High-fat diet and its effects on altered S1P signaling after stroke [Abstract]

Lisa Porschen, Hana Matuskova, Frank Matthes, Anja Meissner

Angaben zur Veröffentlichung / Publication details:

Porschen, Lisa, Hana Matuskova, Frank Matthes, and Anja Meissner. 2023. "High-fat diet and its effects on altered S1P signaling after stroke [Abstract]." Journal of Neurochemistry 166 (S1): 102. https://doi.org/10.1111/jnc.15897.

B 04-08 | High-fat diet and its effects on altered S1P signaling after stroke

Lisa Porschen[1,2], Hana Matuskova[1,2,3,4], Frank Matthes[1,2,5], Anja Meissner[1,2,3,5]

[1]Lund University, Department of Experimental Medical Science, Lund, Sweden; [2]Lund University, Wallenberg Center for Molecular Medicine, Lund, Sweden; [3]DZNE, German Center for Neurodegenerative Diseases, Bonn, Germany; [4]University Hospital Bonn, Department of Neurology, Division of Vascular Neurology, Bonn, Germany; [5]University of Augsburg, Department of Physiology, Institute of Theoretical Medicine, Medical Faculty, Augsburg, Germany

Stroke is a common, multifactorial cardiovascular disease linking to a variety of risk factors, including genetic predisposition, lifestyle factors, and co-morbidities. Metabolic syndrome characterized by obesity, insulin resistance and increased blood pressure links to impaired cerebrovascular function and was associated with increased risk of stroke. Data generated by us and others showed that alterations in the signaling of sphingosine-1-phosphate (S1P) associate with several cardiovascular risk factors and cardiovascular disease, including stroke.

Here, we investigated alterations in S1P signaling post-stroke and how metabolic syndrome induced by high-fat diet alters stroke-associated S1P responses, using a murine middle cerebral artery occlusion (MCAo) model to mimic ischemic stroke.

Mass spectrometry revealed elevated S1P plasma levels post-stroke. Concomitantly, brain S1P concentrations were lowest in the ischemic hemisphere compared to the respective contralateral hemisphere and sham-operated mice. Interestingly, S1Pr3 mRNA and protein expression were specifically augmented in the vascular compartment of the ischemic hemisphere. Additionally, S1Pr3 plasma concentrations were elevated post-stroke. Mice exposed to high-fat diet presented with higher S1P plasma levels compared to mice on control diet and had larger infarct sizes post-stroke. Lastly, plasma S1P and S1Pr3 levels were assessed in a human cohort of stroke patients within 24-h post-stroke and at a 3-month follow-up. S1P plasma levels were lower during the acute phase and were normalized at 3 months post-stroke, while S1Pr3 levels were augmented at both time points post-stroke compared to age- and sex-matched controls. Control individuals were of similar cardiometabolic status, thus making it difficult to determine effects of metabolic syndrome on S1P signaling.

In conclusion, S1P signaling is significantly altered post-stroke and with high-fat diet exposure, suggesting a possible targetability in new therapeutic approaches.