VOLTAMMETRIC AND ATOMIC FORCE MICROSCOPY OF AMYLOID BETA PEPTIDES

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Alzheimer's disease (AD) is an incurable, progressive and terminal neurodegenerative disease, which was first described in 1906 by the German psychiatrist and neuropathologist Alois Alzheimer. The AD brain histopathology is characterized by the presence of extracellular amyloid plaques containing a mixture of amyloid beta (Aβ) peptides: short Aβ fragments in small amount, $Aβ_{1-40}$ (~ 90%) and $Aβ_{1-42}$ (~ 10%). Atomic force microscopy (AFM) and differential pulse (DP) voltammetry have enabled the research in the oxidation and aggregation of Aβ peptides.

The electrochemical behaviour of the Aβ monomers, before the aggregation process and fibrilization started, in freshly prepared chloride free solutions, was investigated. DP voltammetric results showed that the $Aβ_{1-40}$ and $Aβ_{1-42}$ peptides oxidation, at a glassy carbon electrode, occurs in two steps, the first electron transfer reaction corresponding to the tyrosine Y^{10} amino acid residue oxidation, and the second to the three histidine (His^6, His^{13} and His^{14}) and one methionine (Met^{35}) amino acid residues oxidation. The identification of the $Aβ_{1-40}$ and $Aβ_{1-42}$ peptides oxidation peaks, based on the comparison between ten different control Aβ peptide sequences lacking specific electroactive amino acid residues, was achieved. The results showed that, in the absence of aggregation and/or fibrilization, the tyrosine Tyr^{10} and histidine His^{13} were the most reactive amino acid residues.

The fibrilization process of short $Aβ_{01-28}$, $Aβ_{10-20}$, $Aβ_{12-28}$, and long $Aβ_{1-40}$ and $Aβ_{1-42}$ peptides, in chloride free media, by AFM and DP voltammetry, was also investigated. The short Aβ peptides helped to highlight the role played by different amino acid residues domains in the fibrilization process.

Control experiments were done with full length Aβ peptides that: *(i)* do not aggregate (inverse $Aβ_{40-1}$ and $Aβ_{42-1}$, and rat $Aβ_{1-40}$Rat), and *(ii)* lack specific electroactive amino acid residues (mutant $Aβ_{1-40}Phe^{10}$ and $Aβ_{1-40}Nle^{35}$).

The long $Aβ_{1-40}$ and $Aβ_{1-42}$ peptides aggregation was electrochemically detected *via* the electroactive amino acid residues oxidation peak currents decrease that occurred in a time dependent manner, correlated with changes in the Aβ peptides adsorption morphology, from initially Aβ monomers, to aggregates, protofibrils and fibrils, corresponding to the Aβ peptides in a β-sheet configuration, observed by AFM.