INSELGRUPPE

UNIVERSITÄT BERN

Press release

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Established for the first time by Bernese team:

Connection between eye infarction and gut flora

The research group led by Martin Zinkernagel and Denise Zysset at the Department of Ophthalmology at Bern University Hospital and the Department of Clinical Research, Bern University, has demonstrated specific changes in the composition and function of the gut flora in patients with an eye infarction. An imbalance in the gut flora correlates with the occlusion of the ocular artery. Recommendations for the prevention of eye infarctions can be derived from this.

Eye infarctions occur suddenly – mostly in connection with cardiovascular diseases. An eye infarction occurs in more than twice as many diabetic patients compared to people without a diagnosis of diabetes. The search for correlations between this disease and nutrition and for possible preventive measures is ongoing.
Prof. Dr. Dr. med. Martin Zinkernagel's research team in Bern has now dedicated for the first time a study to the question of a possible connection between eye infarction and gut flora. It is known from already existing investigations that imbalances of the gut flora have an important effect in impaired fat metabolism and thus in atherosclerosis (popularly known as arteriosclerosis).

Eye infarction – more frequent than previously known

A retinal artery occlusion (RAO) occurs suddenly and can reduce the eye's vision or even lead to blindness in the affected eye. Minor events often go unnoticed because the remaining, functioning eye can compensate for the visual function. What exactly happens in an eye infarction? Following the same basic pattern as a stroke or a heart attack, an infarction can also occur in the eye. As a rule, the actual event is preceded by a long-lasting vascular disease (atherosclerosis) in which certain blood lipids form deposits on the inner walls of important arterial blood vessels. Blood vessels constricted in this way can suddenly be blocked by a blood clot. Oxygen is withdrawn from the eye; the retina can no longer perform its function and the vision is lost. With immediate specialist intervention, partial or

extensive restoration of the eye is possible. If, on the other hand, there is a long delay an eye infarction can cause permanent damage.

Risk factors: environment, genes and nutrition influence the gut flora

The risk factors for cardiovascular diseases have been well investigated and can be roughly divided into three groups: environmental factors, genetic predisposition and behaviour/nutrition. Frequently cited keywords are in this context environmental pollution and stress, smoking and alcohol as well as lack of exercise and poor nutrition. It is known that these factors are associated with a change in the composition of the gut flora. The latter was of particular interest to the research group. The gut flora – the entirety of the microorganisms that colonise the human intestine – plays a decisive role in digestion and influences the metabolism and the immune system. In a healthy adult, this ecosystem consists mainly of bacteria of which totally up to a hundred trillion colonise the intestine. Their composition varies greatly from person to person. However, imbalances in the gut flora – known as dysbiosis or dysbacteria – can impair the metabolism and contribute to the development of metabolic diseases such as atherosclerosis.

Composition of the gut flora researched via gene analysis

The Bernese research team examined the gut flora (intestinal metagenome) of patients who had suffered an eye infarction and of a healthy control group as well. The intestinal metagenome, the totality of the genomic information of the microorganisms in the intestine, was determined by sequencing. The sequencing allows a precise determination of the amount and type of the gut flora components and replaces earlier, very complex and inaccurate examination methods. The study found differences in both the composition and the function of the gut flora. The class *Actinobacteria* and the species *Bifidobacterium adolescentis*, *Bifidobacterium bifidum*, *Bacteroides stercoris* and *Faecalibacterium prausnitzii* were increasingly found in the intestines of persons who had suffered an eye infarction. Genetic material of *Actinobacteria* was found in deposits on the inner walls of the blood vessels. Furthermore, a reduction of the bacterial strain *Bacteriodetes* in favour of Proteobacteria in patients indicates a dysbiosis and thus a possible atherosclerotic disease.

Amin oxide TMAO: messenger or perpetrator?

Previous studies have shown a link between the production of trimethylamine N-oxide (TMAO) in the intestine and cardiovascular diseases. TMAO is also considered a risk and prognosis marker for atherosclerotic diseases. The Bernese study now found a significant difference in TMAO concentration between patients and persons in the control group. At higher concentrations of TMAO the genus *Akkermansia* appeared more frequently. The genus *Parasuterella* and the family *Lachnospiraceae* showed the opposite behaviour.

Whether an increased TMAO concentration is the cause for the development of atherosclerosis or whether this is only a marker for the differences in the gut flora cannot yet be conclusively proven.

Cardiovascular diseases are closely related to the fat metabolism in the blood. It is known that low-density lipoproteins (LDL) contribute to deposits on the inner walls of the blood vessels. In this context, the isoprene signalling pathway, which provides starting materials for the production of cholesterol, was investigated. It was established that patients who had suffered an eye infarction exhibited increased isoprene biosynthesis.

Consequences and prevention

The data obtained indicate possible ways as to how an eye infarction can be prevented with certain probiotics, antibiotics and an appropriate diet and lifestyle. All results suggest that eye infarction is due to the same causes as stroke and heart attack. It is a metabolic cardiovascular disease. This can be of genetic origin or can be controlled by environmental influences and eating, exercise and addictive behaviour. The general indications of sufficient exercise and avoidance of smoking and alcohol as well as a balanced diet can also be recommended as a measure to prevent eye infarction.

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- Denise C . Zysset-Burri, Irene Keller, Lieselotte E. Berger, Peter J. Neyer, Christian Steuer, Sebastian Wolf & Martin S. Zinkernagel 2019: Retinal artery occlusion is associated with compositional and functional shifts in the gut microbiome and altered trimethylamine-N-oxide levels. https://doi.org/10.1038/s41598-019-51698-5

Insel Gruppe

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