**A48**

**Decreased blood-brain barrier P-glycoprotein function with aging**

Martin Bauer\(^1\), Rudolf Karch\(^2\), Aiman Abrahim\(^1,3\), Claudia C Wagner\(^1\), Kurt Kletter\(^4\), Markus Müller\(^1\) and Oliver Langer\(^1,3\)

\(^1\)Department of Clinical Pharmacology, Medical University of Vienna, 1090 Vienna, Austria

\(^2\)Department of Medical Computer Sciences, Medical University of Vienna, 1090 Vienna, Austria

\(^3\)Department of Radiopharmaceuticals, Austrian Research Centers GmbH – ARC, 2444 Seibersdorf, Austria

\(^4\)Department of Nuclear Medicine, Medical University of Vienna, 1090 Vienna, Austria

E-Mail: oliver.langer@meduniwien.ac.at

**Introduction**

P-glycoprotein (P-gp) acts at the blood-brain barrier (BBB) as an active cell membrane efflux pump for several endogenous and exogenous compounds. The P-gp substrate (\(R\)-\([^{11}\text{C}]\)verapamil (VPM) can be used to measure P-gp-mediated transport at the BBB in vivo with positron emission tomography (PET). The distribution volume (\(DV\)) of VPM has been shown to inversely reflect P-gp function in the BBB [1].

**Materials and methods**

A young (\(n = 7\), mean age: 28.0 ± 3.8 years) and an aged group (\(n = 6\), mean age: 69.4 ± 8.5 years) of healthy volunteers underwent dynamic VPM PET scans and arterial blood sampling. Radiolabelled metabolites of VPM were quantified by a previously described combined solid-phase extraction/HPLC protocol [1]. A whole-brain grey matter region was defined by using the Hammersmith n20r49 brain atlas [2]. The \(DV\) of VPM was estimated by using a 2-rate-constant-1-tissue-compartment model [1].

**Results**

Mean \(DV\)s (± standard deviation) of VPM were 0.50 ± 0.08 for the young and 0.63 ± 0.13 for the aged group (+27% for the aged group, \(p = 0.04\), 2-tailed \(t\)-test). There was no significant difference in VPM metabolism between the young and the aged group (area under the curve of the fraction of polar \([^{11}\text{C}]\)metabolites of VPM versus time in arterial plasma: 12.7 ± 2.4 and 14.1 ± 3.6 for the young and the aged group, respectively, \(p = 0.19\), 2-tailed \(t\)-test).

**Conclusion**

Our data confirm previous results that older subjects show significantly decreased P-gp function in the BBB [1, 3]. Decreased P-gp function can lead to increased accumulation of toxins and drugs in the aging brain and could thus be a risk factor for the development of neurodegenerative disease.

**References**

