

## CROSSTALK

### Crosstalk proposal: There is much to gain from the independent control of human muscle spindles

Michael Dimitriou 

Physiology Section, Department of Integrative Medical Biology, University of Umeå, Umeå, Sweden

Email: mdimitriou@umu.se

Edited by: Francisco Sepúlveda & Vaughan Macefield

Linked articles: This article is part of a CrossTalk debate. Click the links to read the other articles in this debate: <https://doi.org/10.1113/JP281337>, <https://doi.org/10.1113/JP281595>, <https://doi.org/10.1113/JP281594>.

Muscle spindles are encapsulated sensory organs found in most of our skeletal muscles. It is well known that spindles respond to muscle stretch and contribute to proprioception, but these mechanoreceptors are particularly interesting because they have their own motor supply. The majority of efferent projections to mammalian spindles originate from  $\gamma$  motor or 'fusimotor' neurons that supply spindles exclusively (Matthews, 1972). Fusimotor neurons therefore allow for the independent control of muscle spindles.

Human muscle afferent activity can be recorded using the technique of micro-neurography (Vallbo & Hagbarth, 1968) but equivalent documentation of fusimotor activity is virtually impossible. However, recordings from spindle afferents can be used to study fusimotor function:  $\gamma$  neurons project to spindles exclusively, and the spindle organ acts as an integrator of input from mechanoreception and

multiple fusimotor fibres (Matthews, 1972). Recordings from spindle afferents of awake monkeys and cats, including elegant recordings from freely moving cats (Prochazka, 1996; Prochazka & Gorassini, 1998), have provided strong evidence for independent and selective fusimotor control. In humans, a reliable way to induce fusimotor activity is by voluntarily activating the spindle-bearing muscle, which indicates a parallel activation of  $\alpha$  and  $\gamma$  motor neurons (Vallbo, 1970). As often described in medical and neuroscience textbooks, ' $\alpha$ - $\gamma$  co-activation' acts to maintain spindle responsiveness to stretch despite skeletal muscle shortening. Many studies of human spindles have reported no evidence of selective fusimotor drive independent of changes in  $\alpha$  motor activity (e.g. Gandevia & Burke, 1985; Wessberg & Vallbo, 1995; Kakuda *et al.* 1996). However, most human spindle afferent data have been recorded under passive/relaxed conditions, isometric contractions or during very slow active movements in contexts that would tend to favour  $\alpha$ -linked fusimotor activity. Indeed, this limited behavioural repertoire has been put forward as a potential cause for the observed discrepancy between human and feline spindle control (e.g. Prochazka, 1986). One way to address this discrepancy is to record human spindle afferent activity in various fundamental sensorimotor contexts requiring active naturalistic movement. It is difficult to maintain single afferent recordings during naturalistic active movement in humans. However, using newer technologies and pushing the envelope with human micro-neurography has recently allowed the debate concerning the nature of human fusimotor control to advance, as described below. This short article emphasizes

top-down fusimotor control, although cutaneous afferent ('reflexive') projections to fusimotor neurons (Aniss *et al.* 1990; Gandevia *et al.* 1994) are potentially an important source of independent fusimotor control as well.

#### Independent preparatory control of muscle stiffness

It is generally accepted that voluntary movements are prepared before they are executed. Movement preparation is associated with faster reaction times and better movement quality (Rosenbaum, 1980; Ghez *et al.* 1997), but the neural mechanisms involved are unclear. The firing of 'preparatory' neurons in the CNS has been closely linked to movement direction/extent (Kurata, 1993; Messier & Kalaska, 2000) and visual target location (Shen & Alexander, 1997). Despite the vigorous changes in preparatory activity across multiple areas of the brain, there is no concurrent goal-dependent change in skeletal muscle activity that may facilitate execution of the planned movement (Tanji & Evarts, 1976; Gao *et al.* 2018). It was originally believed that preparation represents a subthreshold version of movement-related cortical activity (Tanji & Evarts, 1976). This idea has been contradicted more recently by demonstrating that preparation sets another initial dynamical state that promotes execution of the planned movement (Churchland *et al.* 2010); however, it is still unclear how this brain state results in improved motor performance.

In a recent study (Papaioannou & Dimitriou, 2021), we recorded spindle afferent responses from wrist and finger extensors while fully-alert individuals performed the classic instructed-delay

Michael Dimitriou is a research fellow at the University of Umeå, Sweden. He is the principal investigator at DimitriouLab and his work focuses on human sensorimotor control, with a particular interest in investigating the role of muscle spindle receptors.



reaching task, using their right hand (Fig. 1A, left). We hypothesized that some preparatory activity in the CNS may reflect goal-directed control of spindle sensitivity/gain to muscle stretch. Independent modulation of spindle gain via the fusimotor system could function as movement-related preparation that does not determine concurrent muscle force, but could nevertheless affect movement execution via modulating stretch 'reflex' responses: the negative feedback to the muscle motor drive, which in turn affects the level of mechanical resistance to stretch, i.e. 'stiffness'. As expected, there were no systematic deviations in hand kinematics or muscle EMG during movement preparation in our study. However, we found a consistent decrease in spindle afferent responses when preparing to reach targets in directions associated with stretch of the spindle-bearing muscle (Fig. 1A, right). Because the goal-dependent decrease in background (tonic) firing rate was moderate in size and only observed in type Ia afferents, this suggests a relative suppression of dynamic  $\gamma$  motor neuron

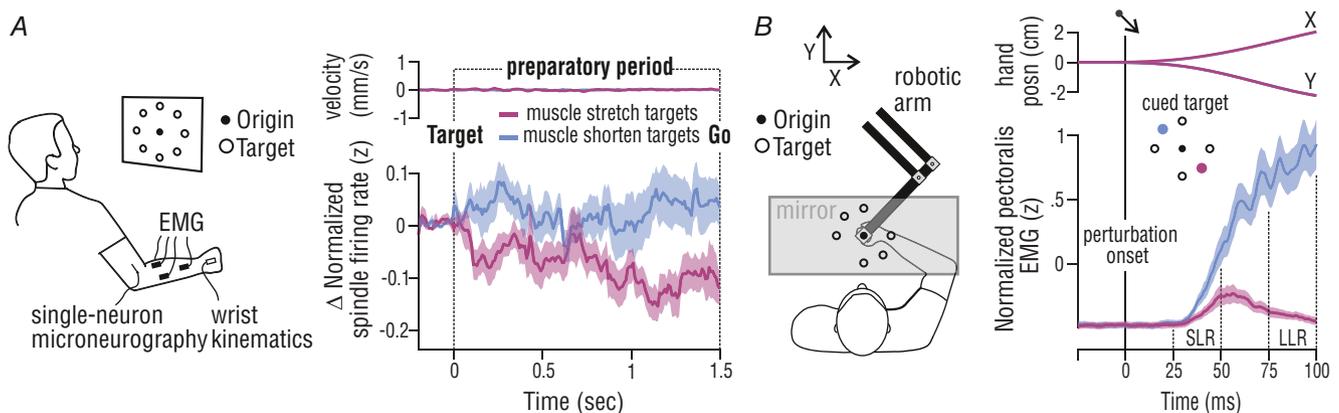
drive to muscles preparing to stretch. 'Dynamic' fusimotor neurons only affect primary spindle receptors (i.e. type Ia responses). Dynamic fusimotor drive is known to induce some increase in tonic Ia firing but has a much stronger positive effect on spindle gain (Matthews, 1972; Emonet-Denand *et al.* 1977; Prochazka, 1996). Accordingly, additional experiments involving whole-arm perturbations during reach preparation demonstrated a modulation of stretch reflex gains that reflects the observed preparatory changes in spindle activity (Fig. 1B).

Prevalent computational frameworks of sensorimotor control (e.g. Wolpert & Miall, 1996) have generally ignored fusimotor control. This is not surprising, as the textbook version of  $\alpha$ - $\gamma$  co-activation essentially describes fusimotor function as ensuring that the stretch sensor remains operational despite skeletal muscle shortening. For voluntary movement, such computational models suggest that the brain predicts the sensory consequences of a motor command and compares internal predictions with incoming sensory

feedback generated by the action. Our study suggests that the 'controller' can also proactively modify the 'plant' (body part) by adjusting the sensitivity of the plant's sensors, in order to facilitate the intended action, e.g. by preventing consequences (negative feedback) that would otherwise interfere with movement execution. Future research will determine whether independent fusimotor control plays a role in adjusting muscle stiffness across different motor tasks (e.g. object interception).

#### Selective extraction of task-relevant information

Hospod *et al.* (2007) recorded spindle afferent activity from relaxed muscles of the lower leg during imposed movements of the foot. When attention was directed at the imposed movement, the firing of 58% of recorded type Ia afferents changed in a way that suggested a selective re-balancing of dynamic and static fusimotor drive. This led the authors to suggest that selective fusimotor drive may help provide more



**Figure 1. Goal-dependent tuning of muscle spindles and stretch reflex gains during movement preparation**

A, left, the microneurography set-up. Movement of the right hand at the wrist controlled the position of a visual cursor. On each trial, a target was first cued and after a delay period ('preparatory period') a Go signal to move the cursor to the target was issued. Right, mean normalized signals across all recorded spindle type Ia afferents  $\pm 1$  SEM ( $n = 8$ , from 6 subjects). Despite no hand movement or goal-dependent changes in EMG, spindle afferents from wrist and digit extensors decreased their firing rates when preparing to reach a target requiring stretch (vs. shortening) of the spindle-bearing muscle. B, left, the same study also used a robotic and virtual reality platform. Participants performed the same delayed-reach task using the whole arm, but here the robot also unpredictably perturbed hand position during preparation to probe stretch reflex responses. Right, mean signals across participants ( $n = 14$ )  $\pm 1$  SEM. As predicted from A, both short- and long-latency reflex gains ('SLR' and 'LLR') were relatively suppressed when preparing muscle stretch. Across all experiments in this study, targets/trials were presented in a block-randomized manner, which ensured no systematic difference in movement history across targets. Moreover, any potential minor (i.e. undetectable) systematic deviations in muscle length and/or EMG that could theoretically have occurred during preparation cannot account for the clear goal-dependent difference in SLR, but rather suggest an independent modulation of spindle gains. Adapted from Papaioannou & Dimitriou (2021).

accurate movement trajectory information to the brain. Similarly, paying attention to the velocity *vs.* final position of imposed ankle movements affected spindle sensitivity in a task-appropriate manner (Ribot-Ciscar *et al.* 2009). But the above task-dependent effects on spindle output have been characterized as small (e.g. Macefield & Knellwolf, 2018) and therefore of questionable behavioural impact (but see also Ribot-Ciscar and Ackerley, 2021). Moreover, any  $\alpha$ -linked fusimotor drive may possibly dominate if similar tasks are performed actively or under a certain degree of muscle co-contraction (Dimitriou, 2014). For example, co-contractions are commonplace when learning a novel motor task (e.g. Thorougman & Shadmehr, 1999), even one that only involves adaptation to visual distortions (Huang & Ahmed, 2014).

Nevertheless, the selective extraction of proprioceptive information has also been demonstrated during naturalistic active movement. We recently recorded spindle afferent activity from wrist extensors while participants executed all stages of a classic visuomotor learning task (Dimitriou, 2016). In this task, participants performed reaching movements with their hand before, during and after a visual distortion equivalent to wearing prism glasses (i.e. 'visuomotor rotation'). Hand movements controlled the position of a visual cursor, and on each trial, the participants had to bring the cursor inside one of eight peripheral visual targets. All targets were symmetrically arranged in a circle. Despite fundamentally identical movements across the task's three stages, there were large differences in spindle output as a function of task state. For example, in the 'washout' stage, the visual distortion is removed and movement direction of the hand and the cursor suddenly re-align. The spindle afferent population encoded muscle length only in the washout stage (e.g. see Fig. 4E in Dimitriou, 2016). That is, both primary and secondary spindle sensors 'linearized' with respect to hand position, likely via the selective and state-dependent increase of 'static' fusimotor drive. This linearization effect occurred only in the stage where there was a need for adaptation and proprioceptive feedback was directly reflective of the task-relevant consequences of the motor commands (cursor direction). A follow-up study has also shown a congruent task-relevant modulation of stretch reflex responses (Dimitriou, 2018).

### Closing remarks

Recent studies indicate that humans make good use of their capability for independent control of muscle spindles, as reflected by the advantageous preparatory tuning of muscle stiffness and the selective extraction of task-relevant information. Future research will determine the full extent to which independent fusimotor control facilitates the robustness, flexibility and adaptability of human motor behaviour. A better understanding of the sensorimotor system (and its dysfunction) can in turn inform new technologies, such as in the areas of prosthetics and robotics control.

### Call for comments

Readers are invited to give their views on this and the accompanying CrossTalk articles in this issue by submitting a brief (250 word) comment. Comments may be submitted up to 6 weeks after publication of the article, at which point the discussion will close and the CrossTalk authors will be invited to submit a 'Last Word'. Please email your comment, including a title and a declaration of interest, to [jphysiol@physoc.org](mailto:jphysiol@physoc.org). Comments will be moderated and accepted comments will be published online only as 'supporting information' to the original debate articles once discussion has closed.

### References

- Aniss AM, Diener HC, Hore J, Burke D & Gandevia SC (1990). Reflex activation of muscle spindles in human pretibial muscles during standing. *J Neurophysiol* **64**, 671–679.
- Churchland MM, Cunningham JP, Kaufman MT, Ryu SI & Shenoy KV (2010). Cortical preparatory activity: Representation of movement or first cog in a dynamical machine? *Neuron* **68**, 387–400.
- Dimitriou M (2014). Human muscle spindle sensitivity reflects the balance of activity between antagonistic muscles. *J Neurosci* **34**, 13644–13655.
- Dimitriou M (2016). Enhanced muscle afferent signals during motor learning in humans. *Curr Biol* **26**, 1062–1068.
- Dimitriou M (2018). Task-dependent modulation of spinal and transcortical stretch reflexes linked to motor learning rate. *Behav Neurosci* **132**, 194–209.
- Emonet-Denand F, Laporte Y, Matthews PB & Petit J (1977). On the subdivision of static and dynamic fusimotor actions on the primary ending of the cat muscle spindle. *J Physiol* **268**, 827–861.
- Gandevia SC & Burke D (1985). Effect of training on voluntary activation of human fusimotor neurons. *J Neurophysiol* **54**, 1422–1429.
- Gandevia SC, Wilson L, Cordo PJ & Burke D (1994). Fusimotor reflexes in relaxed forearm muscles produced by cutaneous afferents from the human hand. *J Physiol* **479**, 499–508.
- Gao Z, Davis C, Thomas AM, Economo MN, Abrego AM, Svoboda K, De Zeeuw CI & Li N (2018). A cortico-cerebellar loop for motor planning. *Nature* **563**, 113–116.
- Ghez C, Favilla M, Ghilardi MF, Gordon J, Bermejo R & Pullman S (1997). Discrete and continuous planning of hand movements and isometric force trajectories. *Exp Brain Res* **115**, 217–233.
- Hospod V, Aimonetti JM, Roll JP & Ribot-Ciscar E (2007). Changes in human muscle spindle sensitivity during a proprioceptive attention task. *J Neurosci* **27**, 5172–5178.
- Huang HJ & Ahmed AA (2014). Reductions in muscle coactivation and metabolic cost during visuomotor adaptation. *J Neurophysiol* **112**, 2264–2274.
- Kakuda N, Vallbo AB & Wessberg J (1996). Fusimotor and skeletomotor activities are increased with precision finger movement in man. *J Physiol* **492**, 921–929.
- Kurata K (1993). Premotor cortex of monkeys: Set- and movement-related activity reflecting amplitude and direction of wrist movements. *J Neurophysiol* **69**, 187–200.
- Macefield VG & Knellwolf TP (2018). Functional properties of human muscle spindles. *J Neurophysiol* **120**, 452–467.
- Matthews PBC (1972). The physiological study of fusimotor fibers. In *Mammalian Muscle Receptors and their Central Actions*, pp. 195–262. Edward Arnold Publishers Ltd, London.
- Messier J & Kalaska JF (2000). Covariation of primate dorsal premotor cell activity with direction and amplitude during a memorized-delay reaching task. *J Neurophysiol* **84**, 152–165.
- Papaioannou S & Dimitriou M (2021). Goal-dependent tuning of muscle spindle receptors during movement preparation. *Sci Adv* **7**, eabe0401.
- Prochazka A (1986). Proprioception during voluntary movement. *Can J Physiol Pharmacol* **64**, 499–504.
- Prochazka A (1996). Proprioceptive feedback and movement regulation. In *Handbook of Physiology, section 12, Exercise: Regulation and Integration of Multiple Systems*, ed. Rowell L & Shepherd JT, pp. 89–127. Oxford University Press, New York.
- Prochazka A & Gorassini M (1998). Ensemble firing of muscle afferents recorded during normal locomotion in cats. *J Physiol* **507**, 293–304.

- Ribot-Ciscar E & Ackerley R (2021). Muscle proprioceptive feedback can be adapted to the behavioral and emotional context in humans. *Curr Opin Physiol* **20**, 46–51.
- Ribot-Ciscar E, Hospod V, Roll JP & Aimonetti JM (2009). Fusimotor drive may adjust muscle spindle feedback to task requirements in humans. *J Neurophysiol* **101**, 633–640.
- Rosenbaum DA (1980). Human movement initiation: specification of arm, direction, and extent. *J Exp Psychol Gen* **109**, 444–474.
- Shen L & Alexander GE (1997). Preferential representation of instructed target location versus limb trajectory in dorsal premotor area. *J Neurophysiol* **77**, 1195–1212.
- Tanji J & Evarts EV (1976). Anticipatory activity of motor cortex neurons in relation to direction of an intended movement. *J Neurophysiol* **39**, 1062–1068.
- Thoroughman KA & Shadmehr R (1999). Electromyographic correlates of learning an internal model of reaching movements. *J Neurosci* **19**, 8573–8588.
- Vallbo AB (1970). Discharge patterns in human muscle spindle afferents during isometric voluntary contractions. *Acta Physiol Scand* **80**, 552–566.
- Vallbo AB & Hagbarth KE (1968). Mechnoreceptor activity recorded from human peripheral nerves. *Electroencephalogr Clin Neurophysiol* **25**, 407.
- Wessberg J & Vallbo AB (1995). Human muscle spindle afferent activity in relation to visual control in precision finger movements. *J Physiol* **482**, 225–233.
- Wolpert DM & Miall RC (1996). Forward models for physiological motor control. *Neural Netw* **9**, 1265–1279.

## Additional information

### Competing interests

None.

### Author contributions

Sole author.

### Funding

This work was supported by grants awarded to M.D. by the Medical Faculty of Umeå University (strategic grant 2.1.6-1119-19) and the Swedish Research Council (project 2020–02140). The views expressed in this article are the author's own.

### Keywords

fusimotor control, human, muscle spindle, proprioception, sensorimotor