Unilateral Neglect Theories and Interventions: Evidence and Implications for OT

Lorie Richards, PhD, OTR/L, Kasey Mitchell, MOT, OTR/L, & Bradley Freestone, O.D.
University of Utah
AOTA 2014
Unilateral Neglect

• Definition
  – A heterogeneous disorder in which the individual fails to report or respond to stimuli presented in the contralateral side of space
  – Most common is Left sided neglect
Neglect Facts

• Present in 10-82% of individuals post-stroke
  – 10-82% after RH stroke
  – 15-65% after LH stroke

• Does improve over time in many individuals, but treatment is indicated because
  – Interferes with success during rehabilitation. (Jehkonen, et al., 2006; Vossel, et al., 2013)
  – Is a long-term disorder for ~33-40% and reduces independence in daily activities. (Kerkhoff & Schenk, 2012; Nijboer, et al., 2013)
  – Associated with falls (Kortte & Hillis, 2009)
Signs and Symptoms

- Omissions of stimuli in L hemispace
- Omissions of L-side of stimuli/body
- Rightward posture/head tilt
- Gaze deviation to R
- Inability or disinclination to move into L hemispace
- Collisions, dressing half of body, ignoring food on L side of mouth, etc.
- Can be in multiple modalities
- Neglect becomes more pronounced when task demands are increased.
Neglect subtypes

- allocentric vs egocentric
- Personal, peripersonal, extrapersonal space
- Sensory modality
- Attention vs Intentional Neglect
  - Typically associated more with parietal lesions vs frontal lesions
Models and Mechanisms

- Interhemispheric dis-inhibition (Kinesbourne, 1987) — hemisphere imbalance
- Deficit in mental representation of space (Bisiach, 1978).
- Now belief is that there are multiple mechanisms.
- Neurological location is also not clear — although a large, multi-region attention loop in involved
Models and Mechanisms

• Part of neglect may involve the dorsal visual system
  (Ungerleider & Mishkin, 1982)
  – from occipital through parietal and frontal lobes
  – Coding of location for purpose of action, independent of identity (“where” or “how” system)
  – Coding may not be fixed based on environmental axes, but may shift dynamically depending on locations of the effectors with respect to the target. (Anderson, et al., 1993)

• Part of neglect may involve the ventral visual system
  – From occipital lobe through temporal lobe
  – Specialized for identification of objects (“What” system)
Threads of Investigation on Neglect
(Buxbaum, et al., 2006)

• Mechanisms
• Assessment of key characteristics
• Spatial frames of reference for coding spatial information (egocentric, object-based)
• Psychophysical aspects (how much processing of unreported stimuli?)
• Assessment of different sensory modalities of neglect and their relationships
• Anatomic substrates
• Role of deficits in arousal and general attention in the neglect syndrome
• Interventions for neglect
Evaluations for Neglect

- “Find the midpoint” tests
- Search tests – usually visual
- Drawing/copying tests
- Perceptual judgment tests
- Reading Tests
- Extinction Tests
- Posture tests
- Eye movements
- Functional Tests
“Find the midpoint” Tests

• Line bisection
  – Established test-retest reliability, construct validity, convergent validity, divergent validity, criterion validity
  – Inter-rater reliability, responsiveness, internal not tested
  – SEM not known

• Auditory Subjective Midline Test or subjective straight ahead test.

• Point to/grab the midline of a rod

• Drive the w/c to the midpoint
Heilman Line Bisection Test

- Distinguishes attentional from intentional neglect
- Bisect lines on computer screen with view of hand occluded under 2 conditions: normal viewing and reversed viewing

Normal error (attentional) = Where bias – aiming bias
Reversed error (intentional) = aiming bias - where bias
Landmark Test  (Bisiach, et al., 1998)

Search Tests

• **Cancellation tests** (letter, star, word, shape, Alberts, Bells, Apples, Balloon)
  – Albert’s, letter cancellation: Established test-retest (.62-.79), convergent validity, divergent validity, predictive validity, construct validity
  – No reliability established for star cancellation, Bell’s, word
  – No evidence for responsiveness; no SEM

• **Find a single (or a few) target(s) among distractors** – no psychometric data found
  – Tray test
  – Cupboard test

• **Fluff Test** – no psychometric data found
Drawing/copying tests

- Clock, flower, house, man
  - Man: established test-retest reliability (.62), inter-rater reliability; construct validity
  - No data on responsiveness or SEM

- Ogden Scene Drawing test — No data found

- Rey Complex Figure
  - Established test-retest & interrater reliability, criterion validity
  - Not specific to Neglect
  - No data on responsiveness or SEM
Perceptual judgement tasks

• Chimeric faces (Is it a real face?; Which is happier?)
• Gray Scales (Which is darker?)
• No psychometric data found
(more) Functional Tests

• Some search tasks (Cupboard, Tray)
• W/C obstacle course
• Baking Tray Test
  – Place cubes (buns) on a baking tray covering the entire tray
  – Score = # in L half of tray/# in R half of tray
  – Established some construct validity, limited ability to detect neglect
  – No data on reliability, responsiveness, or SEM
Test Batteries

• (Rivermead) Behavioral Inattention Test
  – Criterion-referenced test
  – Conventional subtests
    • Line crossing, letter cancelation, star cancellation, figure copying, line bisection, and representative drawing
  – Behavioral subtests
    • Picture scanning, telephone dialing, menu reading, article reading, telling and setting the time, coin sorting, address and sentence copying, map navigation, and card sorting
  – Some psychometrics established (test-retest and interrater reliability, internal consistency, construct validity, criterion validity, convergent validity, discriminability)
  – No data on responsiveness or SEM
Test Batteries

• **Semi-Structured Scale for Functional Evaluation of Hemi-Inattention** *(Zoccoloti, et al., 1992)*
  - Personal neglect subscale
    - Show me how you comb your hair, use the razor/powder yourself, put your eyeglasses on?
  - Extrapersonal neglect subscale
    - Serving tea, card dealing, picture description, environment description
  - Established inter-rater reliability, internal consistency, construct validity, responsiveness
  - No test-retest or SEM
Test Batteries

- **Catherine Bergego Scale**
  - Observe client in grooming L side of face, adjusting left sleeve/slipper, eating food on L side of plate, knowledge of L limbs, collisions with objects on L, cleaning L side of mouth after eating, difficulty looking to L, finding personal belongings, auditory attention to L, difficulty traveling towards L on unit
    - 0 = no neglect;
    - 1 = mild neglect (always explores the R hemispace first and slowly/hesitantly explores the L side);
    - 2 = moderate neglect (constant and clear left-sided omissions or collisions);
    - 3 = severe neglect (only able to explore the right hemispace)
  - Also can ask as a self-report questionnaire to assessment awareness
    - 0 = no difficulty
    - 1 = mild difficulty
    - 2 = moderate difficulty
    - 3 = severe difficulty
Test Batteries

- **Catherine Bergego Scale**
  - Sel-report scale:
    - 0 = No behavioral neglect
    - 1-10 = Mild behavioral neglect
    - 11-20 = Moderate behavioral neglect
    - 21-30 = Severe behavioral neglect
  - Established inter-rater reliability, internal consistency, construct validity, criterion validity, responsiveness.
  - No data on test-retest reliability or SEM
Interventions

- Prism Adaptation
- Visual scanning training
- Sensory stimulation (caloric, neck vibration, optokinetic stimulation, Galvanic stimulation)
- Eye patching
- Limb activation
- Sustained attention training/Alertness training
- rTMS/tDCS
Prism Adaptation

• Relies on 2 processes
  – Strategic Recalibration
    • Conscious error correction on reaches
  – Spatial Realignment
    • Unconscious, gradual, realignment of proprioceptive and visual sensorimotor coordinate system used to plan and execute actions
What’s the evidence for PA?

• 90% of studies show positive effects (see Newport & Schenk, 2012 for review) – many lasting after intervention has ended (Shiraishi, et al., 2008 & 2010; Fortis, et al., 2010; Serino, et al., 2009, but see Farné, et al., 2002; Priftis, et al., 2013)
  – But large number of case studies
  – Almost half had < 5, only 2 randomized between PA and a control group
  – The highest level evidence was for positive results in conventional neglect tests that maintained out at least 1 month (Serino, et al., 2009; Frassinetti, et al., 2002)

• Many with negative results had < 100 prism, or < 10 training sessions (Turton, et al., 2010; Rousseaux, et al., 2006; Nys, et al., 2008), but not all (Mizuno, et al., 2011)
What’s the evidence for PA?

• Not positive results on all tests in all studies
• Appears to improve performance on tasks in which conscious attention is allocated to the left, but not on tasks in which there is no explicit demand to attend to the left - rightward bias remains
  – No change on preference judgments, crossing out only intact apples (Sarri, et al., 2011; Gossmann, et al., 2013; Ferber, et al., 2003)
  – Suggests that prisms influence attention and motor related circuits in the dorsal posterior cortex (traditional neglect tests, target detection – dorsal stream – SPL/IPS which control visually guided motor behavior and attention)
    • Doesn’t influence perceptual aspects of neglect mediated by higher order perceptual areas in ventral temporal cortex (ventral stream) (Striener & Danckert, 2010) because lesions in neglect often sever the communication between the dorsal and ventral streams.
What’s the evidence for PA?

• The terminal-feedback procedure is superior (Ladavas, et al., 2011)

• However, a version in which the “reaching” during manipulation common objects (coins, jars, puzzles, serving tea) with the arm in full view was found to be just as efficacious (Fortis, et al., 2010; Shiraishi, et al., 2010)
What’s the evidence for PA?

• Individual differences in prism adaptation effect:
  – Depends on size of the aftereffect (Fortis, et al., 2010)
  – Importance of neglect subtype?
    • Only those with intention neglect improved (Goedert, 2013)
  – Whether lesion location makes a difference is not clear (Serino, et al., 2006; Sarri, et al., 2008, Fortis, et al., 2010)
    • Occipital lobe
    • R Intraparietal region (white matter deep to inferior parietal lobe)
    • White mater of R middle frontal gyrus
Visual Scanning Training

• Training voluntary orienting of attention toward the L – a behavioral compensatory mechanism
Visual Scanning Training – what’s the evidence?

• Improvements in performance on
  – conventional neglect tests found (see Pizzamiglio, et al., 2006 for review; van Kessel, et al., 2013; Polanowska, et al., 2009; Kerkhoff, et al., 2013; 2014)
  – functional tests, such as the CBS (Priftis, et al., 2013)
  – to every day life activities (Antonucci, et al., 1995).
• But not always on all neglect tests (e.g., Robertson, et al., 1990; Wagenaar, et al., 1992) – only those trained
  – Not awareness of neglect or auditory midline (Kerkhoff, et al., 2013, 2014)
• Type, duration, frequency, and intensity of training has varied across studies
• No always found to be the superior treatment (Kim, et al., 2011)
Sensory Stimulation

• Caloric stimulation
  – Placing ice water into the left external ear canal
  – Activates the horizontal semicircular canal and induces nystagmus (fast beat to left, slow return)
  – Reduces neglect symptoms on conventional neglect test (Rode & Perenin, 1994; Adair, et al., 2003)
Sensory Stimulation

• Neck vibration
  – Vibration to L posterior neck muscles at position that gives illusory horizontal movement of an LED in front of them
  – Improved performance on cancellation test (Johannsen, et al., 2003) that was retained for a year.
  – Neck vibration for 5 minutes before OT, reduced neglect but no retention (Kamada, et al., 2011)
Optokinetic Stimulation/smooth pursuits

- Watching L-ward moving stimuli
- Proposed mechanisms
  - The lefward moving stimuli gives the illusion that visual stimuli are being displaced rightward (Na, et al., 2002)
  - Reorients covert and overt attention (Mattingley, et al., 1994)
  - Central correction of the neural coordinate transformation (to egocentric coordinate FOR) process via asymmetric input (Karnath, 1996)
Optokinetic Stimulation

• Improved performance on standard neglect tests (line bisection, cancellation, reading) and auditory attention tests (Kerkhoff, et al., 2006; 2012; 2013; Thimm, et al., 2009)
  – More than visual scanning (Kerkhoff, et al., 2014)
  – More than exploratory training (Schröder, et al., 2008)

• Increased awareness of neglect behavior (Kerkhoff, et al., 2014)

• But not on word misreadings (Reinhart, et al., 2011) — stimulus-centered neglect — rightward bias?
Galvanic Vestibular Stimulation

• Weak direct current bilaterally on mastoids behind the ears (L anode; R cathode)
  – Polarizes otoliths and semicircular canal afferents so activates vestibular structures
• Activates network disrupted in neglect
• Improved performance on BIT and Barthel that retained 1 month even with only 1 session (Wilkinson, et al., 2014)
Eye Patching

• Block visual input from right hemispace

• Proposed mechanisms
  – Facilitates shifting of eyes L, attention follows
  – Reduces input to overactivated L hemisphere from superior colliculus

• Studied in combo with other task training
  – Scanning training (Zeloni, et al., 2002)
  – Trunk rotation activity (Fong, et al., 2007)
Eye Patching

- Results are mixed
  - Hemispace blinding found to reduce neglect (Zeloni, et al., 2002; see Smania, et al., 2013 for review, but see Fong, et al., 2007)
  - Patching the R eye very mixed results, not convincing evidence for its use (Barrett, et al., 2001; Walker, et al., 1996; Smania, et al., 2013)
Limb activation

• Performing movements in the L space with the L limb – sometimes with scanning training, sometimes FES used to move the limb.

• Proposed mechanism  (Robertson, et al., 2002)
  – Our representation of space consists of multiple overlapping areas (personal, peripersonal, far space)
  – Using the L limb in the L space activates the L space and body schema forcing multiple spatial sectors
  – May also decrease inhibition from the LH and increase activation of the RH
Limb Activation – what’s the evidence?

• Mixed results, some finding reductions in neglect (Luukkainen-Markkula, et al., 2009; Priftis, et al., 2013) others finding no effect (Robertson, et al., 2002)

• Although using the L limb in a task reduces neglect influence on that task (Robertson, et al., 1992)

• Using the R limb at the same time eliminates the effect (Robertson & North, 1994)
Sustained attention/alertness training

• Spatial neglect is part of an integrated attention system
• Individuals with neglect have reduced sustained attention and alertness
• Various attention training paradigms
• Improvement on neglect tests, but failed to retain for 1 month (Thimm, et al., 2006; Robertson, et al., 1993)
• May improve performance on tests that have a non-spatial attention aspect (selective or sustained), but not when those types of attention is not involved. (Pizzamiglio, et al., 2006)
Mirror Therapy

• Typically a treatment for hemiplegia
  – Paretic limb placed within a mirror box
  – Attempt to move both arms
  – Image of moving non-paretic arm in mirror is interpreted as paretic arm moving.

• A few studies have found reductions in neglect performance on tests, such as the BIT (Dohle, et al., 2009; Thieme, et al., 2012)
What about combining therapies?

- **Optokinetic stimulation + VST** *(Pizamiglio, et al., 2004)*
  - Optokinetic stimulation did not increase performance over VST training alone
- **Neck vibration and prism adaptation** *(Saevarsson, et al., 2010)*
  - Combination therapy was better than NV alone
- **Optokinetic stimulation with prism adaptation** *(Keller, et al., 2009)*
  - Optokinetic stimulation with arm tracking of stimuli
    - No additional benefit of prisms
    - Worsening of symptoms with arm tracking
Brain Stimulation: tDCS and rTMS

• **Proposed mechanism** (Kinsbourne, 1987)
  – Left hemisphere is overactive and inhibiting right hemisphere
  – Right hemisphere is underactive

• **tDCS**
  – Electrical
  – Anodal (facilitatory) for R parietal cortex; cathode (inhibitory) over L parietal cortex; both

• **rTMS**
  – Magnetic
  – Low frequency and continuous theta burst = inhibitory
  – High frequency and intermittent theta burst = facilitatory
Brain Stimulation: rTMS
What’s the evidence?

• Very few studies that have done more than 1 session
• Most have small sample sizes
• Only 2 have used sham treatment
• Both low frequency rTMS and cTBS over the L parietal lobe reduce neglect influence in conventional neglect tests, effects can retain out to 6 weeks (Koch, et al., 2012; Cazzoli, et al., 2012; Shindo, et al., 2006, Song, et al., 2009)
• High frequency rTMS over the R parietal lobe also reduced neglect (Kim, et al., 2013)
Brain Stimulation: tDCS
What’s the evidence?

• Even fewer studies have been done
• None found with more than 1 session
• Most have small sample sizes
• Anodal stimulation of R parietal lobe
  – Reduced neglect on conventional neglect tests (Ko, et al., 2008; Sunwoo, et al., 2013; Sparing, et al., 2009)
• Cathodal stimulation of L parietal lobe
  – Reduced neglect on conventional neglect tests (Sparing, et al., 2009)
• Dual stimulation
  – Stronger effect than anodal alone on conventional tests (Sunwoo, et al., 2013)
Summary

• Neglect is a heterogenous condition caused by lesions in many places in the spatial attentional network

• Not clear what interventions are best for what aspects of the condition or how influenced by location of lesion
  – Some combined therapies may prove more effective, but may be based on neglect subtype

• Visual scanning, Prism adaptation, optokinetic stimulation, have some evidence for their efficacy – but high level evidence (high quality RCTs) remains limited

• A recent meta-analysis of RCTs found a lack of evidence for long lasting effects of neglect interventions on more functional tasks (BIT-B) (Yang, et al., 2013)