Methylation analysis of *SST* and *SSTR4* promotors in the neocortex of Alzheimer's disease patients

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Research question and background

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 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.

Methods and tissues used

As methylation of CpG islands plays an important role in gene silencing we studied the methylation status of the CpG islands in the promoters of somatostatin (*SST*) and in that of 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.

Results and conclusion

Bisulphite sequencing of DNA from cortical gray and infracortical white matter showed that the DNA methylation status at the promoters of *SST* and *SSTR4* did not significantly differ between AD and control samples in any of the regions analyzed. We confirmed these results using deep bisulphite sequencing of PCR products from the SST promoter amplified from DNA from the cortical gray of the superior frontal gyrus of all AD patients and non-demented controls. We observed a trend toward increased DNA methylation with increasing age. In conclusion, deregulated somatostatin signalling in the AD cortices cannot be explained by hypermethylation of the *SST* and *SST4* promoter CpG islands.