

Serum Albumin Conformational Disturbances in Melancholic Depression can be Revealed Using Time Resolved Tryptophan Fluorescence



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Mini Review

Depression is one of the most prevalent mental disorders and one of the main causes of disability worldwide. Depression is a risk factor for suicide and many severe somatic diseases [1]. Morbidity of depression is increasing. In the mid-1990s, the World Bank predicted that in 2020 depression would rank second after cardiovascular diseases among the leading causes of disability [2]. Depression is also the most expensive of all brain diseases [3]. Thus, depression now is a very complicated medical and social problem that in the next few years will be only exacerbate. Therefore, investigation of all aspects of pathogenesis of depression is one of the most important problems of the medicine.

Prediction and evaluation of the efficacy of pharmacotherapy of depression is a problem of current importance. All this call forth the necessity of the development of objective methods for the individual prediction of the efficacy of medication on the early stages of antidepressant therapy. There are 3 fluorescent amino acid residues in human serum albumin (HAS) - tryptophan, tyrosine and phenylalanine. In HSA excitation wavelength at 295 - 305 nm is mainly absorbed by tryptophan-214 residues (Trp-214-R) that as inner probe of albumin molecules gives possibility of selective observation of state of albumin molecule and possible conformational changes [4]. The aim of the study was to investigate the kinetics of tryptophan fluorescence decay in serum albumin of patients with melancholic depression (MD) using subnanosecond fluorescent spectroscopy.

Subjects and Methods

There were investigated 14 patients with MD at admission in the clinic of affective disorders of Moscow Research Institute of

Psychiatry and 14 healthy volunteers (controls). Patient's state was defined as a depressive episode in frame of bipolar depressive disorder (type 2) (F32) and in the structure of recurrent depressive disorder (F33). Investigation was performed in accordance with Helsinki Declaration and the conclusion of local ethical committee of the Institute (№ 16 of 13.03.2017).

Fluorescence decay of serum albumin Trp-214-R was measured in subnanosecond range using laser device (LED, Pico-Quant). Excitation wavelength -290±10nm; samples were excited by laser flash (7·10-10 sec). Before measuring each serum, the kinetics of fluorescence decay of the calibrator (a solution of L-tryptophan isomer in buffer and ethanol) were determined. This made it possible to compare the fluorescence intensities measured on different days [5,6]. Using a personal computer based on the AMD Sempron processor, both the measurement process and the processing of experimental data (TimoHarp and FluoFit programs, Picoquant) were automated. The significance of the differences was assessed using the Wilcoxon test (for independent samples). The results were statistically processed using Statistics 6.0 and Excel 2003.

Results and Discussion

In HAS excitation at >295 nm is absorbed mainly by tryptophan 214 (Trp-214) residues thus excitation in the range of 295 - 305nm permits to observe the state of its environment. For the formal description of the kinetics of fluorescent decay of tryptophan it is necessary to use the sum of not less of 3 exponentials [7]:

$$F(t) = A_1 \exp(-t/\tau_1) + A_2 \exp(-t/\tau_2) + A_3 \exp(-t/\tau_3) + \dots$$

where t is the time after light absorption, $F(t)$ is the fluorescence intensity at time t , A_i are the amplitudes of the three exponentials, τ is the decay time of their fluorescence.

Analysis of all fluorescence decay parameters of Trp-214-R in the serum samples of controls and patients before the treatment showed that the mean amplitudes A_1 and A_3 in the serum of these patients were significantly lower than in the group of controls. The application of the Wilcoxon test to independent samples of controls and patients showed a significant difference ($p=0.01$) between these groups: for A_1 - 440 ± 16 v 378 ± 5 and A_3 - 327 ± 15 v 285 ± 7 , respectively (for A_2 - $p=0.1$). Analysis also has revealed the significant ($p=0.01$) differences between controls and depressed patients of ratios A_1/A_3 (1.54 ± 0.04 v 1.16 ± 0.05) and A_1/A_2 (0.75 ± 0.01 v 0.64 ± 0.01), respectively.

Conclusion

It was shown the first time in literature that conformational changes of albumin in mental disorders can be detected by tryptophan-214 residues fluorescence. The properties of albumin binding sites in MD patients before treatment differed from those in controls. The authors suggest that it points to the changes in albumin molecule conformation that may disturb the functional state of the protein. Conformational protein changes may be an important component of the disturbance of molecular processes in the development of pathological process in the body.

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