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Understanding Neuroplasticity and Recovery: Insights From Current Research

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UNDERSTANDING NEUROPLASTICITY AND RECOVERY: INSIGHTS FROM CURRENT RESEARCH

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INTRODUCTION

- This presentation will discuss the following:
 - A framework for understanding principles of neuroplasticity.
 - Contemporary theories of cortical reorganization following injury.
 - Current evidence supporting neuroplastic change following injury.
 - Selected current treatment research relating outcomes to neuroplasticity.

A FRAMEWORK FOR NEUROPLASTICITY

- Neuroplasticity occurs throughout the lifespan.
- The nature of neuroplasticity is *change* whether it is positive or negative.
- We tend to think about neuroplasticity in terms of recovery, but it is important to consider pre-injury variables.
- Both extrinsic factors and intrinsic factors drive neuroplastic change (Cramer et al, 2011; Hotting & Roder, 2013; Plowman & Kliem 2010).
 - Extrinsic: Motor learning and skills, experiences, behavior modification, exposure to drugs, exercise
 - Intrinsic: Age, gender, stage of development, genotype

A FRAMEWORK FOR NEUROPLASTICITY

- Skills are not discrete, isolated events but rather a distribution of interconnections to other areas supporting the function (Kolb, Muhammad & Gibb, 2011).
 - We can see this more readily in motor movements through the networks of the direct activation pathway (pyramidal tract) and indirect activation pathway (extrapyramidal tract).
 - However, language functions also require intricate connections for lexical storage, phonemic representation, auditory/visual memory, etc.
- Experience and practice impacts assignment of the amount of cortical area dedicated to the skill even though the general topography remains constant (Chen, Epstein & Stern, 2010; Grafman, 2000; Kerr, Cheng & Jones, 2011; Mateer & Kerns, 2000; Nudo, 2011; Plowman & Kliem, 2010).
 - Movement from discrete events to smooth interconnected functions.
 - The type of cortical change is specifically tied to the functions of the task.

A FRAMEWORK FOR NEUROPLASTICITY

- Plowman & Kliem (2010): Cortical maps are dynamic. Behavior occurs first, followed by increased synaptic connections (synaptogenesis) and finally cortical change
- True learning can only occur if the brain changes (Kolb).
 - Long-term potentiation.
 - Anything can cause change, including exercise and thoughts.
- Mateer & Kerns (2000):Circuits that fire together build interconnections that are at first temporary, but "wire together" over time (Mateer).
 - Association learning is an example of the establishment of interconnections.
- Attention is gaining importance in facilitating neural connectivity and regulating cognition and perception.

- Grafman (2000): Four Types of Neuroplasticity
 - Homologous Area Adaptation
 - Relevant to early, critical stage human development.
 - Injury causes shifting of functions to homologous opposite hemisphere locations.
 - Complicates function originally assigned to the location especially if it occurs before full development.
 - Makes dual-task performance difficult.

- Grafman (continued)
 - Cross-Modal Reassignment:
 - If an area is deprived of the input that it would normally receive, other areas invade it.
 - Example: Blindness deprives the area of input allowing input from new areas.
 - Map Expansion:
 - The size of the area dedicated to a function is dependent on frequency of use.
 - Dynamic and temporary unless the skill is repeated long enough.
 - Nudo (2011) refers to this as Temporal Contiguity Hypothesis.

- Compensatory Masquerade:
 - Instead of actual recovery of functions, different processes are used to accomplish the task.
 - Grafman presents this example: More than one route to get from home to work. One is automatic with little effort (routine, implicit, covert). Other routes require more effort (needs more cues, explicit, overt processing).
 - After injury spared and preexisting neural networks are reorganized.

- Thompson (2000) and Raymer et al (2008)
 - Research evidence seems to support two of these types of reorganization following injury relevant to language recovery.
 - Homologous Area Adaptation
 - Shift of language functions to homologous right hemisphere locations.
 - Research has also shown that some healthy adults activate right hemisphere locations as well, but not to the same extent.
 - Tends to be more related to comprehension than production.
 - Map Expansion
 - Expansion to spared adjoining areas.

- Mateer & Kerns (2000) cautions that damaged areas may be dominated by intact connecting areas causing suppression of function even if residual skills are present.
 - May seem facilatory at first but becomes detrimental over time.
- Nudo (2011) proposes 3 mechanisms that facilitate spontaneous recovery:
 - The theory of diaschisis and its reversal
 - Functional improvement rather than actual "recovery" of lost skills.
 - Substantial physiological and neuroanatomical change occurs.

- Kliem et al (2004) & Kliem (2011) demonstrate a time course for motor reorganization in rats that may be relevant to human recovery.
 - 3 days post injury: Improvement in *behavior* on trained skills only.
 - 7 days post injury: An increase in the number of *synapses* per neuron.
 - 10 days post injury: Increase in cortical representation.
 - The change in behavior alone is not indicative of cortical change. Cortical changes occur in late stage learning.
 - The change observed is specific to the task demands.

- Raymer et al (2008) provide a literature review outlining principles important to recovery of language.
 - Timing is critical: Intensive treatment immediately following injury may have a negative impact on recovery.
 - The specific "safe" time is not yet known.
 - At the chronic stage of recovery, intensity and an enriched environment is the desirable approach.
 - Use it or lose it: Language has to be used to be improved.
 - Repetition, consistency and experience are important.
 - Meta analysis by Robey demonstrated those patients beginning treatment early had the best outcomes overall.
 - Start early but keep tasks simple; increase intensity over time.

- Ludlow et al (2008) published a literature review tackling the same question from the motor reacquisition point of view.
 - Speech movements improved with practice, but nonspeech movements did not.
 - Diadochokinetic rates may not translate to speech unless speech is used in the training.
 - Early learning engages more cortical activation than routine tasks.
 - Reiterated: experience, repetition, intensity, timing, salience and age all impact outcomes.

- Saur & Hartwigsen (2012) Examined 14 patients with lesions associated with middle cerebral artery infarct over 3 time periods.
 - Less than 4 days post onset: Poor language scores, little left hemisphere activation
 - Approximately 2 weeks post onset: Improved language scores, more left hemispheric activation and significant homologous right hemisphere activation.
 - 4-12 months post onset: Decreased right hemisphere activation, increase in left hemisphere activation.
 - Supports a 3 phase model of recovery: Diaschisis, Subacute and Chronic

- Meinzer, Rodriguez and Rothi (2012) examined results of Constrained-Induced (CI)Treatment Approaches over the last 10 years.
 - 4 main principles: Nonuse, massed practice, shaping and behaviorally relevant treatment settings.
 - Nonuse: Thought to be related to diaschisis, but can be overcome by forcing use of the area to tap into residual skills. In the beginning very strict practice was followed.
 - Massed Practice: The more the engagement of the area, the stronger the neural connections leading to actual cortical change. As high as 3 hours per day over 10 consecutive days.

- Meinzer (continued)
 - Shaping: Through practice, behavior is gradually shaped closer to the desired behavior.
 - Relevant Settings: Activities must be relevant to real life, everyday functions, in the beginning.
 - Generally, CI treatment shows significant improvement over other treatments -- especially if the control treatment does not use the same intensity schedule.
 - Gains appear to be retained over 6 months.
 - No evidence to clarify how long the treatment should continue.

- Hamilton, Chrysikou and Coslett (2011).
 - The role of the right hemisphere activation in language recovery is somewhat controversial.
 - Some researchers argue that it has a facilatory impact while others suggest that it has a negative impact on long term recovery.
 - The size of the lesion in the left hemisphere impacts the amount of right hemisphere activation.
 - The age at which the injury occurs impacts right hemisphere proficiency.
 - The lack of balance between the hemispheres may reduce inhibition, causing the right hemisphere to inhibit residual left functions.

- Heath et al (2013) used fMRI to examine the impact of auditory repetition on naming in patients with aphasia at two time frames.
 - 21 control participants with an average age of 56.9, no significant medical history, right handed.
 - 6 participants with chronic aphasia from a single left CVA with an average age of 57.6
 - Picture stimuli were digital photographs.
 - Aphasia group: Pictures were chosen based on consistent naming ability in a trial task.

- Heath, et al. (continued): 4 tasks
 - Facilitation phase: Participants were required to look at the picture, listen to the name and repeat.
 - These pictures were presented again in the scanner as long-term facilitation task during the experimental phase.
 - Experimental phase: Pictures were presented while in the fMRI scanner.
 - Participants were prompted to either name or repeat the name heard.
 - For the short-term facilitation task new pictures were presented twice in the scanner - once repeated and once not repeated.
 - Unfacilitated task: Naming with no auditory prompt.
 - Follow-up one week after scanning: Naming with no prompt.

- Heath, et al. (continued)
 - All participants with aphasia showed improved naming from baseline to post-testing.
 - Repetition facilitated more accurate naming for all in both the short-term and long-term tasks.
 - fMRI did not show facilitation of phonological networks.
 - Patterns of activation were different for each aphasic participant.
 - Patterns of activation for aphasic participants were different than controls.
 - Activation patterns for both groups employed both phonologic and semantic cortical regions.

- Marcotte et al (2013) examined semantic feature analysis treatment relative to default-mode network connectivity in aphasics and controls.
- Default-mode network: Two main hypotheses
 - DMN regulates attention to internal and external stimuli, monitors the external environment and supports diffuse attention.
 - DMN regulates introspective functions, linked to episodic memory, attention and working memory.

- Marcotte et al (2013)
 - 10 healthy controls and 9 individuals with aphasia from a single left hemisphere incident, all right handed, French speaking adults.
 - In order to compare learning across groups, the control group were asked to complete a computerized Spanish word learning task.
 - Controls Two fMRI scans: 5 days after training (early learning phase) and after 14 training sessions (consolidation phase).
 - During scans, pts named pictures in both Spanish and French.
 - Participants with aphasia: Probed at baseline. Only words incorrectly named over two trials were selected for inclusion in the task.
 - Pts were scanned, then received SFA treatment 1 hour/3 times a week to reach either 80% accuracy or a maximum of 6 weeks.
 - Two post-treatment scans involved only naming.

- Marcotte et al (2013) continued
 - Of specific interest were the interactions both within the anterior and posterior parts of the DMN and between them.
 - All participants with aphasia improved naming and some generalization to untrained stimuli with SFA treatment.
 - Imaging results showed significantly different results for both groups in DMN activation. The control group was stable across participants while the individuals with aphasia showed individual patterns.
 - SFA treatment did result in greater activation of posterior regions.
 - Anterior-posterior disconnection was seen with the aphasia group. SFA did not improve this disconnection.
 - However, a significant correlation between DMN activation and treatment outcome was not found.

- Vallila-Rohter and Kiran (2013)
 - Examined nonverbal learning in individuals with aphasia in an effort to better understand the process of learning.
 - Does aphasia occur in the absence of any cognitive learning deficits or is the language deficit compounded by deficits in learning?
 - 2 groups: 18 individuals with aphasia following a single left hemispheric CVA, all right handed, all tests at least 6 months post onset.
 - 13 control participants matched for age and education level; one was left handed.
 - Stimuli: Cartoon character drawings varying by 10 characteristics.
 - The task was to sort the pictures into two groups.

- Vallila-Rohter & Kiran (continued)
- Each participant completed two category tasks.
 - Task 1 Feedback-based Training: Picture was presented, participants guessed which category it should belong to by pressing a button, feedback was given regarding category and correctness of response.
 - Testing Phase: 45 new examples + 16 seen above were presented with no training.
 - Task 2 Paired-Association Training: Picture was presented with its category affiliation included. Participants pressed the button after seeing the correct answer.
 - Testing Phase: 45 new examples + 16 seen above were presented with no training.

- Vallila-Rohter & Kiran (continued)
 - No effect of task or group, but a group x task interaction did occur.
 - The two groups demonstrated different patterns of learning.
 - For the control group: The more features a character had, the more likely it was categorized correctly. All controls met standards of learning the tasks.
 - Performance for controls did not change as a function of training.
 - Aphasic group: Only 11 participants met the standards of learning (60% accuracy).
 - Aphasic group: 3 performed the same regardless of instruction.

SUMMARY

- Even though emerging evidence shows neuroplastic changes following CVA, the correlation to observable behavior remains unclear.
- More evidence validating animal research as applicable to human neurological function is being demonstrated.
- The brain continues to change in both positive and negative ways in response to behavior and environment.
- Individual characteristics and experiences appear to impact recovery.
- Timing, intensity and task demands play important roles in facilitating functional outcome.
- It remains unclear at this time if "recovery" or "compensation" are responsible for improved outcomes.
- Neuroplastic change is not restricted to a specific time period post injury.
- The role of the right hemisphere in language recoupment remains unclear.

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