

## S28-4 Application of animal PET in drug development

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In the drug discovery and development process, it should be indispensable to assess pharmacokinetics, pharmacodynamics and safety pharmacological aspects. It is expected to apply the molecular imaging method with noninvasive PET measurement in monkeys from the scientific, animal ethical and economical points of view.

We evaluated the chronic MPTP-treated monkeys with PET imaging and behavioral performance test, showing the impaired behavioral performance as well as decreased pre-synaptic dopamine synthesis and transporter availability in the striatum without any changes in post-synaptic dopamine D1 receptor binding. We transfected AADC gene into the striatum of the monkeys, resulting in the improved behavioral performance as well as dopamine synthesis. We developed a stroke model in monkey, have assessed several candidate compounds for strike therapeutic drugs, and suggested the possibility to predict the efficacy of these candidates before clinical trials in humans. We found that cholinergic muscarinic receptor binding was decreased in the brain of aged monkeys as well as impaired working memory performance in comparison with young animals. When anti-Alzheimer disease drug with cholinesterase inhibition was administered, we confirmed the lowered cholinesterase with PET, the increased cholinergic neural transmission with microdialysis and the improved working memory performance.