Our previous studies suggest that in addition to genetic factors, environmental factors play a critical role in the development of Alzheimer's disease. We showed that experience of transgenic mice harboring familial Alzheimer's disease (FAD)-linked APPswe/PS1ΔE9 in a complex environment dramatically reduced extent of amyloid deposition. To examine whether experience in a complex environment would rescue additional deficits in brain plasticity in these mice, FAD-linked APPswe/PS1ΔE9 were exposed to a complex environment for one month right after weaning. Here we show that experience of APPswe/PS1ΔE9 mice in enriched environmental conditions enhanced neural progenitor cell (NPC) proliferation, as well as the number of mature neurons incorporated in the granule layer of the dentate gyrus. Functionally, environmental enrichment significantly enhanced hippocampal long-term potentiation (LTP), without notable alternation in basal synaptic transmission. In addition, these mice exhibit attenuated levels of oligomeric Aβ, the neurotoxic precursor of amyloid deposition, as well as tau hyperphosphorylation. We further observed upregulation of the main anterograde motor protein, kinesin-1, in the brains of transgenic mice that experienced environmental enrichment, suggesting an enhancement of axonal transport. Taken together, this study suggests that environmental experience can modulate neuroplasticity, attenuates neuropathology and enhances synaptic plasticity in FAD-linked mouse model. This study provides evidence for the critical significance of environmental enrichment as a potential therapeutic approach.