TEACHING THE BRAIN NEW TRICKS: ALTERING DISEASE PROGRESSION IN BASAL GANGLIA DISORDERS

LORI QUINN, EdD, PT
Active physiological mechanisms that support recovery and limit future disability.

Physical and cognitive mechanisms, including musculoskeletal linkages, control of basic movement types, ability to plan, etc.

Ability to achieve meaningful goals with consistency, flexibility, and efficiency.

Participation in necessary and desired roles including self-care, social, occupational, and recreational.

Participation
Activities (skills)
Body Structures & Functions
Health

Impairments
Activity Limitation
Restriction
Participation

Health condition (disease/disorder)

Disablement

Rehabilitation

Quinn & Gordon 2016
Exercise to drive neuroplasticity

Exercise
- Goal-based exercise
- Aerobic exercise

Increased synaptic strength
- ↑ Neurotransmitters
- ↑ Receptor density
- ↑ Dendritic spine formation

Improved brain health
- ↑ Trophic factors
- ↑ Blood flow
- ↑ Immune system
- ↑ Neurogenesis
- ↑ Metabolism

Strengthened circuitry
- Basal ganglia
- Cortex
- Thalamus
- Cerebellum
- Brainstem

Improved behaviour
- Motor (conscious and automatic)
- Cognition (executive function)
- Mood and motivation
Huntington’s Disease is a model disease

Well characterised clinical presentation

Motor
- Gait deficits
- Postural instability
- Chorea
- Dystonia

Cognitive
- Deficits in executive function
- Impaired memory
- Attention
- Judgement

Behavioural
- Depression
- Irritability
- Apathy
- Anxiety

Huntington’s disease gene
- Mutant Huntington’s protein
- Aggregation
- Neuronal Cell Death

Caudate, Putamen, Striatum
TRAIN-HD: Task-related TRAINing in Huntington’s disease

Outcomes (blinded)
- PPT
- Sit to stand (30 sec Chair Stand)
- Timed Up & Go
- Quality of Life (HD QOL)
- Balance – Berg Balance Test & Motor function – UHDRS

Randomized control trial:
- Task and context-specific physio in home 2x/wk for 8 weeks
- Usual care
- Focus on walking, balance and sit to stand
- Intensive repetition – task-specific; not just exercise
- Goal-directed feedback
- Goal setting – collaborative effort

Quinn et al. Phys Ther 2014
## Goal Attainment Scaling

<table>
<thead>
<tr>
<th>Type of Goals</th>
<th>No. of goals</th>
<th>% of goals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Walking/stair climbing</td>
<td>17</td>
<td>34%</td>
</tr>
<tr>
<td>Standing balance</td>
<td>9</td>
<td>18%</td>
</tr>
<tr>
<td>Sit to stand</td>
<td>7</td>
<td>14%</td>
</tr>
<tr>
<td>Confidence (balance or walking)</td>
<td>7</td>
<td>14%</td>
</tr>
<tr>
<td>Physical activity</td>
<td>6</td>
<td>12%</td>
</tr>
<tr>
<td>Functional activity</td>
<td>3</td>
<td>6%</td>
</tr>
<tr>
<td>Falls</td>
<td>1</td>
<td>2%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Score at Assessment 2</th>
<th>No. of goals</th>
<th>% of goals</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>23</td>
<td>46%</td>
</tr>
<tr>
<td>1</td>
<td>10</td>
<td>20%</td>
</tr>
<tr>
<td>0</td>
<td>13</td>
<td>26%</td>
</tr>
<tr>
<td>-1</td>
<td>4</td>
<td>8%</td>
</tr>
<tr>
<td>-2</td>
<td>0</td>
<td>0%</td>
</tr>
</tbody>
</table>

Ninety-two percent (92%) of the goals were achieved at the end of the 8 week sessions, with 46% being achieved at much better than expected outcome.
## Outcome Measures

<table>
<thead>
<tr>
<th>Outcome measure</th>
<th>Assessment 1 scores (Mean ± SD)</th>
<th>Assessment 2 scores (Mean ± SD)</th>
<th>Adjusted estimate of visit 2, p-values &amp; effect sizes from ANCOVA</th>
<th>Adjusted estimate of visit 3, p-values &amp; effect sizes from ANCOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control group</td>
<td>Intervention group</td>
<td>Control group</td>
<td>Intervention group</td>
</tr>
<tr>
<td>9 item PPT</td>
<td>24.1 (6.8)</td>
<td>19.1 (5.5)</td>
<td>23.3 (6.9)</td>
<td>19.6 (5.3)</td>
</tr>
<tr>
<td>7 item PPT</td>
<td>18.1 (4.5)</td>
<td>13.5 (3.7)</td>
<td>17.5 (4.7)</td>
<td>13.2 (4.7)</td>
</tr>
<tr>
<td>UHDRS TMS</td>
<td>37.6 (13.8)</td>
<td>52.6 (17.3)</td>
<td>37.3 (10.4)</td>
<td>52.2 (16.4)</td>
</tr>
<tr>
<td>UHDRS Cognitive Scores</td>
<td>181.4 (54.8)</td>
<td>142.6 (55.2)</td>
<td>184.7 (46.3)</td>
<td>148.3 (43.4)</td>
</tr>
<tr>
<td>Berg Balance Scores</td>
<td>47.5 (11.6)</td>
<td>44.3 (8.2)</td>
<td>48.2 (12.4)</td>
<td>44.2 (7.0)</td>
</tr>
<tr>
<td>Gait speed (m/s)</td>
<td>1.2 (0.5)</td>
<td>1.0 (0.3)</td>
<td>1.2 (0.4)</td>
<td>1.2 (0.4)</td>
</tr>
<tr>
<td>Fast Gait speed (m/s)</td>
<td>1.4 (0.5)</td>
<td>1.2 (0.4)</td>
<td>1.5 (0.5)</td>
<td>1.5 (0.5)</td>
</tr>
<tr>
<td>30sec CST</td>
<td>10.2 (4)</td>
<td>7.7 (3)</td>
<td>10.8 (4.8)</td>
<td>7.7 (3.6)</td>
</tr>
<tr>
<td>TUG</td>
<td>12.0 (6.7)</td>
<td>14.0 (6.7)</td>
<td>12.1 (9)</td>
<td>14.6 (10.0)</td>
</tr>
<tr>
<td>Vitality score</td>
<td>5.5 (1.3)</td>
<td>5.3 (1.4)</td>
<td>5.4 (1.0)</td>
<td>5.3 (1.4)</td>
</tr>
<tr>
<td>HADS global score</td>
<td>8.3 (5.7)</td>
<td>6.5 (6.7)</td>
<td>7.5 (6.8)</td>
<td>6.8 (6.8)</td>
</tr>
<tr>
<td>HD QoL summary scale</td>
<td>84.9 (16.6)</td>
<td>80.5 (23.3)</td>
<td>88.6 (14.3)</td>
<td>80.8 (21.7)</td>
</tr>
<tr>
<td>EQ5D Health Index</td>
<td>75 (12.6)</td>
<td>75.2 (26.2)</td>
<td>73.1 (16.5)</td>
<td>75.3 (24.5)</td>
</tr>
</tbody>
</table>

Quinn et al. Phys Ther 2014
ExeRT-HD: Exercise Rehabilitation Trial in HD

- Randomized, controlled trial with 32 participants
  - *Exercise group*: 12 weeks, 3x/week
  - *Control group*: Continue as usual

**Aerobic exercise**
- 25 minutes of exercise on the bike within an aerobic zone (5 min cool down/warm up)
- KEY COMPONENT: Heart rate in aerobic zone

**Strengthening and stretching**
- 15 min on key muscle groups

Quinn et al. Parkinsonism Rel Disord, 2016
Outcomes

Predicted VO₂ max (difference: 493.3 ml.min⁻¹, 95% CI: [97.1, 887.6]

UHDRS modified motor score (intervention arm 2.9 points lower, 95% [-5.42, -0.32])

Quinn et al. Parkinsonism Rel Disord, 2016
Early stage intervention to delay onset or slow progression in Parkinson’s disease

Inpatient multidisciplinary rehabilitation

- Randomized trial (rasagiline vs rasagline plus rehab)
- 3 1-hour daily sessions, 5 times per week
- Physical therapy - Strengthening, range of motion, aerobic exercise on treadmill with visual and auditory cues; 60-70% heart rate reserve
- Occupational therapy – ADLs and hand function
Multidisciplinary inpatient rehabilitation can delay the need for increasing drug treatment.

**Figure 3.** L-dopa equivalent dosage. MIRT, multidisciplinary intensive rehabilitation treatment.
"If exercise could be packaged into a pill, it would be the single most widely prescribed and beneficial medicine in the nation.”

Dr. Robert Butler, founding director of the National Institutes on Aging, NIH
Engage-HD
Supporting Engagement in Activities in HD

Theoretical framework grounded in self-determination theory

**Autonomy**
- Freedom of choice
  - Offer choice
  - Redefine what exercise means

**Competence**
- Perceived self-belief
  - Goal-setting
  - Positive Reinforcement
  - Skill-Specific Feedback

**Relatedness**
- Sense of shared experience
  - Listen
  - Respond to personal needs

Busse et al., Trials. 2014; 15:487
Quinn et al. JNPT 2016;40:1-10
Move to Exercise

An exercise programme for people with movement disorders

Developed by:
Monica Busse PhD MSCP, Lori Quinn EdD PT, Karen Jones MSc MSCP, Matthew Townsend MSc

2.3 Tandem Standing

Purpose: This exercise will improve your standing balance and your balance during walking.

Key points: Place one foot in front of the other. If you can, put the heel of your front foot against the toe of your other foot. If you are unable to keep your balance in this position, put your front foot to the side but as close to the other foot as is comfortable. If you feel comfortable in this position, let go of the support while keeping your hand nearby.

Relatedness

Autonomy

Competence

Busse et al., Trials. 2014; 15:487
Quinn et al. JNPT 2016;40:1-10
Logic model

Inputs

Activities

- Home visits where coaches interact with participants to promote:
  - Autonomy
    - Involving participants in decision making
    - Maximising choices and minimizing control and pressure
    - Tailoring advice and support to the individual
  - Relatedness
    - Acting in a warm, caring way
    - Acknowledging and supporting patients’ perspectives, feelings and values
    - Avoiding judgement or blame
  - Competence
    - Helping to clarify outcome expectations
    - Assisting in realistic goal-setting
    - Assisting in building skills and aiding with activities required to achieve goals
    - Providing positive feedback

Implementation evaluation

- Fidelity (audio transcripts)
  - One of the home visits audio recorded, transcribed and then analysed independently by two researchers and scored according to:
    - Extent to which coach promotes participants’ autonomy (0-4)
    - Extent to which coach promotes participants’ relatedness (0-4)
    - Extent to which coach promotes participants’ competence (0-4)
    - Overall impression of coaches’ performance (0-4)
  - Giving an overall score for each coaching session ranging from 0-16.
  - Self-assessment ratings by coaches

Outputs

- Behavioral change
  - Increased and sustained regular physical activity
  - Greater exercise related self-efficacy

- Behavioral Outcomes
  - Exercise specific skill development
  - Realistic goal setting and review
  - Improved self monitoring of physical activity (pedometers, exercise diaries, goal review, progression of exercise)
  - Competent use of exercise equipment and DVD

- Immediate outcomes
  - Increase in daily physical activity (IPAQ)
  - Stability of disease specific measures (UHDRS mMS, Cognitive)
  - Stability of functional measures (UHDRS Function)
  - Improvement in self-efficacy measures (Lorig scale)
  - Improvement in health-related QoL (EQ5-D)

- Longer term outcomes
  - Sustained physical activity behaviours
  - Longer term stability of disease measures and function
  - Longer term health benefits of regular physical activity

Engage-HD

Physical Activity Workbook

A purpose-designed workbook for HD patients, which aims to:

- Provide information about the benefits of physical activity and exercise
- Provide examples of how other HD patients deal with challenges of PA.
- Introduce patients to goal-setting, exercise diaries and pedometers for self-monitoring
- Encourage safety in exercising

Move to Exercise DVD

A DVD for HD patients which aims to:

- Give participants a step-by-step guide to performing a range of different exercises in the home, depending on interests and needs

Quinn et al. JNPT 2016;40:1-10
Engage-HD

- 2 arm parallel randomized controlled feasibility trial
- 6 sessions over 14 weeks
- Physical activity compared to social contact control

Physical Activity scores 142% higher in physical activity group than in social group at assessment 2 95% CI: [-22, 653]

Busse et al., Trials. 2014; 15:487
Quinn et al. JNPT 2016;40:1-10
Life Space Assessment: a surrogate measure of participation

- Person's usual pattern of mobility during the month preceding the assessment.

- Determines **how far and how often** the person leaves his or her place of residence and the degree of independence the person has.

Lifespace Assessment was 12 points higher in physical activity group than in social group at assessment 2
95% CI: [-2.4, 27]
Improved cognition as measured by SDMT

Physical activity group achieved about 3 more correct answers than social group (treatment effect: 2.9, 95% CI [0.01, 5.9])

Busse, Quinn et al., submitted for publication
What does the future hold?

**INTERVENTION**
- 6 month, 3 times per week exercise program
  - Aerobic exercise using stationery cycling
  - Task specific strengthening exercises
  - Behavioral change strategies – promote autonomy, relatedness & competence

**MECHANISM**
- **Cerebral blood flow**
- **Neuroplasticity** – change in brain structure and function
- **VO₂ max** (surrogate measure of fitness)
- Peripheral biomarkers (surrogates for potential CNS changes);
  Circulating growth factors and inflammatory markers
  - ↑BDNF, ↓ TNFa, ↓ IL-6, ↓ IGF-1, ↓ IL-1B, ↓ VEGF

**SURROGATE MARKERS**

**MOTOR**
- ↑ Disease-specific motor function (UHDRS TMS)
- ↑ HD-specific symptoms (HD-Pro-TIAD)
- ↑ Dual task function (Clinch Token Transfer Task)

**COGNITION**
- ↑ cognitive function (HD-CAB)

**OUTCOMES**
- Improved quality of life for participants and carers
- Increased energy, improved mood
- ↑ Physical activity and sleep (7-day activity monitoring)

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“The next generation of solutions will require new skills among physical therapists to be partners in the treatment of populations of patients across the continuum of health care settings and coach patients and families in lifestyle management and be accountable for sustaining and improving functional status.”
Summary

• Efforts to alter disease progression and affect neuroplasticity via exercise and physical activity must happen in the earliest stages of neurodegenerative diseases.

• Behavioral change interventions that are personalized and adaptive must be incorporated into any rehabilitation interventions to facilitate exercise uptake and maximize participation.

• Future trials of exercise and rehabilitation must incorporate both exercise and task specific practice with sufficient challenge and repetition to drive neuroplasticity and neural repair.
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• Huntington’s Disease Association of UK
A Movement Problem Solving Hypothesis: Practice Conditions Implications from Gentile’s Learning Stages Model

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Teachers College, Columbia University
Motor Learning & Control Program, Dept. of Biobehavioral Sciences

New York University
Dept. of Physical Therapy and
Dept. of Performing Arts and Arts Professions (Dance Ed. Program)
Two Important Terms To Distinguish

**Actions (also called “skills”)**

- Goal-directed activities that involve body, head and/or limb movements
- Evaluated by whether or not action goal achieved
- **Examples:** Sit-to-stand; walk across a cluttered room; catch a ball

** Movements**

- What body, head, or limb segments do when an action is performed
- Evaluated by movement analysis
- **Examples:** Movements used to perform actions
3 Views of Skill Learning Suggest Teaching Differences for Actions and Movements

1. Gentile’s Stages of Learning Model
   Learner’s Goal for Each Stage

   **Initial stage:** Learner’s goal to acquire movement coordination pattern well enough to allow some degree of success at achieving the action goal of the skill
   • For the learner – An action oriented goal

   **Later stages:** Learner’s goal to develop consistency in action goal achievement, efficient use of energy, and adaptability
   • For the learner – A movement oriented goal
2. Bernstein’s View of Optimal Practice Conditions

“The processes of practice ... consists in the gradual success of a search for optimal motor solutions to the appropriate problems. Because of this, practice, when properly undertaken, does not consist in repeating the means of solution of a motor problem time after time, but in the process of solving this problem again and again by techniques which we changed and perfected from repetition to repetition.”

• Bernstein, N. (1967, The co-ordination and regulation of movements, p. 134)
3. Adolph’s View of How Infants Learn to Locomote

Infants acquire locomotion skills by “detecting novel and variable constraints on locomotion, and...discovering new solutions to respond adaptively.”

Movement Problem Solving Hypothesis

Motor skill learning is enhanced to the degree that practice conditions engage learners in movement problem solving.

The movement problem to be solved =
- The action goal
  e.g., stand from sitting in a chair and walk 3 steps

The problem solution (solving the problem) =
- The characteristics of movements that allow action goal achievement
A Teaching / Practice Strategy That Promotes Movement Problem Solving:
Discovery Learning of Movements

What is “discovery learning of movements”? 

- The learner actively determines/discovers the specific movement characteristics needed for action goal achievement rather than having those characteristics prescribed

It occurs when the learner:

- Knows the action goal
- Has a minimum amount of movement information
- Must “discover” the optimal ways to move to achieve the action goal
4 Practice Conditions that Engage People in Discovery Learning

1. Practice focused on discovering movements to achieve the action goal rather than on performing “correct” movements
   - Trial and error vs. errorless practice

2. Learner’s attention focus directed toward effects of movements rather than on movements themselves

3. Movement exploration of environmental variations

4. Feedback that encourages movement problem solving rather than movement solutions
Practice Condition 1: Practice Focused on Discovering Movements to Achieve Action Goal Rather Than on Correct Movements

Mount et al. (2007, NeuroRehabilitation)

Subjects: 33 m & f (m age = 63 y) 21 d post stroke onset

Tasks:
1. Putting on a sock with a sock-donner
2. Preparing a wheelchair for a transfer

Practice Conditions:
Trial and Error - Progressively more specific feedback about an error made trial to trial (from “an error was made” to “here’s how to correct the error”)
Errorless - Each trial performed with therapist showing and directing correct movements
Mount et al. Experiment (cont.)

Practice Sessions: 7 days max. practice [each day start with perform w/o instructions]; end practice = 2 consecutive “correct” trials

Transfer Tests: Variation of practiced tasks

Results:
No. of days to performance criterion:
No statistical difference between practice conditions

Transfer task success:
Trial & Error significantly higher % for both tasks

Conclusion:
Advantage for “trial & error” practice for adapting to new task conditions
Practice Condition 2: Attention Focus on Movement Effects Rather than on Movements

Some Definitions:

Movement effects = The results (i.e. effects) of a movement (e.g., stepping on a stair step)

Attention Focus = Where conscious attention directed

External focus = On movement effects or on environment

Internal focus = On movements

Large amount of research shows: External Focus results in better learning and performance than an Internal Focus

e.g., Wulf et al. (2009, Physical Therapy)
Wulf et al. (2009) Experiment

Subjects: 14 Parkinson Disease m & f (52 – 80 y)  
Hoehn & Yahr stage = II or III

Task: Stand and balance on a rubber ‘Disc O Sit’ for 15 s  
[situated on a portable force platform]

Attention Focus Instructions:

External Focus – “Focus on minimizing movements of the disk”
Internal Focus – “Focus on minimizing movements of your feet”
Control – “Stand still”

Each subject did all 3 4x
Results:
External focus resulted in less postural sway

Conclusion:
Focusing attention on movement effects encourages action goal achievement by engaging in movement problem solving through non-conscious processes.
Suzanne Farrell teaches ballet to experienced students and professional dancers by instructing them to concentrate on the “effect” they want to create with their movements rather than on the movements they use to create the effect they want.

Practice Condition 3: Movement Exploration of Environmental Variations

Research example: Adolph’s research with infants learning locomotion skills

Research goal: Determine what infants do to learn how to navigate variable and novel challenges in their environment

Infants (8 – 18 mo.) observed from first weeks of crawling to well after they begin walking:
- Descending walkways of varying slopes
- Walking over bridges of varying widths w/ and w/o handrails
- Spanning gaps of varying distances
Results of Adolph’s research consistently show:

- Infants learn to achieve action goals by adapting to environmental demands by exploring various ways of moving to adapt to environmental demands.
- This learning achieved with very large amounts of practice.
  - e.g., One study showed that in 1 hr, 14-mo. olds:
    - Took more than 2,000 walking steps
    - Traveled a total distance of 7 football fields
    - Fell 15 times
The infants’ behavior during their learning experiences were consistent with Gentile’s 2 learning stages.

“...in their first weeks of crawling and walking, infants plunged straight down impossibly steep slopes. Over weeks of locomotor experience, exploratory behaviors became more discerning and responses became more adaptive...” (Adolph, 2008, p. 214)

**Conclusion:** Infants learn adaptive locomotor skills by focusing on action goal achievement and by exploring movement solutions in a variety of environmental conditions.
Practice Condition 4: Feedback That Encourages Movement Problem Solving Rather Than Movement Solutions

Winstein et al. (1996, *Physical Therapy*)

Types of feedback compared:
*Concurrent* – Available during performance [i.e., movement solutions]
*Knowledge of Results (KR)* – Available after performance [i.e., movement problem solving]

Feedback conditions:
1. Concurrent feedback
2. KR after every trial
3. KR after every 5 trials

Task: Partial Weight-Bearing

**Goal** = Support 30% body wt. while stepping on bathroom-type scale with preferred leg while on crutches

Practice: 80 trials
Retention Tests (no feedback): 20 trials 2 days post practice
Winstein et al. Experiment (cont.)

**Results**

<table>
<thead>
<tr>
<th></th>
<th>End of Practice</th>
<th>Retention Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concurrent:</td>
<td>~ 1% Error</td>
<td>~ 12% Error</td>
</tr>
<tr>
<td>KR-1:</td>
<td>~ 8% Error</td>
<td>~ 9% Error</td>
</tr>
<tr>
<td>KR-5:</td>
<td>~ 8% Error</td>
<td>~ 9% Error</td>
</tr>
</tbody>
</table>

**Conclusions**

- Practice with post-performance feedback that requires learner to determine movement corrections more effective for learning task than with feedback presented concurrently during performance.

Results consistent with movement problem solving hypothesis.
Research evidence supports a “movement problem solving” hypothesis as a viable basis for developing teaching strategies and practice conditions.

“Discovery learning” is an effective means of engaging people in movement problem solving when learning motor skills.

“Discovery learning” teaching strategies and practice conditions can be implemented in various ways.
4 ways to implement discovery learning teaching strategies and practice conditions:

1. Practice focused on discovering movements to achieve action goal rather than on performing “correct” movements, e.g.,
   - Practice that involves making movement errors

2. Learner’s attention focus on effects of movements rather than on movements themselves

3. Movement exploration of environmental variations

4. Feedback that encourages movement problem solving rather than movement solutions
Motor learning as therapy: A critical appraisal of the legacy of Ann Gentile

November 5, 2016

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Ann Gentile’s Accomplishments

• She worked across an extraordinary diversity of **scientific domains**
• She created a unique and remarkable **intellectual milieu**
• She made significant **contributions to practice** (teaching of skills in PE, special ed, rehab)
• She formulated and stood for **critical ideas**
Scientific Domains

• Neuroscience (Frontal Lobes)
• Recovery & Neural Plasticity
• Motor Development
• Motor Control
• Rehabilitation
• Motor Learning
A Working Model of Skill Acquisition with Application to Teaching

By A. M. Gentile

In writing this paper, the objectives are to present some basic concepts concerning skill acquisition, loosely formulated in terms of a working model, and then to draw some practical applications to teaching. The presentation is far from complete. All possible factors that could affect motor learning are not included. Further, in making applications to teaching, there are many inductive leaps and intuitive jumps from data to general statements.

Why present such a tentative and, at times, speculative model for consideration? First, although specific details within the model undoubtedly will be revised with further investigation, the major relationships already are adequately supported and the general formulation probably represents an accurate picture of the factors involved in skill acquisition.

A second reason for presenting the model at this time pertains to its usefulness for teachers. The writer found that most motor learning textbooks, and her own class presentations, represented a disjointed collection of facts, largely devoid of unifying themes. The area of motor skills seemed to have a supermarket quality: a little massed/distributed practice here, feedback there, stacks of reaction time, mental rehearsal, speed/accuracy, short-term memory, and other distinct topics of interest piled about in disarray. For the novice in the skills area, especially for the teacher-in-training whose entire experience may officially terminate with one undergraduate or graduate course, there seemed to be a need to selectively integrate the material into a package which could be easily handled and serve as a basis for future study or as a guide for operations performed by the teacher of skills.

The paper is organized into three sections. In the first, the motor patterns to which the model pertains are briefly identified. The nature of skill acquisition, partitioned into initial and later stages, is presented in section two. Finally, in the last section, application is made to teaching strategies.
‘Working Model’ and updates


Outline

• 3 important principles from ‘working model’ that need *renewed* emphasis
  – Stages of skill acquisition
  – Importance of task analysis & selection
  – Movement is a means to an end
Two related questions

• Integration of motor learning into PT curriculum?
• Motor learning - a distinct therapeutic approach?
Is motor learning therapy?

• “Motor learning is not something that the therapist does, it’s what the patient does.” (Ann Gentile)
Stages of Skill Acquisition

• Stage 1: “Getting the idea of the movement”
  – Cognitive stage (Fitts, 1962)
• Stage 2: “Fixation/diversification”
  – Associative phase (Fitts)
  – 3\textsuperscript{rd} phase (Fitts) - Autonomous

Gentile’s stages  
A prescriptive formulation

• Defined from perspectives of learner & teacher
• Emphasis on 1st stage
• Forms the interpretive foundation for all motor learning research
  – e.g. blocked vs. random practice
A Taxonomy of Tasks

<table>
<thead>
<tr>
<th>Regulatory Conditions during Performance</th>
<th>Intertrial Variability</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Absent</td>
</tr>
<tr>
<td><strong>Closed Tasks</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Stationary</strong></td>
<td></td>
</tr>
<tr>
<td>• Climbing stairs at home</td>
<td>• Walking on different surfaces</td>
</tr>
<tr>
<td>• Brushing teeth</td>
<td>• Climbing stairs of different heights</td>
</tr>
<tr>
<td>• Unlocking the front door</td>
<td>• Drinking from mugs, glasses, cups</td>
</tr>
<tr>
<td>• Stepping on the bathroom scale</td>
<td></td>
</tr>
<tr>
<td><strong>Consistent Motion Tasks</strong></td>
<td></td>
</tr>
<tr>
<td>• Stepping onto an escalator</td>
<td>• Sitting in a moving automobile</td>
</tr>
<tr>
<td>• Lifting luggage from an airport conveyor</td>
<td>• Catching a ball</td>
</tr>
<tr>
<td>• Moving through a revolving door</td>
<td>• Walking down a crowded hall</td>
</tr>
<tr>
<td></td>
<td>• Carrying a wiggling child</td>
</tr>
</tbody>
</table>
Critical importance of task analysis & selection

• The taxonomy helps us understand the requirements placed on the performer by different types of tasks

• Choice of task is active, not passive
  – The selection of the task is perhaps the most critical decision that a therapist (teacher) makes
  – Therapist chooses tasks that will challenge the patient, promote recovery, and maximize functional ability (skill)
    • Hence, task-oriented therapy
Movement is a means to an end

- Levels of Analysis
  - Action
  - Movement
  - Neuromotor processes
Levels of analysis

Figure 3–1 Diagrammatic representation of the relationship between levels of analysis. At the “Movement” level, filled circles represent the many movement patterns that can be used to successfully achieve the “Action-Goal” (movement equivalence); unfilled circles are unsuccessful patterns. At the level of “Neuromotor Processes,” filled circles represent the many ways neural processes can be organized to produce a specific movement (motor equivalence); unfilled circles are unsuccessful modes of organization.
Movement is a means to an end

• Formulation of the motor plan is primarily the responsibility of the learner
  – Implicit/explicit learning

• Trying to “teach” the correct way to move can actually have negative consequences
  – Short-circuits the learning process
  – “means-end confusion”
Restitution vs. substitution

A false dichotomy?

• aka recovery vs. compensation
  – Question is often framed at the *movement* level of analysis
  – After therapy, is the patient's original function restored, as it was before, or has the patient compensated by using a different movement pattern

• We can ask this question at each of Gentile’s three levels of analysis
  – Action
  – Movement
  – Neuromotor processes
Restitution vs. substitution

A third path

• This question is rarely formulated at the Action level

• The question we should be asking is whether *skill* has been restored
  – ability to achieve a goal consistently, flexibly, and efficiently
Are motor learning principles used in rehabilitation practice?

• DePaul et al surveyed Canadian Physiotherapists (117 replies)
  – Part 1 - test of motor learning principles (MLP)
  – Part 2 - estimation of how frequently principles used in clinical practice

• Conclusions
  – Overall knowledge of MLP was generally high (11/14)
  – Despite awareness, application of MLPs was inconsistent

Assessment of Knowledge-related to Motor Learning

Participants correctly answered an average of 11 of 14 questions on the ML knowledge assessment.

Weak areas: Benefits of random practice schedule and external focus of attention despite strong supporting evidence in healthy literature.

- Def'n: Augmented feedback 98%
- Def'n: Transfer of learning 93%
- Term: Knowledge of performance 93%
- Term: Walking = Continuous skill 89%
- Def'n: Retention 83%
- Term: Dressing = Serial skill 77%
- MLP: Self-evaluation helps learning 97%
- MLP: Assess learning vs performance 96%
- MLP: Continuous skills and whole-task practice 88%
- MLP: Variable practice improves transfer 72%
- MLP: Whole task practice for walking 66%
- MLP: External vs internal focus of attention 55%
- MLP: Random practice enhances learning 44%

Correct answers (%)

Motor Learning Definitions, Terms, and Principles
Application of specific Motor Learning Principles

Participants were asked to estimate how frequently they applied specific MLPs in their practice. Proportions of participants who reported applying each MLP > 50% of the time were calculated.

<table>
<thead>
<tr>
<th>Motor Learning Principles</th>
<th>% of participants who apply &gt;50% of time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole-task practice of cont. skills (walking)</td>
<td>77%</td>
</tr>
<tr>
<td>Feedback should provide new, useful info</td>
<td>73%</td>
</tr>
<tr>
<td>Variable practice improves transfer</td>
<td>73%</td>
</tr>
<tr>
<td>Task and environment specific practice</td>
<td>69%</td>
</tr>
<tr>
<td>Assess learning not performance</td>
<td>67%</td>
</tr>
<tr>
<td>More practice, better learning</td>
<td>65%</td>
</tr>
<tr>
<td>Limited versus constant guidance</td>
<td>58%</td>
</tr>
<tr>
<td>Self-evaluation by learner</td>
<td>42%</td>
</tr>
<tr>
<td>Limited versus abundant feedback</td>
<td>42%</td>
</tr>
<tr>
<td>Random versus blocked practice</td>
<td>39%</td>
</tr>
<tr>
<td>External vs internal focus of attention</td>
<td>35%</td>
</tr>
</tbody>
</table>
Motor learning as therapy

Two views

1. Motor learning principles form a set of rules or guidelines
   – We use these principles to enhance the effectiveness of therapy

2. Motor learning is the therapy
   – Motor learning principles are not merely a set of “rules” – more of a toolbox
   – In “motor learning therapy”, the therapist engages in a dialogue with the patient to select the tasks that will maximize recovery
Task-oriented training

• Patient is viewed as an active problem solver
• Therapist’s primary roles are task selection and structuring conditions of practice
• Rehabilitation is focused on the acquisition of skills
  – “the pursuit of skilled movement, rather than merely functional actions (i.e., ADL)”¹
• Effectiveness of therapy measured using a skill-based framework²


“Task-oriented training has emerged as the dominant approach to motor restoration for stroke-induced motor impairments.”


• See also
Summary points

• The central ideas in Gentiles’ working model are still highly relevant
  – some of these ideas are not given proper emphasis

• It is time for a reconsideration of the role of motor learning in rehabilitation
  – From principles to toolbox

• Motor learning is our “ruby slippers”
  – Our most powerful and meaningful approach

• Our task - to add to and improve the tools in that toolbox
Enhancing motor learning: The OPTIMAL theory

Gabriele Wulf
University of Nevada, Las Vegas
and
Rebecca Lewthwaite
Rancho Los Amigos National Rehabilitation Center
and University of Southern California
THEORETICAL REVIEW

Optimizing performance through intrinsic motivation and attention for learning: The OPTIMAL theory of motor learning

Gabriele Wulf¹ · Rebecca Lewthwaite²³
OPTIMAL theory of motor learning

MOTIVATION
- Autonomy
- Enhanced expectancies

ATTENTION
- External focus

GOAL-ACTION COUPLING

SELF-FOCUS on TASK GOAL

Motor performance

Motor learning
MOTIVATION

Factors that influence or encompass the energization, direction, and intensity of behavior
• Implicit or explicit
• Intrinsic or extrinsic

Social-comparative feedback
Perceived task difficulty
Definitions of success
Self-modeling
Beliefs/illusions/superstitions/placebos
Suggestions, hypnosis
Subliminal primes
Conceptions of ability
Perceptions of ability
Extrinsic rewards
Positive affect
Social-comparative feedback

- All participants received their own error scores (average platform deviation from horizontal)
- 2 practice days, 7 trials each
- Retention test (no feedback) on Day 3
- 3 groups ...

• **Better Group:**
  “The average score on this trial was [20% worse].”
  Inferred performing better than average.

• **Worse Group:**
  “The average score on this trial was [20% better].”
  Inferred performing worse than average.

• **Control Group:**
  No normative feedback
Better > Worse = Control
during both Acquisition and Retention
Perceived task difficulty

- Enhanced expectancy
  “Active people, with your experience, usually do well on this task”
- Control

Participants
Women, 60-74 years

Definitions of success

Groups

• **Large circle:** Balls ending up in the BLUE circle are considered “good” trials

• **Small circle:** Balls ending up in the RED circle are considered “good” trials

OPTIMAL theory of motor learning

- MOTIVATION
  - Autonomy
  - Enhanced expectancies

- ATTENTION
  - External focus

- SELF-FOCUS
  - FOCUS ON TASK GOAL

- MOTOR PERFORMANCE
  - Motor learning
**Enhanced expectancies ...**

- Serve a task-readying function, boosting performance

- *Expectations of positive outcome or experience trigger dopaminergic response.* **Temporal pairing with task practice important.**
  
  Dopamine facilitates short-term performance effects and long-term consolidation for retention/learning.

- *Success with challenge*
  
  Occasional risks to expected success (i.e., challenge) can temporarily dampen dopamine levels – but amplify the impact of subsequent success (Schultz, 2010, 2013).
OPTIMAL theory of motor learning

**Motivation**
- Autonomy
- Enhanced expectancies

**Attention**
- External focus

**Focus on Task Goal**
- Goal-action coupling

**Self-focus**

**Motor performance**

**Motor learning**
Providing autonomy support through self-controlled use of assistive device ...
Providing autonomy support through self-controlled use of assistive device ...

Providing **autonomy** support by giving learners incidental choices ...

**Choices group**

2 choices:

1. Second task: Coincidence timing or hand dynamometer?

2. Which painting should we hang in the lab?

**No Choices group**

was informed of second task and painting

Providing autonomy support by giving learners incidental choices ...

OPTIMAL theory of motor learning
Autonomy ...

- Enhances self-efficacy; promotes task focus
  - Reduces concern about abilities, self-regulatory activity; frees up attentional resources for performance

- Reduces stress
  - Cortisol (stress hormone) down-regulates dopamine/motivation (Montoya et al., 2014)
OPTIMAL theory of motor learning

- **MOTIVATION**
  - Autonomy
  - Enhanced expectancies

- **ATTENTION**
  - External focus

- **Focus on Task Goal**
  - Goal-action coupling

- **Self-focus**

- **Motor performance**
  - Motor learning
Typically instructions are directed at the coordination of *body* movements.

“Move your feet”

“Contract your biceps”

“Concentrate on your diaphragm”

“Focus on your fingers”

“Move your shoulders back”

“Contract that muscle”
INTERNAL FOCUS
Concentration on body movements

EXTERNAL FOCUS
Concentration on effect of movements (e.g., surfboard, cup, sound, piano keys, golf club, beanbag)

“Turn the board”
“Focus on the cup”
“Turn the board”

“Focus on the sound”
“Move the club back”
“Squeeze the beanbag”
An **external focus** enhances movement effectiveness ...

**Internal focus**
“Keep your **feet** horizontal”

**External focus**
“Keep the **markers** horizontal”

**Control**

---

An **external focus** enhances automaticity ...

Platform movements over 90-s trial...

Participant with **internal focus** (feet)

![Graph showing platform movements over 90-s trial with internal focus.]

Participant with **external focus** (markers)

![Graph showing platform movements over 90-s trial with external focus.]

Faster movement adjustments with external focus:
Utilization of reflexive (automatic) control mechanisms

An **external focus** enhances movement efficiency...

Task
Isometric force production:
30% of max. force

**Internal focus:** Calf muscle
**External focus:** Platform

An **external focus** enhances movement efficiency...

Task
Isometric force production: 30% of max. force

**Internal focus**: Calf muscle
**External focus**: Platform

External focus advantages have been found for ...

<table>
<thead>
<tr>
<th>Tasks</th>
<th>Levels of expertise</th>
</tr>
</thead>
<tbody>
<tr>
<td>Balance</td>
<td>Novices</td>
</tr>
<tr>
<td>Golf (long-iron shots, pitch shots, putting)</td>
<td>Experts</td>
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<tr>
<td>Soccer kicks</td>
<td></td>
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<tr>
<td>Volleyball serves</td>
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<tr>
<td>Dart throwing</td>
<td></td>
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<tr>
<td>Tennis</td>
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<tr>
<td>Basketball free-throws</td>
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<tr>
<td>Rowing</td>
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<tr>
<td>Kayaking</td>
<td></td>
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<td>Swimming</td>
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<tr>
<td>Agility</td>
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<tr>
<td>Sprint</td>
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<tr>
<td>Weight lifting</td>
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<tr>
<td>Force production</td>
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<tr>
<td>Vertical jump</td>
<td></td>
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<tr>
<td>Long jump</td>
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<tr>
<td>Gymnastics</td>
<td></td>
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<tr>
<td>Ballet</td>
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<tr>
<td>Playing musical instruments</td>
<td></td>
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<tr>
<td>Singing</td>
<td></td>
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<td>...</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Age groups</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Children</td>
<td></td>
</tr>
<tr>
<td>Young adults</td>
<td></td>
</tr>
<tr>
<td>Older people</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Disability/Conditions</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Parkinson’s disease</td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td></td>
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<tr>
<td>Intellectual disability</td>
<td></td>
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<tr>
<td>ADHD</td>
<td></td>
</tr>
<tr>
<td>Injuries (ankle sprain)</td>
<td></td>
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</tbody>
</table>

...
OPTIMAL theory of motor learning

- **MOTIVATION**
  - Autonomy
  - Enhanced expectancies

- **ATTENTION**
  - External focus

- **FOCUS ON TASK GOAL**

  - SELF-FOCUS

- **Motor performance**
  - Motor learning

Motor performance enhances motor learning, which improves self-focus, leading to better task focus and enhanced expectancies, which in turn supports autonomy in motivation.
External focus of attention ...

- Directs attention to the task goal
- Reduces a focus on the self
OPTIMAL theory of motor learning

MOTIVATION

Autonomy

Enhanced expectancies

ATTENTION

External focus

Focus on task goal

Self-focus

Motor performance

Motor learning

Goal-action coupling
Goal-action coupling

• **Structural brain changes** are the result of formation of new connections by dendritic spine growth (synaptogenesis) and other neuroplastic processes.

• **Functional connectivity** – temporally coherent activity over large and distinct regions of the brain – changes with tasks and with practice. More distinct functional connections are associated with higher skill.
Motor planning brain activation during a pre-shot routine is “radically different” between expert golfers and novices.

Differences are apparent before the golfer swings the club.

Consistent with notion that extensive practice leads experts to develop a focused and efficient organization of task-related neural networks, whereas novices have difficulty filtering out irrelevant information.
Fig. 2. Brain activation derived from 15 s from the onset of the pre-shot routine — control task for (a) a novice and (b) an expert golfer. In each case, the golfer shown represents the one whose overall brain activation was closest to the group mean. The color code gives the $F$ values for the $F$-test of those voxels significantly different between the active and control tasks: red ($6.63 < F < 10$), orange ($10 \leq F < 25$), yellow ($F \geq 25$), where $F = 6.63$ correspond to the whole-brain corrected significance level ($p = 0.05$). The right hand side shows a schematic representation to summarize those brain regions which were activated during the pre-shot routine for the two groups of golfers: (c) novice golfers activated the limbic regions including the cingulate and temporal pole and (d) expert golfers activated the supplementary motor region.
Functional connectivity


Red: Positive correlation
Blue: Negative correlation
Adopting an external focus of attention alters intracortical inhibition within the primary motor cortex

Y.-A. Kuhn, M. Keller, J. Ruffieux and W. Taube

Movement and Sport Sciences, Department of Medicine, University of Fribourg, Fribourg, Switzerland
**Conclusion:** The level of intracortical inhibition was previously shown to influence motor performance. Our data shed new light on the ability to instantly modulate the activity of inhibitory circuits within M1 by changing the type of attentional focus. The increased inhibition with EF might contribute to the better movement efficiency, which is generally associated with focusing externally.
Figure 11  Dynamic salience network-mediated switching of large-scale brain networks. The salience network (SN) plays a crucial role in dynamic switching between the central executive and default-mode networks. The SN recruits the central executive and task control regions to maintain cognitive set and manipulate information in working memory while suppressing the default-mode network to keep attention focused on task-relevant goals. Adapted from Bressler, S. L., & Menon, V. (2010). Large-scale brain networks in cognition: Emerging methods and principles. Trends in Cognitive Sciences, 14, 277–290.
Summary: Connectivity

- Enhanced expectancies and autonomy support facilitate motor learning by making dopamine available for memory consolidation and neural pathway development.
- More positive expectancies and autonomy facilitate efficient switching from the default mode network to motor networks associated with the movement skill.
- An external attentional focus facilitates [internal attentional focus impedes] efficient switching from the default mode network to relevant motor networks.
- Generally, conditions that optimize performance facilitate learning.
OPTIMAL theory of motor learning

Are all 3 factors important for optimal learning?

- Autonomy
- Enhanced expectancies
- External focus

Goal-action coupling

focus on task goal

self-focus

motor performance

motor learning
3 studies compared the effectiveness of combinations of 2 factors with 1 factor or none:

Enhanced expectancies (EE)
Autonomy support (AS)
External focus (EF)
3 studies compared the effectiveness of combinations of 2 factors with 1 factor or none:

Enhanced expectancies (EE)
Autonomy support (AS)
External focus (EF)

3 studies compared the effectiveness of combinations of 2 factors with 1 factor or none:

- Enhanced expectancies (EE)
- Autonomy support (AS)
- External focus (EF)

3 studies compared the effectiveness of combinations of 2 factors with 1 factor or none:

- **Enhanced expectancies (EE)**
- **Autonomy support (AS)**
- **External focus (EF)**

Enhanced expectancies (EE): Positive social-comparative feedback
External focus (EF): Focus on the target
Enhanced expectancies + External focus

Which scenario is more typical?

1. Instructor/therapist ...
   • selects practice tasks, describes how actions should be performed
   • gives corrective feedback
   • gives instructions that refer to body movements

   or

2. Instructor/therapist ...
   • elicits small to moderate learner choices (e.g., feedback when performer asks for it)
   • highlights good aspects of performance, mostly ignores mistakes
   • does not talk about body movements and directs attention externally
Scenario 1:
Instructor/therapist …
- selects practice tasks, describes how actions should be performed
- gives corrective feedback
- gives instructions that refer to body movements
Scenario 2:
Instructor/therapist …
- elicits small to moderate learner choices
- highlights good aspects of performance, mostly ignores mistakes
- does not talk about body movements and directs attention externally

**Diagram:**
- **MOTIVATION**
  - Autonomy
  - Enhanced expectancies
- **ATTENTION**
  - External focus

- **Focus on Task Goal**
  - Goal-action coupling
  - Self-focus

- **Motor performance**
  - Motor learning

**Virtuous cycle**
Thank you!

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rlewhataite@dhs.lacounty.gov

www.optimalmotorlearning.com
Multifactorial Modifiers of Functional Recovery after Spinal Cord Injury: Translating Basic Science to Human Interventions

D. Michele Basso, EdD, PT
11,000 new cases each year
Average age at the time of injury = 40.2
Mostly males = 80%
Even mild injury results in profound burden – physical, emotional, economic
To change disability, our lab strives to manipulate motor learning through cellular and molecular factors.
Promoting Recovery After SCI

Training Improves Functional Recovery & Strength

Buehner, 2012 Archives 93:1530

AIS C and D
n= 225

Pre Training

- Community: 28%
- Non Amb: 31%
- Slow Amb: 41%

Post Training

- Community: 47%
- Non Amb: 22%
- Slow Amb: 31%

Buehner, 2012 Archives 93:1530

Training Improves Functional Recovery & Strength

BUT NOT ENOUGH

AND NOT IN EVERYONE
Injury Mechanisms
(Epicenter/Remote)

Promoting Recovery After SCI

Intervention Timing
(Early/Late)

Task Specific Rehabilitation

Adaptive
Maladaptive

Adaptive
Maladaptive
Human SCI  Animal SCI Model

Lesion Site Pathology
Human SCI

Animal SCI Model

Training Paradigm
Specific Focus:

For Stroke: There is a bad time to start intensive rehabilitation (Human, animal) with neuro-inflammation being a potential factor.

UNKNOWN HOW TIMING AND INFLAMMATION INTERACT IN SCI

Key biomarker of inflammation is Matrix Metalloproteinase 9 (MMP9)

We Manipulate MMP9 to alter Inflammation then assay motor learning with and without treadmill training delivered early or late after SCI.
EARLY REHABILITATION FOR SCI

PROMOTES ROBUST LOCOMOTOR RECOVERY WHEN INFLAMMATION IS BLOCKED WITH GENETIC MUTATION OF MMP9

Hansen et al., 2013 J Neuroscience
Beneficial and Detrimental Effects Last Well-Beyond Training

Hansen et al., 2013
Late training is ineffective in KO and WT mice.

<table>
<thead>
<tr>
<th></th>
<th>Naïve (n=10)</th>
<th>KO Pre (n=6)</th>
<th>KO Post (n=6)</th>
<th>WT Pre (n=5)</th>
<th>WT Post (n=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMS</td>
<td>9</td>
<td>5.7 ± 0.4</td>
<td>5.6 ± 0.2</td>
<td>4.8 ± 0.2</td>
<td>5.0 ± 0.3</td>
</tr>
<tr>
<td>Trunk Displacement</td>
<td>0.54 ± 0.04</td>
<td>1.01 ± 0.31</td>
<td>0.64 ± 0.11</td>
<td>1.24 ± 0.40</td>
<td>0.87 ± 0.26</td>
</tr>
<tr>
<td>Toe Dragging (s)</td>
<td>0.031 ± 0.001</td>
<td>0.067 ± 0.010</td>
<td>0.051 ± 0.004</td>
<td>0.077 ± 0.013</td>
<td>0.078 ± 0.007</td>
</tr>
<tr>
<td>Swing Time (s)</td>
<td>0.113 ± 0.005</td>
<td>0.060 ± 0.012</td>
<td>0.078 ± 0.005</td>
<td>0.055 ± 0.023</td>
<td>0.068 ± 0.019</td>
</tr>
<tr>
<td>Stance Time (s)</td>
<td>0.30 ± 0.01</td>
<td>0.69 ± 0.09</td>
<td>0.52 ± 0.04</td>
<td>0.82 ± 0.14</td>
<td>0.91 ± 0.09</td>
</tr>
<tr>
<td>Peak Ankle Velocity</td>
<td>22.9 ± 1.5</td>
<td>15.5 ± 3.3</td>
<td>19.3 ± 1.6</td>
<td>11.4 ± 4.7</td>
<td>12.3 ± 3.7</td>
</tr>
<tr>
<td>Peak Toe Velocity</td>
<td>30.0 ± 1.8</td>
<td>21.8 ± 4.7</td>
<td>27.7 ± 2.0</td>
<td>16.4 ± 6.8</td>
<td>19.6 ± 5.5</td>
</tr>
<tr>
<td>Gridwalk (% Success)</td>
<td>84.3 ± 1.7</td>
<td>12.3 ± 3.2</td>
<td>11.3 ± 3.1</td>
<td>13.1 ± 1.2</td>
<td>14.6 ± 3.0</td>
</tr>
</tbody>
</table>

Hansen et al., 2013
If we deliver this effective form of training too late, it fails. If we deliver it too early without blocking inflammation, it is harmful.

TAKE AWAY
1. Rehab efficacy depends on more than the type or timing of the intervention. The microenvironment is critical.
Early TM Training makes Invading Inflammatory Monocytes Even More Toxic

- Naïve Control (L1-L3)
- 24h SCI (L1-L3)

![Image showing immunofluorescence with GFP and Ly6 labeling]

**Graphs:**
- MMP-9: naïve, 7day, 7day EX
- Ly6C: naïve, 7day, 7day EX

Norden in prep
Primary Source of EARLY Harmful Inflammation are Bone-Marrow Derived Monocytes and TM training worsens their inflammatory profile

TAKE AWAY
1. Consider the lumbar cord as part of the “Injury Site” rather than relatively protected.
2. Peripheral Inflammatory sources may allow easier, more effective anti-inflammatory treatment of the cord.
Complex Interaction Between Inflammation and Recovery

Effect of High Inflammatory Microenvironment on Lumbar Neuroplasticity, Learning and Function

1. Adaptive vs. Maladaptive Plasticity
Early Lumbar Inflammation Increases Reflex Activity & Prevents Learning

PLASTICITY TAKES ON A MALDAPITIVE PHENOTYPE EARLY AFTER SCI.

IT DOESN’T SUPPORT LUMBAR MOTOR LEARNING

Hansen et al. Frontiers Neural Circuits 2016
Late Lumbar Adaptive Plasticity Supports Segmental Learning

LUMBAR MOTOR LEARNING

EARLY

LATE

Hansen et al. Frontiers Neural Circuits 2016
EARLY AFTER SCI: Maladaptive plasticity worsens with high inflammation and greater SCI severity. It prevents motor learning in putative CPG interneurons.

LATE AFTER SCI: Adaptive plasticity supports lumbar spinal learning but appears insufficient to drive locomotor recovery.

If early rehabilitation is harmful and waiting later until inflammation has resolved is better but largely ineffective then how do we promote recovery?

- Increase Novelty of the task
- Make it more challenging
- Target persistent motor control deficits
• **Eccentric Contraction**
  Lengthening contraction of the muscle to lower a limb or objective in a controlled way.

• **Eccentric Motor Control**
  Highly advanced skill that emerges late in development

• **Requires precise matching of descending drive from brain with afferent signals from the limb.**
  Too much drive = Isometric or Concentric Action
  Too little drive = Collapse
Eccentric Motor Control Deficits
DO NOT respond to Flat TM Training

Worthen-Chaudhari in prep
Task-Specific Eccentric TM Training Improves Recovery Late After SCI

Late TM Training

Normal – TM walking

SCI – Post Flat TM

SCI – Post DH TM

Rat Knee Degrees

Ankle Degrees

Faw/Hansen in prep
Late Eccentric Training Induces Near Normal Paw & Trunk Control

Faw/Hansen in prep
Eccentric Training Improves Learning after SCI

Lumbar Motor Learning

Response Duration (s)

Downhill

\[ r^2 = 0.58 \]

\[ *p<0.05 \]

Flat

\[ R^2 = 0.001 \]

Faw/Hansen in prep
Task-Specific Eccentric TM Training LATE after SCI induces gains in learning and functional recovery that are unattainable with Flat TM Training.

Eccentric form of training reduces lumbar inflammatory cytokines.
Can Task-Specific ECCENTRIC Training Produce Greater Recovery Beyond Flat TM Training in Human SCI?
Eccentric task specific training may be more effective because it is novel and challenging and stimulates white matter plasticity.

New Evidence suggests that Complex Skill Learning relies on myelin plasticity.

- Myelinated decending motor axons are not fully myelinated and have large gaps (Tomassy 2014 Science)

- These gaps have high concentrations of glutamate which attract immature oligos (OPCs) (Gautier 2015 Nature)

- When OPCs are blocked from maturing and myelinating, complex skill learning is prevented. (Mackenzie Science 2014)
Multicomponent $T_2$ Relaxation Imaging (MCRI)

Uses the $T_2$ relaxation signal at multiple echo times to indirectly quantify water molecules between myelin layers

Myelin Water Fraction (MWF)

- Myelin Water Area / Total Signal Area

Laule et al, Neurotherapeutics 2007

Prasloski et al, NeuroImage 2012
A major barrier to functional recovery after SCI is inflammation within the lumbar cord and the primary cellular source is infiltrating bone-marrow derived monocytes.

Applying exercise during an inflammatory state worsens inflammation in the cord and worsens function.

It is useful to consider the lumbar cord as part of the “Injury Site” rather than relatively protected.
Clinical Implications

Selecting the optimal treatment window and the best form of treatment is complex.

Flat Treadmill Training produces robust locomotor recovery BUT only when it is administered during early neuroplasticity periods under low levels of inflammation.

If we deliver this effective form of training too late, it fails. If we deliver it too early without blocking inflammation, it is harmful.
For patients that are non-responders to an intervention, we must ask ourselves:

Is the intervention task-specific enough?

Is an otherwise beneficial treatment being blocked by cellular factors like inflammation?

Have we waited too long to deliver the training and the window of natural repair and plasticity has closed?
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Some reading as a follow-up to Roberta Shepherd talk [November 2016 ]

Textbooks


Articles


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