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Meeting abstract



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

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## 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*)-[$^{11}$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 [$^{11}$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

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