In contrast to the physiological mechanisms underlying the acute cortical alterations monitored with functional magnetic resonance imaging (fMRI) during the migrainous aura (1), the mechanisms underlying increased interictal cortical responsiveness, frequently called ‘hyper-responsiveness’, remain ambiguous. There is substantial evidence that a deficiency in habituation to repetitive external sensory stimuli contributes to this abnormality (2); however, the precise neuroanatomic localisation and the underlying neuronal processes are still poorly defined. The current state of knowledge suggests that not a primary neuronal dysfunction but a sequence of intracranial alterations accounts for the symptoms, including the increased cortical responsivity, observed in migraine. The contribution of these changes to the clinical features of the disease and to the reoccurrence of attacks is only partially understood.

In this issue Coppola et al. (Lateral inhibition in the somatosensory cortex during and between migraine without aura attacks: Correlations with thalamocortical activity and clinical features) (3) imply that deficient dynamic activity of subcortical and cortical networks between attacks meaningfully contributes to the development of the migraine cycle-dependent hyper-responsiveness and correlates with the clinical features of migraine. In their work, somatosensory-evoked potentials (SSEPs) were obtained by electrical stimulation of the right median and/or ulnar nerves at the wrist in 41 migraine patients without aura, between and during attacks. Simultaneous stimulations of two adjacent peripheral nerves elicited smaller SSEPs than separate stimulations of either of the two nerves (e.g. Tinazzi et al. (4)). The mechanism, thought to account for this suppression after the concurrent inputs, is called lateral inhibition. It can also be observed in other modalities, e.g. it has already been shown that in the visual cortex of migraine patients the lateral inhibition is deficient interictally and that this impairment might be responsible for the increased sensitivity of the visual neurons (5).

In their present work Coppola et al. observed that the degree of the lateral inhibition, reflected by the amplitude change of the N20–P25 component of SSEPs, was significantly reduced in patients when the measurements were taken between — but not during — attacks, as compared to the results with healthy individuals. Furthermore, they studied not only the classical SSEPs, but have also extracted high-frequency oscillations from the SSEP measurements (HFOs), which reflects the magnitude of thalamocortical activation. The maximum peak-to-peak amplitude of the pre-synaptic HFO bursts also showed a reduction in interictal migraine patients. Certainly, previous results based on the measurements of spontaneous electroencephalogram (EEG) and evoked potentials in migraine patients between attacks have already suggested that the increased cortical responsivity, an unbalanced ‘teamwork’ of both inhibitory and excitatory neurons, might be the consequence of the deficient thalamic control (e.g. Coppola et al. (6)). The new finding in this clinical study is that the degree of lateral inhibition showed a negative correlation with the number of days elapsed since the last migraine attack, and also with the duration and severity of the monthly attack. However, it correlated positively with the pre-synaptic HFO amplitude. No correlations were observed between the clinical characteristics and the lateral inhibition or HFO amplitude, when these measurements were taken during attacks. These data suggest that the reduced lateral inhibition in migraine, observed between attacks, could indeed be a consequence of deficient thalamocortical activity; furthermore this measurement can also be used as a biomarker for the diagnosis of migraine.

Unfortunately, this study followed a parallel group design; the ictal-interictal electrophysiological measurements were performed in two partly different patient
groups and were taken only once, not repeatedly during the migraine cycle. Furthermore, the study included only patients without aura. These limitations weaken the interpretation and the generalisation of the results.

In order to better understand the complex pathology underlying migraine, future work should investigate the fundamental physiological mechanism of the altered thalamocortical activity between attacks, which might originate from the thalamus, due to functional disconnections between the thalamus and other subcortical areas (7), could be a result of an anomalous cortical feedback to the thalamus or might also be driven by the abnormal functioning of other subcortical areas. For example, the thalamus and the somatosensory cortex are intensively interconnected with the brainstem monoaminergic system, which also shows deficient activity throughout the whole migraine cycle (8).

In summary, the diagnosis of migraine is a complex clinical task and is based on a compatible history and fulfilment of the diagnostic criteria, currently based on the symptoms. Clinically useful laboratory tests for the diagnosis of migraines have not officially been established. Recent studies, including this paper, not only improve our understanding of the pathophysiology of migraines, but also can provide useful biomarkers for the diagnosis and monitoring of migraine.

References