Department of Child and Adolescent Psychiatry/Psychotherapy

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Cooperation Project: “Age-dependent Cell Biological Effects of Psychotropic Substances in Maturing Neuronal Systems”

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In recent years it has been extensively debated if the prevalence of psychiatric disorders in childhood and adolescence is increasing. In contrast, the increased frequency of prescribing psychotropic medications to minors cannot be doubted. Most psychotropic substances are used “off-label”, meaning there is a huge lack of knowledge about the cell biological effects of compounds in the developing brain. Pediatric psychopharmacology can only be properly understood within the context of developmental neurobiology.
In a joint venture between the Department of Child and Adolescent Psychiatry and the Institute of Anatomy and Cell Biology, we are conducting in vitro studies in neuronal cell cultures and in vivo studies in rodents to assess the potential impact of psychotropic substances on cell development. We are interested in the effects of the substances most frequently used in child and adolescent psychiatry: methylphenidate, a psychostimulant and dopamine transporter inhibitor; atomoxetine, a selective norepinephrine transporter inhibitor; (both compounds are used in the treatment of attention deficit hyperactivity disorder); and fluoxetine, a selective serotonin transporter inhibitor and antidepressant. Besides their well-known effects on the presynaptic monoaminergic transporter molecules, all three substances seem to have an impact on cell plasticity. Our working group was able to detect neuroprotective effects of methylphenidate. Fluoxetine and atomoxetine exerted a dose-dependent effect on cell viability and a reduction of neuronal arborisation and synaptic density. In collaboration with the Department of Anesthesiology, we were able to show that atomoxetine inhibits the NMDA-receptor, a mechanism that influences apoptosis in the developing brain. We are currently investigating the possible age-dependency of the effects of atomoxetine and fluoxetine not only on the expression of various monoaminergic transporters and subunits of the NMDA-receptor (PhD work Patrick Udvardi) but also on the expression of PSD scaffolding proteins since the NMDA-receptor is embedded in a much larger complex of proteins associated with the post-synaptic density (PSD).