

## THE INTERACTION OF BRAIN PATHWAYS AND SACRAL REFLEXES FOLLOWING SPINAL LESIONS IN MAN

### Hypothesis / aims of study

Spinal cord injury (SCI) interrupts pathways that normally coordinate bladder and sphincter function. Previous studies have shown that in most people with a complete SCI the so-called "bladder guarding reflex (BGR)," a response which helps to maintain continence by increasing tone in the striated urethral sphincter as the bladder fills, is absent up to the point of neurogenic detrusor overactivity (1). The BGR then becomes exaggerated during detrusor-sphincter dyssynergia causing obstructed voiding (2).

Recently it has been shown that by monitoring the pudendo-anal reflex (PAR) these aberrant sacral reflexes can also be demonstrated in people with incomplete SCI (3). Furthermore, the potential for utilising preserved voluntary pathways in this SCI group may well help to restore normal function by facilitating sacral reflexes such as the PAR. The aim of this preliminary study was to investigate the relationship between the activation of cortico-spinal pathways using transcranial magnetic stimulation (TMS) and the PAR comparing people with and without incomplete spinal cord injuries.

### Study design, materials and methods

Three subjects without spinal cord injuries and two with incomplete ASIA D (ASIA – American Spinal Injuries Association) neurologically graded supra-sacral spinal cord injuries were recruited following appropriate informed consent.

Electromyographic activity of the external anal sphincter (a surrogate for the striated urethral sphincter) was recorded by an anal-probe electrode. The pudendo-anal reflex (PAR) was elicited by electrical stimulation of the pudendal afferent nerves (DPN/DCN - dorsal penile/clitoral nerves) using a doublet pulse (200µs pulse duration at 2ms intervals) at a strength sufficient to evoke a response approximately half maximum (latency range 19-24 ms). Cortical stimulation of the anal sphincter was achieved by transcranial magnetic stimulation (TMS) using a double-cone coil optimally placed and centred over the vertex (Cz) (latency range 24-26 ms). To examine the effect of TMS on the PAR and vice versa, the strength of TMS was set to produce a near threshold sphincter response.

### Results

Figure 1A shows the experimental arrangement of subject, the transcranial magnetic stimulation (TMS) and dorsal penile electrical nerve stimulation (DPENS) with their respective evoked responses, the motor evoked potential (MEP) of the anal sphincter and pudendo-anal reflex (PAR). Conditioning of the PAR by near-threshold transcranial magnetic stimulation TMS of the motor cortex is shown for one non-SCI subject in Figure 1B. Top to bottom: changing conditioning interval from TMS at -80 ms to TMS at +80 ms relative to the DPN stimulation at time zero. The PAR is highlighted by a vertical grey box. Any response to TMS is marked with a star. Note the maximal facilitation of the PAR at -20 ms to 0ms conditioning interval in a non-SCI subject. Interestingly, in this subject, when the PAR became the conditioning stimulus there was sometimes a significant facilitation of the TMS at +20 and +80 ms. The graph (Figure 1C) shows the results of the condition-testing protocol as described in B for the three non spinal cord injured subjects (open circles) and the two incomplete SCI subjects (closed circles).

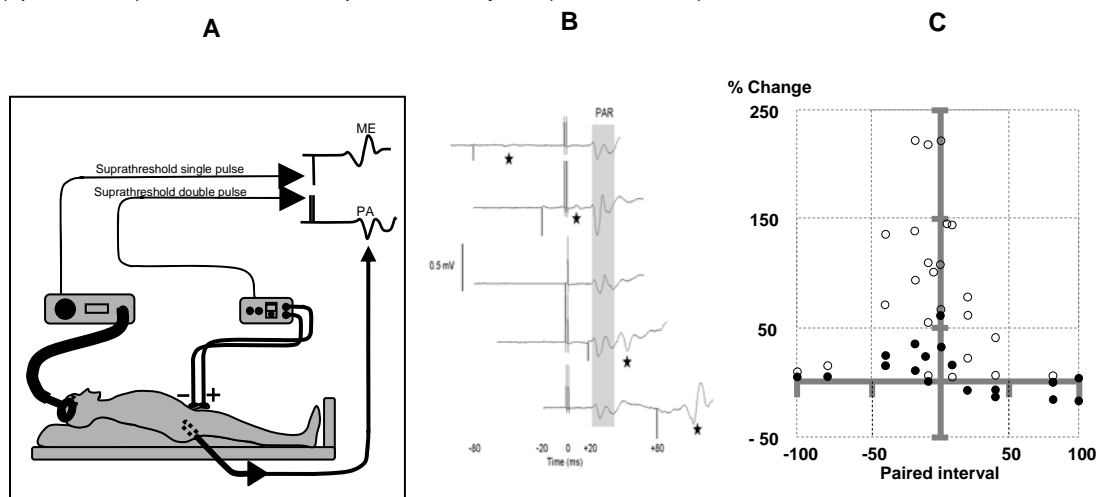


Figure 1.

### Interpretation of results

Conditioning a test PAR response by TMS resulted in facilitation of the PAR. Facilitation started when the TMS preceded DPN stimulation by 25-50 ms, reached a peak for near simultaneous stimuli and was absent when TMS occurred after DPN stimulation. The peak of facilitation was greater than 200% increase in the PAR for the non-SCI subjects. In comparison, the facilitation in the SCI subjects was only about 50% but the time course of facilitation was similar. These findings suggest that such condition-testing will be useful for assessing the efficacy of any technique aimed at restoring normal function of the bladder and sphincter function in spinal cord injury.

#### Concluding message

Further experiments are now being conducted to identify the site(s) of interaction of these pathways and to determine whether the aberrant neural mechanisms in SCI might be responsive to repetitive TMS by tapping into neural plasticity for restoring normal facilitatory function.

#### References

1. J Urol. (1982) 127; 953-957
2. Brit J Urol. (1997) 80; 940-945
3. Prog Brain Res. (2006) 152; 205-219.

**FUNDING:** International Spinal Research Trust and RNOH Academic Research Board

**HUMAN SUBJECTS:** This study was approved by the COREC & RNOH LREC, UK and followed the Declaration of Helsinki Informed consent was obtained from the patients.