

The complexity of the mammalian brain may be based on flexible synaptic strength

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INTRODUCTION

The Brain cells communicate with each other via synapses, which are junctions where neurotransmitters are exchanged. Tens of thousands of synapses can connect a single neuron, allowing it to communicate with thousands of other brain cells. The flexibility of synapse strength is assumed to underpin memory, learning, and other types of cognition, as these connections govern information flow across the brain. According to Gregor Schuhknecht, a neuroscience postdoc at Harvard University, researchers have long assumed that synapses with larger surface areas are stronger, but have lacked experimental confirmation. To address this issue, Schuhknecht and his colleagues discovered connections between neuron pairs in the neocortex area of mouse brain slices while still a graduate student at the Institute of Neuroinformatics at the University of Zurich and ETH Zurich. When an action potential stimulates the release of neurotransmitter-packed vesicles from a neuron's axon terminal, these chemicals travel across the synapse and are detected by receptors in the receiving neuron's dendrite, triggering an action potential in that cell. The researchers utilised a small electrode to detect synapse strength and electron microscopy to quantify synapse size by recording the change in voltage of the receiving neuron. They discovered that synapses with a bigger postsynaptic density area—the region of the dendrite containing neurotransmitter receptors—produced more voltage fluctuations. Stephanie Rudolph, a neuroscientist at Albert Einstein College of Medicine who was not involved in the work, describes it as a “technical tour de force” that validates the association between synapse size and strength, which has long been a source of debate in neuroscience. Some studies have simply counted the number of synapses between two neurons to determine neural connection. According to Schuhknecht, the discovery that bigger synapses are stronger allows connection strength to be attributed to a synapse based on its size, offering “a considerably more precise representation of the connection.” This could help scientists construct maps of the brain's connectome for fruit flies and mice, with the objective of better understanding how information moves through the brain. The number of neurotransmitter release sites in an axon terminal, as well as the likelihood of a vesicle being released, influence the strength of a synapse. Until previously, most neuroscientists' thinking was that synapses in the neocortex could release only a single vesicle of neurotransmitter per action potential, adds Schuhknecht. However, the number of release sites in the mouse brain slices surpassed the number of synapses between each neuron pair, indicating that each synapse may be capable of releasing numerous vesicles. This suggests that synapses in the neocortex—the biggest area in the human brain—are more flexible than previously thought. “It fundamentally changes how we think about the prevailing form of synaptic transmission,” Rudolph adds. “We may speculate that multivesicular release improves the brain's capacity to adapt to both internal and external obstacles, as well as allowing for a wider spectrum of computational processing and information storage.” Neurotransmitters have a role in early human development processes such

as neurotransmission, differentiation, neuron proliferation, and neural circuitry formation. Different neurotransmitters may occur at various stages of development. Monoamines, for example, are present before neurons develop. Even in the very early stages of the embryo, norepinephrine levels are high in the notochord. Serotonin is involved in the process of morphogenesis. Excitatory amino acids occur later in ontogenesis than other amino acids. As new synapses develop, the levels of neurotransmitters and neuromodulators tend to rise. Others, such as glutamate, will appear throughout the perinatal period and then plateau. Hypoxia and drug exposure can disrupt neural circuit development, resulting in long-term negative repercussions in the body. Acetylcholine, glutamate, GABA, glycine, dopamine, norepinephrine, and serotonin are some of the neurotransmitters that the body uses for various activities. The excitatory neurotransmitter glutamate is the most common in the brain. It's also the main player in the nervous system's plasticity. Glutamate has been linked to changeable synapses, which are thought to constitute the brain's memory store components. The principal inhibitory neurotransmitters are Gamma-Aminobutyric Acid (GABA) and glycine, on the other hand. GABA, for example, is responsible for around 40% of inhibitory processing in the brain. Glycine is mostly present in the spinal cord. Another important neurotransmitter, dopamine, is involved in a variety of brain activities such as learning, motor control, reward, emotion, and executive functions. Dopamine has also been linked to neurological and mental problems. Many medicines used in psychiatry and neurology target serotonin, a neurotransmitter that controls many cognitive functions and brain activity. Serotonin influences gastrointestinal functions such as bowel motility, bladder control, and cardiovascular function. The central nervous system and sympathetic nerves produce norepinephrine, which is a monoamine. The brain's locus coeruleus plays an important function in norepinephrine transmission. The brain's release of norepinephrine affects a number of functions, including stress, sleep, attention, concentration, and inflammation. It also plays a function in autonomic nervous system response modulation. Histamine is a neurotransmitter that affects motivational behaviour and mediates homeostatic activities in the body. It stimulates alertness, modifies eating behaviour, and mediates homeostatic functions in the body. The vesicular release of neurotransmitters at presynaptic nerve terminals is used to treat neurotransmission. The release of neurotransmitters into the synapse is enabled by calcium-evoked exocytosis of presynaptic vesicles. The neurotransmitter-containing vesicles are tethered to the plasma membrane by active zones, which are specific regions on the presynaptic plasma membranes. Active zones fuse with vesicles when an action potential causes calcium influx into the presynaptic cleft, facilitating neurotransmitter release. The fusion of neurotransmitter-containing vesicles with the active zone is mediated by a number of proteins. Syntaxin-1, SNAP-25, and synaptobrevin-2 are soluble N-ethylmaleimide sensitive factor attachment protein receptors (SNAREs) that collectively form a SNARE complex, a critical component in membrane fusion and eventually exocytosis. Several proteins involved in this pathway may function as inhibitors.

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