Oscillatory activity in the beta frequency range (15-30 Hz) is a robust phenomenon in the sensorimotor cortex of both humans (Kilner et al, J Neurosci 2000; Neuper & Pfurtscheller, Clin Neurophysiol 2001) and monkeys (Baker et al, J Physiol 1999). Beta oscillations in the primary motor cortex are: (1) produced by local cortical circuits reliant on GABAA-mediated intracortical inhibition (Baker & Baker, J Physiol 2003); (2) particularly pronounced in association with isometric contractions; and (3) phase-locked to activity in contralateral hand and forearm muscles (Baker et al, J Physiol 1997; Mima et al, Clin Neurophysiol 2000) with cortico-muscular coherence mediated by fast cortico-spinal axons and monosynaptic cortico-motoneuronal synapses (Baker et al, Exp Brain Res 1999). There is further evidence that synchronized beta frequency oscillations reflect the integration of activity in the primary motor cortex with that in other cortical areas such as premotor (Feige et al, J Neurophysiol 2000), somatosensory, and posterior parietal areas (Rougeul et al, Electroenceph Clin Neurophysiol 1979), and that they are modulated by attention (Kristeva-Feige et al, Clin Neurophysiol 2002).

We recently reported that beta frequency oscillations are synchronized across distributed sites in motor, premotor, somatosensory, and posterior parietal cortices of macaque monkeys as they maintained pressure on a hand lever (Bressler et al, Soc Neurosci Abstr 2002). The monkeys kept the lever pressed while waiting for stimulus presentation in a visual pattern discrimination task. Once the stimulus was presented, the monkeys were required to discriminate between two stimulus pattern types and make a differential GO/NO-GO response in order to receive a reward. Surface-to-depth event-related local field potentials (LFPs) were simultaneously recorded from bipolar teflon-coated platinum electrodes at up to 16 different cortical locations in the hemisphere contralateral to the hand pressure. The data set consisted of multi-site LFP time series recorded during thousands of task trials in three or more recording sessions for each monkey. All experiments were performed by Dr. Richard Nakamura at NIMH, and animal care was in accordance with institutional guidelines at the time (Bressler et al, Nature 1993).

In the current study, we sought to investigate causal influences existing between the sites that exhibited synchronized beta frequency oscillations. These sites were in cortical areas known to be anatomically connected in a large-scale network (Felleman & Van Essen, Cereb Cortex 1991). Our goal was to learn more about the functional relations that exist between the areas of this network in the maintenance of sustained motor output. Since our ability to determine causal influences is limited to characterization of the statistical predictability of the time series at one site based on the time series at another site, we are unable to definitively specify the axonal pathways by which such influences are manifested. Nonetheless, measures of causal influence provide directional information, and thus have the potential to provide greater insight into functional relations than available from correlation-based measures.

Multivariate autoregressive (MVAR) spectral analysis (Ding et al, Biol Cybern 2000) was performed on the LFPs from the ensemble of trials in each recording session during the pre-stimulus period. Preliminary investigations of causal influence in related sessions from this data set have previously been reported (Liang et al, Neurocomp 2000; Liang et al, Neurorep 2000). Spectral power and coherence were derived from a MVAR time series model fit to the LFPs in a 125-ms-long prestimulus window. All sites and site pairs were tested to determine whether they consistently displayed power and coherence

spectral peaks in the beta frequency range across recording sessions. Significant peaks were observed in this frequency range in power spectra from specific sites in motor, premotor, somatosensory, and posterior parietal cortical areas. Significant peaks were also observed in the coherence spectra between these sites.

For those site pairs showing beta-frequency peaks in the power and coherence spectra, we then computed causal influence in both directions from the MVAR model. The basis for evaluating the direction of influences between channels is the concept of Granger causality. For two simultaneously measured time series, one series is called causal to the second if the residual error for the second series at the present time is reduced by including the past measurements from the first series in the regression model. The method of Kaminski and Blinowska (Biol Cybern 1991) was used to measure causal influence. This method is based on the transfer function, **H(f)**, of the MVAR model, given by:

$$\mathbf{H}(f) = (\sum_{j=0}^{m} \mathbf{A}(j) e^{-2\pi i j f})^{-1}$$

where the MVAR model is:

$$\sum_{k=0}^{m} \mathbf{A}_k \mathbf{X}_{t-k} = \mathbf{E}_t \,.$$

The $\mathbf{A_k}$ are $p \times p$ coefficient matrices, $\mathbf{X}_t = (x_{1t}, x_{2t}, \cdots, x_{pt})^T$ are data from p LFP sites at time *t*, and $\mathbf{E_t}$ is a temporally uncorrelated residual error vector. The Directed Transfer Function (DTF) is defined as the magnitude of the matrix element $\mathbf{H_{ji}(f)}$ which measures the causal influence from site *i* to *j*. Recent work has shown that the DTF function is equivalent to a spectral measure of Granger causality (Kaminski et al, Biol Cybern 2001).

Pairs of sites having beta frequency power and coherence peaks were also found to have peaks in their DTF spectra that were consistent over recording sessions. The across-session means and standard deviations of DTF were used to identify site pairs with beta frequency peaks that were significantly greater than zero and that significantly differed in the two directions of causal influence (i.e. from site *i* to site *j* versus from site *j* to site *i*). A number of site pairs were found that had significant beta DTF peaks, but which did not significantly differ in the two directions. Other site pairs showed pronounced differences in beta DTF between the two directions. In two monkeys, somatosensory sites were identified that exhibited unidirectional driving of primary motor sites. In these same monkeys, evidence was found of unidirectional driving from posterior parietal to premotor cortex. These results tentatively support the hypothesis that in sustained motor output, cortical motor areas are dependent on steady driving by somatosensory and/or posterior parietal cortical areas. (Supported by grants from the National Institute of Mental Health and the National Science Foundation.)