Physiologic Basis of the EEG

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1. EEG Definitions

1.1. The EEG

The electroencephalogram is the difference in voltage over time between two cerebral recording sites. The scalp EEG signal is generated by neurons, organized by neuronal orientation and connections, and is modified by electrode and scalp properties.

1.2. Volume conduction

Volume conduction is the process of current flow through a volume of tissues between the current generator (neurons) and current detector (scalp electrodes).

1.3. Inverse problem

The projection of voltage changes across the array of recording electrode provides a 2 dimensional map across the scalp. The calculation of the source of current from this 2 dimensional map is the "inverse problem" of source localization.

2. EEG Source

2.1. Neuronal source of the EEG

Action potentials are too transient and focal to accumulate enough signal to be recorded at the scalp. Instead, the source of the EEG is the combined synaptic potentials that underlie neuronal activity. In other words, the voltage recorded at the scalp is the sum of underlying excitatory and inhibitory postsynaptic potentials that in turn modulate the activation of action potentials.

2.2. Presynaptic potentials

2.2.1. Resting membrane potential; Em

An energy-dependent sodium-potassium pump in the cell membrane excretes 3 sodium ions out of the cell for every 2 potassium ions brought into the cell. The resulting overall outside-positive/inside-negative potential is kept in balance by the "leaking" of chloride ions out of the cell that in turn is checked by the voltage- and osmotic gradients across the cell membrane. The steady-state voltage measured across the cell membrane is called the resting membrane potential (Em).
Em is approximately -65µV inside the cell compared to outside.

2.2.2. Action potential

The action potential is an all-or-nothing response, meaning that a single neuron, once triggered to "fire", has only a single type of electrical response of one particular amplitude.
The action potential occurs when the Em is perturbed, and when the intracellular potential rises above the cell's *threshold potential* at the cell's trigger point – the *axonal hillock*.

2.2.2.1. Voltage-gated ion channels

The rise of the intracellular potential above the threshold potential (*depolarization*) triggers the activation of voltage-gated channels that allow sodium ions to flow into the cell fueled by voltage- and

osmotic gradients. Voltage-gated calcium channels may also participate, and have different threshold potentials and rates of activation.
The inside of the cell, now fully depolarized, is now positive relative to the outside. Sodium channels close, and sodium begins to be transported back out of the cell.
Voltage-gated potassium channels are activated; potassium ions flow out of the cell down their voltage- and osmotic gradients, causing the cell's potential to again turn negative (*repolarization*).
Rapid repolarization briefly causes *hyperpolarization* and represents a neuron's *refractory period* during which it can not fire again until "reset" at the Em.

2.2.2.2. Propagation

The rapid change in voltage induced by the action potential is conducted along the axon.
The velocity of electrical transmission is aided by saltatory conduction along myelinated axons in which recurrent action potentials are triggered along the axon's course because the current can "jump" between gaps in myelin (*nodes of Ranvier*) because each electrically uninsulated node allows new depolarizations.

2.2.2.3. Termination

Action potentials reach the pre-synaptic membrane and activate local voltage-gated ion channels that control neurotransmitter vesicles. The vesicles migrate to the cell membrane and release neurotransmitters into the synaptic cleft. The neurotransmitters cross the cleft and find receptors located on the post-synaptic membrane located on dendrites of the next neuron of the chain.

2.3. Postsynaptic ligand-mediated channels

Neurotransmitters released from presynaptic vesicles travel across the synaptic cleft to the postsynaptic membrane. Postsynaptic receptors, when activated by reception of their particular neurotransmitter, open channels that can depolarize (excitatory) or hyperpolarize (inhibitory) the postsynaptic membrane. The combined depolarizations and hyperpolarizations must occur with enough consistency in type and timing to activate or suppress the likelihood that the neuron can reach its threshold potential to activate the next action potential in the chain.
These relatively long-lasting fluctuations of excitatory and inhibitory postsynaptic potentials aggregated among a host of dendrites is the source of the EEG.
Some important ligand-mediated channels and some common agonists and antagonists are (in a simplified fashion)

Excitatory amino-acid receptors

Receptor	Ion channel	Agonist	Antagonist
NMDA	Ca^{2+}	glutamate	ketamine
AMPA	Na+, K+, Ca^{2+}	glutamate	parempenal
kainate	Na+, K+	glutamate, kainic acid	ethanol

Inhibitory amino acid receptors

Receptor	Ion channel	Agonist	Antagonist
GABA	Cl–	barbiturates	flumazenil

benzodiazepines

3. Neuronal organization

Neurons arranged higgledy-piggledy would not have recordable potentials at the scalp. Aspects of neuronal type, location, and organization facilitate EEG measurement.

3.1. Neuronal type

Large *pyramidal cells* located in cortical layers 3, 5, and 6 comprise the main population of neurons measured on the EEG.

3.2. Neuronal orientation

These neurons are radially oriented which, in aggregate, create regions of discrete current *sources* and *sinks*. Excitatory currents involving cations flow towards an excitatory synapse; inhibitory ions flow towards an inhibitory synapse. Because the total sum of currents must equal zero (Kirchoff's Law), compensatory and opposite currents flow in opposite directions. The radial, elongated morphology and orientation of these neurons allows physical separation of these currents along the neuron, and in aggregate, generates a current loop orthogonal to the scalp.

Neurons laid out transversely to the scalp may also generate loop currents, but because they may be randomly oriented with respect to each other (in relationship to the overlying scalp), currents cancel out each other and do not create well-demarcated voltage differences from electrode to electrode.

4. Cortical organization

4.1. Columnar organization

The functional organization of groups of neurons into radially-oriented cortical columns facilitates generation of scalp potentials since cortical columns allied for a particular purpose, with overall excitatory or inhibitory activities, are more likely to aggregate postsynaptic potentials of similar timing and amplitude.

4.2. Cortical area

EEG recordable at the scalp requires a threshold number of neurons acting synchronously within a minimum area. Modeling experiments place this area at about $6cm^2$. Human recordings demonstrate that 90% of epileptic spikes seen on cortical recordings are not recorded on the scalp if the cortical area is less than $10cm^2$. The practical importance of this limitation is that abnormalities generated under these thresholds – such as simple partial seizures with limited cortical spread – may be missed on scalp recordings.

5. Corticothalamic circuitry

Synchronous neuronal activity is a requirement for generation of scalp-recordable potentials. Corticothalamic circuits mediate the synchronous and coordinated activation and deactivation of cortical postsynaptic potentials. Thus, corticothalamic circuits define waking (such as the waking alpha rhythm and mu rhythm) and sleep rhythms (sleep spindles, synchronous delta activity).

Pacemaker neurons within the dorsal thalamus send efferent fibers to cortical neurons as well as to thalamic inhibitory neurons, creating what is in effect a servo-regulatory network. Cortical neurons, in turn, send feedback efferents to thalamic neurons. The network of neurons, therefore, mediate synchronous oscillations that form measureable rhythms in the EEG.

The distribution and amount of synchronous activity, in turn, is mediated by ascending brainstem systems that regulate tonic corticothalamic activities into waking, non-REM, or REM sleep states, each identified by their predominant rhythms.
In addition to corticothalamic circuits, cortical regions may maintain intrinsic rhythms (cortico-cortical) with different degrees of independence from corticothalamic circuits. These endogenous rhythms may vary by state or may emerge under certain pathophysiological lesions involving ascending control systems or in corticothalamic circuits.

6. Scalp effects

Several factors alter the EEG signal recorded at the scalp.

6.1. Distance

Since electrical energy diminishes with the square of the distance, electrical sources deep within the brain may occur without registering at the scalp. Brain atrophy, or subgaleal or subdural fluid collections can all attenuate EEG signal.

6.2. Filter effects

The scalp acts as a high frequency filter that selectively attenuates faster EEG frequencies.
Defects in the skull – craniotomy, trauma, yet-to-be closed fontanelles - can alter this filter effect and "restore" high frequency signals, producing breach effects of focal exaggeration of amplitude and of faster frequencies.

7. Effect of brain lesions

Interruptions to the micro- to macro-systems outlined above define pathophysiological changes to state-appropriate EEG.

7.1. Attenuation

Since cortical neurons are the source of EEG signal, and therefore, overall amplitude recorded at the scalp, loss of cortical neurons causes attenuation of EEG. Therefore, lesions that preferentially destroy gray matter result in loss of EEG amplitude.

7.2. Arrhythmic delta activity

Corticothalamic circuits largely define tonic state-mediated EEG rhythms. Lesions to white matter tracts that connect cortical neurons to thalamic control regions, therefore, interrupt normal rhythmicity and frequencies. The most common result of a white matter lesion is arrhythmic delta activity.

7.3. Periodic, sharp activity

Lesions that involve creating islands of cortex disconnected from surrounding cortex and corticothalamic fibers frequently demonstrate slowing with recurrent bursts of epileptiform activity.

7.4. Paroxysmal depolarizing shift and interictal epileptiform discharge

The paroxysmal depolarizing shift (PDS) is the fundamental lesion of epilepsy. In the PDS, a defect in the extent of depolarization (for example, sustained depolarization by a pathological activation of calcium-mediated channels) allows activation of a series of repetitive action potentials. Sustained neuronal firing, in turn, causes abnormal activation of the downstream, postsynaptic neuron.
If the PDS involves a critical number of neurons within a cortical region, an *interictal epileptiform discharge (*or *spike)* that represents the simultaneous, sustained burst of neuronal activity can be

recorded on the scalp. The sustained and simultaneous burst of neuronal activity interrupts ongoing cortical rhythms, giving rise to the characteristic definition of the interictal epileptiform discharge (a sharp, abrupt discharge lasting between 20-200 ms, often followed by a slow wave of the same potential, that stands out from and interrupts background activities).