The centromere plays a fundamental role in accurate chromosome segregation during mitosis and meiosis in eukaryotes. Sequential separation and segregation of centromeres are genetically controlled. This sequence of temporal order is altered in Alzheimer’s, i.e. centromeres divide before their time. This division is called premature centromere separation (PCS) and is seen as a manifestation of genome instability leading to aneuploidy. Results from the FISH method applied to the centromere region of the X chromosome in interphase nuclei of lymphocytes from peripheral blood in AD patients, demonstrated that PCS appears considerably before mitotic metaphase, directly after completion of DNA replication in G2 phase of the cell cycle. Using the fluorescent in situ hybridization (FISH) method, an analysis of premature centromere division of the X chromosomes has been done on histopathologic slides of neurons from the frontal cerebral cortex, in a group of sporadic AD patients and in age-matched controls. The presence of PCS on the X chromosome was verified in all analyzed individuals. The group of AD sporadic patients had an average frequency of this alteration of 8.60 ± 1.81%. Comparison to the control group with an average frequency of 2.96 ± 1.20% shows a highly statistical significance (P < 0.01). Results from our study showing instability of centromere dynamics in the early phases of the cell cycle coincide with re-entry cell cycle alteration of cortical neurons which may give us the possibility to further elucidate the initial processes leading to AD.