Methylation analysis of SST and SSTR4 promoters in the neocortex of Alzheimer's disease patients
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The Alzheimer's disease (AD)-ridden cortex is neuropathologically characterized by major amyloid deposition, extensive neurofibrillary change and reduction of several peptides, including somatostatin. Several observations in recent years have pointed to a major pathogenic role for depletion of somatostatin with respect to amyloid accumulation, which is often thought to be the crucial event in a cascade leading to AD. As methylation of CpG islands may play an important role in gene silencing we studied the methylation status of the CpG islands in the promoters for somatostatin (SST) and its major receptor subtype, SSTR4, in tissue samples from the middle temporal gyrus (Brodmann area 22) and superior frontal gyrus (Brodmann area 9) of 5 severely affected AD patients aged 72-94 years (Braak stages V-C or VI-C) and 5 non-demented controls aged 50-92 years. Methylation analysis at the nucleotide level on DNA from cortical gray and infracortical white matter showed that the DNA methylation status at the promoters for SST and SSTR4 did not differ between AD and control samples in any of the regions analyzed. This result from high resolution methylation analysis of the SST promoter was confirmed using deep amplicon sequencing performed on cortical gray from the superior frontal gyrus of all AD patients and non-demented controls studied. In conclusion, down-regulation of somatostatin in the AD cortices studied does not appear to be due to hypermethylation of the SST and SSTR4 promoter CpG islands.