




Neuroplasticity, Pain and Graded Motor Imagery

Adriaan Louw, PT, PhD (c), M.App.Sc (physio), GCRM, CSMT


Combined Sections Meeting 2012
Chicago, IL – February 8-11, 2012

1



Neuroplasticity, Pain and Graded Motor Imagery

Adriaan Louw, PT, PhD (c), M.App.Sc (physio), GCRM, CSMT



Objectives

Upon completion of this educational session the participants will be able to:

1. Be updated on the neuroplasticity changes in the brain in patients with pain
2. Recognize the fact that patients with pain have distorted body images in the brain
3. Have an updated view of the evidence for graded motor imagery to alter pain and dysfunction in patients with pain
4. Shown a series of graded motor imagery techniques which can be applied into clinical practice
5. Apply the information from the educational session into clinical practice

3



Today's presentation

How the brain process pain



4

Treating false representation



Special thanks and acknowledgement to Dr. Butler and Dr. Moseley

How does the brain process pain?

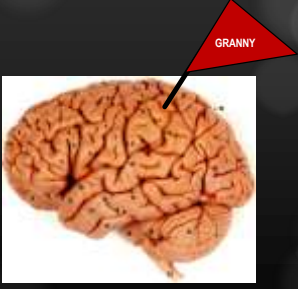
6

Name the area of the brain that processes pain...

7

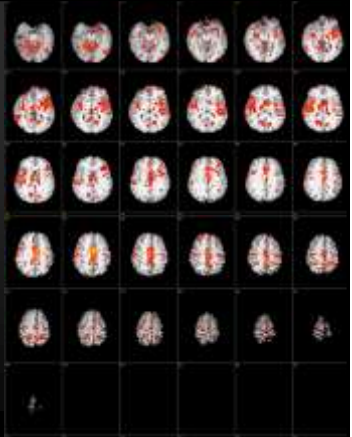
8

Let's do a little experiment...



GRANNY

9



Courtesy Dr. Lorimer Moseley


10

Definitions describing neural processing

- Melzack's neuromatrix
- The map in the brain
- The virtual body
- Schema – "body of knowledge"
- The virtual body in the actual body

Neuromatrix = coding space
 Neurosignature = representation= event space

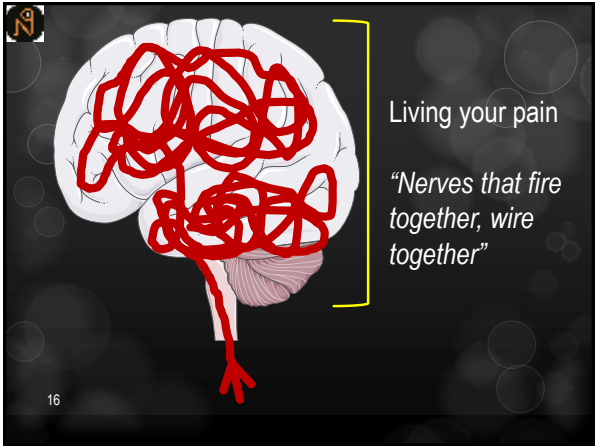
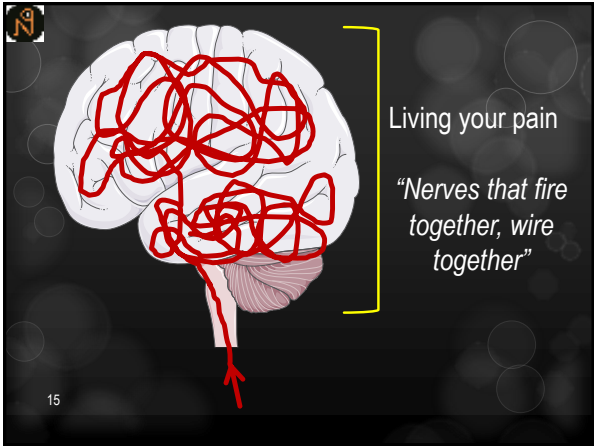
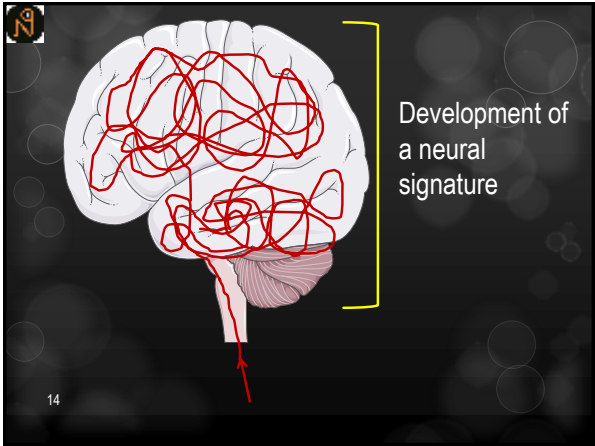
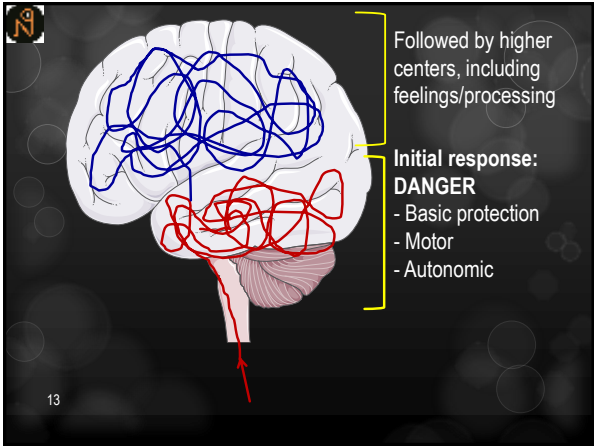
11



Initial response: DANGER

- Basic protection
- Motor
- Autonomic

12



Nº

Mapping of the brain in pain – 6 key points

1. Common areas are frequently “ignited”
 - Pre-motor/motor area
 - Cingulate
 - Hippocampus
 - Amygdala
 - Pre-frontal
 - Sensory cortex
 - Hypothalamus and thalamus
 - Cerebellum
 - Spinal cord

17
Eg. Flor H, Bushnell MC, Casey KL, Petrovic P, Ingvar M

Nº


Representation of Pain in the Brain – 6 key points

1. Common areas are frequently “ignited”
2. Via connections, backfiring neurones, and neurotransmitters, pain is perceived – the pain neural signature

18
Eg. Flor H, Bushnell MC, Casey KL, Petrovic P, Ingvar M.

A TYPICAL PAIN NEUROTAG

1. PREMOTOR / MOTOR CORTEX
impulse and prepare movement.
2. CINGULATE CORTEX
sensitization, focusing
3. PREFRONTAL CORTEX
problem solving, memory
4. AMYGDALA
fear, fear conditioning, addiction
5. SENSORY CORTEX
sensory discrimination
6. HYPOTHALAMUS / THALAMUS
drive impulses, automatic regulation, motivation
7. CEREBELLUM
movement and cognition
8. HIPPOCAMPUS
memory, spatial cognition, fear conditioning
9. SPINAL CORD
going down the highway



From Butler and Moseley
2003 Explain Pain

Feelings can be modulated by anything relevant



20
From: Dr. Moseley with permission

Feelings can be modulated by anything relevant

- Denote synaptic modulation

Beliefs

21

From: Dr. Moseley with permission

The diagram shows a lateral view of a human brain with a network of green lines representing synaptic modulation. The text 'Beliefs' is positioned to the left of the brain. A small logo with the letters 'bim' is in the bottom right corner.

Feelings can be modulated by anything relevant

- Denote synaptic modulation

Beliefs
Knowledge, logic

22

From: Dr. Moseley with permission

The diagram shows a lateral view of a human brain with a network of green lines representing synaptic modulation. The text 'Beliefs' and 'Knowledge, logic' is positioned to the left of the brain. A small logo with the letters 'bim' is in the bottom right corner.

Feelings can be modulated by anything relevant

- Denote synaptic modulation

Beliefs
Knowledge, logic
Other sensory cues

23

From: Dr. Moseley with permission

The diagram shows a lateral view of a human brain with a network of green lines representing synaptic modulation. The text 'Beliefs', 'Knowledge, logic', and 'Other sensory cues' is positioned to the left of the brain. A small logo with the letters 'bim' is in the bottom right corner.

Feelings can be modulated by anything relevant

- Denote synaptic modulation

Beliefs
Knowledge, logic
Other sensory cues
Social context

24

From: Dr. Moseley with permission

The diagram shows a lateral view of a human brain with a network of green lines representing synaptic modulation. The text 'Beliefs', 'Knowledge, logic', 'Other sensory cues', and 'Social context' is positioned to the left of the brain. A small logo with the letters 'bim' is in the bottom right corner.

Feelings can be modulated by anything relevant

- Denote synaptic modulation

Beliefs
 Knowledge, logic
 Other sensory cues
 Social context
 Anticipated consequences



25


From: Dr. Moseley with permission



Feelings can be modulated by anything relevant


- Denote synaptic modulation

Beliefs
 Knowledge, logic
 Other sensory cues
 Social context
 Anticipated consequences
 Family
 media
 previous history
 culture
 GP
 work
 physiotherapist
 education
 activity self-efficacy
 access
 exposure



26


From: Dr. Moseley with permission



Pain


- Denote synaptic modulation

Beliefs
 Knowledge, logic
 Other sensory cues
 Social context
 Anticipated consequences
 Family
 media
 previous history
 culture
 GP
 work
 physiotherapist
 education
 activity self-efficacy
 access
 exposure



27

From: Dr. Moseley with permission



Representation of Pain in the Brain – 6 key points

1. Common areas are frequently “ignited”
2. Via connections, recursive and backfiring neurones, pain is perceived – the pain neural signature
3. Representational “ignition” is not dependant on a specific tissue

28

Eg. Flor H, Bushnell MC, Casey KL, Petrovic P, Ingvar M.

Representation of Pain in the Brain – 6 key points

1. Common areas are frequently “ignited”
2. Via connections, recursive and backfiring neurones, pain is perceived – the pain neural signature
3. Representational “ignition” is not dependant on a specific tissue
4. “Emotional pain” uses similar areas to “physical pain”

29
Eg. Flor H, Bushnell MC, Casey KL, Petrovic P, Ingvar M.

Representation of Pain in the Brain – 6 key points

1. Common areas are frequently “ignited”
2. Via connections, recursive and backfiring neurones, pain is perceived – the pain neural signature
3. Representational “ignition” is not dependant on a specific tissue
4. “Emotional pain” uses similar areas to “physical pain”
5. Ignited areas can be easily modified*

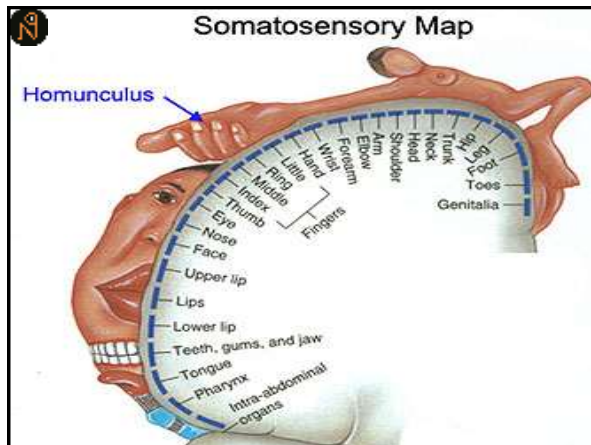
* More on this in the second half...

30
Eg. Flor H, Bushnell MC, Casey KL, Petrovic P, Ingvar M.


Representation of Pain in the Brain – 6 key points

1. Common areas are frequently “ignited”
2. Via connections, recursive and backfiring neurones, pain is perceived – the pain “neurotag”
3. Representational “ignition” is not dependant on a specific tissue
4. “Emotional pain” uses similar areas to “physical pain
5. Ignited areas can be easily modified
6. Smudging of some key “nodes” can occur

31
Eg. Flor H, Bushnell MC, Casey KL, Petrovic P, Ingvar M.



Z9



- Not constrained by gyri and sulci
- Humanoid but not quite (somatopic)
- Use dependent
- Takes on non-organic parts eg collars
- Can be separated from the actual anatomy it represents
- One of many neurosignatures
- Part of a total body matrix

Butler DS, Coppieters MW 2012

Z9 **Neuroplasticity made easy...**

A Participant's hands placed behind screens. Opposite hand visible for Experiment 1.



22 - 23 cm Rubber hand (cm)

B Synchronous manual brushing of real hand and rubber hand.



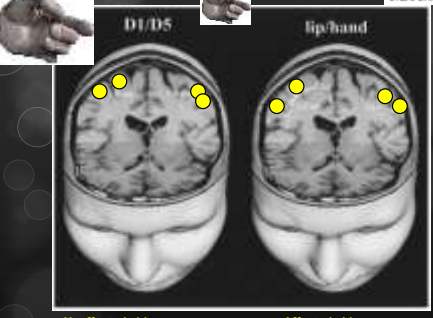
Sites of which skin temperature was measured.

7042 | September 1, 2009 | vol. 105 | no. 35 | 13173

Psychologically induced cooling of a specific body part caused by the illusory ownership of an artificial counterpart

G. Lorimer Moseley^{1*}, Nick Otto², Annelieke Vanema³, Saneeko Des⁴, Marijko Wijers¹, Alberto Gallo⁵, and Charles Spence⁶

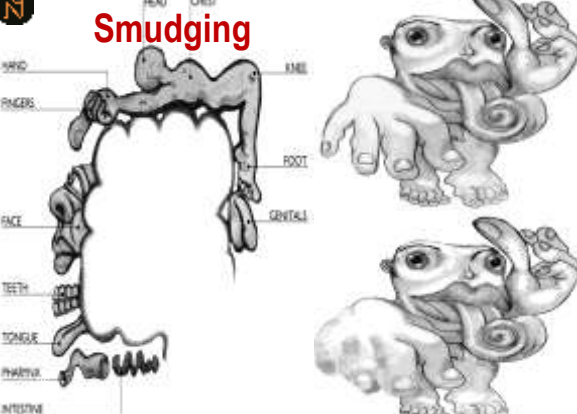
Z9




Patterns of cortical reorganization in complex regional pain syndrome

Christian Malhotra, MD; Hermann D. Handwerker, MD, PhD; Rainerhof Neundorfer, MD; and Frank Doherty, MD

Z9 **Smudging**



Precious information: smudging/brain change are normal



- Occurs as a normal part of life (musicians, blind persons, breast feeding mice)
- "Your brain looks after you"

37

eg. Elbert T et al (1998) *Neuroreport* 9: 3571

Smudging happens quickly

- Web 4 fingers – smudge after 30 minutes
- Lasts 2 hours if webbed for 5 hours

Stavrinou et al 2006 *Cerebral Cortex*

38



Smudging/brain change in pain states

- Phantom limb stories
- Low back, CRPS, carpal tunnel syndrome etc
- Correlations with pain level and chronicity
- Syndactyly stories
- A glial/immune response
- It happens fast (but can change on the weekend)
- Not only somatosensory

Juottonen K et al 2002 Pain 98: 315
 Milligan ED et al 2003 The Journal of Neuroscience 23: 1036
 Flor H. 2000 Progress in Brain Research, 129
 Slavimou et al 2006 Cerebral Cortex

41

42

Two Point Discrimination

- TPD = how far two points have to be away from each other to be recognized as 2 points
- 45 mm is normal for L-spine
- Significant changes in TPD in CLBP and CRPS
- "Tells you what is happening in the brain"

43

Two Point Discrimination

- Chronic LBP – problems with pelvic position
- Major problem with TPD
- Horizontal > vertical
- Skin of the back = smudged

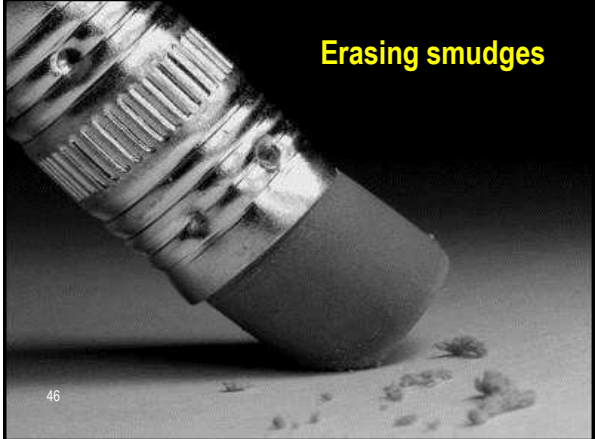
44

Thoughts are nerve impulses



45

Erasing smudges



46

Where are we at right now?

1. With persistent pain and altered processing, the brain develops a "poorer" view of the tissues. The map of the affected area is "fuzzy."
2. The more the map is messed up, the more the pain.
3. Correcting the brain's view of the image is essential to manage pain

47

What is the most common technique to enhance or start urination?

- In 1996 it was shown that the same neurones which fire when performing a motor act, fire when watching another person do the same act.
- They were called "*mirror neurones*" i.e. they reflected acts performed by another person (Gallese, Fadiga et al. 1996).

48

Mirror Neurones

- These neurones also respond to non-visual stimuli such as the sound of an action and imagination of an action.
- Approx 25% of neurones in pre-motor areas are estimated to be mirror neurones.

49


"I feel your pain"

- Knowledge that a loved person is in pain activates similar circuits in your own brain, especially more emotional (limbic/ brainstem) parts of the circuitry (Singer, Seymour et al. 2004). The activation for a loved person is higher than for an unfamiliar person (Singer, Seymour et al. 2006)

50

Embryonic therapies

- Working deep into the neuromatrix – some practicalities



51

Rehabilitation 101

- Do part of movement but no painful part
- Do part of movement with painful part
- Do more
- Increase number
- Increase strength
- Add equipment

52

Rehabilitation 101

- Premotor association areas
- Watching/imagining posture
- Watching/ imagining movement
- Trickery with mirrors
- Do part of movement but no painful part
- Do part of movement with painful part
- Do more
- Increase number
- Increase strength
- Add equipment

53

Virtual body exercises

- Focus placed on synaptic exercises and health
- Brain exercises vs. muscle/joint

54

The Main Techniques


- Laterality
 - Restore accuracy and speed of L versus R
- Motor Imagery
 - Imagining movements/postures
 - Visualization
- Mirror Therapy
 - Mirrors to trick the brain
- Graded Motor Imagery
 - Sequential process of the above

55

**Graded Motor Imagery:
The sequence matters**

Laterality reconstruction
↓
Motor imagery
↓
Mirror therapy


56



GMI Sequence

- In the most recent randomised controlled trial, the graded motor imagery package has demonstrated good evidence for outcome (reduced pain and disability in Complex Regional Pain Syndrome1 (CRPS1) (Moseley 2004; Moseley 2005) and CRPS1 and phantom limb pain (Moseley 2006). It works best if carried out in the sequence of laterality recognition, motor imagery and mirror therapy (Moseley 2006). Note : 2 weeks of each component with graded trial numbers.


57



GMI Sequence

- CRPS and phantom limb pain are severe neuropathic pain states. It would seem that the GMI process would be beneficial for other pain states such as overuse syndromes (variously focal dystonia, repetition strain injury, cumulative trauma disorder) and various arthritic syndromes. Anecdotal evidence supports this contention, suggesting that trials are worthy


58



Laterality

- Laterality signatures as critical premotor association signatures to optimal motor output.
- Loss of laterality is known to occur in patients with CRPS and phantom limb pain. (Schwoebel, Coslett et al. 2002; Moseley 2004; Nico, Daprati et al. 2004).
- An evolutionary biology viewpoint may be that it is a form of protection, maybe neglect. Patients may say their arm belongs or not belongs to them

59



Laterality

- However in experimental pain (Moseley, Sim et al. 2005) and expectation of pain (Hudson, K. et al. 2006) , there is delayed recognition of the opposite limb.
- Limb laterality recognition activates pre motor (association) cortices, not primary motor cortex, imagined movements activate both (Moseley, Schweinhardt et al. 2003), allowing a basis to the GMI progression.

60



Stage 1 GMI Laterality (LRD)

Left/right discrimination is the accuracy and speed of identifying whether a picture or body part is a right or left part of the body (as in the limbs) or tuning to the left or the right (as in the spine). This recognition is altered in some pain states.




61

Judging a left from a right

Rapid initial choice

Mentally manoeuvre body part



Reject or confirmation

(Parsons LM 1987, *Cognitive Psychology*, vol.19, p.178-241)

62


Laterality (L/RD)

1. A critical premotor association neurosignature
2. Known losses in CRPS1 and phantom limb pain. Anecdotally, lost in many ongoing pain states
3. Also altered in ongoing motor perturbations
4. Evolutionary biology perspective
5. Laterality training known to involve pre-motor, not motor areas
6. Seminal work in the area was carried out by Parsons (2001)

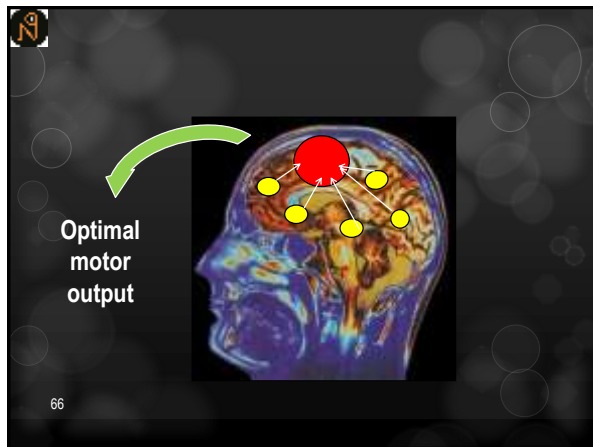
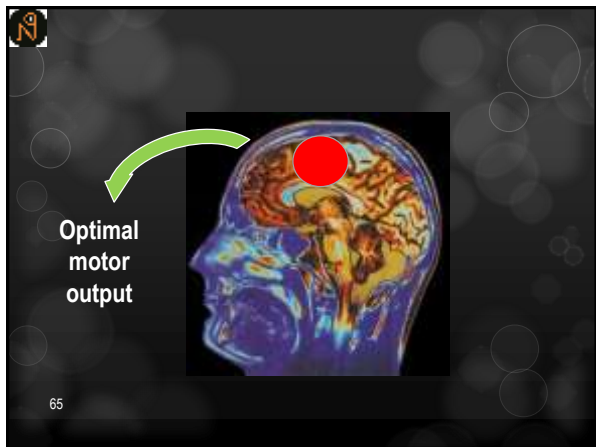
(e.g. Nico D et al 2004 *Brain* 127: 120; Moseley GL 2004 *Neurology* 62: 2186; Parsons L 2001 *Acta Psychologica* 107: 155; Schwobel J et al 2002 *Neurology* 59: 775)

63

Laterality as a premotor neuro signature



64



Acute vs. Chronic

In CRPS1 it takes longer to recognise the affected hand (Moseley GL 2004, *Neurology*, vol.62, p.2182)

Group	Blood response time (ms)
Affected	~7000
Unaffected	~5500
Healthy	~5000
Chronic	~5000

In acute hand pain it takes longer to recognise the non-injected hand (Moseley et al. 2005, *Cognitive Brain Research*, vol.25, p.188, Hudson et al. 2006, *European Journal of Pain*, vol.10, p.219)

67

Laterality reconstruction:

Restoring the brain's ability to recognize left and right

- Recognize: Computer program
- Hands everywhere: Books/magazines/HEP
- Flash cards

68

Recognise online



recognise limb/body laterality online

www.noigroup.com

69

Recognise online

Images of left and right body parts are presented randomly in predetermined;

- numbers (eg 5 to 100)
- time (eg 1 second to 20 seconds)
- Context – vanilla to context to moving

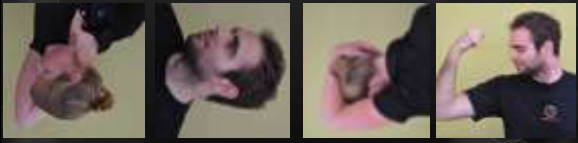
Reaction time and accuracy are scored and graphed.



Images

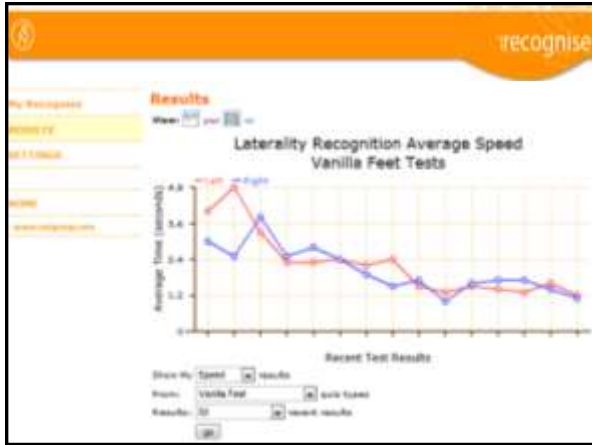
Left - 'a'

Right - 'd'



25% 25% 25% 25%

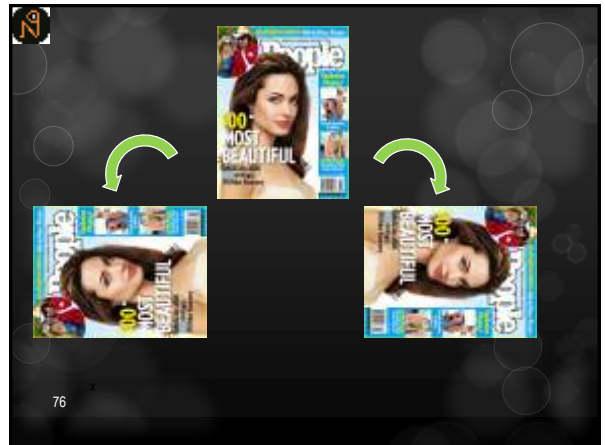


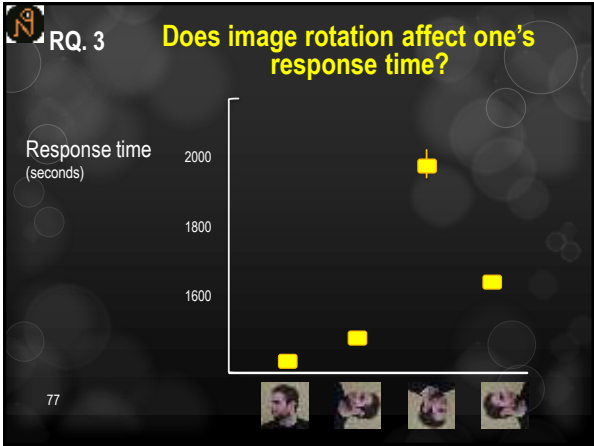


Brand New

○ Recognise™ is the first way to accurately measure the ability to recognize left and right body parts and movements, and to train left/right discrimination as part of a comprehensive rehabilitation program. You can learn more about how left/right discrimination forms part of the graded motor imagery rehabilitation process at www.gradedmotorimagery.com

74







Z⁹ **What is normal ?**

- 1737 participants
(1315 pain-free)
- 65% female
- 40 countries worldwide
- Variety of occupations
e.g. healthcare practitioners,
forestry and farming industry,
education, unemployed

83

Z⁹ **RQ. 1**

a) What is a 'normal' response time?


Necks 1.6 ± 0.5 seconds
Hands 2.0 secs (mean)

b) What is a 'normal' accuracy?

92.5% (median)

84


Recognize/Laterality



- Most people:
 - Correct 90%
 - Ave time = 2.4 sec.
- CRPS
 - Twice as long to recognize (4.7 sec. average)

85

So what?



- Baseline data now available
- No effect of age, gender or handedness
- Rotation effect
- No effect of pain

86

Recent e-mail from a PT

- Hello Again!

First, I'd like to say thank you for the guidance you've given me already; second I'd like to say that I've had success in treating my patient with CRPS, but now I am not sure how to proceed.

- Here's the quick story, we started with looking at pictures of feet--playing games with the pictures (matching, sorting, etc)... and on day 5 the patient woke up with almost total resolution of his pain. He was down to a 2/10. The pain remained low, and by the next day he had 0/10 pain. Yippee!

87

GMI Part 2 Motor Imagery


Mental representation of movement without moving

- The result of conscious access to the neurosignatures representing intention, preparation, carrying out and evaluating a movement
- Note the link to laterality
- Kinaesthetic less visual

88

Part 2 Motor Imagery

It has been used for years in sports, childbirth, healthy people and those with neurological injury. We all do it. (Dickstein and Deutsch 2007)




89

Part 2 Motor Imagery

- Imagined movements can increase pain and swelling in CRPS1 (Moseley 2004)
- May not necessarily be constrained by the biomechanical limitations of the body

90

Motor Imagery Guidelines



- Watch is "less brain effort" than imagining movement
- Static before movement
- Consider (or watch) what it might feel like to have a body part in a certain position
- Consider (or watch) what it might feel like to have a body part doing a certain movement
- Imagining another person less demanding than imagining self

91

Motor Imagery Guidelines

- Could use Recognise, picture books, movies, people, work, dreams etc
- Progression examples
- Smooth gentler movements
- Increase ROM
- Increase speed
- Bring in functional/feared movements
- Use tools
- Alter environment

92

GMI stage 3 Mirror therapy

McCabe S et al 2003
Rheumatology 42:97

Moseley GL 2005
Pain 114:54



93

Practicalities: the mirror box


- Box construction
- Beer cartons can work
- Good quality perspex mirror
- Collapsible to take home



94

Practicalities – from the patients perspective

- Be guided by a clinician who understand brain function
- Sit “evenly” and no jewelry
- Forget the hand in the box at least initially



95

Practicalities – the mirror box

Graded hand activity examples

- Looking at the hand
- Turning hand up and down (elbow movement not hand movement)
- Flattening out the hand
- Flattening the hand and taking some weight through it
- Moving individual fingers
- Finger thumb opposing
- Tapping fingers
- Add increasing muscle activity to each movement
- Use tools (screwdriver, nail cutters, pen scissors etc. – make appropriate to the left or right hand)
- Introduce clinicians' hand
- Touch the face in the mirror

96

Practicalities –the mirror box


Context change

- Place (safe to feared places)
- Emotion
- Time of day
- Try movements distracted (eg while balancing on a chair)
- Music (play a song in your brain) play an external song.
- Sitting, standing, lying
- Use metaphors (eg. Open hand to free a bird, play spiders with the fingers on the mirror)
- Add different smells and noises

97

What about the hand in the box?

- Some move it as well
- Asynchryia
- Move hand in the box as treatment for many hand pains

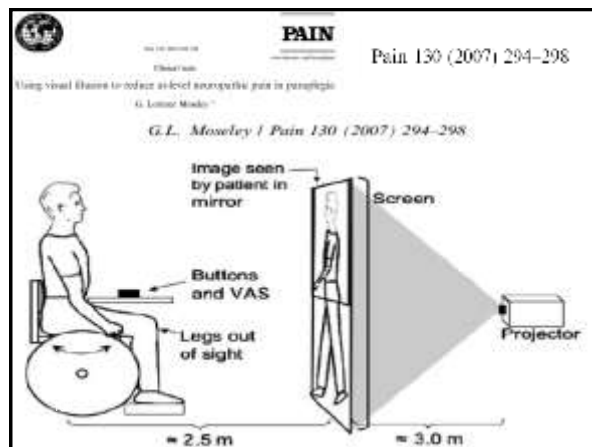


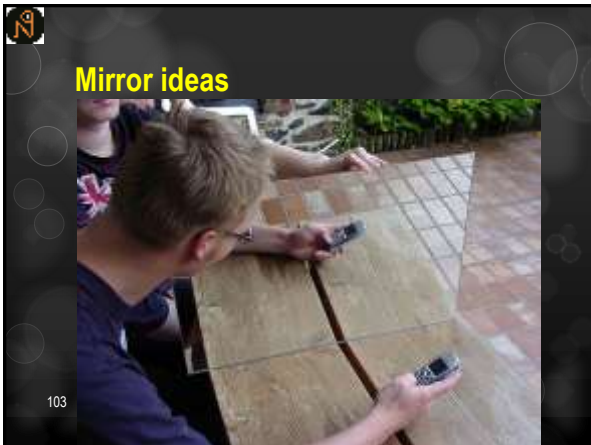
98

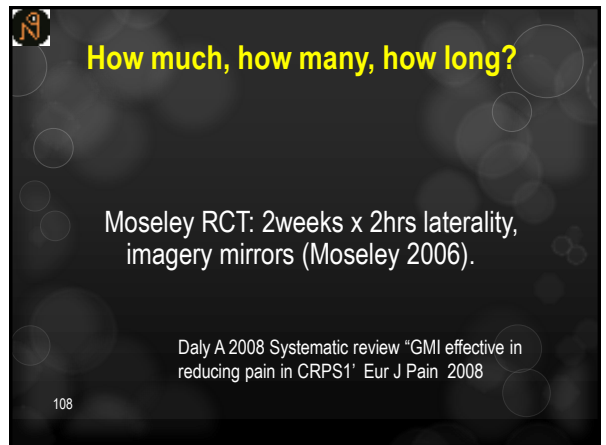
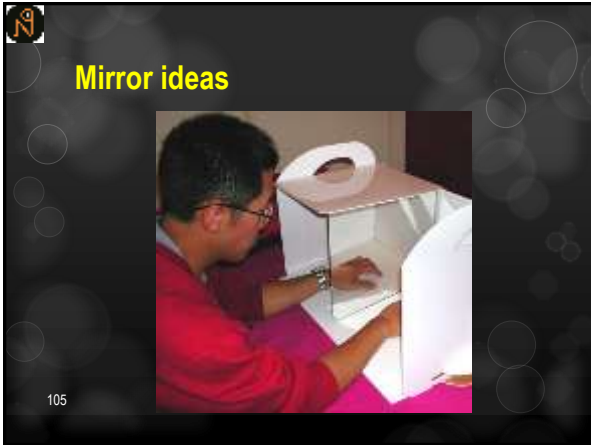
Mirror Therapy

- There is good evidence for the use of mirror therapy alone for acute CRPS (McCabe, Haigh et al. 2003; McCabe, Haigh et al. 2004)
- Mirror therapy alone for phantom limb pain has shown benefits in small trials (Ramachandran and Rogers- Ramachandran 1996; McLachlan, McDonald et al. 2004). There are case reports of successful mirror therapy management of CRPS (Karmarker and Lieberman 2006) and post hand surgery pain (Rosen and Lundborg 2005) in respected medical journals.
- Benefits of mirror box therapy with cognitive behavioural therapy demonstrated in three patients with CRPS1. (Vladimir Tichelar, Geertzen et al. 2007)

99







GMI from the clinical side, anecdotes

1. Around 20% CRPS1 no shift
2. Occasional quick resetting with Left/right discrimination and mirrors (but not like "House")
3. Stress will influence outcomes (L/R discrimination fallouts)
4. May need to go around the whole body with L/R discrimination training
5. May need to do feet for "hot hands" and vice versa
6. Rare "freak-outs"

109

Some clinical anecdotes

8. The place of NS education
9. May help with other perturbed outputs (performance, motor)
10. Mixing treatment not unusual
11. Fun initially: the clinical reasoning, compliance, goal setting and support essential
12. "Learning from the shadows" m- George (www.noigroup.com)
13. Laterality lost in dyslexia

110

Some clinical anecdotes

14. Athletes have superb laterality, but injury may offset it
15. Laterality deficits may be severe enough to use the foot for the hand and vice versa
16. Mirrors used for all hand pains
17. Mirrors for out of plaster stiffness
18. GMI could be pre-emptive
19. Mirrors may be a life time pain management tool for some
20. L/R discrimination may be diagnostic

111

THANK YOU & ACKNOWLEDGEMENTS...

Adriaan@ispinstitute.com

- University of Stellenbosch, South Africa
- Dr. Ina Diener (Stellenbosch)
- David Butler, Neuro Orthopedic Institute
- Dr. Louie Puentedura, UNLV
- International Spine & Pain Institute
- Dr. Lorimer Moseley
- Rockhurst University (Kansas City)
- RehabAuthority (Boise, ID)
- Sports Rehab (Overland Park, KS)
- Orthospineandpain.com
- Iowa PT Association Research Grant



113

Selected References

- Daly AE, Bialocerkowski AE. Does evidence support physiotherapy management of adult Complex Regional Pain Syndrome Type One? A systematic review. *Eur J Pain*. Apr 2009;13(4):339-353.
- Moseley GL. Graded motor imagery is effective for long-standing complex regional pain syndrome: a randomised controlled trial. *Pain*. Mar 2004;108(1-2):192-198.
- Moseley GL. Graded motor imagery is effective for long standing complex regional pain syndrome. *Pain*. 2004;108:192-198.
- Moseley GL. Graded motor imagery for pathologic pain: a randomized controlled trial. *Neurology*. Dec 26 2006;67(12):2129-2134.
- Moseley GL. Graded motor imagery for pathologic pain. *Neurology*. 2006;67:1-6.
- Chapman CR. Neuromatrix Theory. *Pain Forum*. 1996;5:139-142.
- Derbyshire SW, Whalley MG, Oakley DA. Fibromyalgia pain and its modulation by hypnotic and non-hypnotic suggestion: an fMRI analysis. *European Journal of Pain*. May 2009;13(5):542-550.
- George SZ, Wittmer VT, Fillingim RB, Robinson ME. Fear-avoidance beliefs and temporal summation of evoked thermal pain influence self-report of disability in patients with chronic low back pain. *J Occup Rehabil*. Mar 2006;16(1):95-108.
- Melzack R. Phantom limbs and the concept of a neuromatrix. *Trends Neurosci*. 1990;13:88-92.
- Melzack R. Gate control theory: on the evolution of pain. *Pain Forum*. 1996;5:128-138.
- Melzack R. From the gate to the neuromatrix. *Pain*. Aug 1999;Suppl 6:S121-126.
- Melzack R. Pain and the neuromatrix in the brain *Journal of Dental Education*. 2001;65:1378-1382.

114

Selected References

- Moseley GL. A pain neuromatrix approach to patients with chronic pain. *Man Ther*. Aug 2003;8(3):130-140.
- Moseley GL. A pain neuromatrix approach to rehabilitation of chronic pain patients. *Man Ther*. 2003;8:130-140.
- Moseley GL. A pain neuromatrix approach to patients with chronic pain. *Manual therapy*. Aug 2003;8(3):130-140.
- Nielsen JB, Cohen LG. The Olympic brain. Does corticospinal plasticity play a role in acquisition of skills required for high-performance sports? *J Physiol*. Jan 1 2003;556(1):65-70.
- Haggard P, Taylor-Clarke M, Kennet S. Tactile perception, cortical representation and the bodily self. *Current Biology*. 2003;13R170-R173.
- Reddy H, Bendahan D, lee MA, et al. An expanded cortical representation for hand movement after peripheral motor denervation. *Journal of Neurology, Neurosurgery, and Psychiatry*. 2002;72:203-210.
- Flor H. The functional organization of the brain in chronic pain. *Prog Brain Res*. 2000;129:313-322.
- Flor H. The functional organization of the brain in chronic pain. In: Sandkühler J, Bromm B, Gebhart GF, eds. *Progress in Brain Research*, Vol 129. Amsterdam: Elsevier; 2000.
- Flor H. The image of pain. Paper presented at: Annual scientific meeting of The Pain Society (Britain)2003, Glasgow, Scotland.
- Flor H, Birbaumer N, Schugens MM, Lutzenberger W. Symptom specific psychophysiological responses in chronic pain patients. *Psychophysiology*. 1992;29:452-460.
- Flor H, Braun C, Elbert T, Birbaumer N. Extensive reorganization of primary somatosensory cortex in chronic back pain patients. *Neurosci Lett*. 1997;224(1):5-8.
- Flor H, Braun C, Elbert T, Birbaumer N. Extensive reorganisation of primary somatosensory cortex in chronic back pain patients. *Neurosci Lett*. 1997;244:5-8.
- Flor H, Devor M, Jensen T, Phantom Limb Pain. Causes and Cures. In: Dostrovsky JO, Carr DB, Kolzenburg M, eds. *Progress in Pain Research and Management*. Vol 24. Seattle. IASP Press; 2003.

115

Selected References

- Flor H, Elbert T, Knecht C, et al. Phantom limb pain as a perceptual correlate of cortical reorganisation following arm amputation. *Nature*. 1995;375:482-484.
- Flor H, Elbert T, Mühnickel W, Parvez C. Cortical reorganisation and phantom phenomena in congenital and traumatic upper-extremity amputees. *Experimental Brain Research*. 1988;119:205-212.
- Flor H, Turk DC. Integrating central and peripheral mechanisms in chronic muscular pain. An initial step on a long road. *Pain Forum*. 1996;5:74-76.
- van Rijn MA, Marinus J, Putter H, Bosselaar SR, Moseley GL, van Hilten JJ. Spreading of complex regional pain syndrome: not a random process. *J Neural Transm*. Sep 2011;118(9):1301-1309.
- van Rijn MA, Marinus J, Putter H, Bosselaar SR, Moseley GL, van Hilten JJ. Spreading of complex regional pain syndrome: not a random process. *J Neural Transm*. Feb 18 2011.
- Munts AG, Muegge W, Mours TS, et al. Fixed dystonia in complex regional pain syndrome: a descriptive and computational modeling approach. *BMC Neurol*. 2011;11:53.
- Marinus J, Moseley GL, Birklein F, et al. Clinical features and pathophysiology of complex regional pain syndrome. *Lancet Neurol*. Jul 2011;10(7):637-648.
- Harden RN. Objectification of the diagnostic criteria for CRPS. *Pain Med*. Aug 2010;11(8):1212-1215.
- Moseley GL, Wiech K. The effect of tactile discrimination training is enhanced when patients watch the reflected image of their unaffected limb during training. *Pain*. Aug 2009;144(3):314-319.
- Moseley GL, Gallace A, Spence C. Space-based, but not arm-based, shift in tactile processing in complex regional pain syndrome and its relationship to cooling of the affected limb. *Brain*. Nov 2009;132(Pt 11):3142-3151.
- Moseley GL, Zalucki NM, Wiech K. Tactile discrimination, but not tactile stimulation alone, reduces chronic limb pain. *Pain*. Jul 31 2008;137(3):600-608.
- Moseley GL, Zalucki N, Birklein F, Marinus J, van Hilten JJ, Luomajoki H. Thinking about movement hurts: the effect of motor imagery on pain and swelling in people with chronic arm pain. *Arthritis Rheum*. May 15 2008;50(5):623-631.

116

Selected References

- Perez RS, Collins S, Marinus J, Zuromond WW, de Lange JJ. Diagnostic criteria for CRPS I: differences between patient profiles using three different diagnostic sets. *Eur J Pain*. Nov 2007;11(8):895-902.
- Moseley GL, Zalucki NM, Wiech K. Tactile discrimination, but not tactile stimulation alone, reduces chronic limb pain. *Pain*. Dec 1 2007.
- Gallagher RM. Diagnostic criteria for CRPS: balancing the needs of clinicians and investigators. *Pain Med*. May-Jun 2007;9(4):289-292.
- Moseley GL, Sim DF, Henry ML, Souvils T. Experimental hand pain delays recognition of the contralateral hand—evidence that acute and chronic pain have opposite effects on information processing? *Brain Res Cogn Brain Res*. Sep 2005;25(1):188-194.
- Moseley GL, Sim DF, Henry ML, Souvils T. Experimental hand pain delays recognition of the contralateral hand—evidence that acute and chronic pain have opposite effects on information processing? *Brain Res Cogn Brain Res*. Sep 2005;25(1):188-194.
- Moseley GL. Is successful rehabilitation of complex regional pain syndrome due to sustained attention to the affected limb? A randomised clinical trial. *Pain*. Mar 2005;114(1-2):54-61.
- de Jong JR, Vlaeyen JW, Onghena P, Cuypers C, den Hollander M, Rutgrok J. Reduction of pain-related fear in complex regional pain syndrome type I: the application of graded exposure in vivo. *Pain*. Aug 2008;118(3):264-275.
- Acerra NE, Moseley GL. Dysrhythmia: watching the mirror image of the unaffected limb elicits pain on the affected side. *Neurology*. Sep 13 2005;65(5):751-753.
- Moseley GL. Why do people with complex regional pain syndrome take longer to recognize their affected hand? *Neurology*. Jun 22 2004;62(12):2182-2188.
- Moseley GL, Schweinhardt P, Wise R, Tracey I. Virtual, imagined and mirror movements - a novel approach to complex regional pain syndrome (CRPS1). Paper presented at: Europ Fed IASP Chapt Triennial Conference2003, Prague.
- Harden RN. A clinical approach to complex regional pain syndrome. *Clin J Pain*. Jun 2000;16(2 Suppl):S26-32.
- Harden RD. A clinical approach to complex regional pain syndrome. *The Clinical Journal of Pain*. 2000;16:S26-S32.

117

Selected References

- Moseley GL, Olthof N, Venema A, et al. Psychologically induced cooling of a specific body part caused by the illusory ownership of an artificial counterpart. *Proc Natl Acad Sci U S A*. Sep 2 2008;105(35):13169-13173.
- Maihofner C, Handwerker HO, Neundörfer B, Birklein F. Patterns of cortical reorganization in complex regional pain syndrome. *Neurology*. Dec 23 2003;61(12):1707-1715.
- Elbert T, Candia V, Altenmüller E, et al. Alteration of digital representations in somatosensory cortex in focal hand dystonia. *Neuroreport*. Nov 16 1998;9(16):3571-3575.
- Stavrinou ML, Della Penna S, Pizzella V, et al. Temporal dynamics of plastic changes in human primary somatosensory cortex after finger webbing. *Cereb Cortex*. Sep 2007;17(9):2134-2142.
- Joutonen K, Cöckel M, Silen T, et al. Altered central sensorimotor processing in patients with complex regional pain syndrome. *Pain*. 2002;98:315-323.
- Milligan ED, Twining C, Chacur M, et al. Spinal glia and proinflammatory cytokines mediate mirror-image neuropathic pain in rats. *J Neurosci*. Feb 1 2003;23(3):1026-1040.
- Gallese V, Fadiga L, Fogassi L, Rizzolatti G. Action recognition in the premotor cortex. *Brain*. 1996;119:593-609.

118

Selected References

- Singer T, Seymour B, O'Doherty JP, Stephan KE, Dolan RJ, Frith CD. Empathic neural responses are modulated by the perceived fairness of others. *Nature*. 2006;439:466-469.
- Schwoebel J, Coslett HB, Bradt J, Friedman R, Dileo C. Pain and the body schema: effects of pain severity on mental representations of movement. *Neurology*. 2002;59:775-777.
- Schwoebel J, Friedman R, Duda N, Coslett HB. Pain and the body schema. *Brain*. 2001;124:2098-2104.
- Nico D, Daprati E, Rigal F, Parsons L, Siragu A. Left and right hand recognition in upper limb amputees. *Brain*. 2004;127:120-132.
- Hudson ML, McCormick K, Zalucki N, Moseley GL. Expectation of pain replicates the effect of pain in a hand laterality recognition task: bias in information processing toward the painful side? *Eur J Pain*. Apr 2006;10(3):219-224.
- Parsons AA, Stribos PJ. The neuronal versus vascular hypothesis of migraine and cortical spreading depression. *Curr Opin Pharmacol*. Feb 2003;3(1):73-77.
- Dickstein R, Deutsch JE. Motor imagery in physical therapist practice. *Physical therapy*. Jul 2007;87(7):942-953.
- McCabe CS, Haigh RC, Ring EFR, Halligan P, Blake DR. A controlled pilot study of the utility of mirror visual feedback in the treatment of complex regional pain syndrome (type 1). *Rheumatology (Oxford)*. 2003;42:97-101.