Interhemispheric Interactions between the Human Primary Somatosensory Cortices

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Abstract

In the somatosensory domain it is still unclear at which processing stage information reaches the opposite hemispheres. Due to dense transcallosal connections, the secondary somatosensory cortex (S2) has been proposed to be the key candidate for interhemispheric information transfer. However, recent animal studies showed that the primary somatosensory cortex (S1) might as well account for interhemispheric information transfer. Using paired median nerve somatosensory evoked potential recordings in humans we tested the hypothesis that interhemispheric inhibitory interactions in the somatosensory system occur already in an early cortical processing stage such as S1. Conditioning right S1 by electrical median nerve (MN) stimulation of the left MN (CS) resulted in a significant reduction of the N20 response in the target (left) S1 relative to a test stimulus (TS) to the right MN alone when the interstimulus interval between CS and TS was between 20 and 25 ms. No such changes were observed for later cortical components such as the N20/P25, N30, P40 and N60 amplitude. Additionally, the subcortically generated P14 response in left S1 was also not affected. These results document the existence of interhemispheric inhibitory interactions between S1 in human subjects in the critical time interval of 20–25 ms after median nerve stimulation.

Introduction

One of the basic principles in the organization of the human brain is that each cerebral hemisphere processes information from the opposite side of the body. Based on animal experiments, there is convincing evidence that callosal projections contribute to interhemispheric integration and transfer of information. That such projections can convey information between the hemispheres in human subjects is suggested by e.g. the detection of evoked potentials over primary motor cortex (M1) following electrical or magnetic stimulation of the contralateral M1 [for review see [1]]. Maladaptive functioning of interhemispheric interactions such as alterations in interhemispheric inhibition (IHI) has been described in chronic stroke and is thought to be one of the key candidates for motor impairments in these patients [2]. For example, an abnormally high interhemispheric inhibitory drive from M1 of the intact to the lesioned hemisphere has been shown to be associated with poor motor performance [3].

Compared to the findings in the motor cortex, evidence for the existence of interhemispheric transfer in other modalities such as the somatosensory system still remains elusive. There is some evidence that interhemispheric information transfer may be an exclusive attribute of the secondary somatosensory cortex (S2), which receives extensive interhemispheric projections from the contralateral body part [4,5]. Evidence for interhemispheric transfer of tactile information in human subjects comes from patients that underwent resection of the posterior half of the corpus callosum [6,7]. These studies demonstrated that bilateral activation of S2 requires the integrity of the posterior body of the corpus callosum. Furthermore, it has been shown that the size of the intermediate callosal truncus contributes to the timing and amplitude of the ipsilateral S2 source activity [5]. The transcallosal conduction time between homologous S2 was estimated in previous studies and is supposed to range between 10–20 ms [5,8].

Recent animal studies indicate that also parts of the primary somatosensory cortex (S1) such as area 2 have relatively dense callosal connections while areas 3b and 1 have only few connections. This in turn provides another potential substrate for interhemispheric transfer of tactile information [for review see [9,10]]. Therefore, it is reasonable to assume that normal interhemispheric transfer of tactile information might take place not only between S2 but also at an earlier sensory processing stage such as between S1 [11,12,13,14,15]. For example, Hlushchuk and colleagues (2006) found that unilateral touch of fingers is associated, apart from activation in contralateral S1, with a deactivation of the ipsilateral S1 [16]. They suggest that the observed ipsilateral S1 deactivation might result from transcallosal inhibition between both S1.

Assuming that interhemispheric information transfer in humans occurs already between S1, it remains to be determined which critical time window contribute to interhemispheric transfer of sensory information. Furthermore, it is still unclear whether

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Interhemispheric communication in S1 relies predominately on inhibitory or excitatory interhemispheric interactions. Based on these considerations we hypothesized the existence of interhemispheric inhibitory interactions linking the two S1 in humans at an early stage of somatosensory processing.

Materials and Methods

Experimental procedures

Subjects. We studied twelve healthy volunteers between 22 and 32 years of age (26.8±2.9 years (SD); 4/12 females). They gave written informed consent to participate in the experiment according to the declaration of Helsinki and the ethics committee of Leipzig approved the study. Prior to participation, all volunteers underwent a comprehensive neurological examination and were without acute or chronic medication. According to the Oldfield questionnaire for the assessment of handedness [17], all subjects were right-handed (laterality score: +100±11 (median ± range) over a range of -100 (fully left-handed) and +100 (fully right-handed)).

Main Experiment

Interhemispheric interactions between homologous primary somatosensory cortices (S1) were studied using a novel paradigm consisting of paired median nerve somatosensory evoked potential recordings (PMNSEPs) at suprathreshold (1.60±0.79 V for left median nerve, 1.46±0.49 for right median nerve (mean ± stdev.)) intensities. In the paired median nerve paradigm, peripheral stimulation of the left median nerve (MN) served as conditioning stimulus (CS) and always preceded right MN stimulation (test stimulus (TS)) by 5–30 ms while recording somatosensory evoked potentials (SEPs) over the left (target) S1. Additionally, SEP responses to a CS (left MN) and TS (right MN) alone were recorded over left S1 (see Fig. 1). Using this design, we were able to study possible interhemispheric interactions from right to left S1. Changes in early SEP components in the PMNSEPs relative to TS alone would give information about interhemispheric facilitation or inhibition between right and left primary somatosensory cortices.

Using a visual analogue scale (VAS), healthy volunteers rated their attention level toward the task (range 1–10; 1 = no attention, 10 = high attention), their perception of fatigue (range 1–10; 1 = strong fatigue, 10 = no fatigue) as well as their discomfort (range 1–10; 1 = no discomfort, 10 = strong discomfort) twice during the experiment (before and after the PMNSEP recordings).

Paired median nerve somatosensory evoked potential recordings (PMNSEPs)

SEPs were recorded after paired electrical median nerve stimulation of the right and left hand (PMNSEPs). Electrical pulses were generated and triggered using Spike2 software package (Version 5.04, Cambridge Electronic Design, Cambridge, UK) together with a CED Power 1401 interface (Cambridge Electronic Design Ltd., UK) and presented to the subjects using a DS5 isolated bipolar constant current stimulator (Digitimer Ltd, Welwyn Garden City, Hertfordshire, UK). For PMNSEP

Figure 1. Experimental design of the paired median nerve somatosensory evoked potential recordings (PMNSEPs). (A) Interhemispheric interactions between homologous primary somatosensory cortices (S1) were studied using paired median nerve somatosensory evoked potential recordings (PMNSEPs). In the paired median nerve paradigm, suprathreshold peripheral stimulation of the left median nerve (MN) served as conditioning stimulus (CS) and always preceded right MN stimulation (test stimulus (TS)) by 5–30 ms while recording SEPs over the left (target) S1. Additionally, SEP responses to a CS (left MN) and TS (right MN) alone were recorded over left S1 (for details see text). Analysis of PMNSEPs was performed at electrode CP3. (B) Example traces of an individual subject illustrating the subtraction method used. In brief, the response of a left MN CS alone stimulation (middle trace) over left S1 was subtracted from the raw CS+TS response over left S1 (upper trace). Final analysis of the PMNSEP data was performed on the CS+TS SEPs (CS+TS raw data – CS alone, lower trace). For details see text. Amplitudes of interest (P14, N20, N20/ P25, N30, P40, N60) are marked on the lower trace.

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recordings, standard block-electrodes were placed to the right and left median nerve (MN) at the level of the wrist (cathode proximal). MN stimulation was performed using a pulse width of 100 μs and a repetition rate of 2 Hz. Electrical stimulation intensity was adjusted for the the left and right MN individually to produce a small but visible muscular twitch in the thumb (1.60 ± 0.79 V for left MN, 1.46 ± 0.49 V for right MN (mean ± sd)). The chosen stimulation intensity was not perceived as uncomfortable or painful by the subjects.

PMNSEP recordings were performed using a MR compatible electroencephalogram (EEG) system (Brainvision (UK) Ltd., BrainAmp MR plus) from 32 scalp positions evenly distributed over both hemispheres according to the International 10–20 system. During recordings, the midfrontal electrode (FPz) was used as reference and an electrode at the sternum served as ground electrode. The skin electrode impedance was always kept below 5 kΩ. PMNSEPs were acquired with a band-pass filter between 0.1 and 1000 Hz and digitized with a sampling rate of 5000 Hz (sampling interval 200 μs) in epochs from 100 ms before and 400 ms after the stimulus pairs.

During PMNSEPs, left MN stimulation always preceded right MN stimulation using 6 different interstimulus intervals (ISIs, CS+TS) ranging from 5–30 ms in 5 ms steps (see Fig. 1A). The choice of ISIs was motivated by previous studies showing transcortical conduction times in the somatosensory system (S2) ranging between 10–20 ms [8]. Since transcortical conduction times between homologous S1 might slightly differ as compared to S2 we therefore tested a broader range of ISIs (5–30 ms). Additionally, a test stimulus (TS alone, right MN) as well as a control stimulus (CS alone, left MN) was applied while recording PMNSEPs over the left (target) hemisphere. The order of the conditions (CS+TS (5–30ms), TS and CS alone) was pseudo-randomized during the experiment. A total number of 1200 stimulus related epochs were recorded with 150 epochs for each condition (6 ISIs (CS+TS), TS alone and CS alone).

PMNSEPs were analyzed offline using a custom built program running under Matlab environment (Mathworks, Sherborn, MA, USA, Version 7.7). Epochs were digitally filtered using a standard 3rd order band-pass Butterworth filter (1–200 Hz) and each condition was averaged. Analysis was performed on electrode CP3 over the left (target) hemisphere.

A potential problem using the PMNSEP technique is that after paired-pulse stimulation (CS+TS) the response to the second (test) stimulus (TS) might be influenced by an ipsilateral response component (rather than the transcortical effect to be tested) of the first (conditioning) stimulus (CS). Therefore, the response of a left MN CS alone stimulation over left S1 was subtracted from the raw CS+TS response over left S1. We used the following procedure for subtraction: In a first step, the average SEP response at electrode CP3 (left S1) was calculated for each condition (6 ISIs (CS+TS raw data)) and for CS alone stimulation (left MN). Subsequently, the resulting SEP (epoch from 100 ms before and 400 ms after MN stimulation) for the CS alone stimulation was subtracted from each of the 6 CS+TS raw conditions (ISI 5–30 ms, see also Fig. 1B). Final analysis of the PMNSEP data was performed on the CS+TS SEPs (CS+TS raw data – CS alone).

For all subjects, the following SEP amplitudes with cortical origin were analyzed separately: N20, N20/P25 complex, N30, P25, N30/P300, P300.
P40 and N60. The subcortical P14 component [18] was additionally assessed but could only be reliably identified in 8 out of 12 subjects. The N20 amplitude was assessed as the difference between the onset (around 14–16 ms) and the first negative peak usually ranging around 17–22 ms after stimulus onset (see also [19]). In case the P14 could be detected in some subjects, the N20 response was measured from the peak of the P14 to the peak of the N20. The amplitude of the N20/P25 complex was measured as the difference between the N20 peak and maximum subsequent positivity. The N30 amplitude was measured as the difference between the N20/P25 complex peak and maximum subsequent negativity; the P40 amplitude as the difference between the N30 peak and maximum subsequent positivity as well as the N60 amplitude as the difference between the P40 peak and maximum subsequent negativity. The subcortical P14 component was assessed, if possible, as the difference between the baseline and the first positive peak ranging around 12–17ms post stimulus onset.

Statistical analysis
Data were analyzed using the PASW software package for Windows version 18. For statistical analyses, we first used two-way repeated measures ANOVA (ANOVARM, if necessary corrected for non-sphericity) with factor AMPLITUDE (N20, N20/P25, N30, P40 and N60) and ISI (TS alone, 5, 10, 15, 20, 25, 30 ms). In a second step, we performed six one-way ANOVARM with factor ISI for all amplitudes tested. Subsequently, post-hoc tests (Bonferroni-corrected) were performed to identity differences in specific PMNSEP amplitudes of each ISI compared to TS alone. For post-hoc tests, the significance level was set to p = 0.006 to correct for multiple comparisons. All figures represent group data. Error bars refer to the standard error (s.e.m.) of the measurements.

Results
There was no statistically significant change in our assessment of attention (pre: 8.25±0.51, post: 8.00±0.42; p>0.05; range 1–10; 1 = no attention, 10 = high attention), fatigue (pre: 7.87±0.48, post: 7.87±0.45; p>0.05; range 1–10; 1 = no fatigue, 10 = strong fatigue) or discomfort (pre: 1.00±0.00, post: 1.00±0.00; p>0.05; range 1–10; 1 = no discomfort, 10 = strong discomfort) before (pre) and after (post) the experiment. None of the subjects reported any discomfort during the paired median nerve somatosensory evoked potential (PMNSEP) recordings.

A two-way ANOVARM revealed a significant effect of AMPLITUDE (N20, N20/P25, N30, P40 and N60: F(4,44) = 5.031; p = 0.031) and ISI (TS alone, 5–30 ms CS+TS: F(6,66) = 3.746; p = 0.027) on PMNSEP.

Conditioning the right S1 by electrical median nerve stimulation of the left MN (CS) resulted in a significant reduction of the N20 response to right MN stimulation in the target (left) S1 (one-way ANOVARM with factor ISI (TS alone, 5–30ms): F(6,66) = 3.951; p = 0.031, see Figures 2 and 3). No such changes could be observed for the other amplitudes tested (N20/P25: F(6,66) = 2.380; p = 0.083; N30: F(6,66) = 0.847; p = 0.458; P40: F(6,66) = 0.920; p = 0.463; N60: F(6,66) = 2.691; p = 0.066).

Post-hoc analysis revealed that the N20 response of the left S1 (relative to TS alone) was inhibited from 1.66±0.33 μV (TS alone) to 1.22±0.38 μV at a CS+TS ISI of 20 ms (CS+TS/TS ratio: 39.90±8.20%; paired T-Test: p = 0.0030). We also found an inhibition of the N20 response at a CS+TS ISI of 25 ms from 1.66±0.33 μV (TS alone) to 1.28±0.35 μV (CS+TS/TS ratio: 54.15±8.41%; paired T-Test: p = 0.0013; see Figures 2 and 3 and Table 1). No such changes on other PMNSEP components were observed for CS+TS ISIs of 3, 10, 15 and 30 ms (p>0.05, see Table 1).

To investigate if the attenuated effect on the N20 component (CS+TS/TS ISI 20 and 25 ms) of the left S1 occurred already at a subcortical level, amplitude changes of the subcortically generated P14 component of left S1 for all CS+TS conditions were identified and analyzed in 8 out of 12 subjects. We found that the P14 component did not change in response to the CS+TS ISIs relative to TS alone (one-way ANOVARM with factor ISI (TS, 5–30ms): F(6,12) = 1.051; p>0.05, see Table 1).

Discussion
Our results demonstrate that a conditioning stimulus reaching the right S1 attenuates the early cortical N20 response in the left S1 activity at interstimulus intervals of 20 and 25 ms, providing direct evidence for transcallosal information transfer at an early stage of cortical processing in the human somatosensory system. Previous work reported that transcallosal information transfer of proprioceptive information from distal body parts can take place in the secondary somatosensory cortex [S2] [10,20]. The bilateral activation of S2 following unilateral sensory stimulation has been related to the presence of dense transcallosal connections between both S2 [21].

Early tracer injection studies in animals indicated that callosal connections between the postcentral gyri exist for face and trunk areas [22]. More recently, it has been shown that homologous representations in the postcentral gyrus in Brodmann areas (BA) 1, 2 and 3b are directly or indirectly connected via callosal fibers.
information transfer in early processing stages of the somatosensory cortex. Any other interstimulus interval between CS and TS was delivered either 20 or 25 ms before the peripheral test stimulus [10]. It seems best explained by an inhibitory drive from the right to the left hemisphere [11]. The latter finding is in line with our results in human subjects. The reduced N20 component amplitude across hemispheres [11]. The former finding is consistent with previous findings showing that callosal fibers [10, 23]. This is in line with previous findings showing that callosally mediated ipsilateral potentials in the barrel cortex disappeared after applying a lesion to the contralateral sensory cortex [12, 24]. Furthermore, disruption of function in the postcentral gyrus (BA3) by cooling resulted in an augmentation of activity and enlargements of receptive fields of neurons in the homologous S1 suggesting that a functional asymmetry of the sensory thalamus is preserved [12]. This is in line with previous findings showing that callosally mediated potentials are not well understood, animal data seems to indicate that it is important to consider that the reduction of the N20 response in the left S1 is mediated by an inhibitory drive from the right to the left S1 via S1-M1-M1-S1 connections. In the present study, however, the operation of a more direct S1-S1 functional connection may be at least partially mediated by altered processing already in subcortical regions such as the ventroposterior parietal nucleus (VPL). The authors would like to thank Sylvia Stasch for excellent technical support during the PMNSEP recordings and Drs. Yves Vandermeeren and Mickael Camus for critical conceptual discussion.

Author Contributions
Conceived and designed the experiments: PR LGC AV. Performed the experiments: PR TN. Analyzed the data: PR TN. Contributed reagents/materials/analysis tools: PR TN LGC AV. Wrote the paper: PR TN LGC AV. Final version is approved by all authors.

References
1. Chen R (2004) Interactions between inhibitory and excitatory circuits in the human motor cortex. Exp Brain Res 154: 1–10.
2. Völler B, Floel A, Werhahn KJ, Ravindran S, Wu CW, et al. (2006) Contralateral hand anesthesia transiently improves poststroke sensory deficits. Ann Neurol 59: 385–398.
3. Louis GN, Perreault EF (2007) Side of lesion influences interhemispheric inhibition in subjects with post-stroke hemiparesis. Clin Neurophysiol 118: 2656–2663.
4. Hescheler K, Rupp A, Stanack A, Meineck HM, Steimlich C, et al. (2001) Interaction of tactile input in the human primary and secondary somatosensory cortex—a magnetoencephalographic study. Neuroimage 14: 759–767.

Interhemispheric Inhibition in S1

Table 1. PMNSEP amplitudes [µV] for electrode CP3 of the left (target) S1 for unilateral (TS alone) and bilateral (5–30 ms) median nerve stimulation.

| Amplitude | TS alone | 5 ms | 10 ms | 15 ms | 20 ms | 25 ms | 30 ms |
|-----------|----------|------|-------|-------|-------|-------|-------|
| P15 (n=8) | 0.17±0.05 | 0.28±0.06 | 0.25±0.06 | 0.33±0.06 | 0.29±0.06 | 0.39±0.11 | 0.29±0.10 |
| N20       | 1.60±0.33 | 1.74±0.44 | 1.44±0.38 | 1.47±0.30 | 1.22±0.38** | 1.29±0.36** | 1.46±0.39 |
| N20/P25   | 4.83±1.55 | 5.26±1.67 | 4.94±1.53 | 5.08±1.48 | 4.80±1.36 | 4.49±1.28 | 4.44±1.34 |
| N30       | 2.36±1.11 | 2.86±1.41 | 2.60±1.33 | 2.66±1.37 | 2.55±1.12 | 2.76±1.22 | 2.37±1.11 |
| P40       | 1.88±0.36 | 2.25±0.46 | 1.96±0.44 | 1.89±0.38 | 1.96±0.38 | 1.79±0.28 | 1.99±0.30 |
| N60       | 2.63±0.57 | 3.62±0.76 | 2.99±0.65 | 3.01±0.67 | 2.57±0.51 | 2.89±0.50 | 2.95±0.46 |

Asterisks represent significant differences relative to TS alone (significance level p<0.008, corrected for multiple comparisons).

Table 1. PMNSEP amplitudes [µV] for electrode CP3 of the left (target) S1 for unilateral (TS alone) and bilateral (5–30 ms) median nerve stimulation.

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5. Stanček A, Hoehnsetter K, Tintera J, Vrana J, Rachmanová R, et al. (2002) Source activity in the human secondary somatosensory cortex depends on the size of corpus callosum. Brain Res 936: 47–57.

6. Fabri M, Del Pesce M, Paggi A, Polonara G, Bartolini M, et al. (2005) Contribution of posterior corpus callosum to the interhemispheric transfer of tactile information. Brain Res Cogn Brain Res 24: 73–80.

7. Fabri M, Polonara G, Del Pesce M, Quattrini A, Salvolini U, et al. (2001) Posterior corpus callosum and interhemispheric transfer of somatosensory information: an fMRI and neuropsychological study of a partially callosotomized patient. J Cogn Neurosci 13: 1071–1079.

8. Frot M, Mauguière F (1999) Timing and spatial distribution of somatosensory responses recorded in the upper bank of the sylvian fissure (SI) area in humans. Cereb Cortex 9: 854–863.

9. Iwamura Y (2000) Bilateral receptive field neurons and callosal connections in the somatosensory cortex. Philos Trans R Soc Lond B Biol Sci 355: 267–273.

10. Iwamura Y, Taoka M, Iriki A (2001) Bilateral activity and callosal connections in the somatosensory cortex. Neuroscientist 7: 419–429.

11. Clarey JC, Tweddel R, Calfof MB (1996) Interhemispheric modulation of somatosensory receptive fields: evidence for plasticity in primary somatosensory cortex. Cereb Cortex 6: 196–206.

12. Pidoux B, Verley R (1979) Projections on the cortical somatic I barrel subfield from ipsilateral vibrissae in adult rodents. Electroencephalogr Clin Neurophysiol 46: 715–726.

13. Werhahn KJ, Mortensen J, Van Boeck RW, Zeumer KE, Cohen LG (2002) Enhanced tactile spatial acuity and cortical processing during acute hand deafferentation. Nat Neurosci 5: 906–938.

14. Blankenburg F, Ruff CC, Bestmann S, Björnottm O, Edel N, et al. (2008) Interhemispheric effect of parietal TMS on somatosensory response confirmed directly with concurrent TMS-fMRI. J Neurosci 28: 13202–13208.

15. Staines WR, Graham SJ, Black SE, McCleod WE (2002) Task-relevant modulation of contralateral and ipsilateral primary somatosensory cortex and the role of a prefrontal-cortical sensory gating system. Neuroimage 15: 190–199.

16. Oldfield RC (1971) The assessment and analysis of handedness: the Edinburgh inventory. Neuropsychologia 9: 97–113.

17. Lee EK, Seyal M (1998) Generators of short latency human somatosensory-evoked potentials recorded over the spine and scalp. J Clin Neurophysiol 15: 227–234.

18. Sonoo M, Kobayashi M, Genha-Shamian K, Mannen T, Shimizu T (1996) Delineated description 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.

19. Manzoni T, Barbaresi P, Conti F, Fabri M (1989) The callosal connections of the primary somatosensory cortex and the neural bases of midline fission. Exp Brain Res 76: 251–266.

20. Picard N, Lepore F, Pito M, Guillemot JP (1996) Bilateral interaction in the second somatosensory area (SII) of the cat and contribution of the corpus callosum. Brain Res 356: 97–104.

21. Killackey HP, Gould HJ, 3rd, Canick CG, Pons JP, Kaas JH (1983) The relation of corpus callosum connections to architectonic fields and body surface maps in sensorimotor cortex of new and old world monkeys. J Comp Neurol 219: 364–419.

22. Iwamura Y, Iriki A, Tanaka M (1999) Bilateral hand representation in the postcentral somatosensory cortex. Nature 369: 554–556.

23. Devor A, Tian P, Nishimura N, Teng IC, Hillman EM, et al. (2007) Suppressed neuronal activity and concurrent arteriolar vasodilation may explain negative blood oxygenation level-dependent signal. J Neurosci 27: 4452–4459.

24. Allison T, McCarthy G, Wood CC, Jones SJ (1991) Potentials evoked in human and monkey somatosensory cortex by stimulation of the median nerve. A review of scalp and intracranial recordings. Brain 114(Pt 6): 2465–2503.

25. Wolters A, Schmidt A, Schramm A, Zeller D, Naumann M, et al. (2005) Timing-dependent plasticity in human primary somatosensory cortex. J Physiol 563: 1039–1052.

26. Goldring S, Aras E, Weber PC (1976) Comparative study of sensory input to motor cortex in animals and man. Electroencephalogr Clin Neurophysiol 29: 537–550.

27. Reit J, Swayne OB, Vandermeeren Y, Camus M, Dimyan MA, et al. (2008) Contribution of transcranial magnetic stimulation to the understanding of cortical mechanisms involved in motor control. J Physiol 586: 325–351.