Functions of the Neuronal Circuits

Principles of neuronal operation (Eccles 1973)

The principle of neural operation as defined by Eccles in 1973 are:

1. All transmission at a distance is by the propagation of nerve impulses (all-or-nothing messages)
2. Divergence: wide dispersal of signals
3. Convergence: opportunity for integration of signals from different sources
4. Electrical transmission is periodically converted to chemical: opportunity for signal processing
5. Transmission of a relevant signal is accompanied by a strong background noise
6. Inhibition sharpens signals and controls neuronal discharges
7. Everything that goes on in our brain has a basis in neuronal events and can be measured in terms of signals.

Divergence

The signal diverges from one → many. It consists of 2 types:

1. Amplifying type of divergence - the input signal is spread > 1 neuron per synapse. Example: a single pyramidal cell in the motor cortex is able to excite up to 10,000 muscle fibers (corticospinal tract).
2. Divergence into multiple tracts - the signal is deviated in at least 2 separate directions. Example: signals from dorsal columns follow two courses in the brain: into cerebellum and into the thalamus and eventually cerebral cortex (spinothalamic tract with branching afferents to inferior peduncles of cerebellum).

Convergence

Multiple inputs converge to a single neuron (many → one). It consists of 2 types:

1. From a single source - multiple synaptic terminals from the pre-synaptic neuron communicate with a single post-synaptic neuron → anatomical basis of *spatial summation* of multiple EPSPs, to finally excite the post-synaptic neuron.
2. From multiple sources (excitatory or inhibitory) - this allows different tracts to excite a single neuron thus allowing summation of information from different sensory organs → high-level analysis of the afferent signals.
    - Example: optical inputs and proprioception of ocular movements, auditory inputs and proprioception of head (ear) movements (cerebral cortex).
    - Example: interneurons of the spinal cord receive converging signals from:
        1. Peripheral proprioceptive and cutaneous nerve fibers entering the cord
        2. Propriospinal fibers passing from one segment of the cord to another
        3. Corticospinal fibers
        4. Other pathways that begin from the brain and project to the spinal cord
    - Example: spinothalamic neurons receive sensory and pain afferents from the skin and from internal organs → hypersensitivity or pain in the skin accompanying disease processes of the internal organs.

Summation of postsynaptic potentials

When a synapse excites a typical neuron, the neuronal membrane remains highly permeable for only 1 to 2 milliseconds. However, the EPSP dissipates over next 15 or more milliseconds (as explained here). Similar duration have also the IPSPs. During excitation in a neuronal pool, many presynaptic terminals are usually stimulated at the same time (divergence and convergence) and their effect can summate (spatial summation). Also a second opening of the same synapse in a sufficiently short interval can increase the PSP (temporal summation).

Presynaptic modulation of the signal

Presynaptic Inhibition

The inhibitory action is affected by depressing the output of excitatory transmitter by a presynaptic terminal located over the excitatory terminal (axo-axonic terminal). Activation of this synapse by stimulation of the presynaptic axon results in the following:

1. The release of neurotransmitter (e.g., GABA) → Opening of Cl^- channels in the terminal of the excitatory axon →
2. Increased chloride conductance decreases the amplitude of the action potential in the terminal of the excitatory axon →
3. The amount of transmitter released is reduced → less transmitter is released → smaller EPSP is evoked in the motoneuron.

Presynaptic inhibition can also change the K^+ conductance, or it involves modulation of voltage-gated Ca^{2+} channels by intracellular second messenger system. It requires many milliseconds to develop and can last as long as minutes or even hours (postsynaptic inhibition normally lasts for only a few milliseconds). Presynaptic inhibition is very widespread and powerful especially at lower levels of the brain (primary afferent level, thalamus, lateral geniculate body). Special elements of the presynaptic inhibition are reciprocal synapses - for example, they are present in olfactory bulb: the mitral dendrite is presynaptic (excitatory synapse) to the dendrite-like branches of the inhibitory granule cells, which in turn is presynaptic to the mitral dendrite (inhibitory synapse). Such system can exert its inhibitory function without generating an action potential in the inhibitory neuron, leading to a very effective inhibition.

Presynaptic facilitation

The excitatory action is effected by further increasing the output of excitatory transmitter by a presynaptic terminal located over the excitatory terminal (axo-axonic terminal). Facilitation can be mediated by serotonin release from the presynaptic terminal, leading to the following:

1. Activation of a second messenger system in the postsynaptic terminal (cAMP) →
2. Partial inactivation of K^+ voltage-gated channels →
3. Prolongation of the Action Potential continues unimpeded →
4. More Ca^{2+} enters the terminal → the amount of transmitter released is increased →
5. Larger EPSP is evoked

Prolongation of signals

This is the process where a single signal can result in a prolonged output discharge (the afterdischarge). The duration of such afterdischarge can last from a few milliseconds up to many minutes. This process can occur by the following ways:

1. **Synaptic afterdischarge**: the EPSP lasts for several milliseconds leading to a sustained signal output
2. **Reverberatory circuits**: essentially positive feedback within the neuronal network, resulting into a vicious circle of excitation which is limited only by the availability of the neurotransmitter and receptor (fatigue of synapse and downregulation of receptors).

Continuous signal output:

1. **Intrinsic Neuronal Excitability**: the membrane potentials of many neurons even at rest are high enough to cause them to emit action potentials (e.g., large neurons in cerebellum, interneurons in the spinal cord). The frequency rates of these impulses can be increased by facilitatory signals or decreased by inhibitory signals.
2. **Reverberating circuits**: they can also be a source of continual impulses. Excitatory and inhibitory signals modulate the level of intensity of the output of such circuits. This *carrier wave system* allows a decrease in signal intensity as well as an increase. The autonomic nervous system makes use of such circuits to control vascular tone, gut tone, mydriasis/miosis and heart rate.

Rhythmical Signal Output

Many neuronal circuits emit rhythmic output signals (e.g., respiratory signals originating in the reticular substance of the medulla and pons), as a result of the activity of reverberating circuits. Facilitatory or inhibitory signals can affect rhythmic signal output similarly as a continuous signal (e.g., influence of the carotid body stimulation by arterial oxygen deficiency on the frequency and amplitude of the ventilatory movements).

Stabilization of the neuronal circuits

As the neuronal connections in the CNS are abundant, there is a certain danger of arising of uncontrolled reverberating signals (signals that would be transmitting no information, but block transmission of relevant information. Such situation can occur in widespread areas of the brain during epilepsy convulsions. To prevent it, 2 basic mechanisms function throughout the CNS:

1. **Inhibitory circuits**: These are feedback-inhibition circuits that inhibit the same initial excitatory neurons in the same pathway - these circuits occur in virtually all sensory nervous pathways and inhibit either the input neurons or the intermediate neurons in the sensory pathway when the termini become overly excited. A prime example of such neuronal pool with a great amount of inhibitory activity are some circuits basal ganglia in the brain.
2. **Fatigue of synapses** (2 mechanisms):
    1. Short-term adjustment in synaptic sensitivity: To keep circuits function in an effective range of sensitivity pathways are used more or less depending on their sensitivity. Decreased sensitivity of pathways is a result of overusing and fatigue. On the other hand, a pathway that is underused and thus gets to rest, has increased sensitivity.
    2. Long-Term adjustments in Synaptic Sensitivity: they are caused by automatic downregulation/upregulation of synaptic receptors. Upregulation occurs when there is underactivity, and downregulating the receptors when there is overactivity. This occurs as follows: there is normally continual production of receptors, but when there is saturated binding of these receptors (synapse overuse), most of them are inactivated and removed from the membrane (down-regulation). This mechanism is the basis for the rebound-effect in various drugs such as β-blockers (→hypertension) and

benzodiazepines(→severe anxiety and insomnia).

Links

Related articles

- Inhibitory Neuronal Circuits
- Transformation of Synaptic Input into Action Potential
- Post-Synaptic Potentials
- Integration activity of neurons

Sources

- Lecture Notes: Prof. MUDr. Jaroslav Pokorný DrSc.

Bibliography

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Further reading