β-amyloid (Aβ) aggregates are known to induce synaptic dysfunction, and thus are involved in learning and memory deficits, making Aβ deposits a target for prevention or treatment. Microglia, especially bone marrow-derived microglia, is thought to play important roles in internalizing and phagocytosing Aβ. Stromal cell-derived factor 1α (SDF-1α) is an important chemoattractant for hematopoietic progenitor cells (HPCs). To explore whether treatment with SDF-1α can regulate the chemotaxis of microglia and decrease Aβ deposition, it was given to APP/PS1 double transgenic mice by lateral ventricle injection weekly from 7 to 9 months of age. The results of immunohistochemistry and Western blotting showed that SDF-1α increased the number of microglia in the parenchyma, decreased the number of senile plaques and decreased the volume of Aβ deposits. These results suggest that SDF-1α might be considered as a promising therapeutic intervention in treating Alzheimer’s disease by improving the recruitment of microglia and elimination of toxic senile plaques.