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View at the anticonvulsive and Nootropic effects from position of new imagination on understanding of the structure and function GABA-Benzodiazepine receptor complex on the basis of the investigation of the molecular geometry and quantum-chemical characteristics main group anticonvulsants, inhibitor amino acids and some convulsive agent

Statement of the Problem: Until these days, searching of endogen agonists of benzodiazepine receptors is actual task, because a lot of problems clinical medicine neurology, Epileptology, Narcology deepened the understanding mechanism of action and function of GABA benzodiazepine receptor complex to elaborate new perspective anticonvulsive and nootropic compounds.

Purpose: Investigate quantum mechanics characteristics and molecular geometry has three conformational states GABA: linear (GABA-1 conformer), bucket-like (GABA-3 conformer) agonists of which is bucket-like conformer of GABA and isoguvacine, but antagonists are picrotoxin and bicuculline; cyclic (GABA-2 conformer) agonists of which are cyclic conformer of GABA, glycine and β-alanine,but antagonists are bemegride, pentilentetrazol and strychnine; and GABA-3 receptors; maine anticonvulsant's groups. Investigate nootropic's and anticonvulsants effects one-valence salts of glycine and GABA.

Method: Molecular geometry of the benzodiazepine's pharmacophores, main GABA conformers and glycine where studied in the approximation of molecular mechanics with the use of the MM2 force field. Influence introperitonial injection different one-valence salts of glycine and GABA on the cerebral neurophisiological activity in white rats (taking of EEG) and their anticonvulsant activity using strychnine, picrotoxin, pentylenetetrazol and maximal electro seizure models.

Results: It was show, that anticonvulsive and other behavioral effects of derivatives of barbituric acid, benzazepine, benzodiazepine, gidantoine, succinimide and oxasolidindione are realized probably via GABA-2 receptors to switch on them the following functional centers of their structure are nessesary: α, and [δ-ε] for barbitirates; β, [δ-ε] and γ for carbamazepine; β and [δ-ε] for benzodiazepine derivatives, gabapentine and vigabatrine; α, β, γ and [δ-ε] for gidantoine and oxasolidindione derivatives; α, β, γ for succinimide derivatives. The expression of any (including nootropic) behavioral effects of anticonvulsants and inhibitory amino acids depends on power, location and numbers of hydrogen bounds developed between active centers of pharmacophore of anticonvulsant or inhibitory amino acids and active centers of functional skeleton of GABA-2 receptorcomplex.

Conclusion: 1. The more stronger the charge on the atoms of the pharmacophore of the GABA agonist, the more expressive its anticonvulsant effect and Vice versa, the weaker the charge on the atoms, the more expressive the nootropic effects appear 2. There are perspectives of synthesis of compounds, pharmacophore of which should be like as cyclic conformer of GABA, glycine and β-alanine on their quantum mechanics characteristics and molecular geometry.

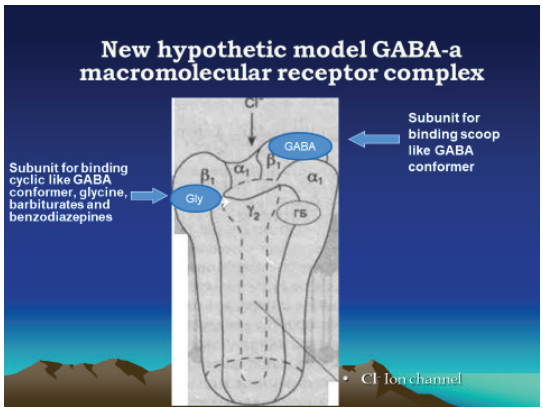

Figure 1. New hypothetic model GABA-a receptor complex

Speaker Biography

George N Shilau has completed his PhD at age of 29 years old from Byelorussian State Medical University. He long time work as senior scientific worker in the laboratory of the biochemistry of neurohormones and neurosurgery over mention University and then as leading scientific worker central scientific-investigating laboratory of Byelorussian Medical Postgraduate Academia and neurologist practitioner, and also as MRY diagnostician. Then he worked as deputy Director of the center of Medical Information "EOCEN" and continues his scientific work in close cooperation with Laboratory of free-radical process chemistry of the Research Institute of Physical Chemical Problems of the Belarusian State University. Now he works as MRY diagnostician of the Republican Clinic Medical Center of the Presidential Administration. He has published more than 40 papers in reputed journals. His interests include neuropharmacology (GABA-benzodiazepine and glycine receptors and their interactions), the clinic of epilepsy.

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