The cortical correlate of the Piper rhythm in humans manifests a further tendency to rhythmic oscillations at a frequency of 35–60 Hz. This was first noted by Hans Piper in the EMG of strong voluntary contractions (Piper 1907). When this pronounced, this high-frequency drive to muscle can be very powerful, leading to the entrainment of nearly all the motor units in a muscle (Merton 1981).

Hill (1921) was the first to appreciate the ubiquitous nature of the Piper rhythm. He recorded the sound emitted by different contracting muscles, rather than the EMG activity, and demonstrated that the rhythm was present in differing grades of muscle contraction, not just the strongest. More recent studies of muscle sound have shown that the Piper rhythm is lost in untreated Parkinson’s disease (Brown 1997), and it was suggested that the loss of Piper activity plays a critical role in the pathophysiology of this common disorder (Brown 1997; Brown and Marsden 1998). However, despite the fundamental character of the Piper rhythm, its origin was unclear. Here we provide evidence that the Piper rhythm of human muscle is driven by the contralateral motor cortex. A preliminary account of this work appeared in abstract form (Brown et al. 1998).

METHODS

Data collection

With the informed consent of each subject (according to Declaration of Helsinki), we recorded whole scalp magnetoencephalographic (MEG) signals simultaneously with surface EMG from 10 healthy right-handed subjects (4 females, 6 males; mean age 32 yr, range 21–46 yr). EMG was picked up from the forearm extensor muscles and tibialis anterior with surface bipolar electrodes. Activity was recorded during repeated (intermittent) and sustained isometric contractions (wrist extended to ~30° against a plastic plunger) and phasic movements (rhythmic self-paced wrist flexion and extension through an arc of 100° at ~0.2 Hz). Subjects were asked to look at a projected screen (blank except for a digital clock) rather than their active hand. Intermittent contractions were limited to periods of 6–12 s to avoid fatigue and were repeated 25–40 times, with rests of ~20 s in-between. Sustained contractions and phasic movements were continued for ~120 s. Contractions were either maximal, moderate, or weak (with mean rectified EMG levels either 100, 60–80, or 20–40% of those during maximal contraction).

Cortical signals were recorded with a whole scalp neuromagnetometer in a magnetically shielded room, simultaneously with surface EMG from the contracting muscle. The subject supported the face EMG from 10 healthy subjects. In eight subjects, coherence across the primary motor cortex and electromyogram (EMG) activity in the 20- to 30-Hz range similarly for both forearm and foot. The lag between EMG and MEG activity in the leg was ~15 ms greater than that seen in the forearm, an interval appropriate for conduction in fast pyramidal pathways. It is concluded that the Piper rhythm in muscle may be driven by a comparable oscillatory activity in the contralateral motor cortex. This cortical rhythmicity can be picked up in several types of movement and seems distinct from the 20- to 30-Hz rhythmicity recorded during weak sustained contractions.

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for off-line analysis. The exact position of the head with respect to the sensor array was determined by measuring magnetic signals from three indicator coils placed on the scalp. The coil locations, with respect to three predetermined landmarks on the skull, were identified with a three-dimensional digitizer, and this information was used to superimpose sources for the MEG signals on individual magnetic resonance images obtained with a 1.5-T Siemens Magneton device.

**Data analysis**

Coherence spectra between MEG and rectified EMG were calculated with a frequency resolution of 1.8 Hz and were averaged across trials for each subject. To establish the noise level for the spectral values, we calculated coherence amplitudes with EMG signals shifted by 1 s (and any true coherence thereby abolished). The amplitudes of these random coherences remained below our significance level (Fig. 2, dashed lines) at 99% probability. We obtained cross-correlograms in the time domain by applying an inverse Fourier transform to the averaged cross-spectrum. Latencies for upper and lower limbs were compared with Student’s unpaired two-tailed t-test.

Sources of oscillatory signals were modeled in time domain as equivalent current dipoles (Hämäläinen et al. 1993), found by a least-squares search of the distribution of the strongest cross-correlogram peaks. The planar gradiometers in our whole scalp magnetometer show the largest signal above the cortical source current; thus we restricted our source analysis to sets of 40 detectors centered over the Rolandic area in each hemisphere, well covering the signal extrema. The locations, orientations, and strengths of the equivalent current dipoles were determined at the strongest cross-correlogram peak corresponding to an anterior (forearm contraction) or lateral (foot contraction) current direction; only sources that accounted for >85% of the field variance were accepted.

**RESULTS**

**Coherence between the Piper rhythm and activity in the motor cortex**

We recorded MEG and surface EMG signals during repeated maximal isometric contractions of the forearm extensor muscles of the dominant hand in 10 healthy subjects. Figure 1A illustrates the spectrum of the coherence between the right forearm EMG and an MEG channel in one subject, revealing a peak in coherence at ~45 Hz. This peak was strongest in the channels overlying the contralateral (left) Rolandic cortex (Fig. 1B). The cross-correlogram from the channel illustrated in Fig. 1B confirms the parallel rhythmicity between MEG and EMG (Fig. 1C). It also shows that cortical activity precedes EMG activity in the forearm.

Eight subjects had a significant peak in their MEG-EMG cross-correlograms, and six also had significant MEG-EMG coherence in the 35- to 60-Hz frequency band (solid lines in Fig. 2). Source modeling of the major peak in the cross-correlograms demonstrated a focus near or in the anterior wall of the central sulcus, contralateral to the active limb (lateral filled circles in Fig. 3). Currents oscillated in the posteroanterior direction, perpendicular to the central sulcus. Two subjects with clear coherence also had their nondominant hand tested, with practically identical results (solid lines in the bottom two spectra in Fig. 2).

Muscle sound recordings suggest that the Piper rhythm is not restricted to maximal contractions (Brown 1997; Hill 1921). Moderate (60–80% of maximal) contractions of the wrist extensors and slow rhythmic extension movements of the wrist were therefore recorded in the three subjects with the highest MEG-EMG coherence during maximal isometric contraction. All three showed qualitatively similar peaks of coherence in the 35- to 60-Hz band during both the moderate contractions and the last 20–30° of phasic wrist extension (Fig. 4). Coherence between MEG and forearm extensor EMG was not seen during the remainder of the movement cycle. One subject also performed slow bilateral extension movements of the wrists (with both sides moving in phase). Clear coherence was seen between EMG and the MEG signal from the contralateral motor cortex but not between the right and left motor cortex or between right and left forearm extensor muscles.
CORTICAL CORRELATE OF THE PIPER RHYTHM IN HUMANS 2913

(dashed lines), recorded during sustained weak (20–40% of maximal) contractions of the wrist extensors and tibialis anterior. There was a clear peak of coherence in the 20- to 30-Hz band, but little at higher frequencies. Note that subjects 5 and 6 show no simple harmonic relationship between the two coherent activities picked up during the different conditions (Fig. 2).

Source modeling confirmed that the 20- to 30-Hz activity displays a somatotopy similar to that found for the 30- to 60-Hz activity recorded during maximal contractions (Salenius et al. 1997). Although the source analysis suggested slightly different generators in the motor cortex for the higher and lower band coherence in some subjects (Fig. 3), no systematic differences were obtained across subjects. However, the frequency of the coherent activity during maximal contraction was generally ~10 Hz lower for leg than forearm contractions in the same subject (mean frequency ± SE in 4 subjects: hand = 47 ± 2 Hz, foot = 36 ± 1 Hz; P < 0.001; Fig. 2A). In contrast, the frequency at the peak of the coherence spectrum in weak contractions did not differ markedly between upper and lower limb (hand = 25 ± 1 Hz, foot = 24 ± 1 Hz), in agreement with previous results (Salenius et al. 1997).

The coherent cortical activity in the 40-Hz band present

In the four subjects tested, the EMG activity was also coherent with MEG during repeated brief isometric maximal contractions of the right or left tibialis anterior muscles (solid lines in Fig. 5). Source modeling indicated that the coherent activity arose in the bank of the interhemispheric fissure, in the region of the contralateral foot area (medial filled triangles in Fig. 3), with the currents oscillating in the mediolateral direction, almost perpendicular to the interhemispheric fissure. Thus the 35- to 60-Hz coherent activity displayed a somatotopy consistent with an origin within the motor cortex.

Relationship between the Piper rhythm and other descending drives to muscle

Recent MEG recordings demonstrated that during weak tonic contractions the cortical signal from the human primary motor cortex and EMG are coherent at 20–30 Hz (Conway et al. 1995; Salenius et al. 1997), in keeping with findings in the monkey (Baker et al. 1997; Murthy and Fetz 1992). Such cortical oscillations were considered a function of the motor cortex acting in a “holding” postural mode (Baker et al. 1997). Figures 2 and 5 show such coherence spectra

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**FIG. 2.** Coherence spectra between EMG from the right (top: subjects 1–6) and left (bottom: subjects 1–2) forearm extensors and an MEG channel above the contralateral Rolandic cortex. Solid lines correspond to brief maximal and dashed lines to sustained weak (20–40% of maximal) contractions.

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**FIG. 3.** Sources of cortical oscillatory signals associated with contractions of different muscles in subject 1, superimposed on the surface rendering of her brain. The black lines indicate the current directions associated with the major upgoing peaks in the cross-correlograms. Filled circles and triangles represent the sources for the forearm extensors and tibialis anterior, whereas filled and unfilled signals represent maximal and weak (20–40% of maximal) contractions.
during contraction may not be harmonically related to the coherence at ~20 Hz for the following reasons: 1) in at least two subjects (5 and 6) the different oscillatory activities showed no simple harmonic relationship during forearm activity, and 2) the Piper-frequency MEG–EMG coherence was at a different frequency in the leg and the arm, even in the same subject, although no such frequency shift was seen with the 20- to 30-Hz coherence present during sustained weak contractions of the arm and leg. Nevertheless, coherences in the two frequency bands were both seen in contractions of moderate strength (Fig. 4), with the lower and higher frequency coherences tending to alternate during the contraction. Under these circumstances, the frequencies of the two activities remained distinct, without evidence of a gradual slide from the 40- to 50-Hz into the 20- to 30-Hz band as submaximal contraction was maintained. This last observation makes it unlikely that the oscillatory cortical activity is directly tailored to the optimal fusion frequency of muscle, which drops gradually as contraction is maintained (Bigland-Ritchie et al. 1983).

**Lag between cortical and muscle activity**

Our results suggest that the coherent cortical 40-Hz activity between brain and muscle arises in the motor cortex and is functionally distinct from the lower frequency coherent activity previously reported in humans and monkeys. We hypothesized that a cortical drive to muscle should be associated with lags between muscles comparable with those seen after percutaneous magnetic stimulation of the motor cortex, which is known to involve fast pyramidal pathways (Rothwell et al. 1991). This was reported for the 20- to 30-Hz MEG–EMG coherences during weak contractions (Salenius et al. 1997) and also turned out to be the case here. Figure 6 summarizes the lags from the major up-going peak in the cross-correlograms to the EMG in forearm or leg in the different subjects. The excess lag from cortex to tibialis anterior over that to the forearm extensor muscles was 16 ± 1 ms for both maximal and weak contractions.

Figure 7 shows examples of MEG–EMG phase-spectra for subject 1. The phase depended linearly on frequency in the frequency range of significant coherence, thereby confirming the interpretation of a fixed delay between the MEG and EMG signals. For this subject, the slopes were 2.7±Hz for right hand and 6.6±Hz for right foot contractions in the frequency ranges of 27–59 and 22–45 Hz, respectively. Across subjects, the slopes of the phase spectra suggested an excess lag of 15 ± 1 ms from cortex to tibialis anterior over that to the forearm extensors, again with no difference between weak and maximal contractions and in excellent agreement with the lags determined from the cross-correlograms.

**FIG. 4.** Coherence spectra between EMG from the right forearm extensors and an MEG channel above the contralateral Rolandic cortex. The signals were recorded during intermittent submaximal contractions (60–80% of maximal contraction strength) and the last 20–30° of slow (0.1 Hz) phasic wrist extensions (movement).

**FIG. 5.** Coherence spectra between EMG from the right and left tibialis anterior muscles and an MEG channel above the contralateral medial Rolandic cortex for subjects 1–4. Solid lines correspond to brief maximal and dashed lines to sustained weak (20–40% of maximal) contractions.
MEG-EMG latencies

**FIG. 6.** *Top:* cross-correlograms between peri-Rolandic MEG and EMG from the right forearm extensors and right tibialis anterior muscles during maximal and weak (20–40% of maximal) contractions for subject 1. *Bottom:* MEG-EMG time lag (t) determined from the major up-going peak of the cross-correlogram between MEG and EMG, corresponding to anteriorly (laterally for foot muscles) directed current flow in the precentral gyrus.

**DISCUSSION**

*Piper rhythm in muscle is driven by the contralateral motor cortex*

The principal finding of this study is that the Piper rhythm of human muscle is linearly correlated with focal activity in the contralateral motor cortex. This was true of both submaximal and maximal isometric contractions and phasic movements and suggests that a parallel rhythmicity of motor cortex and muscle at ~40 Hz may be a fundamental feature of the organization of various forms of motor activity. Indeed, it seems likely that the Piper rhythm is actually driven by the oscillatory activity in the contralateral motor cortex. This conclusion is supported by the lag between the MEG and EMG signals. In particular, the lag to tibialis anterior was consistently 15 ms longer than that to the forearm extensor muscles and therefore similar to that previously reported for coherent activities in the 20- to 30-Hz range (Salenius et al. 1997). Such an interval is appropriate for conduction in fast pyramidal pathways (Rothwell et al. 1991).

The question of the absolute lag between cortex and muscle is more difficult to settle. A current dipole explained the signal distribution best during the major up-going cross-correlogram peak of signals arising in the motor cortex contralateral to the movement. This peak implies intracellular current direction from surface to the depth of the cortex and is consistent with surface negativity of the motor cortex in the anterior wall of the central sulcus. However, the descending efferent motor signal did not necessarily leave the motor cortex during the surface-negative phase of the cortical oscillation. In monkeys,
pyramidal neurons in the motor cortex tend to discharge near the peak of the negative deflection of oscillatory field potentials in lamina V (Baker et al. 1997; Murthy and Fetz 1996a). Such a deep negative field potential is associated with a surface positivity (Creutzfeldt and Houchin 1974; Murthy and Fetz 1996b). An analogous surface positivity preceding involuntary muscle discharge with an interval appropriate for conduction in fast pyramidal pathways was reported in direct recordings from the motor cortex of a patient with cortical myoclonus (Kugelberg and Widén 1954). Comparable findings were also made with scalp EEG in other patients with cortical myoclonus (Obeso et al. 1985). If we measure our lags from the major down-going cross-correlogram peak (consistent with surface positivity over the motor cortex), then an additional 10–15 ms may be added to the measured lags shown in Fig. 6. This would make the absolute delays to forearm and leg muscles comparable with those seen after percutaneous electrical or transcranial magnetic stimulation of the motor cortex (Rothwell et al. 1991). However, whether the major down-going or up-going peak is taken for lag measurements two critical observations remain true; cortical activity precedes EMG and the difference in lag between forearm and leg is appropriate for conduction in fast pyramidal pathways.

**Role of high-frequency oscillatory activity in the motor cortex**

It seems unlikely that the coherence between cortical activity and the Piper rhythm can be accounted for by a simple reafference mechanism. The Piper rhythm can be picked up from most muscles of the body, including those with few or no muscle spindles, whereas in those muscles with spindles there is no causal relationship between afferent spindle volleys and the rhythmic muscle discharge (Hagbarth et al. 1983). Moreover, in our *subject 4* the frequency at the peak of the coherence spectrum was higher in the lower than upper limb, despite the greater reafference delays from the leg. The difference in coherent frequencies between hand and foot was striking and may reflect differences in the intrinsic functional connectivity between the motor cortical hand and foot areas.

The greatest coherence between motor cortex activity and Piper activity in muscle was seen during maximal voluntary contractions and during the last 20–30° of phasic extension, when EMG activity in the forearm extensor muscles was at its strongest. Moderate contractions were characterized by two coherence peaks, one at ~20–30 Hz and another at 35–60 Hz. Weaker tonic contractions showed consistent MEG–EMG coherence only in the lower frequency band. The Piper coherence thus seems related directly or indirectly to the degree of force exerted in tonic and phasic contractions. More forceful contractions may entail a stronger excitation...