 Neural oscillations are rhythmic fluctuations over time in the activity or excitability of single neurons, local neuronal populations or "assemblies," and/or multiple regionally distributed neuronal assemblies. Synchronized oscillations among large numbers of neurons are evident in electrocorticographic, electroencephalographic, magnetoencephalographic, and local field potential recordings and are generally understood to depend on inhibition that paces assemblies of excitatory neurons to produce alternating temporal windows of reduced and increased excitability. Synchronization of neural oscillations is supported by the extensive networks of local and long-range feedforward and feedback bidirectional connections between neurons. Here, we review some of the major methods and measures used to characterize neural oscillations, with a
focus on gamma oscillations. Distinctions are drawn between stimulus-independent oscillations recorded during resting states or intervals between task events, stimulus-induced oscillations that are time locked but not phase locked to stimuli, and stimulus-evoked oscillations that are both time and phase locked to stimuli. Synchrony of oscillations between recording sites, and between the amplitudes and phases of oscillations of different frequencies (cross-frequency coupling), is described and illustrated. Molecular mechanisms underlying gamma oscillations are also reviewed. Ultimately, understanding the temporal organization of neuronal network activity, including interactions between neural oscillations, is critical for elucidating brain dysfunction in neuropsychiatric disorders.

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Ultimately, understanding the temporal organization of neuronal network activity, including interactions between neural oscillations, is critical for elucidating brain dysfunction in neuropsychiatric disorders.
Resting or Baseline Neural Oscillations

When spontaneous neural oscillations are recorded over time without intervening stimulus events, as in resting EEG or during baseline intervals between task trials (Figure 1), the principal quantitation approach is to decompose the time series data spectrally using a Fourier transformation, yielding estimates of power at each frequency.6 Because the EEG in these time windows is not time or phase locked to specific events, oscillation phase information is not considered, and no baseline period exists from which to calculate a change in power. Moreover, when analyzing EEG epochs in the baseline periods preceding stimulus trials, power is estimated from individual trial epochs. This is because little or no baseline power survives averaging over trials in the resulting event-related potential (ERP) (Figure 1) owing to the random phase of the oscillations across trials. The power of specific frequencies can differ between individuals and groups (eg, baseline gamma power in Figure 1, A vs B). However, because absolute EEG power can vary by an order of magnitude between individuals, outliers should be excluded and/or the distribution normalized using an appropriate transformation (eg, logarithmic transformation).

Event-Related Neural Oscillations

When neural oscillations are recorded during tasks in which stimuli are presented over many trials, several event-related measures can be calculated.4 First, single-trial EEG epochs time locked to stimulus onsets can be averaged, yielding an ERP (Figure 1). Second, using time-frequency decomposition methods (eg, Morlet wavelets), one can estimate the change in EEG power relative to the prestimulus baseline for various frequencies as a function of time after the stimulus. These changes can be averaged over trials to yield total power6 (Figure 1). When a stimulus induces an increase in the amplitude of oscillations without resetting their phases across trials, the magnitude of the resulting induced oscillations is termed induced power, which is only evident in the total power estimate (Figure 1, B). Third, the same computational methods can be used to quantify the degree to which the phase of poststimulus oscillations is consistent across trials, a measure known as intertrial coherence. When a stimulus resets the phase of ongoing oscillations or evokes new oscillations such that their phases are consistently aligned across trials, the principal quantitation approach is to decompose the time series data spectrally using a Fourier transformation, yielding estimates of power at each frequency.6 Because the EEG in these time windows is not time or phase locked to specific events, oscillation phase information is not considered, and no baseline period exists from which to calculate a change in power. Moreover, when analyzing EEG epochs in the baseline periods preceding stimulus trials, power is estimated from individual trial epochs. This is because little or no baseline power survives averaging over trials in the resulting event-related potential (ERP) (Figure 1) owing to the random phase of the oscillations across trials. The power of specific frequencies can differ between individuals and groups (eg, baseline gamma power in Figure 1, A vs B). However, because absolute EEG power can vary by an order of magnitude between individuals, outliers should be excluded and/or the distribution normalized using an appropriate transformation (eg, logarithmic transformation).

Cross-Site Oscillation Coherence

The degree to which oscillations from 2 recording sites are correlated or coherent may reflect aspects of neural connectivity.1 Seven
eral coherence measures have been developed that reflect the correlation of the magnitudes and/or phases of oscillations at specific frequencies between sites; these measures can be calculated for resting or baseline spontaneous oscillations and for event-related oscillations. Magnitude-squared coherence reflects both magnitude and phase consistency, whereas phase coherence reflects only phase synchrony between sites (Figure 2). Phase coherence is high if the phase difference between oscillations at 2 sites is consistent across trials even when the phase at individual sites is inconsistent across trials (Figure 2). This sensitivity to the consistency of the cross-site phase lag across trials, rather than the consistency of the phase across trials, distinguishes cross-site phase coherence from the intertrial coherence calculated from a single site. Moreover, the phase coherence of synchronized oscillations between sites is equivalently high irrespective of whether the phase lag between them is small or large (Figure 2). A methodological challenge for EEG and/or magnetoencephalography is the spurious cross-site coherence that can arise when oscillations from a single source are volume conducted to both sites. Approaches have been proposed to mitigate this challenge, but controversies remain.

Cross-Frequency Coupling

Neural oscillations can be organized hierarchically such that the phase of slower oscillations modulates the amplitude, frequency, or phase of faster oscillations, a phenomenon generally termed cross-frequency coupling. For example, the magnitude of gamma oscillations in the cortex and hippocampus systematically varies with the phase of hippocampal theta oscillations in rodents, and similar theta-gamma coupling has been observed in humans. Such temporal coupling of gamma oscillations with the phase of slower oscillations may constitute the fundamental element of a syntactic code for temporally chunking information arising from distinct neuronal assemblies, as described during the encoding of items in short-term memory or spatial locations while moving through the environment. In principle, different oscillation frequencies may exhibit coupling across all combinations of phase, power, or frequency. However, coupling involving increased gamma oscillation magnitudes during the peaks of coincident theta oscillations within or between recording sites (Figure 3) is the most intensively studied example to date.

Focus on Gamma Oscillations

Gamma oscillations have generated particular interest for many reasons. The duration of a gamma cycle corresponds to the 10- to 30-millisecond window of temporal integration for postsynaptic neurons and for spike-timing dependent synaptic plasticity and also corresponds to the time constants of \( \gamma \)-aminobutyric acid (GABA-A) and \( \alpha \)-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA)
In this scheme (Figure 4), termed the parvalbumin neuron–interneuron network gamma (PING), a gamma cycle (lasting 10-30 milliseconds) constitutes the time needed for pyramidal neuron spikes to elicit spikes in PV interneurons (a few milliseconds) plus the time for PV interneuron–mediated inhibitory currents in pyramidal neurons to decay (about 5-20 milliseconds). Parvalbumin interneurons are interconnected, providing a second mechanism for gamma generation. If a population of PV interneurons receives somewhat homogeneous excitatory input, many will spike. In fact, PV interneurons are connected by electrical synapses, which enhance their tendency to spike together. Once a group of PV interneurons spikes, they inhibit each other and are then unable to spike again until this inhibition wears off. Because the kinetics of inhibitory currents are similar across PV interneurons, they will tend to spike again at the same time, initiating a new gamma cycle. This mechanism is termed the interneuron network gamma (ING). Thus, in addition to the functions outlined above, gamma oscillations represent an important barometer for healthy PV interneuron function.

Mechanisms Underlying Gamma Oscillations

A class of inhibitory interneurons, identified by their expression of the calcium-binding protein parvalbumin (PV) and/or their fast-spiking electrophysiologic properties, are critical for generating gamma oscillations. Parvalbumin interneurons may contribute to gamma oscillations through 2 mechanisms. First, PV interneurons are reciprocally connected with excitatory pyramidal neurons (Figure 4). Thus, when pyramidal neurons are active, they will excite PV interneurons, causing PV interneurons to spike. Spikes in PV interneurons then lead to inhibitory synaptic potentials in pyramidal neurons, silencing them. When this inhibition wears off, pyramidal neurons spike again, leading to reexcitation of the PV interneurons and starting a new cycle.

Active pyramidal neurons excite PV interneurons, causing PV interneurons to spike and leading to inhibitory synaptic potentials in pyramidal neurons, silencing them. When this inhibition wears off, pyramidal neurons spike again, leading to reexcitation of the PV interneurons and starting a new cycle.

Spontaneous Gamma Oscillations in Schizophrenia

Based on theoretical considerations and empirical evidence, dysfunction in the generation and/or coordination of neural oscillations is increasingly implicated in the pathophysiology of psychiatric disorders. Hirano et al have reported that patients with schizophrenia have reduced auditory evoked-gamma phase synchrony, which is consistent with the findings of prior studies, as well as increased gamma power during the baseline intervals between task stimuli. Gamma oscillations during task baselines may reflect neural noise in the sense that they do not appear to participate in processing the stimulus at hand. Indeed, this noise interpretation is supported by their inverse relationship with subsequent stimulus-evoked gamma synchrony. Rodent studies have shown that disruptions in PV interneurons similarly increase spontaneous gamma power, suggesting that PV interneuron abnormalities in schizophrenia may underlie their increased baseline gamma power. This increase in gamma power was not present in the spontaneous EEGs recorded from patients during rest, which underscores the need to consider how task context may influence gamma oscillations during baseline intervals between task stimuli and dissociate it from the spontaneous gamma oscillations recorded during task-free rest periods. This distinction warrants further attention, because it has not been emphasized in prior animal and human studies focused on spontaneous neural oscillations.