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Excitability of the motor cortical representation of the external anal sphincter

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Abstract This study was designed to assess the excitability of the motor cortical representation of the external anal sphincter by using transcranial magnetic stimulation (TMS). In six healthy volunteers, the rest motor threshold and the duration of the cortical silent period were determined with single TMS pulses, and the intracortical inhibition and facilitation were measured with paired TMS pulses. Values obtained from the anal sphincter were compared with those obtained from a muscle in the right hand. All subjects completed the study. Rest motor threshold and intracortical facilitation were similar in both muscles. In contrast, cortical silent period duration and intra-cortical inhibition were less for the anal sphincter than for hand muscle. This study has opened new perspectives for the investigation of anal sphincter cortical control in humans.

Keywords Anal sphincter · Clinical neurophysiology · Cortical excitability · Electromyographic silent period · Motor cortex · Motor-evoked potentials · Paired pulses · Transcranial magnetic stimulation

Introduction

The role played by the motor cortex in anorectal pathophysiology is not completely understood (Vodusek 2004), but is certainly critical. For instance, pure cortical lesions can result in various bowel dysfunctions, such as faecal incontinence and constipation, e.g. in case of stroke (Brittain et al. 1998; Robain et al. 2002) or multiple sclerosis (Hinds and Wald 1989). The motor cortex

contributes to anal continence by commanding the voluntary contraction of the external anal sphincter. Neurophysiological investigation of this command might thus be of clinical value.

For 15 years, transcranial magnetic stimulation (TMS) has been used to produce motor-evoked potentials (MEPs) for study of central motor conduction time regarding anal sphincter cortico–spinal pathways (Opsomer et al. 1989; Herdmann et al. 1991; Ghezzi et al. 1992; Jost and Schimrigk 1994; Pelliccioni et al. 1997; Welter et al. 2000). In addition to conduction time measurement, TMS has gained widespread acceptance for appraising the excitability of motor cortical circuitry (Abbruzzese and Trompetto 2002). For this purpose, various tests have been proposed, e.g. the determination of rest motor threshold (RMT) and the duration of the cortical silent period (CSP) using single TMS pulses and the calculation of intracortical inhibition (ICI) or facilitation (ICF) using paired TMS pulses. These excitability parameters are classically measured in hand muscles. A few excitability studies have been performed in lower limb muscles (Robinson et al. 1993; Chen et al. 1998; Salerno et al. 2000; Tremblay and Tremblay 2002), in facial muscles (Leis et al. 1993; Werhahn et al. 1995; Cruccu et al. 1997), and in the diaphragm (Lefaucheur and Lofaso 2002; Demoule et al. 2003), but never in pelvic floor muscles. The goal of the current TMS study was to characterize the main properties which determine cortical excitability of the external anal sphincter, compared with hand muscle, in normal subjects.

Materials and methods

Six right-handed healthy volunteers (four men, two women), free from any anorectal or neurological disease, gave their informed consent for this study. One subject was chosen for each decade from 20 s to 70 s to determine the effect of age on the results.

Anal MEPs were recorded using two pairs of pre-gelled disposable surface electrodes (Medtronic Functional Diagnostics, Skovlunde, Denmark; #9013S0241), the active

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electrode being placed over the anal sphincter, at the right side of the anal verge, and the reference electrode being placed 3 cm more laterally. An intra-rectal ground electrode was used, consisting of the stimulating tip of a commercially available electrode (Inomed, Teningen, Germany; #525 340), which was first designed as an intra-rectal monopolar stimulator (Lefaucheur et al. 2001). The placement of the ground electrode between the site of magnetic stimulation and the site of MEP recording led to a substantial reduction of the stimulus artefact and made the recording of a reproducible MEP possible for all subjects (Lefaucheur 2004). Anal MEPs were recorded through a 20–1000 Hz bandpass using a Phasis II EMG machine (Esaote, Florence, Italy), the subjects lying in left lateral position.

Magnetic stimulation was performed using a Magstim 200 stimulator and a double cone coil (Magstim, Whitland, Carmarthenshire, Wales, UK; #9902-00). The use of a double cone coil improves the rate of successful stimulation of the cortical representation of anal musculature, which is a deep motor strip located in the inter-hemispheric fissure (Herdmann et al. 1995). The coil was moved over the scalp to determine the position eliciting MEPs of maximum amplitude. The procedure for cortical excitability testing included the determination of RMT, CSP duration, ICI and ICF.

The RMT was defined as the minimum intensity required to produce MEPs of 50 μ V amplitude in at least 5 out of 10 trials while muscle was at rest (Rossini et al. 1994). The CSP, corresponding to a post-MEP interruption of the electromyographic signal, was determined in single-pulse trials performed at 140% RMT during a tonic voluntary contraction. Four rectified traces, each consisting of a block of three averaged trials, were superimposed. The minimum CSP duration was measured from the stimulus artefact and from the end of the MEP until the first re-occurrence of voluntary EMG activity. A paired-pulse paradigm using a BiStim module (Magstim) was applied for ICI and ICF determination. The intensity of the conditioning stimulus was set to 80% RMT and the intensity of the test stimulus was set to 120% RMT, while muscle was at rest (Kujirai et al. 1993). Inter-stimuli intervals (ISIs) of 2 and 4 ms to determine ICI, and of 10 and 15 ms to determine ICF, were randomly applied and intermixed with control trials (test stimulus alone). On the whole, eight trials were recorded and averaged for the test

pulse alone and four trials for each ISI. Peak-to-peak amplitudes were measured for the different MEPs and ICI and ICF were expressed as a percentage of the test MEP amplitude. Only maximum values of ICI and ICF were retained for analysis (Chen et al. 1998).

In the same session, cortical excitability parameters were measured by recording MEPs in the first dorsal interosseus muscle of the right hand using the same procedure as for the anal sphincter. Hand muscle study differed only by the use of a figure-of-eight double 70 mm coil (Magstim; #9925-00) for cortical stimulation and of a Velcro bracelet (Medtronic; #9013S0711) strapped around the forearm as the surface ground electrode. Results obtained for the anal sphincter and for the hand muscle were compared with the Wilcoxon matched-pairs signed-ranks test, a value of $P < 0.05$ being considered as significant.

Results

The study was completed for all the subjects. Because RMT values were lower than 71%, it was possible to determine CSP duration at a stimulus intensity corresponding to 140% RMT in all cases. Cortical excitability results are listed in Table 1 and illustrated in Fig. 1 for the anal sphincter. Significant differences between anal sphincter and hand muscle were found for CSP duration (Wilcoxon test, $P = 0.03$) and ICI ($P = 0.03$) but not for RMT ($P = 0.84$) and ICF ($P = 0.69$). In an overall view of the results, age effects did not appear critical, but the sample size was probably too small to conclude.

Discussion

Various electrodiagnostic tests, in particular anal sphincter electromyography (Podnar 2003), have proved to be valuable tools for assessment of anorectal dysfunction. The current study first showed that several parameters of cortical excitability, such as RMT, CSP, ICI and ICF could be measured in the anal sphincter as in any skeletal limb muscles.

In upper limb muscles, the CSP was found to result from the activation of both spinal and cortical circuits (Cantello et al. 1992; Inghilleri et al. 1993; Ziemann et al.

Table 1 Values of motor threshold (MT, in % of maximum stimulator output), cortical silent period duration (CSP, in ms), and intra-cortical inhibition and facilitation (ICI and ICF, in % of test MEP amplitude) measured in the anal sphincter or in a hand muscle. CSP duration was measured from the end of the motor-evoked potential or from the stimulus artefact (values in brackets)

Subject	Age	Anal sphincter				Hand muscle			
		MT	CSP	ICI	ICF	MT	CSP	ICI	ICF
1	25	55	43 (98)	63	121	56	78 (130)	23	118
2	38	65	39 (93)	56	139	57	96 (145)	25	131
3	49	60	85 (135)	63	128	62	90 (142)	29	132
4	56	55	62 (114)	61	142	67	94 (145)	29	129
5	62	70	51 (105)	73	117	62	110 (158)	18	133
6	71	65	60 (116)	74	115	66	87 (142)	21	146
Mean	50.2	61.7	56.7 (110.2)	65.0	127.0	61.7	92.5 (143.7)	24.2	131.5
s.d.	16.7	6.1	16.6 (15.1)	7.1	11.4	4.5	10.7 (9.0)	4.4	9.0

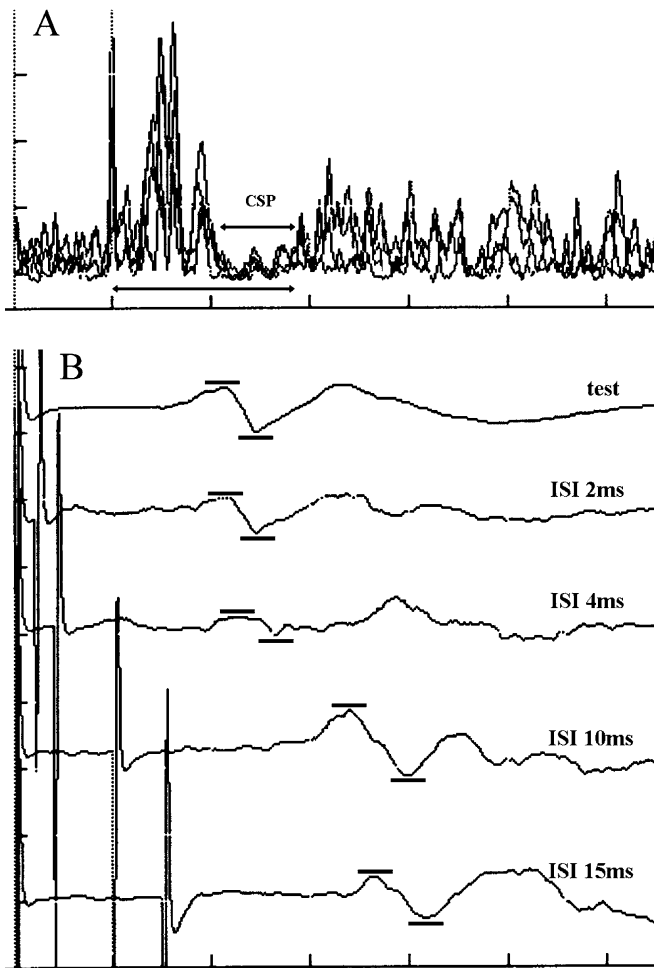


Fig. 1 **A** Cortical silent period (CSP) recorded in the anal sphincter muscle to cortical stimulation. Values of CSP were measured from the end of the motor evoked potential and from the stimulus artefact. **B** Motor evoked potentials (MEPs) recorded in the anal sphincter muscle after single or paired pulses of motor cortex stimulation. Paired pulses determined MEP inhibition or facilitation, compared with the test MEP, according to the inter-stimuli interval (ISI). Sweep: 50 (**A**) and 10 (**B**) ms/division; gain: 100 (**A**) and 500 (**B**) μ V/division

1993). In contrast, the CSP recorded in facial muscles probably originates solely from intra-cortical mechanisms, because the R1 component of the blink reflex can be elicited during the whole facial CSP (Leis et al. 1993; Cruccu et al. 1997). Regarding anal sphincter CSP, a spinal contribution remains possible, even if we failed to evoke any anal reflex to pudendal nerve stimulation during CSP (performed in only one subject, data not shown).

CSP duration seemed to be shorter in the anal sphincter than in hand muscle. Short CSP mean duration has also been reported for facial muscles (22–32 ms; Desiato et al. 2002) and the diaphragm (27–39 ms; Lefaucheur and Lofaso 2002). These differences could originate in the type or length of the inhibitory circuits explored by this test or in the strength of the cortico–spinal projections regarding the anatomical location of the muscle (Brouwer and Ashby 1990). Indeed, neural control of anal sphincter contraction differed from that of limb muscles by the

nature of the proprioceptive feedback (absence of tendon joints, reflex regulation by rectal distension), by the segmental organization of the spinal motoneurons (within the Onuf's nucleus) or by the coordination between somatic and autonomic motor systems (for modulating anal sphincter reflex contraction) (Vodusek 2004).

Unlike CSP, the origins of ICI and ICF are considered to be solely intra-cortical (Kujirai et al. 1993; Chen et al. 1998) but resulting from different cortical networks (Ziemann et al. 1996; Liepert et al. 1998). The circuits involved in ICF express higher thresholds than those involved in ICI (Ilic et al. 2002). These parameters, classically recorded in muscles at rest, are known to decrease during voluntary contraction, particularly ICI (Ridding et al. 1995). Thereby, the continuous motor unit firing at rest, which exists in the external anal sphincter, in contrast with limb muscles, might contribute to the difference in ICI observed between sphincter and hand muscles. The functional role of the cortical inhibitory circuits assessed by ICI, and maybe also by CSP, is probably to reduce unspecific overflow in the cortico–spinal drive and then to focus neuronal activity on to appropriate motor pathways involved in an intended movement (Liepert et al. 1998; Tergau et al. 1999). The fact that the anal sphincter is involved in a tonic motor task, mainly regulated by segmental spinal reflexes, limits the requirement for fine and selective activation of cortical motoneurons, in contrast with limb muscle. Interestingly, ICI was found to be quite absent (Hopkinson et al. 2004) and CSP to be very short (Lefaucheur and Lofaso 2002) in the diaphragm, another muscle with continuous and strong reflex motor activity.

The cortical control of the external anal sphincter has rarely been appraised in humans. Using functional magnetic resonance imaging, anal sphincter contraction was found to be associated with overactivity of various cortical regions (Kern et al. 2004). More specifically, the motor cortical representation of the anal sphincter was mapped with the TMS technique (Turnbull et al. 1999). Cortical excitability studies regarding the anal sphincter, as initiated by the present work, will be able to provide additional valuable information on anal sphincter pathophysiology. Indeed this neurophysiological testing is easy to perform, well tolerated by the subjects, and repeatable. However, the inter- and intra-individual variability is quite high, both for CSP (Fritz et al. 1997; Orth and Rothwell 2004) and for ICI/ICF (Borojerdj et al. 2000; Orth et al. 2003). Therefore, rigorous technique and standardized methods will be required for clinical application. This testing might improve understanding of various anorectal dysfunctions. In particular, diseases in which the “brain–gut axis” is involved are concerned, such as faecal incontinence in patients with cerebral palsy, chronic constipation with outlet obstruction syndrome, irritable bowel syndrome or anismus (Mertz 2003; Mulak and Bonaz 2004). This might also contribute to better diagnosis or follow-up of these diseases. In conclusion, new and exciting perspectives for assessing the cortical control of

anal sphincter contraction are opened by using this simple neurophysiological tool.

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