C137

Shaping of respiratory drive currents by phasic inhibition in hypoglossal motoneurones and modulation of inhibition by protein kinase A

S.A. Saywell and J.L. Feldman

Department of Neurobiology, UCLA, Los Angeles, CA 90095, USA

Inspiratory drive to hypoglossal (XII) motoneurones is mediated predominantly via AMPA receptors (Funk *et al.* 1993). The effect of inhibition upon inspiratory drive currents, and its functional significance for respiratory-related motor output is unclear. Here, we describe phasic inhibition in XII motoneurons, its effect on inspiratory drive currents, and modulation of this inhibition by protein kinase A (PKA).

Neonatal rats were anaesthetized by hypothermia and rapidly decerebrated. A 700 μm medullary slice that generates a respiratory-related rhythm (Smith *et al.* 1991) was cut. Slices were superperfused with ACSF (28 °C, $[K^+]$ 9 mM). The activity of the hypoglossal nerve was amplified, rectified, integrated and used to define the inspiration. All measurements were normalized to the duration of the corresponding inspiratory period and expressed as a percentage of that period. Whole-cell voltage-clamp recordings ($V_h = -70$ mV, -100 mV for reversal) were made from XII motoneurones. IPSCs were reversed immediately after whole-cell patch formation. Drugs were either included in the patch electrode or bath applied.

Motoneurones were divided into three groups based upon the level of inhibitory drive: non-inhibited (NIM) ($n = 6$), late-inspiratory inhibited (LIM) ($n = 15$) and inspiratory inhibited (IIM) ($n = 7$). In LIMs inspiratory drive currents were truncated (56 ± 28 %) compared with the NIMs (101 ± 5 %, $P < 0.01$) with no significant difference in the duration of nerve activity. Inhibition in LIMs persisted 131 ± 33 % into post-inspiration. IIMs were inhibited through the inspiratory period in the apparent absence of excitatory drive currents. Bicuculline (200μM) abolished inspiratory and post-inspiratory inhibition, increased the duration and amplitude of inspiratory drive currents in LIMs ($n = 9$, $P < 0.01$), whereas in NIMs it did not markedly alter the currents. In IIMs bicuculline revealed excitatory currents ($n = 4$), indicating that phasic inhibition gated out excitatory drive currents.

Intracellular dialysis of the catalytic subunit of PKA (250 units ml^{-1}) ($n = 7$) and Sp-cAMP ($n = 6$) both increased inhibitory charge transfer, the amplitude of inspiratory phased inhibitory currents and expiratory phased IPSCs ($P < 0.01$). Mini-analysis of IPSCs suggested that these effects are mediated postsynaptically.

Phasic GABAergic inhibition is common in XII motoneurones and is important in gating and shaping motoneurone output. These inputs are modulated by PKA. Results are given as means $\pm$ s.d., $P < 0.05$ is considered significant (unpaired *t* tests).

Funk GD *et al.* (1993). *J Neurophysiol* **70**, 1497–1515.

Smith JC *et al.* (1991). *Science* **254**, 726–729.

C138

Contribution of feline group IV muscle afferents to a reflex increase during acute muscle inflammation

E.D. Schomburg and H. Steffens

Institute of Physiology, University of Göttingen, Humboldtallee 23, 37073 Göttingen, Germany

The contribution of group III and IV muscle afferents from free nerve endings to pathological motor phenomena resulting in chronic muscle pain is still under debate. The hypothesis that muscular nociceptors support their own activation by an increase of muscle stiffness via the gamma-spindle-loop has been questioned since gamma-activity was inhibited during artificial myositis (Mense & Skeppar, 1991).

Therefore, we investigated the effect of an acute carrageenan-induced myositis of the gastrocnemius-soleus (GS) on mono-synaptic reflexes of flexors (posterior biceps semitendinosus, peroneus) and extensors (GS, quadriceps, anterior biceps semimembranosus, tibialis) and on spinal motor reflex pathways from group III and group IV muscle afferents (activated by injection of KCl or bradykinin into the muscle artery of GS) without and with blocking all myelinated fibres in the GS nerve by TTX (100 μM). With approval of the local ethical committee the experiments were performed in anaemically decapitated high spinal, paralysed (pancuronium bromide) cats (initial anaesthesia before decapitation and paralysis: O_2/N_2O, 1:2, halothane initially 2.5 %, then increasingly replaced by ether, as required for full anaesthesia; for technical details, see Schomburg *et al.* 2001). Finally the animals were humanely killed.

In experiments without application of TTX, i.e. with intact conduction in group III and group IV afferents, the monosynaptic reflexes of flexors and extensor showed a distinct increase after infiltration of GS with carrageenan (1 %) and a slight increase of the facilitation of the flexors by chemically activated group III and IV afferents. The inhibition from these afferents to the extensors reacted less uniformly. The effects of carrageenan started within 1 h, reached their maximum after 1.5 h and generally returned to the control values after about 3.5–4 h.

After application of TTX, i.e. with a block of myelinated fibres, but intact conduction in group IV fibres (Schomburg & Steffens, 2002) the effects of carrageenan and their time course were similar to those without TTX block.

The results show that the input from acutely inflamed muscles may induce an increase of the reflex responsiveness of flexors and extensors, which is not mediated via the gamma-spindle-loop. Since the effects also occurred after a block of all myelinated fibres from the inflamed muscle by TTX, a distinct part of the effects can be assumed to be induced by group IV muscle afferents.

Mense S & Skeppar P (1991). *Pain* **46**, 201–210.

Schomburg ED & Steffens H (2002). *Neurosci Res* **44**, 213–223.

Schomburg ED *et al.* (2001). *J Physiol* **536**, 605–613.

C139

Receptive fields of cerebellar Golgi cells to widely separated peripheral inputs

T. Holtzman, T. Rajapaksa and S.A. Edgley

Department of Anatomy, University of Cambridge, Dowming Street, Cambridge, UK

Golgi cells are an important element of the cerebellar cortical circuitry. They inhibit granule cells, which are the only excitatory cells in the cerebellar cortex, and are thus in a position to mediate transmission into the cortex through the mossy fibre pathway. Previous work has shown that these neurones respond to activation of an excitatory peripheral receptive field with brief accelerations of their spike activity (e.g. Vos *et al.* 2000). In this study we describe a different response to peripheral inputs.

The experiments were performed in seven rats under general anaesthesia (urethane 1000 mg kg^{-1} I.P., supplemented if required). At the end of the experiments the animals were killed with an overdose of the anaesthetic. Using a multiple microelectrode device we were able to record from up to seven Golgi cells simultaneously within a small (1 mm^2) area of cortex over crus II. Brief electrical stimuli delivered through percutaneous pins were used to activate peripheral afferents. We characterised the responses of Golgi cells into three stereotypical types: short latency excitations (as described previously), short latency depressions of firing and long latency depressions of firing. The latter was the most common response we encountered (69 % of cells tested). Furthermore this response was frequently evoked from multiple peripheral sites (bilaterally, from fore- and hindlimbs and face). From studies in which we directly stimulated isolated peripheral nerves we were able to evoke these responses with weak stimuli (< 2 T). Thus large myelinated mechanoreceptive afferents are likely to contribute to them.

The nature of these responses is puzzling: there are few known candidates that could mediate postsynaptic inhibition of Golgi cells. Purkinje cell collaterals are one possibility, but Purkinje cells local to the Golgi cells we recorded seldom responded to the stimuli we used, so local collaterals were unlikely to have mediated these effects. The depression in firing rate was often sustained and substantial, suggesting that it would be accompanied by a powerful effect on granule cells. The widespread nature of the long latency depressions in Golgi cell firing suggest that they are evoked through a pathway with widespread convergence. The identity of this pathway is currently under investigation.

Vos BP *et al.* (2000). *Prog Brain Res* **124**, 95–106.

C140

Activity of Group II interneurones during fictive locomotion and scratch in the feline spinal cord

S. Chakrabarty, K. Stecina, J.S. Riddell*, S. Gosgnach, M. Lafreniere-Roula, S.J. Shefchyk and D.A. McCrea

*Department of Physiology, University of Manitoba, Winnipeg, Canada and *Institute of Biomedical and Life Sciences, University of Glasgow, Glasgow, UK*

Activity in muscle spindle secondary (group II) afferents can have powerful actions on the step cycle, with some afferents (e.g. those from tibialis anterior, TA) causing a prolongation of ongoing flexion and others (e.g. extensor digitorum longus, EDL) advancing the onset of extension (Perreault *et al.* 1995; McCrea *et al.* 2000). In decerebrate cats with intact spinal cords, neither of these actions appears to be a part of the flexion reflex. Here we report on interneurones that are excited by group II muscle afferents located in lower lumbar (L6–L7) segments, during fictive locomotion (*n* = 19) or fictive scratch (*n* = 3) in four decerebrate cats.

Adult cats were anaesthetised with halothane and subsequently decerebrated at a precollicular level. Fictive locomotion was induced by electrical stimulation of the mesencephalic locomotor region (MLR; e.g. see Perreault *et al.* 1995) and fictive scratch was produced by topical application of curare to the cervical dorsal roots (Feldberg & Fleischhauer, 1960). Electrical stimuli (up to 5 T) were applied to peripheral nerves to identify interneurones and perturb the step cycle. Rhythmic EMG activity was recorded from hindlimb muscle nerves and recordings made from interneurones using glass microelectrodes. All protocols followed conformed to local guidelines (for full details of the preparation, see Perreault *et al.* 1995).

Half (11/22) of the group II excited interneurones were either completely or partially inhibited in both the flexion and extension phases. Five interneurones were active during flexion, three during extension, while three fired action potentials through the transition between flexion and extension or *vice versa*. Two of the interneurones active through the transition, between extension and flexion, during locomotion were active only in the extension phase during scratch. Activity of group II interneurones during fictive behaviours in the absence of afferent input indicates that some of the interneurones are part of the central pattern generating network. In addition, the excitability of some interneurones with input from ankle flexor group II afferents is centrally regulated to relay proprioceptive spindle secondary input to the spinal cord at particular times. Identification of the targets and actions of these interneurones will be an important goal for further understanding how these systems regulate stepping.

Feldberg W & Fleischhauer K (1960). *J Physiol* **151**, 502–517.

McCrea DA *et al.* (2000). *Soc Neurosci Abs* **26**, 460.2.

Perreault MC *et al.* (1995). *J Physiol* **487**, 211– 220.

C141

High-frequency modulation of the excitability of the human motor cortex by median nerve stimulation

A.J.S. Webb and S.A. Edgley

Department of Anatomy, Downing Street, Cambridge CB2 3DY, UK

Activation of corticospinal neurons by transcranial magnetic stimulation (TMS) is complex, the most notable features being recurrent discharges attributed to indirect activation (I-waves) at intervals of about 1.6 ms, which may vary dependent on coil type and orientation (e.g. Di Lazzaro *et al.* 2001). The interval between the I-waves is interesting since stimulation of the median nerve evokes synchronous oscillatory discharges in the somatosensory cortex at about 600 Hz (Gobbele *et al.* 1998), thus the interval between successive waves is about 1.6 ms. It is unknown whether these phenomena are linked. We have investigated this in the current experiments.

Experiments were performed on sixteen healthy volunteers with informed consent (11 males, 5 females) aged 20–43 years. The University of Cambridge Human Biology Research Ethics Committee approved the experiments. In each subject we first recorded the EEG response to median nerve stimulation (1.0 × motor threshold at the wrist). The oscillatory potentials at ~600 Hz in the somatosensory cortex were identified in the averaged (> 2000 sweeps) EEG response after digital filtering (500–700 Hz bandpass). After identifying the timing of the major peaks, an experimental protocol was set up so that TMS stimuli could be delivered at one of eight intervals spaced at 0.4 ms intervals after the median nerve stimulus, to span the first two complete cycles of the EEG oscillation. Stimuli at the different intervals were delivered in random sequence, interspersed with TMS only stimuli. Muscle-evoked potentials (MEPs) were recorded from hand muscles (thenar and first dorsal interosseus) and forearm muscles (extensor digitorum and flexor digitorum superficialis).

For initial analysis we examined whether the amplitudes of MEPs recorded at the eight points showed two peaks or two troughs, separated by 1.6 ms. 49 % of the data sets fulfilled this criterion, whereas by binomial distribution 21 % of data sets would be expected to. A Monte Carlo test showed that the presence of a modulation was highly probable ($P < 0.01$). Grouped analysis was undertaken by combining data across subjects aligned to the peak of the EEG burst in each case. The data for the thenar muscles showed a clear tendency for modulation at ~600 Hz, which was shown to be highly significant ($P < 0.01$) by a Monte Carlo test and Fourier analysis of the resultant waveforms.

The results suggest that the oscillatory activity set up in somatosensory cortex by median nerve stimulation is correlated with excitability changes in motor cortex, seen as modulations of the amplitude of MEPs evoked by TMS at different intervals after the median nerve stimulus. These findings may have implications for the origin of I-waves and sensorimotor integration.

Di Lazzaro V *et al.* (2001). *Exp Brain Res* **138**, 268–273.

Gobbele R *et al.* (1998). *Electroencephalogr Clin Neurophysiol* **108**, 182–189.

C142

Cutaneomuscular responsiveness of the first dorsal interosseous muscle to distant stimulation is altered in a chronic partial median nerve entrapment at the wrist in man

L.C. Turner, L.M. Harrison and J.A. Stephens

Department of Physiology, University College London, Gower Street, London WC1E 6BT, UK

In a previous study, Caccia *et al.* (1973) described the reflex responses of hand muscles to stimulation of the digital nerves of different fingers in man. In this study, we have found that reflex cutaneomuscular responsiveness to stimulation of the digital nerves of the little finger is altered in subjects with carpal tunnel syndrome, a chronic partial median nerve entrapment at the wrist (CPNE).

Recordings were obtained from the preferred hand of 17 adult subjects with CPNE and 12 healthy subjects. CPNE subjects were diagnosed using nerve conduction studies. With ethical approval and informed consent, surface EMG was recorded from first dorsal interosseous (1DI) muscle and the sensory nerve action potential (SNAP) recorded from the ulnar nerve whilst electrically stimulating the digital nerves of the little finger (2.5 × sensory threshold, 100 μS, 5 Hz). Subjects performed a sustained weak abduction of the index finger against resistance. EMG was rectified. EMG and SNAP were averaged time-locked to the stimulus for 256 sweeps.

Three reflex components may be identified: a short latency spinal component E1, followed by I1 and E2 components (Jenner & Stephens, 1982). In the present study, the size of each reflex component was expressed as % EMG modulation (mean values shown in brackets). The E2 reflex component recorded from 1DI following stimulation of the digital nerves of the little finger was present in 70 % of CPNE compared with 16 % of control subjects. The size of the E2 component recorded from the CPNE (6.9 %) and control subjects (1.4 %) was significantly different (Mann-Whitney test, $P < 0.05$). In contrast, the size of the E1, I1 components recorded from the CPNE (2.9 %, 3.7 %) and control subjects (5.1 %, 4.2 %) were not significantly different (Mann-Whitney, $P > 0.05$). There was no significant difference in SNAP size recorded from the ulnar nerve in healthy and CPNE subjects (Mann-Whitney, $P > 0.05$).

We conclude that the E2 component associated with distant digital nerve stimulation of the little finger seen in subjects with CPNE reflects 'reorganisation' within the CNS, resulting from interruption of afferent input to the primary sensory cortex following median nerve entrapment.

Caccia MR *et al.* (1973). *J Neurol Neurosurg Psychiat* **36**, 960–977.

Jenner R & Stephens JA (1982). *J Physiol* **333**, 405–419.

C143

Focality of central fatigue after exercise in man: a transcranial magnetic stimulation study

Katherine E. Williams, Adrian T. Humphry, Paul H. Strutton and Nick J. Davey

Division of Neuroscience, Imperial College Faculty of Medicine, Charing Cross Hospital, London W6 8RF, UK

Stimulation of the motor cortex using transcranial magnetic stimulation (TMS) and electromyographic (EMG) recordings have shown corticospinal excitability to be depressed following exercise (Brasil-Neto *et al.* 1993). We have further examined the central fatigue processes in response to discrete rhythmic exercise of an upper arm muscle on one side of the body to investigate whether this fatigue-related depression spreads to non-exercising muscles of the same limb or to muscles in the contralateral limb.

With local ethical approval and informed consent, eight healthy volunteers (7 males; aged 19–25 years) were seated with their arms relaxed on horizontal armrests and bilateral surface electromyographic (EMG) recordings taken from the first dorsal interosseous (FDI) and biceps brachii (BB) muscles. TMS was applied using a MagStim 200 stimulator connected to a 9 cm circular coil centred over the vertex. A train of six stimuli was delivered each minute, alternating between trials producing stimulation of right arm (coil A-side up) and left arm (coil B-side up) muscles. The stimulus intensity was set to $1.2 \times$ threshold for evoking responses in the relaxed BB muscle. Four trials were completed before starting the exercise protocol; 30 s after cessation of exercise a further 60 trials were conducted. Before exercise a 3.5 kg weight was strapped to the wrist. Subjects first completed a heavy exercise protocol by producing right-armed biceps curls, to a tone repeating at a frequency of 0.8 Hz, until exhaustion. On a second occasion, at least 3 days later, six of the subjects completed a light exercise protocol by performing the same exercise routine for 25 % of the time previously achieved. The amplitude of motor evoked potentials (MEPs) was measured in all four muscles at 2 min intervals while relaxed before and after exercise.

After the heavy exercise protocol the exercised BB showed depressed MEP amplitudes (ANOVA, $P < 0.05$) falling to a mean level ($\pm$ S.E.M.) of 25.8 $\pm$ 5.0 % of the pre-exercise values. Mean MEP amplitudes werre still depressed ($P < 0.05$), but had recovered to 58.3 $\pm$ 15.0 % 60 min post-exercise, indicating central fatigue processes were still operating an hour after exercise. The non-exercised BB showed significant (ANOVA, $P < 0.05$) MEP depression 9.5 min post-exercise (60.6 $\pm$ 4.9 %), which returned to pre-exercise levels after 40 min. No significant changes were seen in the FDI of either hand. Following the light exercise protocol a lower level of MEP depression, lasting 10 min (ANOVA, $P < 0.05$), was seen in the exercised BB (53.4 $\pm$ 10.1 %), whilst none was seen in the non-exercised BB or either FDI.

We conclude that post-exercise MEP depression seen in non-exercised BB represents spread of cortical depression, possibly via homotopic inhibitory connections (Meyer *et al.* 1995) in the corpus callosum. The presence of contralateral MEP depression only at higher levels of exercise suggests that this spread occurs when central fatigue processes have reached a substantial level. The spread of post-fatigue depression to the other cortex may operate similarly to the transcortical facilitation observed during unilateral contraction of hand muscles (Stedman *et al.* 1998).

Brasil-Neto JP *et al.* (1993). *Exp Brain Res* **93**, 181–184.

Meyer BU *et al.* (1995). *Brain* **118**, 429–440.

Stedman A *et al.* (1998). *Muscle Nerve* **21**, 1033–1039.

C144

Examination of intercostal muscle facilitation evoked by transcranial magnetic stimulation (TMS) in man

Sophie Theodorou, Maria Catley, Paul H. Strutton and Nick J. Davey

Division of Neuroscience, Imperial College Faculty of Medicine, Charing Cross Hospital, London W6 8RF, UK

Latency measurements in a study using transcranial magnetic stimulation (TMS) with surface electromyographic (EMG) recordings from intercostal muscles have been used to evaluate patients with cervical myelopathy (Misawa *et al.* 2001). We have now extended this technique in a group of control subjects to examine the pattern of facilitation with changing voluntary effort at all six intercostal muscle levels.

With local ethical approval and informed consent, nine healthy volunteers (aged 29–59 years; 5 males, 4 females) were recruited and seated comfortably. TMS was delivered using a MagStim 200 stimulator connected to 9 cm circular coil centred over the vertex with the induced current flowing clockwise. Surface electrodes were placed in each intercostal space on the right side of the body at approximately 2 cm from the sternal edge (1st−4th spaces), at the mid-clavicular line (6th space), and half way between (5th space). Recordings were made at maximum expiratory effort (MEE), at 50, 25, 10 and 5 % of MEE and at maximum inspiratory effort (MIE). Subjects breathed through a tube with a slow leak connected to a pressure meter, which was used to give them feedback of their effort. TMS intensity was set to $1.2 \times$ threshold for evoking motor-evoked potentials (MEPs) at 10 % MEE. MEPs were rectified and averaged for each trial and the areas of the resulting MEPs were measured at each recording site.

MEPs were recorded from each muscle in all subjects at each voluntary effort. The mean ($\pm$ S.E.M.) latencies of MEPs recorded during MEE were 8.8 $\pm$ 0.9 ms (1st space), 9.4 $\pm$ 1.2 ms (2nd space), 8.9 $\pm$ 0.5 ms (3rd space), 11.5 $\pm$ 1.6 ms (4th space), 10.3 $\pm$ 1.6 ms (5th space) and 10.8 $\pm$ 1.5 ms (6th space). Areas of MEPs recorded during MIE were 126 $\pm$ 52 % of those recorded during MEE (1st space), 103 $\pm$ 47 % (2nd space), 64 $\pm$ 18 % (3rd space), 89 $\pm$ 14 % (4th space), 65 $\pm$ 14 % (5th space) and 75 $\pm$ 22 % (6th space); due to the high level of variability, the difference was significant (paired *t* test, $P < 0.05$) only at the 3rd space. The area of MEPs became larger with increasing voluntary effort at all recording sites (ANOVA with Tukey correction; $P < 0.05$). For example, at the 1st space the mean area of MEPs was 23 $\pm$ 4 % of that at MEE (at 5 % MEE), 38 $\pm$ 8 % (at 10 % MEE), 45 $\pm$ 7 % (at 25 % MEE) and 70 $\pm$ 7 % (at 50 % MEE). There were no differences (ANOVA on ranks; $P > 0.05$) in MEP areas (relative to MEE) between recording sites at any given voluntary effort.

The pattern of facilitation of MEPs with increasing effort is altered in hand muscles of patients with incomplete spinal cord injury (Davey *et al.* 1999). We anticipate that these control data from intercostal muscles will help us to differentiate both the neurological level and degree of completeness of high thoracic spinal cord injury.

Davey NJ *et al.* (1999). *Exp Brain Res* **127**, 382–390.

Misawa T *et al.* (2001). *J Spinal Dis* **14**, 439–444.

C145

A transcranial magnetic stimulation study of back muscles in patients with low back pain

Paul H. Strutton*, Maria Catley*, Sophie Theodorou*, Alison H. McGregor† and Nick J. Davey*

*Division of Neuroscience and Psychological Medicine and †Department Musculoskeletal Surgery, Imperial College Faculty of Medicine, Charing Cross Hospital, London W6 8RF, UK

This study has examined motor-evoked potentials (MEPs) and inhibition of voluntary contraction induced by transcranial magnetic stimulation (TMS) of the motor cortex in the paraspinal muscles of the lumbar region in patients suffering from chronic low back pain (LBP).

With local ethical approval and informed consent eighteen patients with LBP were recruited from the orthopaedic and fracture clinic at Charing Cross Hospital and compared with ten control subjects. The patients were on the waiting list for surgery or caudal epidural drug injections to alleviate the symptoms. Electromyographic (EMG) recordings were made bilaterally from the erector spinae (ES) muscles at the L4 spinal level using self-adhesive surface electrodes. TMS was delivered using a MagStim 200 stimulator connected to an angled double-cone coil, which was positioned with its cross-over above the vertex, and the induced current in the brain flowing in a posterior to anterior direction. The threshold (expressed as percentage of maximum stimulator output, %MSO) for inducing MEPs in muscles contracted to 20 % of their maximum voluntary contraction (MVC) was assessed. TMS was delivered in steps equivalent to $0.1 \times$ threshold starting at a minimum intensity of $1.2 \times$ threshold and working downwards. Sets of a minimum of six stimuli were delivered during voluntary contraction to 20 % MVC of ES muscles. The duration and latency of the MEPs were measured and the duration and extent (percentage of voluntary EMG remaining) of the subsequent inhibition were measured even at stimulus intensities subthreshold for inducing MEPs. Statistical comparisons were made using Student's *t* test within patients between the left and right muscles (paired) and between patients and control subjects (unpaired). Statistical significance was taken when $P < 0.05$.

At $1.2 \times$ threshold TMS there was no difference in latency or duration of the MEPs between the left and right back muscles in the patients or controls; the data for both sides were therefore pooled and there were no differences between the patients and the control subjects. The duration and extent of inhibition over a range of stimulus strengths were not different between left and right muscles in the patients or between the patients and the control subjects. There were no significant differences in the thresholds for MEPs or inhibition between left and right muscles in the patients or in the controls. However, the mean ($\pm$ S.E.M.) thresholds for eliciting MEPs and inhibition in the ES muscles were higher in the patients (MEPs: 42.85 ± 1.63 %MSO; inhibition: 37.12 ± 1.78 %MSO) than in the control subjects (MEPs: 35.80 ± 2.32 %MSO; inhibition: 29.60 ± 1.70 %MSO).

The changed excitatory and inhibitory thresholds seen in LBP patients indicates altered corticospinal excitability in the ES muscles, possibly related to protective strategies. The raised inhibition threshold, in particular, suggests altered neurophysiological function at a cortical level. We will investigate whether the changed excitability persists after remission of pain, as this could help to explain why patients are vulnerable to further episodes of LBP.

C146

Cessation of paraplegic spasms by combined neuromuscular stimulation and standing

Jonathan A. Norton*, Duncan E. Wood† and Brian L. Day*

*Human Movement Group, Sobell Department of Motor Neuroscience and Movement Disorders, Institute of Neurology, University College London, London WC1N and †Department of Medical Physics and Biomedical Engineering, Salisbury District Hospital, Salisbury, UK

Patients with complete paraplegia frequently suffer from muscle spasms. In a pilot study, electrical stimulation of the posterior nerve roots was demonstrated to stop spasms in a paraplegic patient (Craggs *et al.* 2000). In the present study we have investigated whether spasms could be altered by neuromuscular stimulation and/or load-bearing standing. All experiments were approved by the local ethics committee and the patient gave informed consent.

The patient, a 59-year-old male, had a complete spinal cord lesion at the 10/11th thoracic level of 20 years duration and a S2–5 posterior rhizotomy. He commonly experienced dorsiflexion spasms at rest. Kinematic and EMG recordings showed that a spasm involved ankle and knee flexors and extensors bilaterally with an interspasm interval of between 3 and 30 s. The spasms showed significant coherence between muscles at various frequencies within and between legs (Fig. 1).
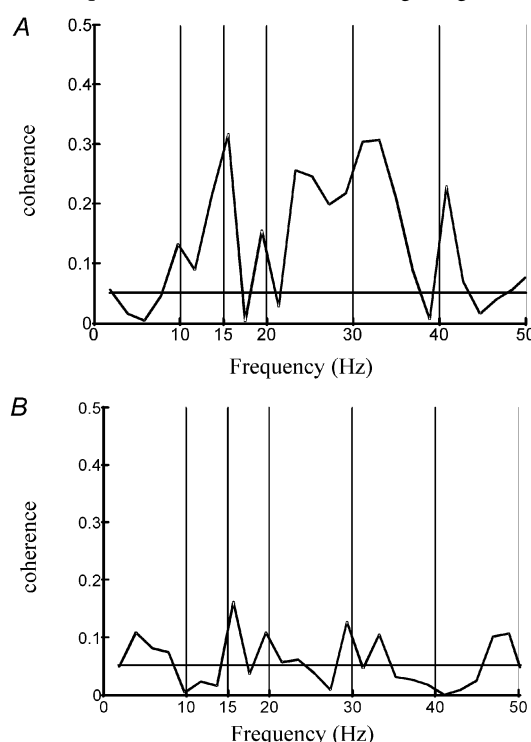

Figure 1. Coherence during muscle spasm: *A*, between tibialis anterior and quadriceps within a leg showing peaks at 8 and 16 Hz, and *B*, between tibialis anterior in right and left legs showing peaks at 8 and 13 Hz. The horizontal line is the 95 % confidence limit.

When he stood with the assistance of 20 Hz stimulation of both quadriceps muscles the spasms stopped entirely. At the end of the

stimulated stand the spasms did not reappear for periods up to 7 h, although rapid passive dorsiflexion would restart the spasms with the same resting characteristics as before. Passive standing, without stimulation in a standing frame, stopped the spasms but only for approximately 5 min. The legs bore $68 \pm 4\%$ and $61 \pm 1\%$ body weight (mean $\pm$ S.D.) during stimulated and passive standing, respectively. With the subject supine, bilateral stimulation of quadriceps, either on its own or in conjunction with manual pressure applied to the soles of the feet, had no effect on the spasms.

The coherence analysis suggests that components of the spasm arise from common sources, possibly driven by spinal oscillators. The results imply that the spinal circuits responsible receive inputs from the periphery, which are capable of modulating the spasm source. It appears that in this subject spasm suppression is maximally effective when the afferent input is generated by the combination of muscle stimulation and load-bearing standing.

Craggs M *et al.* (2000). Sacral nerve neuromodulation for lower spasm and spasticity in spinal cord injury. *Spinal Injury,* New Horizons Conference.

C147

The 5-HT$_{1A}$ receptor agonist 8-OH-DPAT enhances opiate-induced rigidity when applied intrathecally

M.H. Gladden, S.M. Cain, L. Johnston, N.A. Kelley and R. Thomson

Institute of Biomedical and Life Sciences, University of Glasgow, Glasgow G12 8QQ, UK

Muscle rigidity can occur during induction of anaesthesia using potent opiates (see Benthuysen *et al.* 1986). The opiate fentanyl initially induces apnoea, bradycardia and a fall in blood pressure when administered I.V. to urethane-anaesthetised rats. γ-Motoneurone activity is depressed, as indicated by a fall in output of muscle spindles monitored by in-continuity recordings from muscle nerve branches. Presumably this is similar to inhibition of α-motoneurone activity by opiates (see Duggan & North, 1984). However, providing that there are no rhythmic respiratory movements for 15–55 s, γ-motoneurone activity returns strongly, accompanied by a rise in blood pressure and an exophthalmos (Gladden & Sahal, 2000; Gladden *et al.* 2001). Muscle contraction, indicated by EMG activity, follows the rise in γ-motoneurone activity. These changes subside when artificial ventilation is commenced, but thereafter the same responses to apnoea can be elicited repeatedly by stopping ventilation. We investigated the effect of the 5-HT$_{1A}$ receptor agonist 5-OH-DPAT because Jaros & Kolasiewicz (1995) reported that it abolishes opiate-induced rigidity in non-anaesthetised rats if given intraperitoneally 40 min before or 20 min after fentanyl I.P.

Six Sprague-Dawley rats were anaesthetised with urethane (170 mg 100 g^{-1} I.P.). In-continuity recordings were made from S1 dorsal and ventral roots and a nerve branch to the longissimus caudae muscle which supplies 4–9 spindles. The blood pressure and F_{ET,CO_2} were also monitored. After the experiments all animals were killed with an overdose of anaesthetic. Fentanyl (40 mg kg^{-1} I.V.) induced the sequence of changes outlined above. After 5 min of artificial ventilation, recorded variables returned to pre-opiate levels and were unchanged when 5-OH-DPAT (0.04–0.1 mg ml^{-1}) was applied to the exposed sacral spinal cord. However, when the ventilator was stopped 5 min later, the neural responses to apnoea were increased. The mean dorsal root activity measured 40 s after initiation of apnoea was compared with the value 20 s before apnoea. It was $197 \pm 22\%$ (mean $\pm$ S.E.M.) with fentanyl alone, but increased significantly after the administration of 5-OH-DPAT ($302 \pm 26\%$, $P < 0.01$, paired t test). We suggest that 8-OH-DPAT acts supraspinally to abolish opiate-induced rigidity.

Benthuysen JL *et al.* (1986). *Anesthesiology* **64**, 440–446.

Duggan AW & North RA (1984). *Pharmacol Rev* **35**, 219–281.

Gladden MH & Sahal A (2000). *J Physiol* **527.P**, 136P.

Gladden MH *et al.* (2001). *J Physiol* **531.P**, 144P.

Jaros T & Kolasiewicz W (1995). *Pol J Pharmacol* **47**, 19–25.

PC91

Plasticity in the visual system of solitarious and gregarious locusts

T. Matheson, R. Basu Roy, M. Copeland, H. Krapp and S.M. Rogers

Department of Zoology, University of Cambridge, Downing Street, Cambridge CB2 3EJ, UK

Desert locusts *Schistocerca gregaria* exist in a range of forms between two morphologically and behaviourally distinct extremes, the solitarious and gregarious phases. One marked difference in behaviour is that solitarious animals fly individually, whereas gregarious locusts fly in dense swarms. We show that there are changes in identified visual neurones that can be related to this change in behaviour.

Touching hairs on the hindlegs of a solitarious locust can within 4 h transform that animal's behaviour so that it acts gregariously (Rogers *et al.* 2001). We can also drive this change by electrically stimulating a leg sensory nerve.

We have analysed the responses of a visual interneurone, the descending contralateral motion detector (DCMD), and the properties of its output connections onto a leg motor neurone, the fast extensor tibiae (FETi) that is important in escape jumping. DCMD responds maximally to the sight of an object looming towards the locust on a collision course.

The responses of DCMD were tested using simulated looming objects of various sizes and velocities, presented at 1 min intervals. DCMD in gregarious locusts showed little adaptation to repeated stimulation, but in solitarious locusts it showed a pronounced adaptation to 30 % of the value recorded in gregarious locusts.

A spike in DCMD elicited a monosynaptic excitatory postsynaptic potential in the metathoracic FETi, the amplitude of which was approximately 150 % larger in solitarious locusts than in gregarious locusts. Thus although fewer action potentials were elicited in DCMD by visual stimuli in solitarious locusts, each carried a far greater weight at this output synapse. This tunes the visual pathway in solitarious animals so that it is maximally sensitive to infrequent visual stimuli (which is likely to be the normal situation for these animals living singly in large expanses of desert). The same visual pathway of gregarious locusts is tuned by virtue of its resistance to adaptation but weaker synaptic strength so that it continues to function effectively even when the visual environment surrounding the locust contains moving

objects. This may help gregarious locusts avoid collisions with conspecifics when they walk or fly in large swarms, or it may serve to maintain the sensitivity of the escape circuit to the sight of an approaching predator even when surrounded by many other locusts.

Rogers SM *et al* (2001). *6th Int Cong Neuroethol Bonn* 345.

This work was supported by the BBSRC.

PC92

Modulation of cutaneous reflexes during bicycling in man: electromyographic (EMG) and kinematic responses to non-nociceptive sural nerve stimulation

K. Mileva*, D.A. Green* and D.L. Turner†

*Sports & Exercise Science Research Centre, South Bank University, London and †School of Life & Sport Sciences, University of Surrey Roehampton, London, UK

The few published studies of cutaneous reflex modulation during cyclic movement have focused mainly on EMG responses (Zehr *et al.* 2001). The purpose of the present investigation was to extend muscle activation studies and to involve functional measures of lower limb kinematic responses during steady-state bicycling to brief electrical stimulation of the sural nerve, which innervates the dorsolateral foot surfaces.

Seven healthy male subjects (26.7 ± 7.2 years, 82 ± 13.7 kg, 182 ± 4.8 cm) gave informed consent and participated in the study approved by the local ethics committee. Subjects performed cycle ergometry (90–100 W; 60 r.p.m.). EMG was recorded from the ankle flexor tibialis anterior (TA) and ankle extensor soleus (SOL) using surface bipolar electrodes ipsilateral to the stimulation. Electrogoniometers positioned over the Achilles tendon recorded ankle angular position (dorsi/plantar flexion and eversion/inversion). Sural nerve was stimulated at an intensity equal to 75 % of the predetermined pain threshold via electrodes placed inferior to the lateral malleolus. The stimulation trains (5 × 1.0 ms pulses at 200 Hz) were delivered pseudorandomly at eight equidistant points in the crank cycle. Two stimuli were separated by at least two non-stimulated cycles. Net reflex responses were obtained by averaging 30 crank cycles for each of nine conditions (8 with and 1 without stimulation, control) followed by average control subtraction from the corresponding stimulation data.

The main observations of this study were: (1) cutaneous reflexes were dependent upon the point of delivery within a crank cycle and were predominantly inhibitory for both TA and SOL (Fig. 1) in contrast to mainly facilitatory responses observed during static contractions and walking (e.g. Zehr *et al.* 1998); (2) ankle kinematic responses were suppressed by sural stimulation as a result of TA and SOL response inhibition; (3) in both muscles the reflex peak occurred at latencies at or above 100 ms, suggesting that transcortical reflex pathways may contribute to reflex burst generation in bicycling as during human walking (Nielsen & Sinkjaer, 2002).

We conclude that cutaneous reflexes are an important part of the sensory feedback used by the central drive to modulate muscle activation during bicycling as a protective mechanism against sudden ankle movement disturbance.
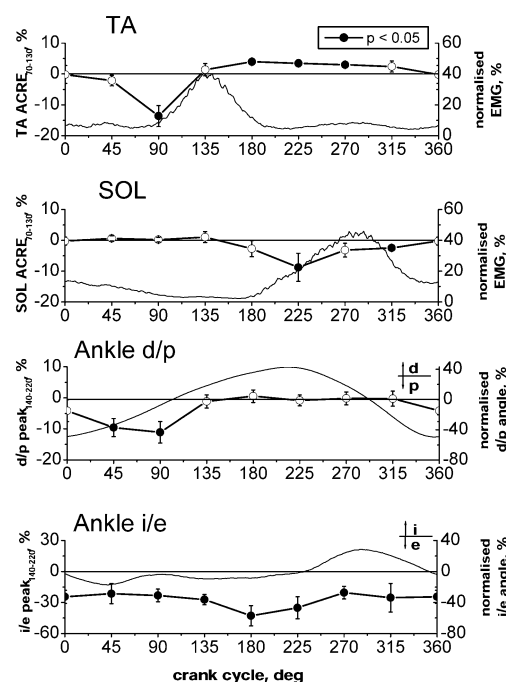

Figure 1. Average EMG (tibialis anterior (TA) and soleus (SOL)) and kinematic (dorsi/plantarflexion (d/p) and eversion/inversion (e/i)) reflex responses as a function of the phase in the crank cycle (mean ± S.E.M., *n* = 7). The corresponding background activity is shown in thin black lines. Data are normalized with respect to the maximal control value observed in each cycle. ACRE, average cumulative reflex EMG. Responses underwent a Wilcoxon signed rank test (significance level *P* < 0.05).

Nielsen JB & Sinkjaer T (2002). *J Electromyogr Kinesiol* **12**, 213–217.

Zehr EP *et al.* (1998). *J Physiol* **507**, 305–314.

Zehr EP *et al.* (2001). *J Neurophysiol* **85**, 1178–1184.

All procedures accord with current local guidelines and the Declaration of Helsinki.