NEUROPLASTICITY

Implications for rehabilitation

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Outline

• What is neuroplasticity?

• Evidence

• Impact on stroke recovery and rehabilitation
Human brain

• Human brain is the most complex and extraordinary structure in the known universe

• Contains over 100 billion neurons interconnected by over a trillion synapses

• Previous thinking – brain “hard wired” with each part performing a single function, and unable to change or have the capacity for repair and regeneration
Neuroplasticity - definition

• “The ability of the nervous system to respond to intrinsic stimuli by reorganising its structure, function and connections; can be described at many levels, from molecular to cellular to systems to behaviour; and can occur during development, in response to the environment, in support of learning, in response to disease, or in relation to therapy” Cramer et al 2011

• Can be adaptive when associated with a gain in function, or maladaptive when associated with negative consequences such as loss of function or increased injury
Neuroplasticity

• Lifelong ability

• Brain can adapt and learn during development, throughout the normal lifespan, and in response to injury

• Neural plastic changes are enhanced by experience and learning – “use it or lose it”

• Neuroplasticity forms the basis of the brain’s capacity to retain memories, improve functions such as movement, and perform daily tasks
Neuroplasticity

- **Components:**
  - Cell genesis, and repair
    - New neurons can be born throughout life
      - e.g. adult neurogenesis in the hippocampus is thought to contribute to memory formation
  - Alteration of existing neuronal pathways
  - Formation of new neural connections
Why didn’t we know about neuroplasticity?

• Lack of technology to study or view the brain

• The mechanistic belief that the brain was “hard wired”

• Use of other means to explain recovery following brain injury
Neuroplasticity – clinical examples

• Motor recovery after stroke
  • Intra-hemispheric changes, such as representational maps e.g. the hand area can shift dorsally to the shoulder region or face region
  • Inter-hemispheric balance can shift such that the uninjured hemisphere has supranormal activity in relation to movement
  • Diffuse adaptive changes, including changes in the connections between network nodes
  • Molecular changes including growth-related processes that evolve over time

• Neglect and language deficits after stroke
  • Similar results described

• Cognitive recovery after stroke
  • Less studied
Neuroplasticity interventions

- Plasticity after injury is often experience dependent

- Interventions that aim to promote plasticity can be expected to have maximum impact when coupled with optimal training and experience

- Plasticity may be time-sensitive, occur with considerable specificity, vary with the nature of the environment and be strongly influenced by the extent of the concomitant training

- Motivation and attention can be critical modulators of plasticity
Neuroplasticity interventions

- Non-invasive brain stimulation
  - Transcranial magnetic stimulation

- Deep brain stimulation

- Neuropharmacology
  - Can increase neuroplasticity through molecular manipulation of numerous cellular and synaptic pathways
    - Growth promoting factors
    - Granulocyte colony-stimulating factor
    - Stem cell implants
Neuroplasticity interventions

• Physical training and exercise
  • Many physical rehabilitation interventions have been reported to induce functional improvements
    • Constraint induce movement therapy for the arm and hand
    • Body weight-supported treadmill training
    • Robotic devices
    • Behavioural shaping
    • Bilateral arm training
    • Task-orientated physical therapy

• Aerobic exercise
  • Extension of activity-based therapies for promoting plasticity
  • Associated with increased neurogenesis
  • Benefit cognitive function
Neuroplasticity interventions

- Cognitive training
  - An extension of physical therapy to the non-motor aspects of the brain
  - Broad potential as part of rehabilitation therapy of patients with stroke
Neuroplasticity – clinical trials

- Very few large multicentre RCTs in the area of physical rehabilitation following stroke

- Three significant trials conducted in past 6 years
  - Extremity Constraint Induced Therapy Evaluation (EXCITE)
    - Tested effect of constraint therapy in 224 patients 3-9 months post stroke and with mild-moderate upper limb impairment
  - Robot-Assisted Upper-Limb Neurorehabilitation in Stroke Patients (UL-Robot)
    - Tested effect of robot-assisted therapy in 127 patients more than 6 months post stroke and with moderate-severe upper extremity impairment
  - Locomotor Experience Applied Post-Stroke (LEAPS)
    - Tested the effect of locomotor training in 408 patients more than 2 months post stroke and with moderate-severe walking impairment
Neuroplasticity – clinical trials

• Only the EXCITE trial demonstrated a clear superiority of the experimental intervention compared to the control group, but all interventions were superior to usual care
  • EXCITE – 2 weeks of intense (6 hours per day) rehabilitation focused on guided use of the hemiparetic upper extremity with behavioural shaping enabled participants to perform functional tasks faster and increased self reported arm use and movement quality
  • UL-Robot – no difference in outcome between robot assisted and intensive therapy groups (but improvement cf control group)
  • LEAPS – no difference between intervention groups (body weight support and a treadmill vs HEP)
Rehabilitation following stroke

• Outcomes often limited, based on compensation and interventions that are not always evidence based

• Need to adopt more restorative approaches

• Current evidence suggests that the time window for learning-based approaches to restoring capacities and skills is open. Much longer than “days / weeks / months” sometimes suggested
Rehabilitation following stroke

• Need to promote neuroplasticity in patients post stroke

• Need to be aware of “active ingredients” that drive beneficial neural plasticity leading to positive functional outcomes

• Important “active ingredients”
  • Intensity
  • Progression
Rehabilitation following stroke

• Intensity
  • RCTs demonstrate that intervention providing intense therapy is more beneficial than usual care
  • In locomotor rehabilitation, intensity of walking shown to be more important for recovery than the treatment mode
  • In upper limb therapy, movement repetition shown to be important as a driver of neuroplasticity i.e movement repetitions per session rather than duration of the session.
  • Optimal number of repetitions required for learning is unknown
Rehabilitation following stroke

• Progression
  • Animal model studies suggest that the greatest neuroplastic changes are associated with the generation and repetition of novel movements rather than the repetition of already known movements e.g. systemically progressing the difficulty of a reaching task in a rat post stroke resulted in cortical changes, whereas repeating the task without progressive difficulty had no effect on cortical mapping

  • Requires monitoring of patient responses to guage if the intervention is of appropriate intensity, and a well defined hierarchy of task requirement to that level of difficulty is increased to maintain the appropriate challenge
Theoretical model for recovery after stroke

Curr Opin Neurol 2013
Environmental enrichment

- Elicits various plastic responses in the young and adult brain

- Animal studies show that an enriched environment promotes sensorimotor recovery after stroke

- Should provide sensory, cognitive and motor stimulation

- Multimodal stimulation includes tactile massage, therapeutic gardens, music, rhythm, cognitive challenges, motor imagery and mental training etc
Intensity of therapy - the current situation

- Peter James Centre
  - Weekend therapy project 2011/12
    - Low level of physical activity in patients receiving orthopaedic rehabilitation – median 398 steps per day

- Angliss
  - Intensity of therapy project 2012
    - Stroke patients received median 81 minutes therapy per day (range 52 – 135 minutes)
Conclusion

• Recognition of neuroplasticity has potential to lead to new therapeutic opportunities for people receiving rehabilitation following stroke by:
  • Enriching the environment
  • Increasing motor activity
  • Developing pharmacologic agents that will enhance plasticity

• Optimal rehabilitation interventions still remain unclear

• Further research indicated involving combination of medical interventions facilitating adaptive neuroplasticity and rehabilitation interventions incorporating intensity and progression
Questions

• How can we incorporate interventions promoting neuroplasticity into our neuro rehabilitation programs?

• How can we create an enriched environment for out patients?
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