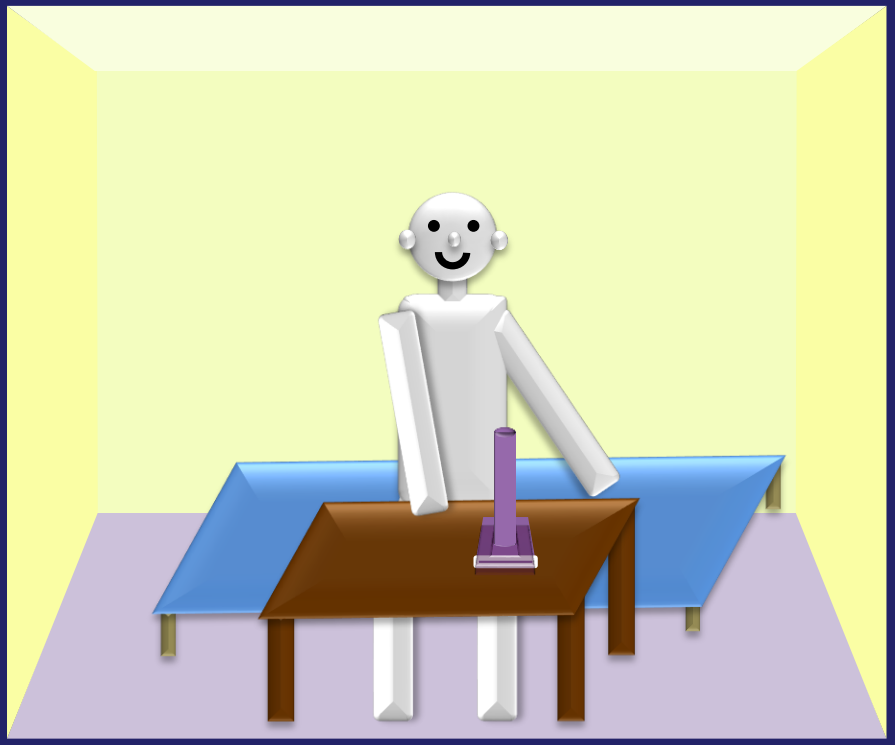
- Treatment of neglect
  - Vast majority of treatment studies focus on left-sided visuospatial egocentric attentional neglect
  - Generally not clinically significant to improve neglect performance on neuropsychological tests if improvement doesn't generalize to everyday life, participation in rehabilitation therapies, etc; or if isn't sustained over time
    - Effective interventions do show this generalization and show lasting improvement

Behavioral Therapies

Prism glasses

Before prism training

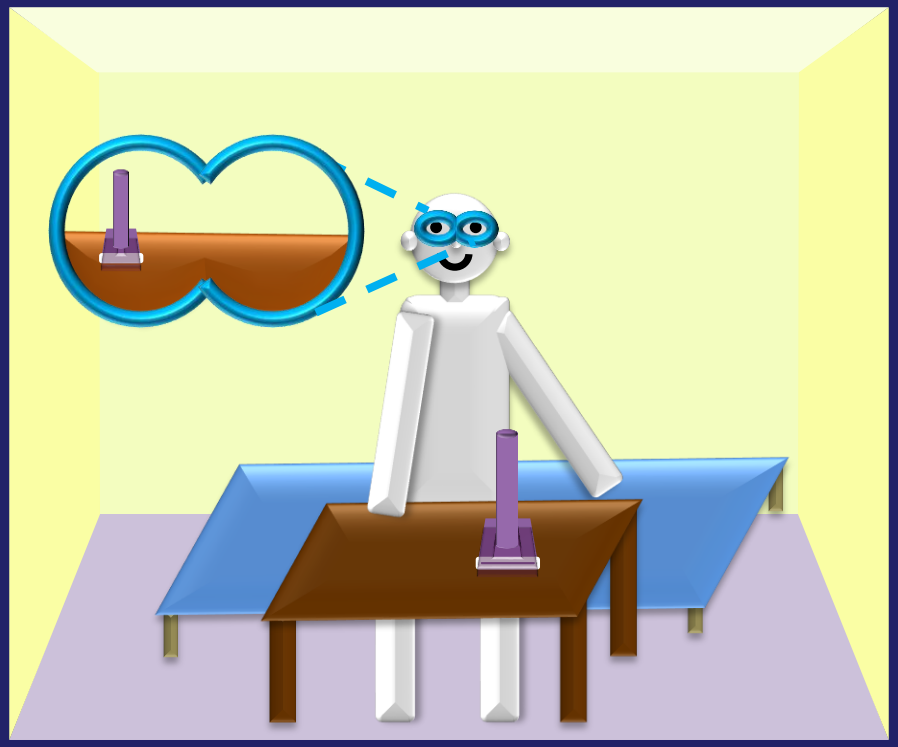


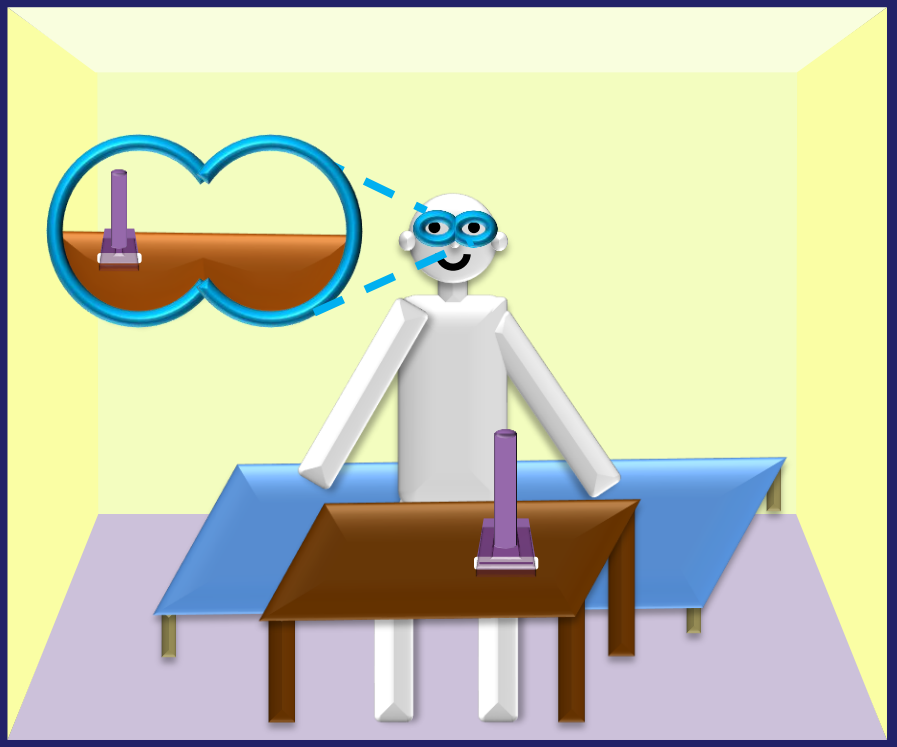


Prism glasses

- Patients train wearing Fresnel lenses which shift environment to the right

Beginning of prism training

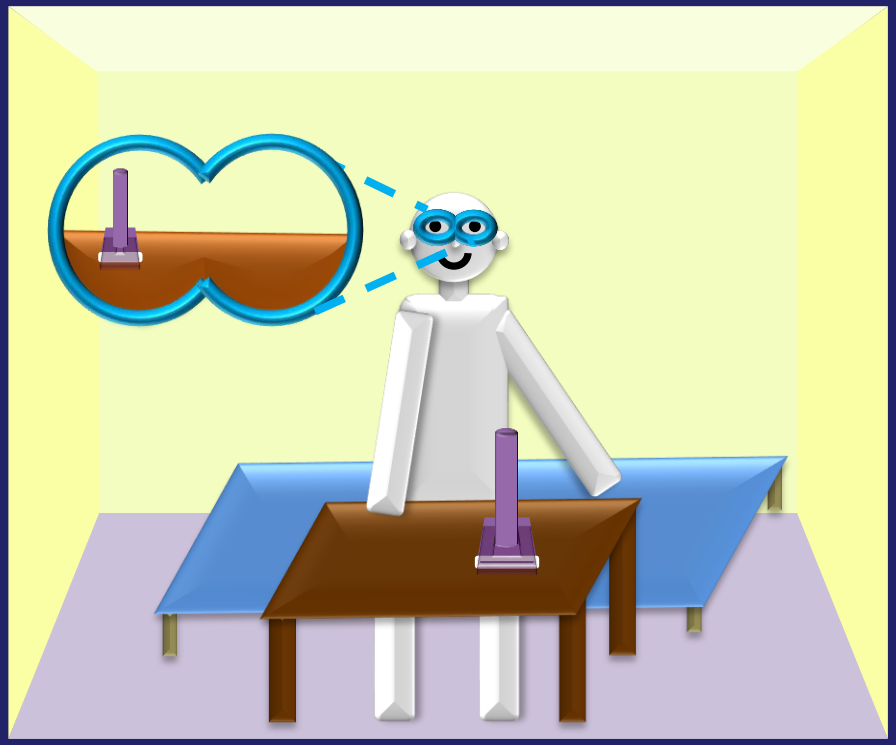


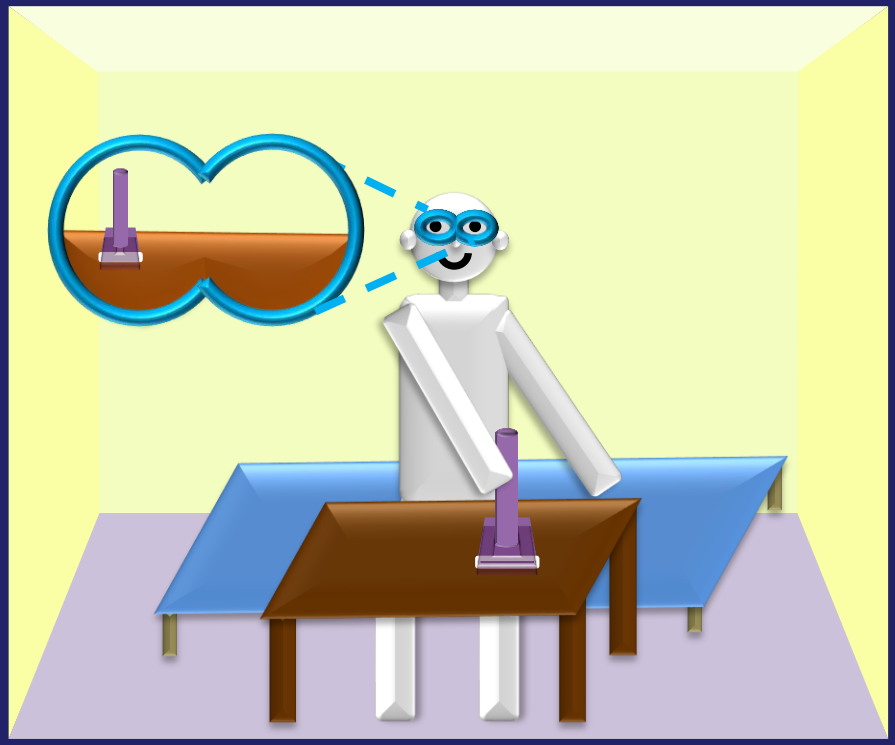


Prism glasses

- With training, patients learn that when reaching for a target with the lenses on, they must shift their actions to the left of where they perceive the target

End of prism training

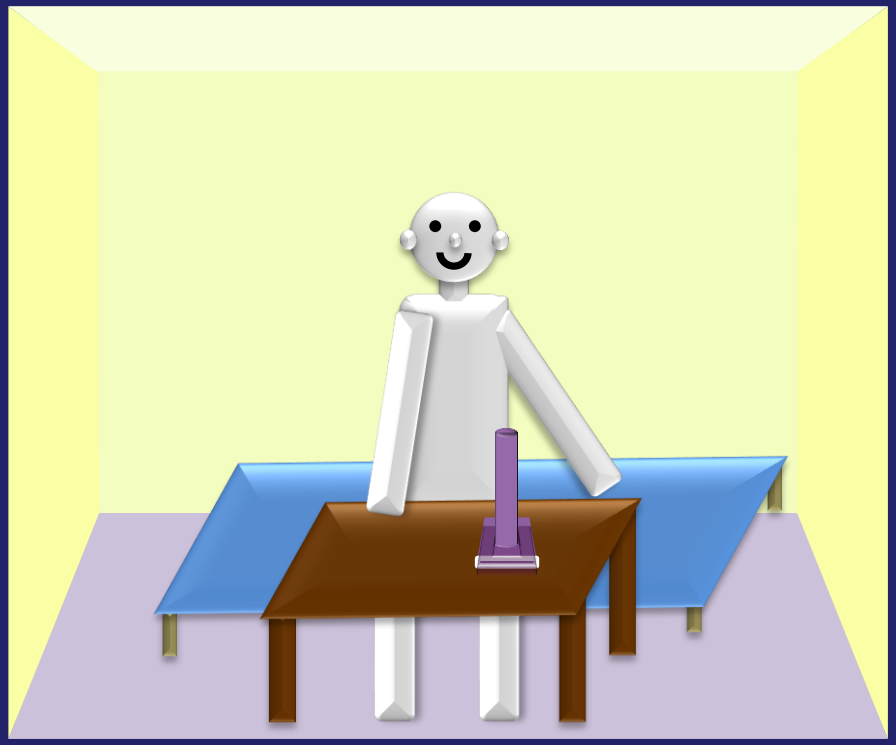


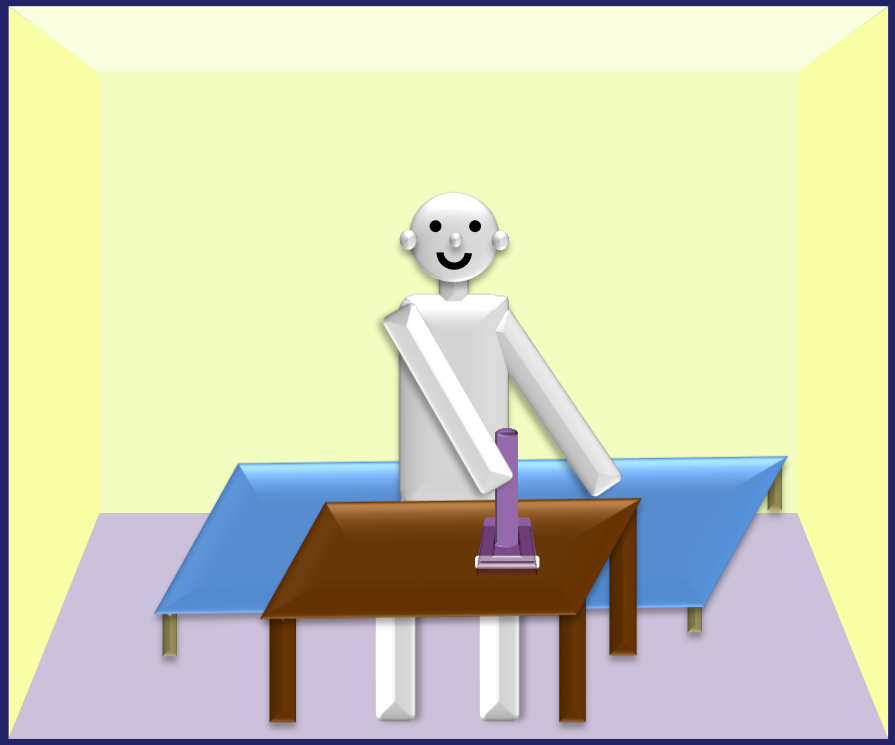


Prism glasses

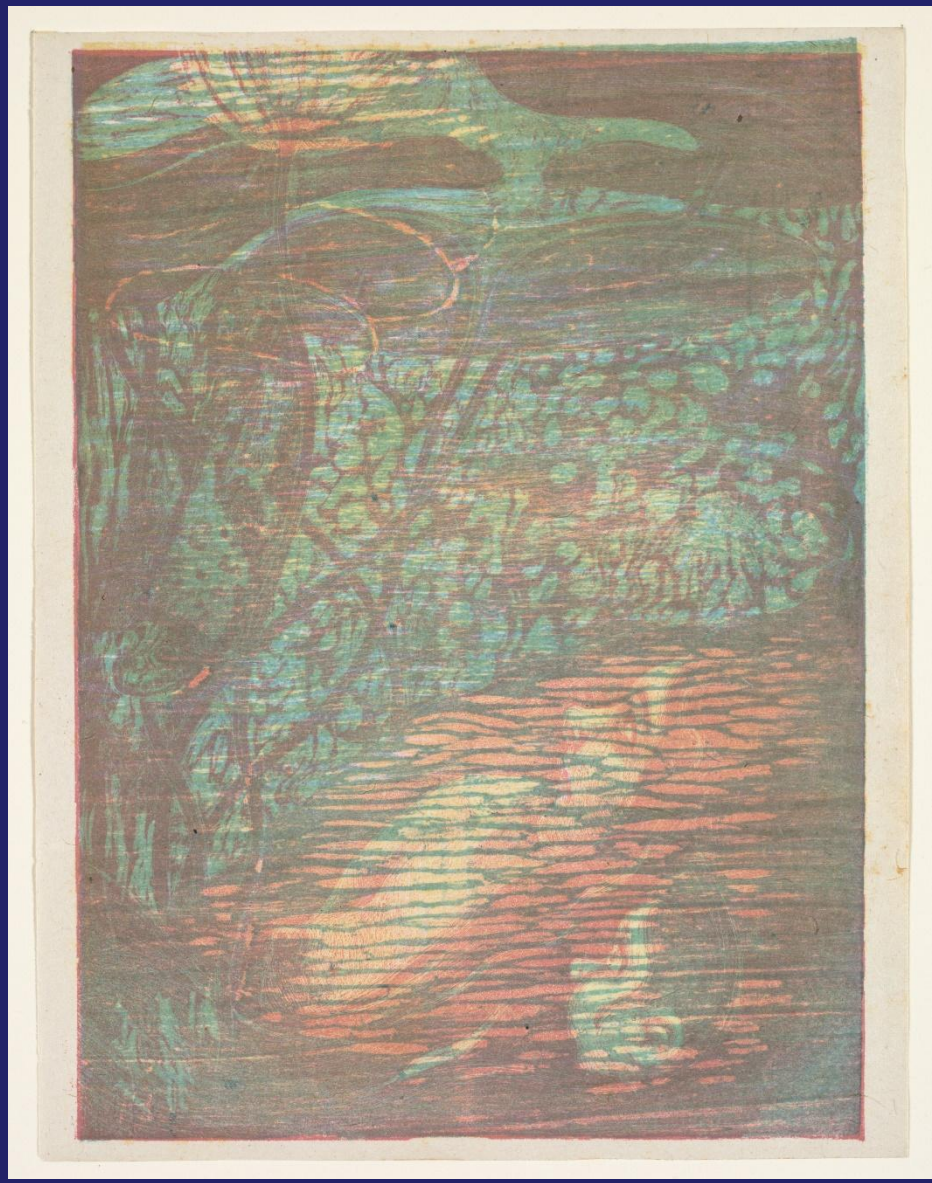
- After removing lenses, patients continue to overcompensate to the left—making up for their left-sided neglect

After prism training



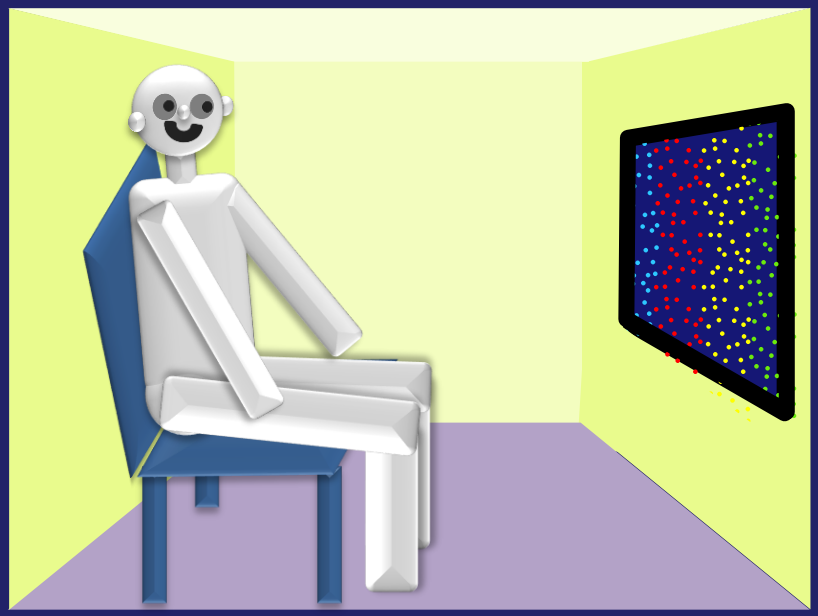


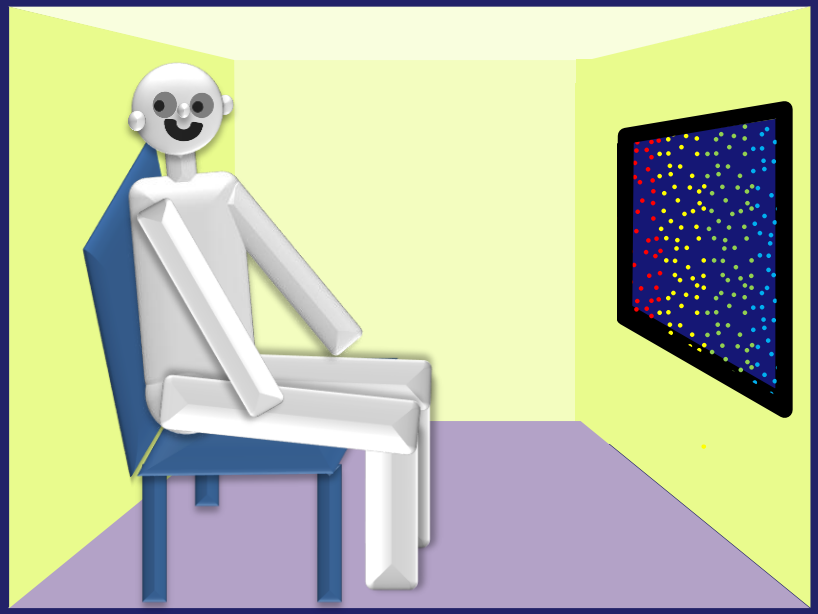
- Prism glasses
  - One meta-analysis found prism glasses to be the best-validated/most effective treatment for neglect
  - Mechanism unclear: may contribute to LTP of networks directing attention and action-intention to neglected space
  - May improve ADLs, with benefits lasting up to 2 years



Optokinetic stimulation

- Patients track images moving to the left
- Make leftward smooth pursuit eye movements





- Optokinetic stimulation
  - May work by upregulating systems that allocate attention to left hemispace
  - Reduces visual AND auditory neglect on neuropsych testing for up to 2 months
    - May involve general upregulation of attention systems, not just those subserving visual modality

Vestibular rehabilitation

- Patients taught specific head movements
- One RCT of vestibular rehab done ≥ 30 min 5x a week for 1 month
  - Improved neuropsych neglect measures, balance, and ADLs during the month of the intervention

- Salience and arousal interventions
  - Neglect is involuntary, but measures which increase the salience of the neglected space may improve performance
  - How to increase salience/arousal?
    - Reward performance
    - Sustained attention training
    - Novel cues in neglected hemispace
    - Use of left-sided body parts during tasks

- Reward interventions
  - One RCT found that when patients were offered a monetary reward for every target they detected, they detected more targets in neglected hemispace
  - Role of dopamine?
    - 2/10 participants in the study did not improve in the reward condition; these individuals had strokes that damaged part of the DA system
    - One hypothesis:
      - DA-mediated effect on attention and salience contributes to the efficacy of reward for improving task performance in neglect

- L-sided novelty and use of L side
  - Novel stimuli command attention
    - Novel visual, auditory, and tactile cues presented in L hemispace can help patients direct their attention towards the formerly neglected side
  - Performing line bisections and cancellations with L hand improves accuracy
  - Any attempted movement of the left arm—even movements unrelated to the task under study, or when the arm remains out of view—can improve performance

- Forced-use therapies
  - Force patients to attend to / initiate movements into neglected left hemispace, by constraining body parts on the right side
  - One RCT showed constraint-induced therapy of LUE lessened neglect behaviors in ADLs
  - Another RCT found that placing power wheelchair joystick on the L improved driving accuracy
    - Acted as spatial cue to attend to L?

Somatic Treatments

- Pharmacotherapy of neglect
  - Evidence preliminary at this time
    - But perhaps easier to apply widely than intensive rehabilitation therapies?
  - Some data to support:
    - Dopamine agonist
    - Cholinesterase inhibitors

  - Careful assessment before/after medication initiation to make sure patients really improve
  - Neglect can spontaneously improve
    - Consider periodically withdrawing medication withdrawal with before-and-after testing to make sure the medication caused the improvement.

- Neurostimulation
  - Repetitive transcranial magnetic stimulation (rTMS) and transcranial direct current stimulation (tDCS) can activate or inhibit cortical electrical activity
    - Effects may persist beyond the duration of the stimulus by influencing brain plasticity
  - Can neurostimulation therapies reduce right-sided attention bias and help with neglect?
    - Data encouraging so far, but much more study needed

- Electrical / vibration stimulation of left hemibody
  - On left hand or muscles of left side of neck
  - 3 RCTs have found such stimulation can reduce left hemineglect on neuropsych tests for up to one week following intervention

Other Interventions

- Optimize standard rehabilitation and nursing interventions
  - Family member participation in rehab can improve ADLs as well as performance on neuropsych tests in patients with neglect

- Optimize the environment
  - Important tasks/conversations should take place in ipsilesional (non-neglected) hemispace
    - However, if patients never have to interact with neglected hemispace, may impede recovery
  - Minimize distractions, multitasking
    - Have patient do most important actions first, since often have impaired sustained attention

Photo: Library of Congress, 1912

- Treatments for neglect exist and can help improve outcomes
- Developing more effective and readily accessible rehabilitation strategies for neglect: an essential yet not fully realized goal

Questions?

Me with Ken Heilman, the “Godfather of Neglect”