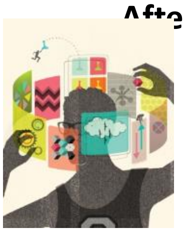
Neuroplasticity Mechanisms: How Therapy Changes the Brain After Injury Part 2

MSHA



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Objectives

Describe the early physiological recovery processes after stroke and how they affect assessment in early post-stroke acute care settings.

Utilize research on treatment driven neuroplastic recovery mechanisms to select evidence-based post stroke treatment content for OT, PT and Speech.

Utilize research on treatment driven neuroplastic recovery mechanisms to maximize upregulation of neuromodulators of motivation including dopamine.

Utilize research on treatment driven neuroplastic recovery mechanisms to maximize upregulation of neuromodulators of attention including acetylcholine and norepinephrine.

Design treatment programs that are balanced with appropriately selected content and methods that maintain patient confidence and maximize outcomes.

What is Neuroplasticity (Cramer et.al. 2011)

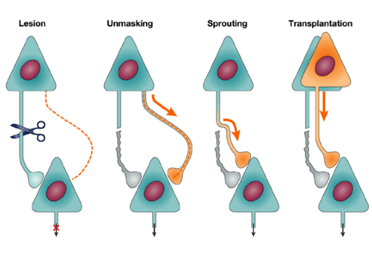
- the ability of the nervous system to respond to intrinsic or extrinsic stimuli
- by reorganizing its structure, function and connections.

I. Overview of neuroplasticity mechanisms after stroke

- Neurophysiology of diaschesis
- Neurophysiology of neural recruitment
- Neurophysiology for white matter tract recovery

Spontaneous Recovery of Function After Stroke (Pekna,M., Pekny, M., Nilsson,M.,2012)

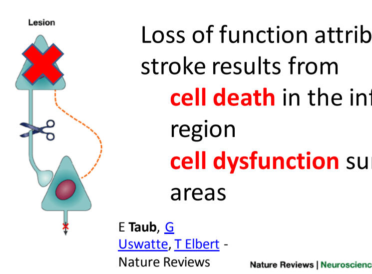
- Loss of function attributable to stroke results from
  - **cell death** in the infarcted region
  - **cell dysfunction** surrounding areas
- In addition, the function of remote brain regions (including the contralateral areas) connected to the area of tissue damage, is compromised because of ***diaschisis*** which includes:
  - hypometabolism,
  - neurovascular uncoupling, and
  - aberrant neurotransmission



E **Taub**, G Uswatte, T Elbert - Nature Reviews Neuroscience, 2002

Four Processes of Spontaneous Recovery after Brain Injury

Spontaneous Recovery of Function After Stroke (Pekna,M., Pekny, M., Nilsson,M.,2012)



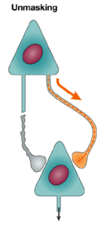
Loss of function attributable to stroke results from
cell death in the infarcted region
cell dysfunction surrounding areas

E **Taub**, G Uswatte, T Elbert - Nature Reviews Neuroscience, 2002

Functional spontaneous recovery involves 3 (likely) overlapping, phases:

(Pekna,M., Pekny, M., Nilsson,M.,2012)

– (1) **reversal of diaschisis**, activation of cell genesis, and repair;



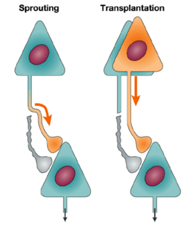
E **Taub**, G Uswatte, T Elbert - Nature Reviews Neuroscience, 2002

Nature Reviews | Neuroscience

Functional spontaneous recovery involves 3 (likely) overlapping, phases:

(Pekna.M., Pekny, M., Nilsson,M.,2012)

(2) **change** in the properties **of existing neuronal pathways;**
(3) neuroanatomical plasticity leading to the formation of **new neuronal connections.**[1]



The basic processes underlying phases 2 and 3 also are involved in normal learning

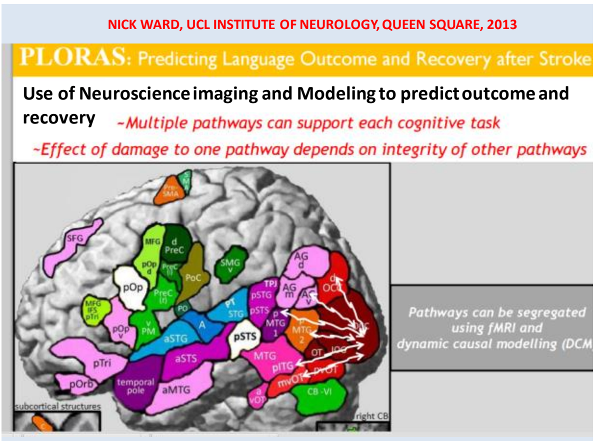
E **Taub**, G Uswatte, T Elbert - Nature Reviews Neuroscience, 2002

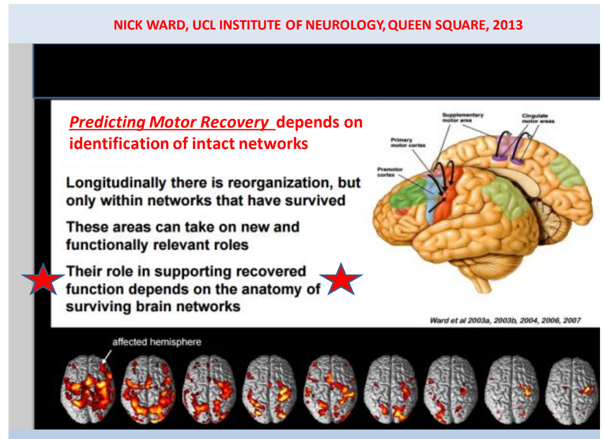
Experience-Dependent Plasticity of the Cerebral Cortex (Pekna,M., Pekny, M., Nilsson,M.,2012)

- *"The ability to adapt in response to the changing environment is the most fundamental property of the nervous tissue and constitutes the basis for learning*."
- ***Neural plasticity*** - neurobiological basis for ability to adapt & learn in an **experience-dependent manner**
  - At the structural level, neural plasticity could be defined in terms of
    - dendritic and axonal arborization,
    - spine density,
    - synapse number and size,
    - receptor density,
    - and in some brain regions also the number of neurons.

Experience-Dependent Plasticity of the Cerebral Cortex

- The structural constituents of neural plasticity jointly determine
  - the complexity of ***neuronal networks*** and their **activity** and
  - contribute to recovery of function after stroke and other CNS injury



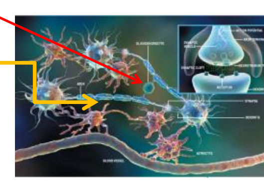


The relationship between clinical phenotypes, neuroplasticity, therapeutic interventions and assessment of function (adapted from Cramer, 2011)

Clinical Phenotypes for Adult Rehab Neurotrauma **Stroke** Neurodegeneration Aging	⟷	***Neuroplasticity*** Adaptive/Maladaptive Alternate/Latent Pathways
↕		↕
Assessments Behavioral Neural – fMRI and DCM Functional	⟷	***Interventions*** Physical Training Language Training Cognitive Training Adjunctive Therapies

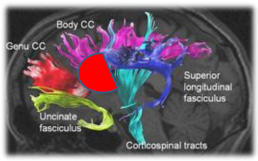
Neurophysiology of white matter tract recovery (Jiang, Q 2010)

- Neurorestorative treatment of stroke significantly increases both ***progenitor and mature oligodendrocytes in the ipsilateral hemisphere of the ischemic brain***.
- Oligodendrocytes generate myelin and contribute to the ***integrity of white matter tracks in the brain.***
- **Stimulation and amplification of these cells may lead to restructuring of axons and myelin.**



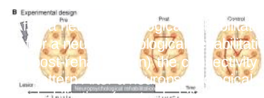
Neurophysiology of white matter tract recovery (Jiang, Q 2010)

- White matter architecture in the ischemic boundary is altered by neurorestorative treatment,
- axonal density in the peri-infarct area is significantly increased after treatment. (see especially Jiang Q et al., (2006) MRI detects white matter reorganization after neuralprogenitor cell treatment of stroke. *Neuroimage.* 32: 1080–1]



Nazareth P. Castellanos et al. Brain 2010;133:2365-2381

Illustration of experimental protocol and hypothesis:



After Rehab the connectivity pattern of the same group of patients was calculated. These pre- and post-rehabilitation networks were compared with those from the group of healthy controls

- Functional connectivity patterns from patients with traumatic brain injury were calculated a few months after injury (pre-rehabilitation condition).

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Maladaptive neuroplasticity

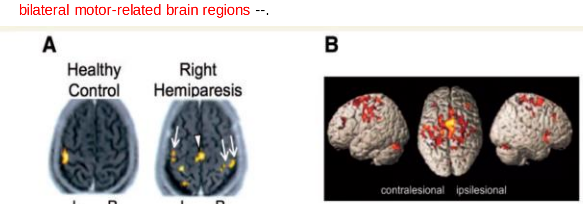
- Another principle is that not all plasticity has a positive impact on clinical status—in some cases, plasticity might have negative consequences.
  - new onset epilepsy is a common complication of cerebral trauma,

Studies of the upper extremity motor system after stroke illustrate a number of forms of brain plasticity.

A & B Spontaneous Recovery

Several patterns of change arise spontaneously during the weeks following stroke onset.

A.In typical right hemiparesis, movements were associated with a shift in motor cortex laterality towards the right hemisphere + increased recruitment of left dorsal premotor & bilateral supplementary motor area
B. In fMR grip task using paretic hand, poorer recoverers recruited a number of bilateral motor-related brain regions --.



Steven C. Cramer et al. Brain 2011;134:1591-

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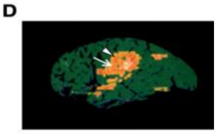
Motor Recovery – Parallel changes

- Studies of motor recovery after stroke also illustrate that injury to a region of the motor network can result in spontaneous (*during the weeks after stroke*) intra-hemispheric changes:
- such as in representational maps where the hand area can shift dorsally to invade the shoulder region (Nudo et al., 1996; Muellbacher et al., 2002)

Motor Recovery – Parallel changes

Or where the hand area can shift into face region (Weiller et al., 1993; Cramer and Crafton, 2006).

D



Steven C. Cramer et al. Brain 2011;134:1591-1609

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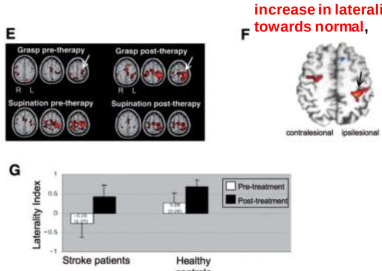
Behavioural gains result from effective treatment

E–G Brain plasticity associated with treatment-induced recovery

E. **increase in the volume of activity and excitability of motor cortex**

increase in laterality, back towards normal,



G. **with a greater predominance of activity in *stroke-affected motor cortex rather than bilateral activation***

Steven C. Cramer et al. Brain 2011;134:1591-1609

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Goals of Neuroplasticity Research in Stroke (Cramer, et al, 2011; Ward, 2013; Price, 2014)

TO BETTER UNDERSTAND:

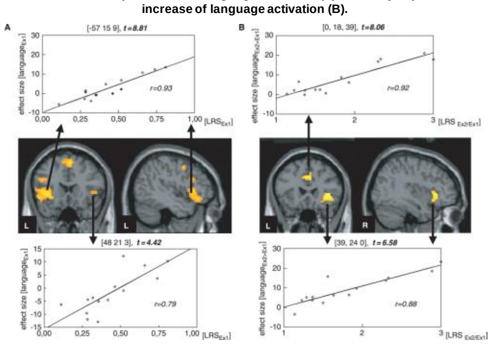
- time sensitivity (the "When" of therapy)
- experience dependence (the "What" of therapy)
  1. Task specific practice (as opposed to typical environmental stimulation) – choice of evidence-based procedures is important
  2. Understanding variability ("Why" some patients respond better than others)
  3. Dosage ("How Much" of therapy)
- the "How" of therapy – altering neuromodulators and "how" Adjunctive therapies enhancing outcomes
- Ultimate Goal predicting outcomes ("What to expect")

Treatment considerations – “When” components of aphasia intervention

Aphasia Therapy (Saur et al 2006)

- The data suggest that brain reorganization during language recovery proceeds in three phases:
  - a strongly reduced activation of remaining left language areas in the acute phase
  - is followed by an upregulation with recruitment of homologue language zones, which correlates with language improvement.
  - Thereafter, a normalization of activation is observed, possibly reflecting consolidation in the language system.

Correlation of initial impairment and language activation (A) and early improvement and increase of language activation (B).



Dorothee Saur et al. Brain 2006;129:1371-1384

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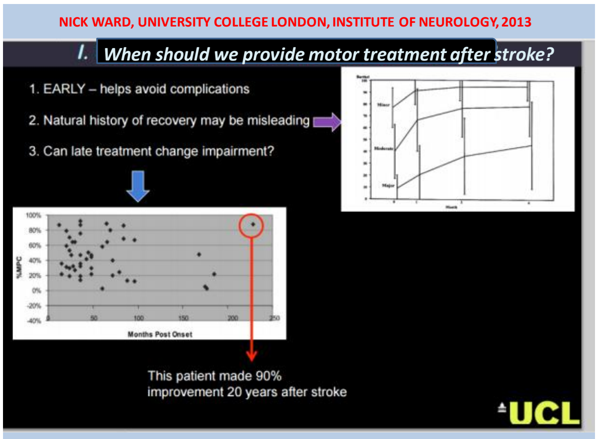
Saur et al 2006 model – Three phases of Language Recovery in Aphasia (see also Turkstra, 2013)

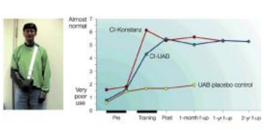
1. The early (compensatory) upregulation of the language network after vessel recanalization could be utilized for -
   - early ***unspecific language therapy*** mostly consisting of ***stimulation techniques***, because all potential areas of language processing are activated with the goal to compensate the deficit.
2. *Targeted* ***task specific goals*** based on deficits identified through thorough assessment ***with continuous adaptation*** as specific changes occur
3. Chronic phase of language recovery – intensive systematic model-orientated therapy ***to*** **evoke recurrent phases of upregulation in the language network**



The "What" of Therapy – **Task Specific Treatment** based on deficits has been studied most extensively

- Effects have been studied using various imaging technologies
- This has led to accumulation of "evidence based therapies"
  - UE motor function
  - Neglect
  - Language
  - Cognition

UE motor function – Constraint Induced Movement Therapy



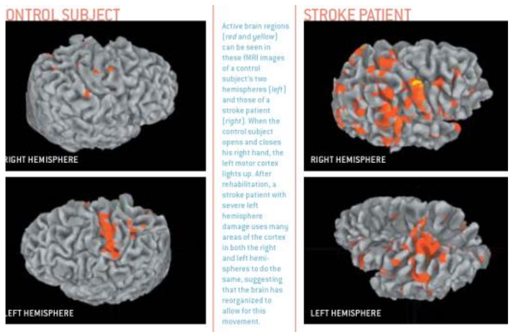
- Constraint-Induced (CI) Movement therapy involves constraining the movement of the extremity that is less affected by cerebral nervous system injury and, more importantly, 'shaping' the affected limb (an arm in this case) for many hours a day for two or three consecutive weeks.

Constraint Induced Therapy

Constraint Induced therapy

- The constraint, by a sling or a mitt, forces the individual to make use of the more affected extremity. The quality or skill of the movements is systematically improved by a shaping procedure.

E **Taub**, G Uswatte, R Pidikiti - Journal of rehabilitation (1999); J Liepert, H Bauder, WHR Miltner, E **Taub**, C Weiller - Stroke, 2000; E **Taub**, G Uswatte, T Elbert - Nature Reviews Neuroscience, 2002



The data show a large increase in real-life arm use in a CI therapy group trained at the University of Alabama at Birmingham (UAB), and the close replication of this result in a group treated at the University of Konstanz. A placebo group that received a general fitness programme did not show a significant change over time.

Cortical Map Rearrangements (Pekna,M., Pekny, M., Nilsson,M.,2012)

- When normal input to a specific area of the primary somatosensory cortex is altered because of genetics or because of experience
  - **rapid structural and functional reorganization results** in this area being **activated by sensory stimulation of the surrounding intact body regions**

The Journal of Neuroscience Cortical Recovery After Nerve Regeneration in Monkeys 219

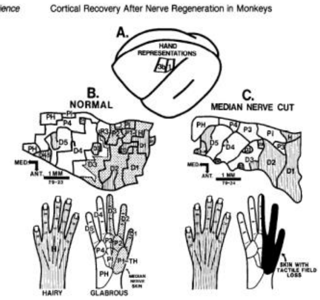
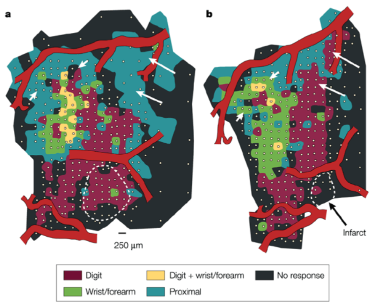


Figure 1. Somatosensory cortical representations of the hand in owl monkeys with normal and transected median nerves to the hand. *A*, Area 3b and 1 hand representations are located in a flat region on the dorsolateral surface of parietal cortex. *B*, Hand representation in area 3b of a normal owl monkey. Cutaneous inputs from the glabrous (*unhatched and stippled*) and hairy (*hatched*) hand surfaces are topographically represented in area 3b. The median nerve innervates the thumbward half of the glabrous hand (*bottom, stippled*), and normally provides inputs to the lateral part of the hand representation (*top, stippled*). *PH*, Hypothenar pad; *PI*, insular pads; *P1-TH*, pad 1 and thenar pad; *P2–4*, pads 2–4; *D1–5*, digits 1–5; *H*, hairy hand proximal to knuckles. *C*, Hand representation in area 3b of an owl monkey with a transected and chronically ligated median nerve (from Merzenich et al., 1983a). No area 3b neurons had cutaneous receptive fields on skin regions normally innervated by the median nerve (*bottom, blackened zone* on hand), but, due to the nerve injury, the lateral part of the hand representation (*top*) had reorganized and acquired substitute inputs from hairy (*hatched*) and glabrous (*unhatched*) skin regions bordering the denervated skin (e.g., hairy D1 and 2, glabrous P3 and I). Area 3b hand representations illustrated in *B* and *C* have been rotated counterclockwise 90° from the orientation shown in *A*.

Cortical Map Rearrangements (Pekna,M., Pekny, M., Nilsson,M.,2012)

- Also, **motor maps** in the primary motor cortex change in response to **task-specific training** or **injury**.
- **Training human subjects** or animals to perform a **specific task** leads to **an increase in the area of motor cortex that controls the muscles used during the task.**



E **Taub**, G Uswatte, T Elbert - Nature Reviews Neuroscience, 2002

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a | Before infarct. b | After infarct and rehabilitative therapy. Note the large increase in the cortical representation of the wrist/forearm after therapy. Adapted with permission from Ref. 51 © 1996 American Association for the Advancement of Science

Cortical Map Rearrangements (Pekna,M., Pekny, M., Nilsson,M.,2012)

- **Cortical areas recruited after injury** play a role in functional recovery in humans
  - supported by a study showing that in well-recovered stroke patients, the ipsilesional dorsal motor cortex shows increase in activity (Gerloff, et al. 2006)
- **Functional redundancy** due to **substantial overlap within and across brain regions** also contributes to the ability of the brain to adapt to injury (Warraich Z, Kleim JA 2010)

Cortical Map Rearrangements (Pekna,M., Pekny, M., Nilsson,M.,2012)

- spinal cord injuries also
  - lead to both unmasking of existing latent connections
  - as well as changes in somatosensory cortex anatomy attributable to the growth of new lateral connections.
- Functional and structural rearrangement has been studied for decades and is well-documented for neural networks within the cerebral cortex,
  - The **plasticity responses** induced by stroke at the **level of the spinal cord** have been demonstrated more recently
  - Using a rat stroke model, Liu et al (2009) showed that the spontaneous behavioral motor recovery highly correlates with the remodeling of corticospinal tract axons in the cervical spinal cord as well as the reorganization of pyramidal neurons in the cerebral cortex of both hemispheres.

General Principles of Experience Dependent Neural Plasticity Kleim & Jones 2008)

- 1. Use It or Lose It - Failure to drive specific brain functions can lead to functional degradation.
- 2. Use It and Improve It - Training that drives a specific brain function can lead to an enhancement of that function.
- 3. Specificity -The nature of the training experience dictates the nature of the plasticity.

General Principles of Experience Dependent Neural Plasticity (Kleim & Jones 2008)

- 4. Repetition Matters - Induction of plasticity requires sufficient repetition.
- 5. Intensity Matters - Induction of plasticity requires sufficient training intensity.
- 6. Time Matters - Different forms of plasticity occur at different times during training.
- 7. Salience Matters -The training experience must be sufficiently salient to induce plasticity.

General Principles of Experience Dependent Neural Plasticity (Kleim & Jones 2008)

- 8. Age Matters - Training-induced plasticity occurs more readily in younger brains.
- 9. Transference - Plasticity in response to one training experience can enhance the acquisition of similar behaviors.
- 10. Interference - Plasticity in response to one experience can interfere with the acquisition of other behaviors.

Task specific neuroscience approaches in children

Childhood Apraxia of Speech

- Kadis, D et al. (2013) Cortical Thickness in Children Receiving Intensive Therapy for Idiopathic Apraxia of Speech. *Brain Topography:A Journal of Cerebral Function and Dynamics*

Turken and Dronkers (2011) motor speech planning, fluency and grammar pathways

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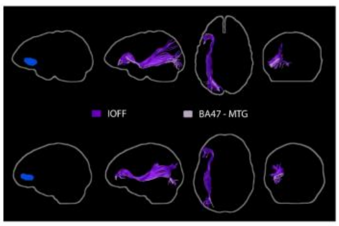


Figure 8. Pathways associated with the BA47 ROI (left, blue). Streamline tractography results from two subjects are presented as exemplars. The inferior occipito-frontal fasciculus as well as a group of IOFF fibers associated with the posterior MTG ROI were identified.

Cortical Thickness of Children with CAS

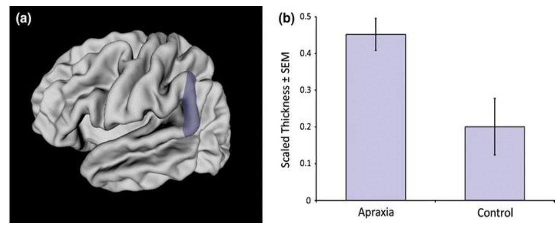


Fig. 1a Left posterior supramarginal gyrus ROI, represented as a *shaded region* on a mid-surface rendering of an average brain; **b** children with idiopathic apraxia (n = 11) had thicker left posterior supramarginal gyri compared to Controls (n = 11) at baseline, $t(20) = 2.84$, $p \leq 0.05$. *Mean scaled cortical thickness* (*±SEM*), shown for each group (Color figure online)

Cortical Thickness Changes Following Prompt

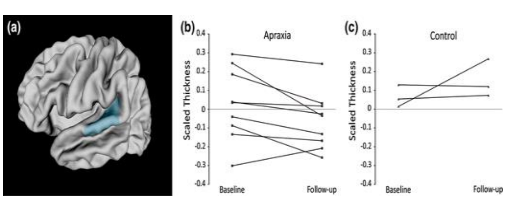


Fig. 2a Left posterior superior temporal gyrus (Wernicke's area), represented as *shaded region*; **b** children with idiopathic apraxia (n = 9) experienced significant thinning of Wernicke's over the course of therapy, ($t(8) = 2.42$, $p \leq 0.05$); **c** baseline and follow-up scaled cortical thickness of Wernicke's area in the small subset of Controls with appropriate serial imaging (n = 3)

Findings

- Only one significant difference was observed: children with idiopathic apraxia had **significantly thicker left posterior supramarginal gyri** than Controls
- Left posterior supramarginal gyrus thickness did not correlate with any of the baseline measures of speech performance in the clinical group
- **In children receiving therapy for apraxia, ROI analyses revealed significant thinning** in the posterior superior temporal gyrus, canonical **Wernicke's area**
- Decreasing thickness in Wernicke's over the course of therapy was not significantly correlated to change scores on any of the standardized speech measures
- The clinical significance of thicker left supramarginal gyri in children with idiopathic apraxia is not clear.

Working Memory Training

- Klingberg, T (2010) Training and plasticity of working memory. *Trends in Cognitive Sciences* 14: 317–324
  - Although WM capacity has been viewed as a constant trait, recent studies suggest that it can be improved by adaptive and extended training.
- This training is associated with changes in brain activity in frontal and parietal cortex and basal ganglia, as well as changes in dopamine receptor density.
- Transfer of the training effects to nontrained WM tasks is consistent with the notion of training-induced plasticity in a common neural network for WM.

Cog Med (visual working memory) Research with ADHD

- Klingberg, T. et al. (2005) Computerized training of working memory in children with ADHD – a randomized, controlled trial. *J. Am. Acad.Child Adolesc. Psychiatry* 44, 177–186
- Kerns, K.A. et al. (1999) Investigation of a direct intervention for improving attention in young children with ADHD. *Dev. Psychol*. 16, 273–295
- Holmes, J. et al. (2009) Working memory deficits can be overcome: impacts of training and medication on working memory in children with ADHD. *Appl. Cogn. Psychol*. 12, 9–15

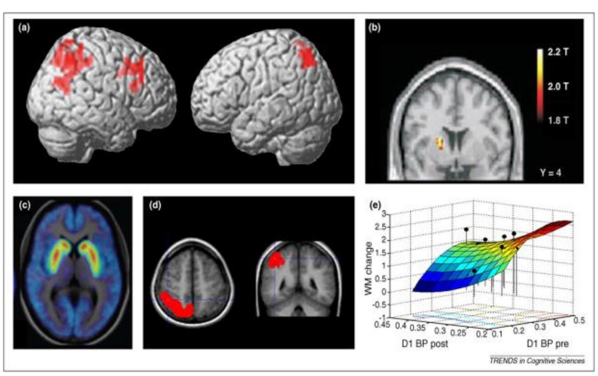
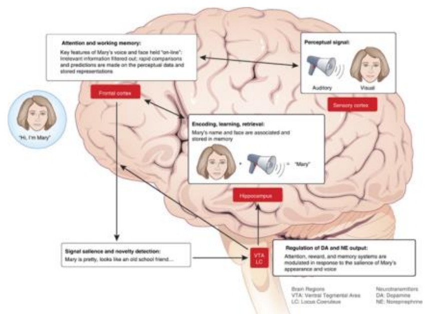


Figure 1. Training-related effects on brain activation and dopamine receptor density from neuroimaging studies. (a) Increases in frontal and parietal activity after training of WM (reproduced with permission from [33]). (b) Increased activity in the caudate nucleus after training of WM tasks requiring updating (reproduced with permission from r

Multisensory Neurorehabilitation

- Specific examples of multisensory neurorehabilitation are
  - mirror therapy and action observation,
  - motor imagery and mental training,
  - virtual reality training, and
  - music-related therapies.



In order for prefrontal cortical operations to engage in efficient decision-making and adaptive behavior, the brain must be able to continuously make accurate predictions about the near future. These predictions rely on rapidly and accurately comparing high-fidelity perceptions of our current internal and external environments with past experiences. Vinogradav, et al2012

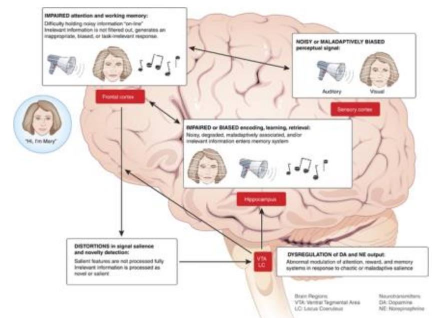
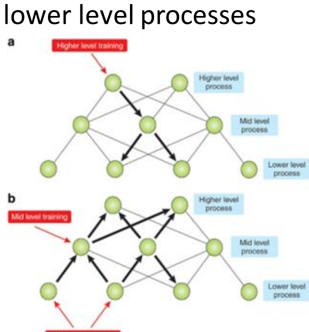


Figure 5
If lower-level perceptual and/or attentional processes are degraded or abnormally biased, the brain will have difficulty adaptively performing other more complex multimodal operations, predictions, or decisions on the data.

The key is balancing high level processing tasks with mid and lower level processes

- Targeted intervention that increases perceptual brain mapping (bottom up processes) and language (top down processes) **simultaneously can build maps, stimulate long fiber tract development, and perhaps improve pruning through intensive, repetitive stimulation** Vinogradav, et al 2012;Ahissar *et al* (2009).



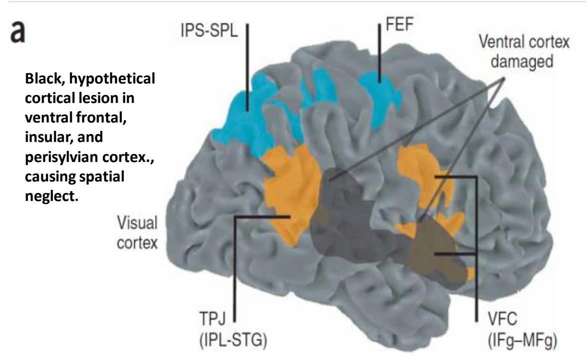
Task-Specific Training (Naoyuki Takeuchi and Shin-Ichi Izumi, 2013)

- All training after stroke should include goals relevant to the **functional needs** of the patient
- Task-specific training to facilitate activities of daily living or other relevant motor tasks is a well-accepted principle of stroke rehabilitation
  - Task-specific training can effectively recover a wide array of motor behaviors involving the upper limbs, lower limbs, sit-to-stand movements, and gait after stroke
  - Compared to traditional stroke rehabilitation approaches such as simple motor exercises, **task-specific training induces**
    - **long-lasting motor learning**
    - **associated cortical reorganization**

Treatment of Neglect

- Treatments that focus on reorienting of attention
  - Principles of Visual Scanning Training (Haskins, et al, 2012)
    - Locus of the Stimulus (left more problematic)
    - Anchoring (verbal and visual cues)
    - Pacing (slowing down by reciting targets aloud)
    - Density
    - Information Load

Figure 1. Functional anatomical model of attention. A. The dorsal (BLUE), top down)and the ventral (ORANGE, stimulus driven) regions of the human visual spatial attention system.



Corbetta et al., 2005

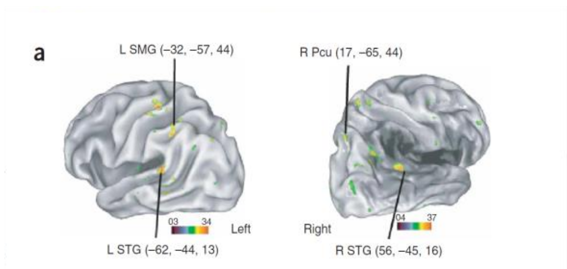
Lighthouse Strategy for Attention Reorienting

- With any task requiring visual attention:
  - Picture of lighthouse placed in farthest spot of L visual field
  - Pt imagines his/her eyes are the beam – sweeping all the way to the left and the right of the horizon to guide ships to safety

Lighthouse Strategy (continued)

1. With scanning sheet or objects on table, therapist asks, what if the light could only stream to the right?
2. Introduce visual stimuli on the table-top in a range the pt should be able to scan to assure pt can succeed
3. If pt misses some, say, “Look you missed ____ on the left – do it again and pretend you are the lighthouse – therapist can model head turning
4. Move to room – identify objects on left and right walls – use tactile or verbal cues as necessary
5. FOR PT Eventually can move to ambulation, identification of people or objects in a room

Figure 7. BOLD correlates of attention reorienting
Regions involved in recovery of reorienting.

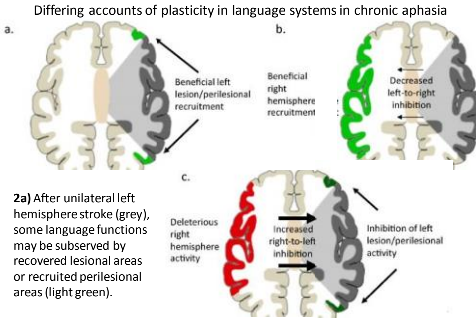


Corbetta et al., 2005

Language Interventions in Aphasia

- During early spontaneous recovery – generalized stimulation
- During acute active recovery stage – treatment should be specific - targeted to unique needs of each patient and adaptive ***ONE SIZE DOES NOT FIT ALL***
- During the chronic recovery stage intensive generalized left-hemisphere targeted interventions (grammatical, phonological eg.) may be most effective

Differing accounts of plasticity in language systems in chronic aphasia



2a) After unilateral left hemisphere stroke (grey), some language functions may be subserved by recovered lesional areas or recruited perilesional areas (light green).

2b) Right perisylvian areas (light green) may be recruited to subserve some language functions, a process facilitated by decreased transcallosal inhibition of the right hemisphere by the damaged left hemisphere.

2c) By contrast, right hemisphere activity may be deleterious. Released from interhemispheric inhibition, right hemisphere structures (red) may exert increased inhibitory influence on left perisylvian areas, impeding functional recovery of lesional and perilesional areas in the left hemisphere (dark green).

Brain Lang. 2011 Jul; 118(1-2): 40–50.

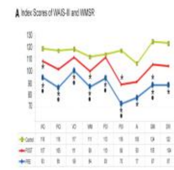
Cognitive Intervention – May follow the same staged guidelines

Cognitive Recovery Research (Nazareth P. Castellanos et al. Brain 2010;133:2365-2381)

- Patients completed a neurorehabilitation program that was ***adapted to each individual's requirements***.
  - Individual sessions of intensive neuropsychological-based rehabilitation, 1 hour. 3–4 days a week.
  - In some cases, cognitive intervention was coupled with other types of neurorehabilitation therapies (PT, OT, SLT)
- Depending on the **severity** and ***deficit features*** of each case, strategies of
  - restitution,
  - Substitution,
  - and/or compensation were applied
  - as well as training in daily living activities,
  - external aids or the application of behavioural therapy

Nazareth & Castellanos (2010) outcomes

- **Means of the general scores in the WAIS-III and some indexes of the Wechsler Memory Scale–R pre- (blue line) and post-rehabilitation (red line) and in controls (green line).**



BRAIN A JOURNAL OF NEUROLOGY

Assist PT's with including cognitive interventions during gait training

- Identification of Cognitive influences on gait
  - Volition - Loss of mobility due to reduced motivation. Decreased inner drive to move. May be mistaken for bradykinesia.
  - Self-awareness - Careless walking: Poor or inaccurate estimation of one's physical limitations may lead to inappropriate evaluation of environmental hazards and increase the risk of falling.
  - Planning - Deficits in decision-making abilities while walking in a complex environment. Inefficient, faulty or even risky choices. Losing the way or wasting time or effort to arrive at the desired destination.
  - Distractibility in complex environments
  - Attention and Multi-tasking

PT task that includes cognitive components

- Stop walking while talking
  - `Subject walks while conducting a conversation with the examiner (for example, answering questions regarding one's medical history)
  - Outcome measure - Walking speed & number of stops (walking).
  - Examiner should be consistent with the questions and level of question difficulty.

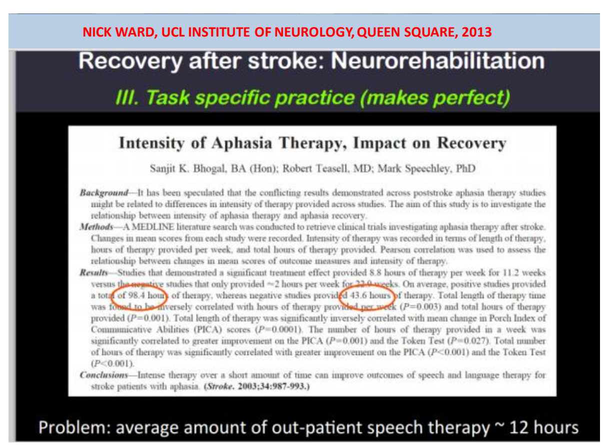
PT task that includes cognitive components

- Arithmetic task (digit span, backward counting, serial 3 or 7 subtractions)
  - Subject walks while counting back from 100 (or any other number), or subtracting 3's or 7's.
  - Outcome measures.
    - Walking speed
    - Number of stops
    - Mistakes in calculations Number of calculations completed

Best Source for Evidence-Based Cognitive Rehabilitation Approaches

Importance of Dose

- How much therapy is necessary?
- Is there such thing as an overdose of therapy?



Other Considerations

Enriched Environment (Naoyuki Takeuchi and Shin-Ichi Izumi, 2013)

- Enriched environments
  - Provide greater opportunity for physical activity and motivation
  - Facilitated by a well coordinated multidisciplinary team
  - Patient involvement in patient-centered interdisciplinary goal setting has been shown to encourage their motivation and engagement in therapy
- Reported benefits of multidisciplinary care extend to patients of all ages and to patients with varying stroke severity

Preventing Maladaptive Plasticity *(***Naoyuki Takeuchi and Shin-Ichi Izumi, 2013)**

- From a PT and OT perspective maladaptive plasticity that weakens motor function and limits recovery
- From a speech perspective – maladaptive plasticity results in recurrent utterances and hyperfluent neologisms in aphasic patients
- From a nursing and family perspective – maladaptive plasticity results in repetitive habits that interfere with re-acclimation in the home, community or vocational setting

Multisensory Neurorehabilitation

- Specific examples of multisensory neurorehabilitation are
  - mirror therapy and action observation,
  - virtual reality training, and
  - motor imagery and mental training,
  - music-related therapies.

Integration between Motor Learning and Multisensory Feedback (Naoyuki Takeuchi and Shin-Ichi Izumi, 2013)

- *Action Observation* -The neurophysiological basis for this recruitment is associated with mirror neurons
- *Brain Computer Interface (BCI)* -record, decode, and translate measurable neurophysiological signals into effector actions or behaviors without the use of peripheral physiological activities
- *Virtual Reality (VR)* -VR is a computer-based technology that engages users in multisensory simulated environments, including real-time feedback (e.g., visual, auditory, and tactile feedback),allowing users to experience simulated real-world objects and events

Language and cognition involve complex intertwining networks

- New research suggests that most patients (children and adults) with language dysfunction have multiple "nodes" of involvement (Finn et al, 2014)
- Combinations of Top-Down and Bottom-up treatment goals hold the greatest promise for complex patients

Cognitive Function in Cerebrovascular Accident (CVA) & Traumatic Brain Injury (TBI) – Part One

A Meta-Analysis of the Research

frontiers in Psychology

Neuroscience illuminating the influence of auditory or phonological intervention on language-related deficits

Sari Ylinen and Teija Kujala

Published online 2015 Feb 17.

- **IS NEUROSCIENTIFIC RESEARCH USEFUL FOR EDUCATORS?**
- **DOES THE CONTENT OF THE INTERVENTION MATTER?**
- **HOW LONG-LASTING ARE THE REMEDIAL GAINS IN THE BRAIN?**

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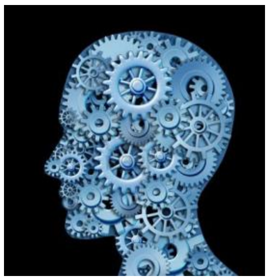
IS NEUROSCIENTIFIC RESEARCH USEFUL FOR EDUCATORS? (Ylinen and Kujala, 2015)

- Neuroscientific research has demonstrated that improved behavioral performance is coupled with changes in both brain function and brain anatomy.
- Especially in the study of dyslexia, neuroscientific studies have illuminated the location of aberrant brain functions, which has enabled to specify the models of the impairment.



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DOES THE CONTENT OF THE INTERVENTION MATTER? (Ylinen and Kujala, 2015)

- Interventions and training programs involving phonological and auditory tasks have repeatedly gained remedial effects in dyslexia, SLI, and LLI.

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HOW LONG-LASTING ARE THE REMEDIAL GAINS IN THE BRAIN?

(Ylinen and Kujala, 2015)

- The activation pattern of previously hypoactive areas had normalized, probably reflecting cumulative learning effects following intervention.
- These follow-up studies thus show that treatment-induced neurobiological changes, coupled with improvement in behavioral performance, can be long-lasting and may enable cumulative gains in language-related skills.

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The "How" of Therapy - Neurochemistry

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Neuromodulators that Build Brains

Different dimensions of cortical plasticity are enabled by the behaviorally-context-dependent release of:

- acetylcholine (focused attention/reward) (Kilgard, Bao)
- dopamine (reward, novelty) (Bao)
- norepinephrine (novelty) (Bollinger)
- serotonin (Bollinger)
- et alia

In adults, learning-induced changes are complexly "nuanced" by differences in behavioral context that result in the differential release of 6 or 7 modulatory neurotransmitters.

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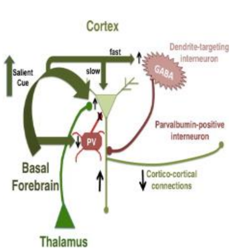
Acetylcholine (Picciotto, Higley and Mineur. 2012)

- Acetylcholine (Ach) is an arousal neuromodulator -both excitatory and inhibitory
- ACh increases behaviors that are ***environmentally adaptive***
- ACh decreases ***responses*** to ongoing stimuli ***that don't require immediate action***

Picciotto, Higley and Mineur (2012)



- Salient cues induce acetylcholine release onto the cortical pyramidal neurons, resulting in rapid inhibitionof pyramidal cells.
- Activation enhances stimulation of pyramidal neuron firing from the environment
- Acetylcholine also suppresses corticocortica ltransmission through inhibitory M2 mAChRs on pyramidal cell axon terminals
- reducing distraction while preserving attention to an environmental stimulus

Net Effect - ACh Reduces distraction while preserving attention to an environmental stimulus

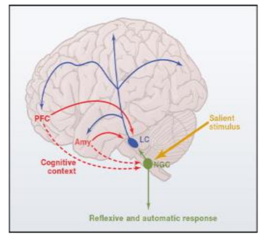
Take away from Picciotto, Higley and Mineur (2012)

- To upregulate ACh in your patients– think TV commercials – (they are louder and grab you with color and quick relevance)
  - **Put the patient in charge** of when information is presented ("raise your hand when you are ready")
  - **Move**, **establish eye contact** with non-attending patients, use **"bells and whistles"**

Norepinephrine (Sara and Bouret, 2012)

- Norepinephrine [noradrenalin (NA)] regulates mood, motivation and arousal
- NA drives a reallocation of neural resources toward regions involved in attention, vigilant perception, and behavior control

Sara and Bouret (2012)



- A salient stimulus will result in a release of noradrenaline in its numerous target regions (bluearrows), including cerebral cortices, limbic structures, thalamus, cerebellum,brainstem, and spinal cord.
- This surge of NA would facilitate sensory and motor processing and, for the reorganization of distributed functional networks,

NA promotes behavioral adaptation.

Take away from Sara and Bouret (2012)

- Making treatment content “emotionally relevant” is the key to increased norepinephrine
  - The “ah hah” moment
  - The “wow that is cool” response to information
- Novelty also works well
  - Try presenting the information several different ways
  - This is where the creativity of a teacher really comes into play

Dopamine (Tritsch and Sabitini, 2012)

- The prefrontal cortex is the major cortical recipient of Dopaminergic inputs
- Dopamine (DA) is believed to play a critical role in several cognitive processes conducted by Pre Frontal Cortex networks, including
  - working memory,
  - attention
  - decision making

Tritsch and Sabitini (2012)

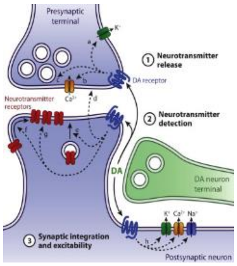


Figure 1. Potential Sites of Modulation of Synaptic Transmission by DA

Dopamine
The neuromodulator of Reward

Take away from Tritsch and Sabitini (2012)

- Keep your treatment personal and emotionally relevant to your patients
  - A personal example, a family member request, etc.
- Strive to provide some novel element to each session
- **REWARD, REWARD, REWARD**
  - Know what is rewarding – it may not be "good job"
  - ADL's are only rewarding if they are relevant to the patient
  - Intermittent reinforcement is preferable

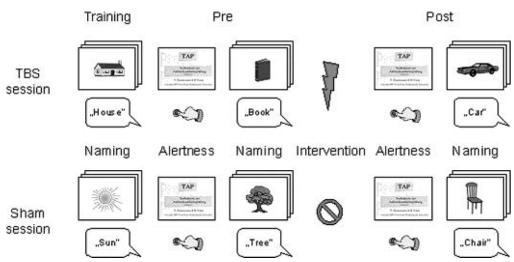
Lesch and Waider (2012)

- Serotonin (5-HT) shapes brain development influencing social cognition and emotional learning
- Key for clinicians
  - The treatment environment should feel safe
  - The therapist must be trusted

Adjunctive Therapies – Increasing Outcomes

- Theta Burst Stimulation (TBS) in Broca's aphasias
- Aerobics as adjunctive to PT

Effects of Theta Burst Stimulation in RH homologue of Broca's area - Experimental procedure, tasks, and sequence of events.



Jochen Kindler et al. Stroke. 2012;43:2175-2179

American Heart Association.
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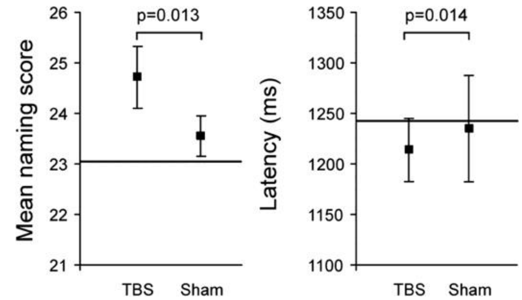
Mean naming scores (left) and naming latencies (right) postintervention.



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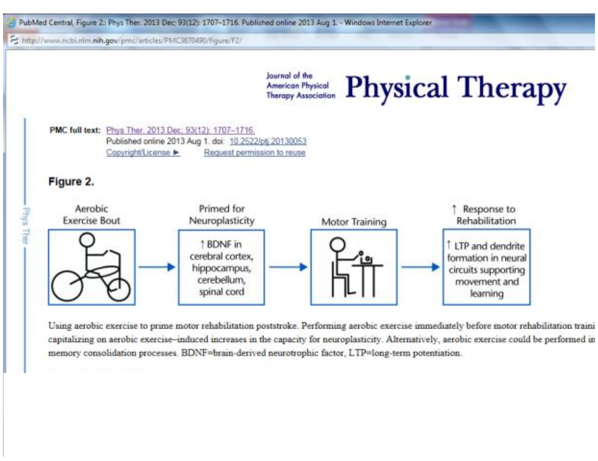
PubMed Central, Figure 2.: Phys Ther. 2013 Dec; 93(12): 1707–1716. Published online 2013 Aug 1. - Windows Internet Explorer

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3870490/figure/F2/

Journal of the American Physical Therapy Association Physical Therapy

PMC full text: Phys Ther. 2013 Dec; 93(12): 1707–1716.
Published online 2013 Aug 1. doi: 10.2522/ptj.20130053
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Figure 2.

Using aerobic exercise to prime motor rehabilitation poststroke. Performing aerobic exercise immediately before motor rehabilitation traini capitalizing on aerobic exercise–induced increases in the capacity for neuroplasticity. Alternatively, aerobic exercise could be performed in memory consolidation processes. BDNF=brain-derived neurotrophic factor, LTP=long-term potentiation.

1. Balance Brain Stimulation

Chapman (2013)

- Active mental stimulation is required to improve or recover lost cognitive functions
- 80% rule (Merzenich & Jenkins)
  - Too low challenge creates boredom
  - Too high challenge creates frustration agitation
- Tasks need to be ratcheted up a notch to constantly achieve brain wiring

"Zone of Proximal Development"

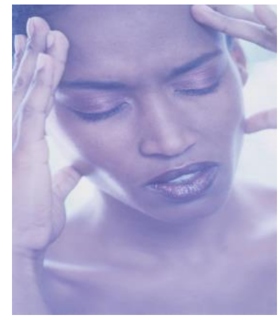
- New concepts/skills are maximally learnable/processed because
  - they should be just difficult enough to engage the client/patient
  - yet easy enough to maintain high spirits

2. Strengthen Strategic Attention

Chapman (2013)

See especially research by Kim et al (2012); Bonnell et al (2012); Chen et al (2011) Goal Directed Attention

- Keep background stimulation as low as possible
  - The brain has to work harder to process input while blocking out extraneous distractions
  - **The processing impaired/injured brain tires faster when there are extraneous stimuli**
- **Therapist can gradually add distractions during tasks to build tolerance**



3. Prioritize

after Chapman (2013)

- Teach client/patient with executive function problems to prioritize tasks
  - Avoid trying to do two things at once (multitasking is very difficult after brain injury)
- Teach patient/client to identify top two tasks from to-do lists
  - The brain becomes quickly overwhelmed with long to-do lists

4. Practice Integrated Reasoning

Chapman (2013)

Start with higher-order processing

SLP's

- Restate or write down big ideas
- ❖ Strategic Memory and Reasoning Training (SMART) Transfer to higher levels of functionality

Vas et al (2011)

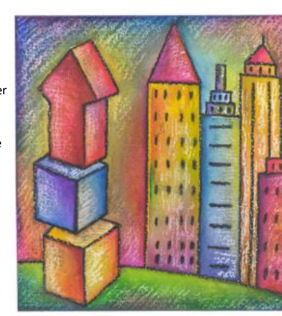
- ❖ Paradigms with possible relevance to rehabilitation strategies

Irimia, A. (2012) et al (also, table of cortical regions affected in TBI)

PT and OT's (Burns added) – strategic motor planning (cognitive control of action)

Caeyenberghs et al (2012)

Patel, R. et al (2012)



Q & A