EVIDENCE FOR A WINDOW OF ENHANCED NEUROPLASTICITY FOLLOWING ISCHAEMIC STROKE

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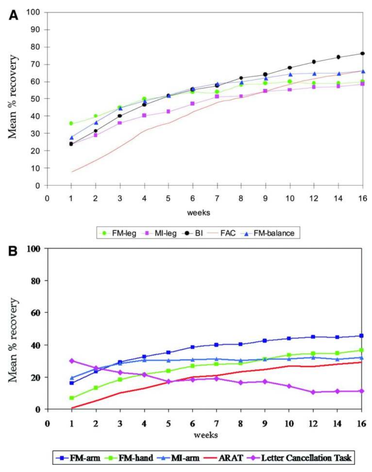
Recovery following stroke tends to asymptote between 3 and 6 months across a variety of functional measures (Kwakkel et al, 2006).

In animal models of stroke, a bihemispheric increase in dendritic sprouting is observed lasting 10-14 days.



from Kwakkel et al, 2006

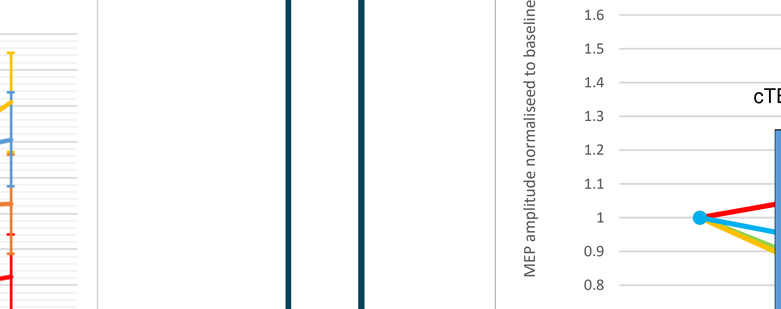
These facts combined have giving rise to the theory that a critical "window" of enhanced neuroplasticity exists in human stroke patients.

We set out to delineate for the first time the duration of any such enhanced neuroplasticity following ischaemic stroke.

How does TMS probe neuroplasticity?

Transcranial magnetic stimulation over motor cortex can depolarise the cortico-spinal tract, evoking a motor-evoked-potential (MEP) in contra-lateral skeletal muscle.

Repetitive TMS can produce transient changes in CST excitability that resemble synaptic Long Term Depression (LTD) and Potentiation (LTP), providing a non-invasive marker of neuroplasticity in the motor cortex.



Subjects

29 patients (average age 68.2yrs) attended for recording from the contralesional hemisphere (UCL) at 2, 4, and 6 weeks and 6 months (TIME) after first ischaemic stroke. 15 patients (average age 68yrs) had recordings from the ipsilesional hemisphere (UoA) at weeks 2, 3, 4 and 8. All subjects had made a good functional recovery with FMUL > 58 or ARAT > 55 after 4 weeks.

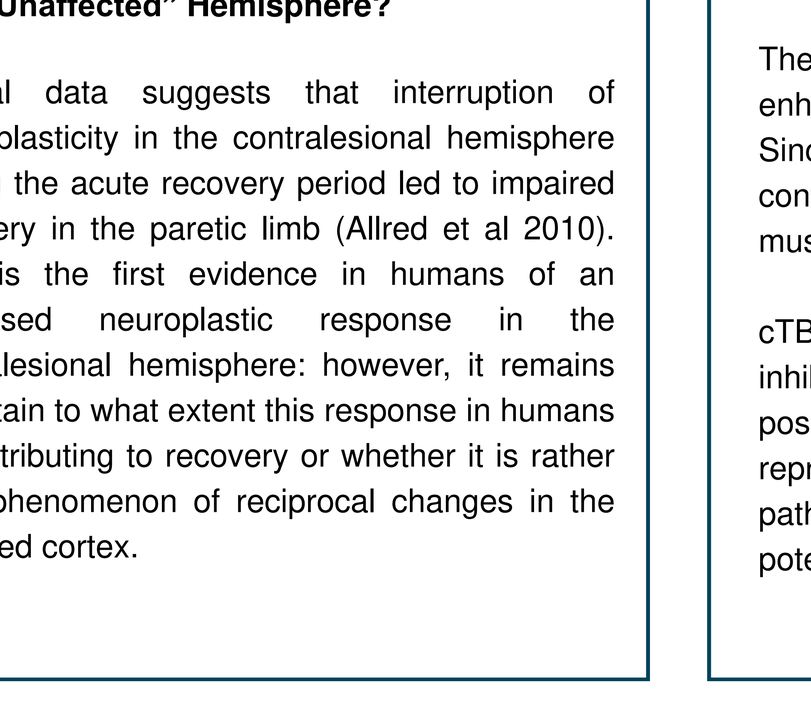
Methods

Subjects received TMS in a spaced theta burst protocol (Goldsworth et al, 2012) to either ipsilesional or contralesional M1, with change in motor evoked potentials (MEPs) over 30/45 minutes as a measure of neuroplastic effect (PLASTICITY).

Averaged normalised MEPs were analysed for each group in a two-way rmANOVA with factors TIME and PLASTICITY.

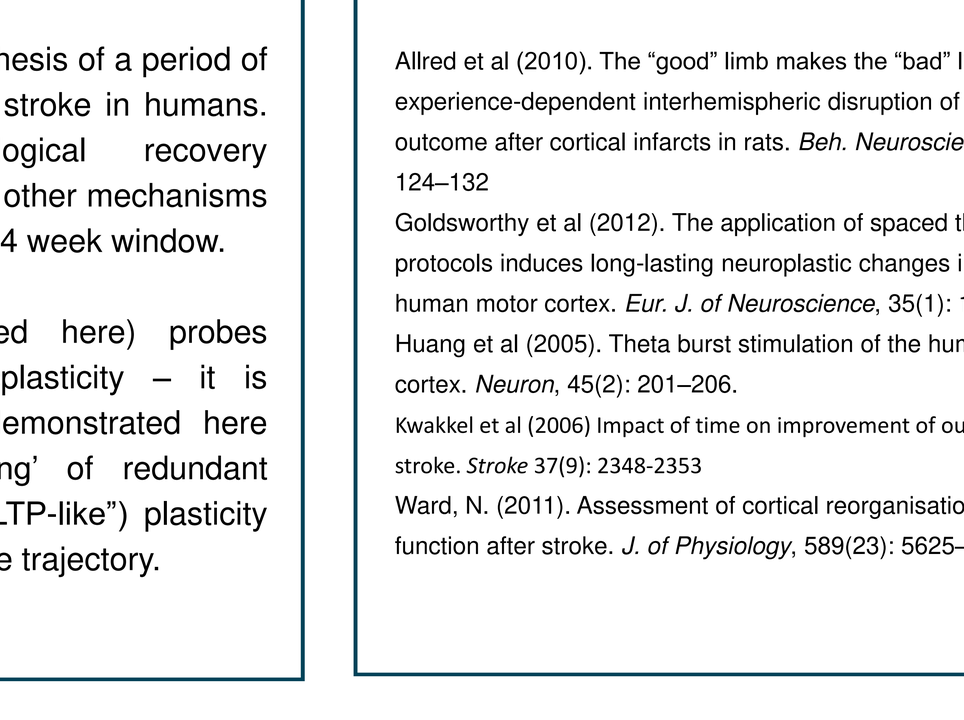
RESULTS – Contralesional Hemisphere

There was no difference in baseline excitability between the stroke and non-stroke hemisphere (p=0.46). There a significant PLASTICITY*TIME interaction (p=0.01), with greater inhibitory plastic response in weeks 2 and 4.



RESULTS– Ipsilesional Hemisphere

There was also a significant effect of WEEK (p=0.04) in the ipsilesional motor cortex, with greatest inhibition of MEPs in weeks 3 and 4.



The "Unaffected" Hemisphere?

Animal data suggests that interruption of neuroplasticity in the contralesional hemisphere during the acute recovery period led to impaired recovery in the paretic limb (Allred et al 2010). This is the first evidence in humans of an increased neuroplastic response in the contralesional hemisphere: however, it remains uncertain to what extent this response in humans is contributing to recovery or whether it is rather an eiphenomenon of reciprocal changes in the lesioned cortex.

A Critical Period?

These data support the hypothesis of a period of enhanced plasticity following stroke in humans. Since spontaneous biological recovery continues beyond this period, other mechanisms must be at play outside this 2-4 week window.

cTBS, (the protocol utilised here) probes inhibitory ("LTD-like") neuroplasticity – it is possible that the window demonstrated here represents an early 'pruning' of redundant pathways, with facilitatory ("LTP-like") plasticity potentially following a separate trajectory.

REFERENCES

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