Medical Xpress

Scientists determine structure of brain receptor implicated in epilepsy and PMT

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Scientists funded by the Biotechnology and Biological Sciences Research Council (BBSRC) have published new research in the journal *Molecular Pharmacology* identifying the structure of a receptor in the brain implicated in conditions such as epilepsy and pre-menstrual tension. The same receptor has also been reported to be highly sensitive to alcohol.

The University of Cambridge team, in collaboration with colleagues at Aston University and the University of Alberta, have determined the arrangement of the constituent parts of an uncommon but important type of GABA receptor in the brain. GABAA receptors in the central nervous system play important roles in the body's response to gamma-aminobutyric acid (GABA), a chemical used by the brain to control certain functions. By understanding how the receptors' sub-units are arranged, scientists may now be able to develop drugs to block or stimulate them, providing hope for sufferers of a range of conditions.

Different types of GABAA receptor have been shown to play various roles in the body's control of behaviour and development. The Cambridge scientists are the first to determine the structure of a type of GABAA receptor containing the so-called delta sub-unit. This receptor type is found in small numbers in the body but is thought to be disproportionately important in controlling our state of consciousness; it is highly sensitive to anaesthetics, and has been linked to epilepsy and pre-menstrual tension, and to the body's response to alcohol.

The team used an atomic force microscope to detect the receptors. They

applied tags to the receptors that bind to different sub-units. These can then be identified with the microscope, which scans a probe over the surface of a sample. By identifying the tags the team could identify where the various sub-units were located. Armed with this information, researchers can now build detailed models of the receptor which can be used to develop drugs to intervene in the signals that it receives.

Dr Mike Edwardson, who led the research team, said: “This type of GABA receptor plays a crucial role in the body’s response to a range of stimuli. Scientists think that when there is a problem in the signalling, conditions such as epilepsy and PMT can occur. Now we have identified the detailed structure of the receptor we are in a better position to design drugs that bind to it.”

Professor Nigel Brown, BBSRC Director of Science and Technology, commented: “Basic bioscience research has a crucial role to play in understanding conditions that affect the health and quality of life for millions of people. If we learn the detailed mechanisms by which the body functions, medical scientists and the pharmaceutical industry can develop treatments to intervene when it goes wrong.”

Source: Biotechnology and Biological Sciences Research Council