Exp Brain Res (2013) 231:397–403
DOI 10.1007/s00221-013-3704-0

RESEARCH ARTICLE

Selective changes in cerebellar-cortical processing following motor training

H. Haavik · B. A. Murphy

Received: 12 July 2013 / Accepted: 3 September 2013 / Published online: 25 September 2013

Abstract The aim of this study was to investigate the effect of varying stimulation rate and the effects of a repetitive typing task on the amplitude of somatosensory evoked potential (SEP) peaks thought to relate to cerebellar processing. SEPs (2,000 sweep averages) were recorded following median nerve stimulation at the wrist at frequencies of 2.47, 4.98, and 9.90 Hz from 12 subjects before and after a 20-min repetitive typing task. Typing and error rate were recorded 2-min pre- and post-typing task. Effect of stimulation rate was analysed with ANOVA followed by pairwise comparisons (paired t tests). Typing effects were analysed by performing two-tailed paired t tests. Increasing stimulation frequency significantly decreased the N30 SEP peak amplitude ($p < 0.02$). Both the 4.98 and 9.90 Hz rates lead to significantly smaller N30 peak amplitudes compared to the 2.47 Hz ($p \leq 0.01$). The N24 amplitude significantly increased following the typing task for both 4.98 and 2.47 Hz ($p \leq 0.025$). In contrast, there was a highly significant decrease ($p < 0.001$) in the N18 peak amplitude post-typing at all frequencies. Typing rate increased ($p < 0.001$) and error rate decreased ($p < 0.05$) following the typing task. The results suggest that the N24 SEP peak amplitude is best recorded at 4.98 Hz since the N30 amplitude decreases and no longer contaminates the N24 peak, making the N24 visible and easier to measure, while still enabling changes due to repetitive activity to be measured. The decrease in N18 amplitude along with an increase in N24 amplitude with no change in N20 amplitude may be explained by the intervention reducing inhibition at the level of the cuneate nucleus and/or interior olives leading to alterations in cerebellar-cortical processing.

Keywords Cerebellum · Cortical plasticity · Repetitive movement · Somatosensory evoked potentials · Human

H. Haavik
Research Division, New Zealand College of Chiropractic, Auckland, New Zealand

B. A. Murphy (✉)
Faculty of Health Sciences, University of Ontario Institute of Technology, 2000 Simcoe St North, Oshawa, ON L1H 7K4, Canada
e-mail: Bernadette.Murphy@uoit.ca

Introduction

The mechanisms that underlie use-dependent cortical reorganisation are not yet well understood. A potentially important area in use-dependent plasticity is the role of the cerebellum. The cerebellum is known to be important for motor learning (for review see Attwell et al. 2002; Bloedel 2004; Ioffe et al. 2007; Manto and Bastian 2007; Molinari et al. 2007), and there is emerging evidence that it may play a role in the plasticity and adaptation of motor circuits (Del Olmo et al. 2007; Apps and Garwicz 2005). In particular, the cerebellum is thought to facilitate the development of motor learning by fine tuning and coupling sensory signals with motor responses (Manzoni 2007). The cerebellum plays a fundamental role in the early stages of learning, as seen in functional magnetic resonance imaging and positron emission tomography studies (Doyon et al. 2002, 2003; Penhume and Doyon 2002).

Functional imaging studies have also determined that there are differences in brain activity associated with areas of executive function in motor execution of simple, sequential movements and longer, more complex sequential tasks (Catalan et al. 1998; Sadato et al. 1996). However to our knowledge, there is only one study that has used somatosensory evoked potentials (SEPs) to investigate cortical

changes that occur with motor training (Haavik Taylor and Murphy 2007). The task used involved the repetitive typing of the sequence of numbers 7, 8, and 9 in ascending order (Haavik Taylor and Murphy 2007). This work found that there were cortical changes following the learning task; however, subcortical changes were not seen (Haavik Taylor and Murphy 2007).

Two SEP peaks in particular are thought to reflect processing related to the cerebellum, namely the N24 and possibly the N18. The N18 SEP potential is thought to reflect inhibitory activity at the level of the medulla, most likely in the dorsal column nuclei (for review see Sonoo 2000). However, there is also a possibility that the N18, in part, is generated via collaterals that diverge from the medial lemniscus within the medulla oblongata, i.e., due to the activity in the cuneocerebellar tract, the cerebellum itself, or accessory olives (Noel et al. 1996), although this remains more controversial (for review see Sonoo 2000). Whether the N18 reflects direct spinal-olivary-cerebellar connections or not, the cuneate nuclei not only appear to serve a role in tactile sensation and kinaesthesia by topographically relaying precise cutaneous and proprioceptive information through the thalamus to the cerebral cortex, but its efferent connections also appear to serve complex, feedback-regulated roles in sensorimotor 'cerebellar' integration by systematically channelling and transmitting a variety of other types of somatic information to other parts of the nervous system (Berkley et al. 1986; Hand and Winkle 1977). Thus, alterations in N18 SEP amplitudes may well reflect alterations in this cerebellar sensorimotor integration.

Dipole source analysis has demonstrated that the frontal N24 and parietal P24 SEP peak originates in the primary somatosensory cortex (S1) (Restuccia et al. 2001). This same group also demonstrated a significant decrease in the amplitude of the frontal N24 and parietal P24 SEP after stimulation of the affected side in patients with unilateral cerebellar lesions (Restuccia et al. 2001), suggesting that the cerebellum influences the early phases of somatosensory processing. Despite the widespread cerebellar-cortical connections, it is interesting to note that only the N24 and P24 SEP peak amplitudes were affected in patients with unilateral cerebellar lesions, suggesting that these SEP components selectively reflect the cerebellum influences in the early phases of somatosensory processing and may therefore be utilised as a method to explore cerebellar influences on sensory function in an experimental setting.

However, the N24 amplitude is difficult to measure as it is partially obscured by the later broad N30 SEP wave. The N24 peak is often described as a notch on the rising slope of the N30 wave (Garcia Larrea et al. 1992).

One way of selectively enhancing the ability to view the amplitude of the N24 SEP peak is to increase the stimulation rate (Garcia Larrea et al. 1992). At higher stimulation rates, the amplitude of the N30 peak decreases thus revealing the underlying N24 peak.

Murphy et al. (2003) have previously shown persistent changes in N18 and N30 SEP peak amplitudes following 20 min of a repetitive motor learning in a non-utilised muscle. As the N18 amplitude is thought to reflect inhibitory activity at the level of the cuneate nucleus (for review see Sonoo 2000), the alteration in N18 amplitude may well reflect motor learning induced changes in the complex, feedback-regulated sensorimotor 'cerebellar' integration systems, via well-known cuneate nucleus efferent connections (Berkley et al. 1986; Hand and Winkle 1977). If the motor task is impacting cerebellar function in this manner, the same motor training task may also affect the N24 SEP peak amplitude, as the N24 SEP peak has been shown to be selectively reduced in patients with unilateral cerebellar lesions (Restuccia et al. 2001). Therefore, this study sought to investigate the effect of varying stimulation rate on the amplitude and properties of the SEP peaks thought to relate to cerebellum processing and motor learning.

A similar design to previous work (Murphy et al. 2003) was utilised to (1) explore the optimal stimulation rate to enable easy and accurate recording of the N24 SEP peak amplitude without contamination of the N30 SEP peak and (2) investigate whether a 20-min motor learning task alters early median nerve SEP peak amplitude from a non-utilised muscle that may potentially relate to cerebellum processing (i.e. N18 and/or N24).

Methods

Subjects

Twelve right-handed subjects (7 women and 5 men), aged 19–47 (mean age 24.5 ± 9.7 years), with no history of neurological disorders, participated in this study. Informed consent was obtained and the local ethical committee approved the study.

SEP stimulating parameters

The stimulating electrodes (anode distal) were placed over the median nerve at the wrist of the dominant arm. Three different stimulation frequencies were utilised (2.47, 4.98, and 9.90 Hz) through 7-mm Ag/AgCl disposable, adhesive electrodes (Hydrospot from Physiometrix) (impedance <5 kΩ). Previous work by Fujii et al. (1994) has demonstrated that at stimulation rates greater than 3 Hz, the N30 SEP peak is attenuated. We therefore selected a rate below 3 Hz that we have used in previous studies (Murphy et al. 2003; Haavik Taylor and Murphy 2007) as our starting point in order to ensure that we could get clear SEP peaks.

We then doubled this rate and doubled it again, as we suspected that a very high stimulation rate may not allow identification of potential changes from an intervention due to collision of afferents, and hence chose the 9.9 Hz, which is well above the rate that is needed to clearly visualise the N24, based on previous studies (Garcia Larrea et al. 1992). Stimuli consisted of electrical square pulses of 0.2 ms duration. The stimulated arm was immobilised with a splint to ensure stable stimulating conditions throughout the experiment. The stimulus intensity was at motor threshold, which was defined as the lowest intensity that produced a visible muscle contraction of the abductor pollicis brevis (APB) muscle.

SEP recording parameters

The subjects were installed in a quiet room and seated in a reclining chair. Throughout the course of the experiment, the subjects were asked to sit still and as quietly as possible. During the SEP recordings, the lights in the room were also turned off and subjects' eyes were closed.

All SEP recording electrodes were 10-mm disc, 2-mm hole gold cup EEG electrodes (Grass Technologies, An Astro-Med, Inc. Subsidiary, Rockland, MA). They were placed according to the International Federation of Clinical Neurophysiologists (IFCN) recommendations (Nuwer et al. 1994). Recording electrodes were placed on the ipsilateral Erb's point, over the C6 spinous process (Cv6), and 2 cm posterior to contralateral central and frontal scalp sites C3/4, which will be referred to as Cc, and on a more frontal site (6 cm in front and 2 cm lateral to Cz), which will be referred to as the 'Rossi site' (as first described by Rossi et al. 2003). The C6 spinous electrode was referenced to the anterior neck (tracheal cartilage). The Erb's point electrode was referenced to the contralateral shoulder. Finally, the central Cc' electrode was also referenced to the contralateral shoulder, as SEP components originating from subcortical regions are best recorded with a noncephalic reference (Ulas et al. 1999). An additional gold cup disinfected EEG electrode was placed in the mouth of subjects and acted as a ground electrode.

The scalp electrodes were securely attached with EC2 adhesive electrode paste (Grass Technologies, An Astro-Med, Inc. Subsidiary, Rockland, MA). The other electrodes were attached to their appropriate sites with tape. The impedance of all recording and reference electrodes was maintained at less than 5 kΩ throughout the experiment.

Experimental protocol

The subjects were first given written and verbal explanations of the study. All subjects attended two sessions. The order of the interventions was randomised.

Somatosensory evoked potential peaks (average of 2,000 sweeps) were recorded following median nerve stimulation at the wrist at three different frequencies (2.47, 4.98, and 9.90 Hz), before and after a 20-min repetitive typing task, which is described below. Typing and error rate were recorded 2-min pre- and post-typing task. Amplitudes were measured from the peak of interest to the preceding and/or succeeding peak of opposite deflection, or if not possible then from the peak of interest to baseline.

Motor learning task

The motor learning intervention consisted of a 20-min thumb abduction task, where the subject pressed a key on an external keyboard repeatedly. The subjects were required to type for 20 min at a typing speed equivalent to 180 key-strikes per minute. Their speed was displayed graphically via the computer monitor using a custom-designed LabView 7.1 program to provide visual feedback for the subject. Subjects' dominant arm was resting on the armchair with about 90 degrees of elbow flexion with the hand pronated. The arm was splinted to minimise changing postures of the forearm, and the splint was fastened to the armchair. The external keyboard was fastened to the splint in a comfortable position for the subject's thumbs. The thumb abductions were of low force, i.e., only the force required to press the key on the external keyboard for the LabView 7.1 program to register the rate of contractions. This equated to between 5 and 10 % of their APB's MVC. Subjects uniformly reported some mild discomfort at about 5 min into the typing task which disappeared by itself within an average of 5 min. Two subjects reported their thumbs felt fatigue towards the end of the 20-min period, but the rest of the subjects did not report this. No further discomfort was reported. The three pre- and post-intervention trials consisted of two lots of 1,000 sweeps at each of the three stimulation intensities. The trials therefore took 2 × 6.75 min at 2.47 Hz, 2 × 3.35 min at 4.98 Hz, and 2 × 1.68 min at 9.9 Hz to record (i.e. a total of 23.56 min for all three trials). The order of these six sets of SEP data (i.e. 6 × 1,000 sweeps) both pre- and post-intervention was randomised. Allowing for time to check impedance, all data collection prior to and after the typing intervention was completed within 30 min.

Data collection and analysis

The signals were passed to a Grass® Model 15 Neurodata acquisition system via an IMEB Model Bio-Potential Isolator Electrical Board (Grass®). The signals were band-pass filtered (3–1,000 Hz) (−6 dB octave roll-off), amplified (gain 100 000), and then passed to a National Instruments® Data Acquisition Board (NI-AT-MIO-46E-3) via a

specially shielded cable and National Instruments Cable box (SC2056). LabView 7®, a commercial software package, controlled the NI-AT-MIO-46E-3 board. The LabView program controlled the data acquisition, signal averaging, and graphing functions for data analyses.

The EEG was digitised at a sample rate of 5,000 samples per second and recorded with a sweep length of 55 ms (5 ms pre-stimulus and 50 ms post-stimulus). A total of 2,000 sweeps were averaged and displayed on an analysis panel from which the waveforms of interest were measured for amplitude and latency. To ensure a stable peripheral nerve volley, the N9 peak amplitude was analysed first, as the N9 SEP peak amplitude, which is recorded over Erb's point, reflects the afferent volley at the peripheral level (i.e. at the brachial plexus). If the N9 peak amplitude pre- and post-intervention was within ±10 % of baseline values, the other peaks from these trials would be included for analysis. This was instituted because of the fact that the participant's hand and arm position may have been altered following the motor training task, and we needed to ensure that the peripheral volley was stable in order to be able to ensure that any changes in SEP peak amplitude could indeed be attributed to central changes. No trials needed to be excluded based on this criterion.

Somatosensory evoked potential amplitudes were measured, from the averaged (2,000 sweeps) non-rectified traces, from the peak of interest to the preceding or succeeding peak of opposite deflection, according to international recommendations (Nuwer et al. 1994), and past studies in this field (Cheron and Borenstein 1987, 1991; Rossini et al. 1996; Sonoo et al. 1996). The amplitude and latency of the following SEP components were identified and measured: the peripheral N9, the spinal N13, the far-field N18 (P14-N18 complex), the parietal N20 (P14-N20 complex), the frontal N24 (P22-N24 complex), and the frontal N30 (P22-N30 complex). The latencies were recorded from stimulation onset to their maximal peak or trough for each SEP component.

To investigate the effect of stimulation rate and the typing task, ANOVAs with factors time (pre vs. post) and rate (2.47, 4.98, and 9.9 Hz) followed by pairwise comparisons (two-tailed paired *t* tests) were carried out for the averaged median nerve SEP peak amplitudes and latencies utilising SPSS™ statistical software (version 17.0). Typing effects were analysed by performing two-tailed paired *t* tests. The level of significance was set at $p < 0.05$.

Results

Effects of stimulus rate

The ANOVA revealed there was a significant effect of rate for the N30 SEP peak amplitude [$F(2, 30) = 4.51$, $p = 0.019$]. Increasing the frequency of stimulation rate resulted in a significant decrease in the N30 SEP peak amplitude. At both the stimulus rates of 4.98 Hz ($p \leq 0.001$) and 9.90 Hz ($p \leq 0.002$), the N30 SEP peak amplitudes were significantly smaller than at the 2.47 Hz stimulation rate (see Fig. 1). At the stimulus rate of 4.98 Hz, the N30 SEP peak amplitude decreased by 45 % compared to its amplitude when recorded with a stimulation rate of 2.47 Hz. At the stimulus rate of 9.90 Hz, the N30 SEP peak amplitude decreased by almost 52 % compared to its amplitude when recorded with a stimulation rate of 2.47 Hz. There was no significant difference between the rates at 4.98 and 9.90 Hz ($p \leq 1.052$). The N30 SEP amplitudes were similar at these two stimulation rates, with the amplitude of the N30 at 9.9 Hz 12.5 % lower than at 4.98 Hz. There were no other significant changes found due to altering stimulation rate. See Table 1 for all the raw SEP peak amplitudes at the various stimulation rates pre- and post- motor training task.

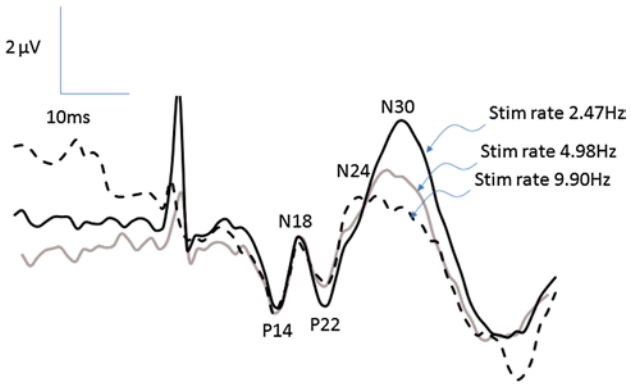

Fig. 1 Figure depicting the effect of increased stimulation rate on the SEP peak amplitudes from one representative study participant. It shows traces from the Rossi site at both the 2.47 Hz (405 ISI), 4.98 Hz (201 ISI), and 9.90 Hz (101 ISI) frequencies. The figure demonstrates that as the frequency is increased, the P22-N30 SEP peak complex decreases in size and the N24 peak becomes more prominent, while there are not changes in the P14-N18 SEP peak complex amplitude

Effects of motor training

Typing rate increased ($p < 0.001$) and error rate decreased ($p < 0.05$) following the typing task. There was also a significant increase in the N24 SEP peak amplitude following the typing task at both 4.98 Hz ($p = 0.024$) and 2.47 Hz ($p = 0.020$) (see Fig. 2). Although there was a trend towards a larger amplitude for the N24 peak following the repetitive typing task, there was no significant difference at the stimulus rate of 9.90 Hz ($p = 0.152$). In contrast, the results showed a highly significant decrease ($p < 0.001$) in the N18 peak amplitude post-typing at all frequencies (see Fig. 2).

Table 1 Mean raw amplitude (μV) data with standard deviations of individual SEP components for each of the three stimulation rates (2.47, 4.98, and 9.9 Hz), pre- and post-motor training intervention

	N13		N18		N20		N24		N30	
	Amplitude	SD	Amplitude	SD	Amplitude	SD	Amplitude	SD	Amplitude	SD
Stim rate 2.47Hz										
Pre	2.08	0.96	1.21 **	0.53	3.40	1.27	1.69 *	0.66	2.63	1.66
Post	2.61	0.84	1.16 **	0.43	3.50	1.30	1.81 *	0.56	2.47 *	1.43
Stim rate 4.98Hz										
Pre	2.29	0.82	1.17 **	0.38	3.02	1.21	1.65 *	0.91	* 1.43	0.85
Post	2.07	0.73	1.12 **	0.54	3.16	1.10	1.87 *	0.86	1.51	0.91
Stim rate 9.90Hz										
Pre	2.04	0.79	1.21 **	0.48	2.98	1.26	1.96	0.81	1.27	0.74
Post	1.98	0.76	1.12 **	0.43	3.21	1.22	2.13	0.69	1.31	1.02

* $p < 0.05$; ** $p < 0.001$

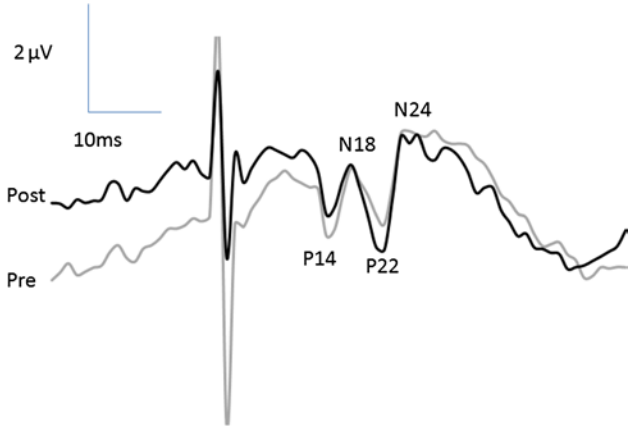

Fig. 2 Figure representing the difference between pre-typing (*grey line*) and post-typing (*black line*) trials for the N18, N24 SEP peaks recorded at a stimulation rate of 4.98 Hz (201 ISI) before and after the 20-min repetitive typing task for a single representative study participant. The figure demonstrates that there was an increase in the P22-N24 SEP peak complex amplitude post-typing task, while the P14-N18 SEP peak complex amplitude decreased

Discussion

The results of this study suggest that the N24 SEP peak is best recorded at a stimulation rate that is above 2.5 Hz but below 9.9 Hz. At 2.48 Hz, the N24 was still contaminated by the N30 peak, and it is therefore difficult to ensure accurate measurements of its amplitude. With the stimulation rate of 4.98 Hz, the N24 peak was clearly more visible (see Fig. 1), as the N30 amplitude decreases and no longer contaminates the N24 peak to the same degree. At this stimulation rate, it was also possible to record changes due to repetitive activity. It is possible that 4 Hz or 6 Hz would work equally well but we did not test these frequencies in order to avoid excessive numbers of repetitive stimuli. At the higher stimulation rate of 9.9 Hz, the N24 peak was also less contaminated by the N30, but no peak amplitude changes could be detected following the motor training task. This could mean that at a stimulation rate of 9.90 Hz, there is too much afferent interference from the high stimulus rate (Fujii et al. 1994), which gates the N24 peak and masks the amplitude increase that occurred following the typing intervention. This study also confirmed previous work that the N30 is best recorded at stimulus rates less than 2.5 Hz (Valeriani et al. 1998).

The N18 peak amplitude decreased following the typing task, as previously shown (Murphy et al. 2003). This decrease in the N18 SEP peak amplitude was a consistent and robust finding at all three stimulation rates. This SEP peak therefore appears to be less influenced by stimulation rate. As the N18 peak amplitude decreased while the N24 peak amplitude increased following the typing intervention, this may suggest that there was a reduction in inhibition at the level of the cuneate nucleus and/or possibly inferior olives following the motor training task resulting in altered sensorimotor cerebellar integration and increased processing occurring at S1 (reflected by the increased N24 peak amplitude).

Several studies have suggested that the N18 SEP peak reflects inhibitory activity at the level of the medulla, most likely in the dorsal column nuclei (Manzano et al. 1998; Rossi et al. 2003; Noel et al. 1996; Sonoo 2000). The N18 SEP peak may therefore reflect a level of afferent processing in the brainstem where information is filtered prior to cortical processing. A reduction in this filtering effect is likely to be an important and necessary part of early motor learning to allow for coupling functionally relevant information together to establish new connections. This process has been referred to as 'chunking' by Miller (1994). To greatly improve efficiency in motor skill learning, bits of information are processed as packages or 'chunks' of information that can be learned and therefore be treated as individual entities in motor memory.

However, N18 SEP peak findings in this study must be interpreted with caution. We recorded the N18 SEP peak, as others have also done (Rossi et al. 2003), from a frontal site contralateral to the side of stimulation. Such a setup also picks up N20 and N24 responses. Others have shown that the N18 is far less contaminated from cortical components when the active electrode is placed on the central region ipsilateral to the stimulus (Sonoo et al. 1991, 1992). Using such a setup would have provided greater reliability of the N18 amplitude.

The N24 and P24 SEP peak amplitudes have been shown to be selectively decreased after stimulation of the affected side in patients with unilateral cerebellar lesions (Restuccia et al. 2001), suggesting that the cerebellum influences the early phases of somatosensory processing, as dipole source analysis has demonstrated that the frontal N24 and parietal P24 SEP peak originates in the primary somatosensory cortex (S1) (Restuccia et al. 2001). Despite the widespread cerebellar-cortical connections, it is interesting to note that only the N24 and P24 SEP peak amplitudes were affected in patients with unilateral cerebellar lesions, suggesting that these SEP components selectively reflect the cerebellum influences in the early phases of somatosensory processing and may therefore be utilised as a method to explore cerebellar influences on sensory function in an experimental setting. As our results found a selective increase in the N24 following the motor task, this may reflect changes in processing of afferent information at the S1 due to altered cerebellar sensorimotor integration (Restuccia et al. 2001). This would support previous work that suggests the cerebellum is important in early motor learning (Attwell et al. 2002; Bloedel 2004; Ioffe et al. 2007; Manto and Bastian 2007; Molinari et al. 2007; Del Olmo et al. 2007; Apps and Garwicz 2005; Manzoni 2007). Our findings may indicate that early motor learning preferentially alters processing in cuneate-olivo-cerebellar-cortical pathways. This is in accordance with previous authors who have argued that the cerebellum facilitates early motor learning by fine tuning and coupling sensory signals with motor responses (Manzoni 2007).

Acknowledgments The authors would like to thank Jessica Bosse and Julian Daligadu for assistance with the data collection process.

References

Apps R, Garwicz M (2005) Anatomical and physiological foundations of cerebellar information processing. Nat Rev Neurosci 6:297–311

Attwell PJE, Cooke SF, Yeo CH (2002) Cerebellar function in consolidation of a motor memory. Neuron 34(6):1011–1020

Berkley K, Budell R, Blomqvist A, Bull M (1986) Output systems of the dorsal column nuclei in the cat. Brain Res 396:199–225

Bloedel JR (2004) Task-dependent role of the cerebellum in motor learning. Prog Brain Res 143:319–329

Catalan MJ, Honda M, Weeks RA, Cohen LG, Hallett M (1998) The functional neuroanatomy of simple and complex sequential finger movements: a PET study. Brain 121(2):253–264

Cheron G, Borenstein S (1987) Specific gating of the early somatosensory evoked potentials during active movement. Electroencephalogr Clin Neurophysiol 67(6):537–548

Cheron G, Borenstein S (1991) Gating of the early components of the frontal and parietal somatosensory evoked potentials in different sensory-motor interference modalities. Electroencephalogr Clin Neurophysiol 80(6):522–530

Del Olmo MF, Cheeran B, Koch G, Rothwell JC (2007) Role of the cerebellum in externally paced rhythmic finger movements. J Neurophysiol 98:145–152

Doyon J, Song AW, Karni A, Lalonde F, Adams MM, Ungerleider LG (2002) Experience-dependent changes in cerebellar contributions to motor sequence learning. Proc Natl Acad Sci USA 99:1017–1022

Doyon J, Penhune V, Ungerleider LG (2003) Distinct contribution of the cortico-striatal and cortico-cerebellar systems to motor skill learning. Neuropsychologia 41(3):252–262

Fujii M, Yamada T, Aihara M, Kokubun Y, Noguchi Y, Matsubara M, Yeh MH (1994) The effects of stimulus rates upon median, ulnar and radial nerve somatosensory evoked potentials. Electroencephalogr Clin Neurophysiol 92(6):518–526

Garcia Larrea L, Bastuji H, Mauguiere F (1992) Unmasking of cortical SEP components by changes in stimulus rate: a topographic study. Electroencephalogr Clin Neurophysiol 84(1):71–83

Haavik Taylor H, Murphy B (2007) Altered cortical integration of dual somatosensory input following the cessation of a 20 minute period of repetitive muscle activity. Exp Brain Res 178(4):488–498

Hand P, Winkle T (1977) The efferent connections of the feline nucleus cuneatus. J Comp Neurol 171:83–110

Ioffe ME, Chernikova LA, Ustinova KI (2007) Role of cerebellum in learning postural tasks. Cerebellum 6(1):87–94

Manto M, Bastian AJ (2007) Cerebellum and the deciphering of motor coding. Cerebellum 6(1):3–6

Manzano GM, Negrao N, Nobrega JAM (1998) The N18 component of the median nerve SEP is not reduced by vibration. Electroencephalogr Clin Neurophysiol 108:440–445

Manzoni D (2007) The cerebellum and sensorimotor coupling: looking at the problem from the perspective of vestibular reflexes. Cerebellum 6(1):24–37

Miller GA (1994) The magical number seven, plus or minus two: some limits on our capacity for processing information. Psychological Review 101(2):343–352

Molinari M, Leggio MG, Thaut MH (2007) The cerebellum and neural networks for rhythmic sensorimotor synchronization in the human brain. Cerebellum 6(1):18–23

Murphy BA, Haavik Taylor H, Wilson SA, Oliphant G, Mathers KM (2003) Rapid reversible changes to multiple levels of the human somatosensory system following the cessation of repetitive contractions: a somatosensory evoked potential study. Clin Neurophysiol 114(8):1531–1537

Noel P, Ozaki I, Desmedt JE (1996) Origin of N18 and P14 far-fields of median nerve somatosensory evoked potentials studied in patients with a brain-stem lesion. Electroencephalogr Clin Neurophysiol 98(2):167–170

Nuwer MR, Aminoff M, Desmedt J, Eisen AA, Goodin D, Matsuoka S, Mauguiere F, Shibasaki H, Sutherling W, Vibert JF (1994) IFCN recommended standards for short latency somatosensory evoked potentials. Report of an IFCN committee. International federation of clinical neurophysiology. Electroencephalogr Clin Neurophysiol 91(1):6–11

Penhume VB, Doyon J (2002) Dynamic cortical and subcortical networks in learning and delayed recall of timed motor sequences. J Neurosci 22:1397–1406

Restuccia D, Valeriani M, Barba C, Le Pera D, Capecci M, Filippini V, Molinari M (2001) Functional changes of the primary somatosensory cortex in patients with unilateral cerebellar lesions. Brain 124(Pt 4):757–768

Rossi S, della Volpe R, Ginanneschi F, Ulivelli M, Bartalini S, Spidalieri R, Rossi A (2003) Early somatosensory processing during tonic muscle pain in humans: relation to loss of proprioception and motor 'defensive' strategies. Clin Neurophysiol 114(7):1351–1358

Rossini PM, Caramia D, Bassetti MA, Pasqualetti P, Tecchio F, Bernardi G (1996) Somatosensory evoked potentials during the ideation and execution of individual finger movements. Muscle Nerve 19(2):191–202

Sadato N, Ibañez V, Deiber M-P, Campbell G, Leonardo M, Hallett M (1996) Frequency-dependent changes of regional cerebral blood flow during finger movements. J Cereb Blood Flow Metab 16(1):23–33

Sonoo M (2000) Anatomic origin and clinical application of the widespread N18 potential in median nerve somatosensory evoked potentials. J Clin Neurophysiol 17(3):258–268

Sonoo M, Sakuta M, Shimpo T, Genba K, Mannen T (1991) Widespread N18 in median nerve SEP is preserved in a pontine lesion. Electroencephalogr Clin Neurophysiol 80(3):238–240

Sonoo M, Genba K, Zai W, Iwata M, Mannen T, Kanazawa I (1992) Origin of the widespread N18 in median nerve SEP. Electroencephalogr Clin Neurophysiol 84:418–425

Sonoo M, Kobayashi M, Genba-Shimizu K, Mannen T, Shimizu T (1996) Detailed analysis of the latencies of median nerve somatosensory evoked potential components, 1: selection of the best standard parameters and the establishment of normal values. Electroencephalogr Clin Neurophysiol 100:319–331

Ulas UH, Odabasi Z, Ozdag F, Eroglu E, Vural O (1999) Median nerve somatosensory evoked potentials: recording with cephalic and noncephalic references. Electromyogr Clin Neurophysiol 39(8):473–477

Valeriani M, Restuccia D, Di Lazzaro V, Le Pera D, Barba C, Tonali P, Mauguiere F (1998) Dipolar sources of the early scalp somatosensory evoked potentials to upper limb stimulation; effects of increasing stimulus rates. Exp Brain Res 120:306–315