Infragranular glutamatergic neurons are excitatory neurons located in the deep layers (V and VI) of the cerebral cortex, specifically beneath the granular layer (layer IV). These neurons primarily use glutamate as their neurotransmitter and play a critical role in transmitting excitatory signals to other regions of the brain and the spinal cord. Below is an overview of their key features, functions, and relevance.

Key Features: Location:

Infragranular neurons are located in layers V and VI of the neocortex, which are situated below the granular layer (layer IV). Layer V is the main output layer of the cortex, while layer VI primarily modulates inputs to the cortex itself. Glutamatergic Nature:

These neurons are excitatory and release glutamate, the principal excitatory neurotransmitter in the central nervous system (CNS). Glutamate acts on various receptors, including NMDA and AMPA receptors, to mediate excitatory synaptic transmission. Projection Neurons:

Infragranular glutamatergic neurons are typically projection neurons, meaning they send long-range axonal projections to other brain regions or the spinal cord. Layer V neurons often project to subcortical targets like the brainstem and spinal cord, playing key roles in motor control and sensory processing. Layer VI neurons send projections primarily to the thalamus, regulating the thalamocortical circuitry, which is important for sensory and motor processing. Morphology:

Many of these neurons are pyramidal neurons, characterized by their triangular-shaped cell bodies and long apical dendrites that extend towards the surface of the cortex, making connections with other layers. Functions: Motor Control:

Neurons in layer V of the motor cortex project to spinal motor circuits and are essential for controlling voluntary movements. Damage to these neurons can result in motor deficits, as seen in conditions like amyotrophic lateral sclerosis (ALS). Sensory Processing:

In sensory regions of the cortex, infragranular glutamatergic neurons process information coming from sensory pathways (e.g., somatosensory or visual) and relay it to subcortical structures. They help integrate information and contribute to high-level functions such as perception and attention. Thalamocortical Modulation:

Layer VI neurons project back to the thalamus, forming feedback loops that regulate sensory inputs to the cortex. This thalamocortical interaction is critical for maintaining sensory precision and filtering unnecessary stimuli, which is relevant for attention and focus. Cognitive Functions:

These neurons are involved in higher-order cognitive processes such as decision-making, memory, and learning, as they integrate signals from multiple cortical and subcortical regions. Relevance in Neurological Conditions: Neurodegenerative Diseases:

In diseases like ALS, Parkinson's disease, or Alzheimer's disease, degeneration of infragranular glutamatergic neurons in layer V can impair motor function and cognitive abilities. Epilepsy:

Hyperexcitability of glutamatergic neurons can contribute to seizures. Infragranular neurons are often involved in the spread of excitatory signals across cortical and subcortical areas during epileptic events. Schizophrenia and Autism:

Dysregulation in the excitatory-inhibitory balance, often involving glutamatergic neurons, has been linked to disorders like schizophrenia and autism. Alterations in synaptic plasticity and connectivity in these neurons could underlie cognitive and sensory processing deficits observed in these conditions.

Conclusion: Infragranular glutamatergic neurons are fundamental components of the cortical circuitry, mediating excitatory signaling to subcortical and cortical regions. Their role in motor control, sensory processing, and cognition highlights their importance in both normal brain function and neurological disorders. Understanding their pathways and mechanisms offers valuable insights into therapeutic targets for treating various brain diseases.