Alzheimer's disease (AD), one of the most progress neurodegenerative brain diseases that leading cause of dementia, has been extensively researched for years. However, our knowledge of its synaptic structure, which is a basis to understanding neurodegenerative disorders, is still unclear. Defining the structures of neurons and their synaptic connections are significant goals of brain research. To study synaptic connectivity, three-dimensional (3D) reconstructions of the nervous system are very helpful. In this study, the 3D structure of brain synapses in the Drosophila was analyzed using focused ion beam scanning electron microscopy (FIB/SEM). This technique is one of the most useful for 3D reconstruction, as the process of obtaining serial images is fully automated and thus avoids the problems inherent in hand-operated ultrathin serial sectioning. In this study, we visualized and quantitatively analyzed the ultrastructural characteristics of the calyx region of a Drosophila mushroom body, which is a neuropil organ that plays an important role for learning and memory in insects. We used transgenic line of Drosophila melanogaster Swedish mutant APP (Swe-APP), which is characterized by early onset AD and increased Aβ production. The 3D images of normal and AD brains reported in this study reveal characteristic features of AD such as appearance of autophagy, abnormal axon formation, and increased mitochondrial size. This 3D analysis reveal structural change as a basis for understanding neurodegenerative disorder.
Fig. 1: Ultrastructure of axon terminals. Comparison of axon terminal ultrastructure between normal (A, B) and AD models (C–E). Note that the AD model occasionally demonstrates aberrant large (C) or normally sized (D, E) axon terminals. The active zone, which is the site of neurotransmitter release (arrowhead), can also be observed. Scale bar, 1 μm.

Fig. 2: 3D reconstruction of nine individual presynaptic axons each from the normal (A) and AD models (B). Axons pass in many different trajectories other than the parallel direction. In the normal model (A), most axons appear long and straight. However, in the AD model (B), axons are relatively short and of various sizes.