Lilly Background Talk „Care for Alzheimer's Disease

Alzheimer's: Is early detection the key?

The bad news is that the number of people who will suffer from dementia in this country in the future will increase. Based on demographic trends alone - based on an estimate and assuming current treatment options and excluding any special consequences such as co-occurrences with corona, which Federal Health Minister Prof. Dr. Karl Lauterbach warned against (see p. 38) - around 2.8 million Germans will suffer from dementia in 2050, plus around 2 million with Alzheimer's dementia. The good news afterwards: the disease could soon lose its horror. However, this will only happen if the conceptual understanding of dementia changes, biomarker tests are carried out at a very early stage and innovative (but already foreseeable) treatment options close the resulting knowledge-therapy gap. This became clear at a background discussion organised by the research-based pharmaceutical company Lilly entitled „Care for Alzheimer's disease". The following question was raised and discussed with the speakers: „Is early detection the key?"

>> In any case, the currently foreseeable pipeline of substances that can be used to treat Alzheimer's dementia in the future is quite encouraging. As Prof. Dr. med. Oliver Peters (Charité Berlin) explained in his lecture on the prevalence, pathophysiology and causes of Alzheimer's disease, there are currently 143 active substances in development, 31 of which are in phase 3. Many of them work with the two proteins amyloid (15%, 20 active substances) and tau (9%, 13), which trigger the course of Alzheimer's in the biomarker model. In the biomarker model, these two proteins trigger the course of Alzheimer's, or if they were influenced favourably, they would be able to delay the course of the disease, which takes place in six stages and cascades - possibly even significantly, depending on the start of therapy.



Fig. 1: Lilly background talk „Care for Alzheimer's disease", lecture „Alzheimer's disease: prevalence, pathophysiology and causes"; Prof. Oliver Peters, MD, Charité, 2023.

This makes the crux of the matter clear: According to the current understanding of the disease, a person only has dementia when the onset of clinical symptoms with pathological changes in the nervous system accompanied by cognitive and functional impairments can be detected. However, as Peters, senior physician at the Department of Psychiatry and Psychotherapy at the Benjamin Franklin Campus of the Charité and head of the working group at the German Centre for Neurodegenerative Diseases (DZNE), explained, there is „a very, very long period of time" before this, which can span several decades, during which biological processes take place insidiously and unrecognised if there is a corresponding predisposition. Although in the early stages those affected are usually not restricted in their everyday life and independence, the pathological degradation of amyloid precursor proteins and the ever-progressing formation of amyloid plaques in the brain has long since begun. Already here in the asymptomatic stages 0 and 1 (see Fig. 1), it would be possible to apply innovative biomarker-based diagnostics in order to use the resulting „window of opportunity" for the early start of a suitable and perhaps soon available targeted therapy strategy.

„We are trying to get further and further retrograde," says Peters, indicating a quite possible direction of travel in the fight against Alzheimer's disease. At the moment, however, symptomatic treatment is still state of the art, because there have been approved anti-dementia drugs for a long time. Peters: „What we would like to do, and what is a step into the future, is secondary prevention, in which treatment is given immediately when the symptoms start - with the aim of achieving greater clinical effectiveness." The nature of chronic degenerations is that the later therapeutic intervention takes place, the less can be achieved. However, since Alzheimer's dementia can already be treated

Since, however, in the case of Alzheimer's dementia, brain damage that has already occurred (even in the asymptomatic area) cannot be reversed, the idea is: „The earlier we begin to treat, the more effectively we can intervene in the pathological process that leads to dementia". This is even with the goal, which in his opinion is extremely realistic, that „ideally, perhaps one day, dementia will no longer occur at all". However, Peters continues, „only if we succeed in primary prevention, i.e. treating before the very first clinical symptoms have appeared. In a few years, this approach could help to maintain the quality of life and independence of those affected for much longer and, on top of that, reduce later costs associated with Alzheimer's disease. Could. Because it costs money in the first place. In his lecture on the „Importance of early diagnosis and

possibilities for early detection“, Prof. Dr. med. Timo Grim-mer(Technical University of Munich) explainedthat biomarker-based diagnostics should be established because the previous exclusively clinically-based diagnostics of Alzheimer's disease are not sufficient for diagnosing the early stages.

For the early diagnosis of Alzheimer's disease, cerebrospinal fluid tests for amyloid and tau proteins, PET scans* with radioactive tracers and, in the medium term, simpler blood-based biomarker tests that are still being developed and clinically validated should be used. In the USA alone, there are already approved tests.

In general, however, the more markers that are positive, the more likely dementia is to develop in the next few years. But also: the earlier a therapy is applied, the greater this effect will be. It is important, he says, not only to make a prognosis, but to accompany it with a therapy option, whereby „we hope that more modifying therapies will be available to us in the future.“ Says Grimmer, „We need to be able to detect and treat those with dementia but who are still asymptomatic, when they are not yet in need of help.“ In this way, serious courses of the disease could be averted or at least slowed down. Achieving this would be a great achievement for those affected and their relatives, but also for society. But since the early diagnosis necessary for this does not happen, „we miss out on people because no one looks at an early stage“.

Grimmer sees less of an obligation for specialised institutions such as the Polyclinic for Psychiatry and Psychotherapy of the Klinikum rechts der Isar and the Centre for Cognitive Disorders of the Technical University of Munich, where he works, and more of a genuine obligation for the treating family doctors. Together with the general practitioners, it is possible to address many of the modifiable risk factors for the development of dementia even without biomarker-based diagnostics, which by their very nature have not yet sufficiently arrived in the GP setting (see Fig. 2, above).

Grimmer hopes that this, too, would have „a huge potential to favourably influence the prevalence of dementia.“ It should be noted that the more tests are available, the greater the challenge is to interpret the results as correctly as possible. All tests have limitations. Especially with blood tests, one must always keep in mind that a certain number of false-positive and false-negative results can occur. Especially the occurrence of false-positive results is a big communicative task. It can happen that people who are confronted with a diagnosis of a disease - whether correct or incorrect - can have a knee-jerk reaction, or at least unnecessary anxiety and social disturbances. <<

by: MVF Editor-in-Chief Peter Stegmaier

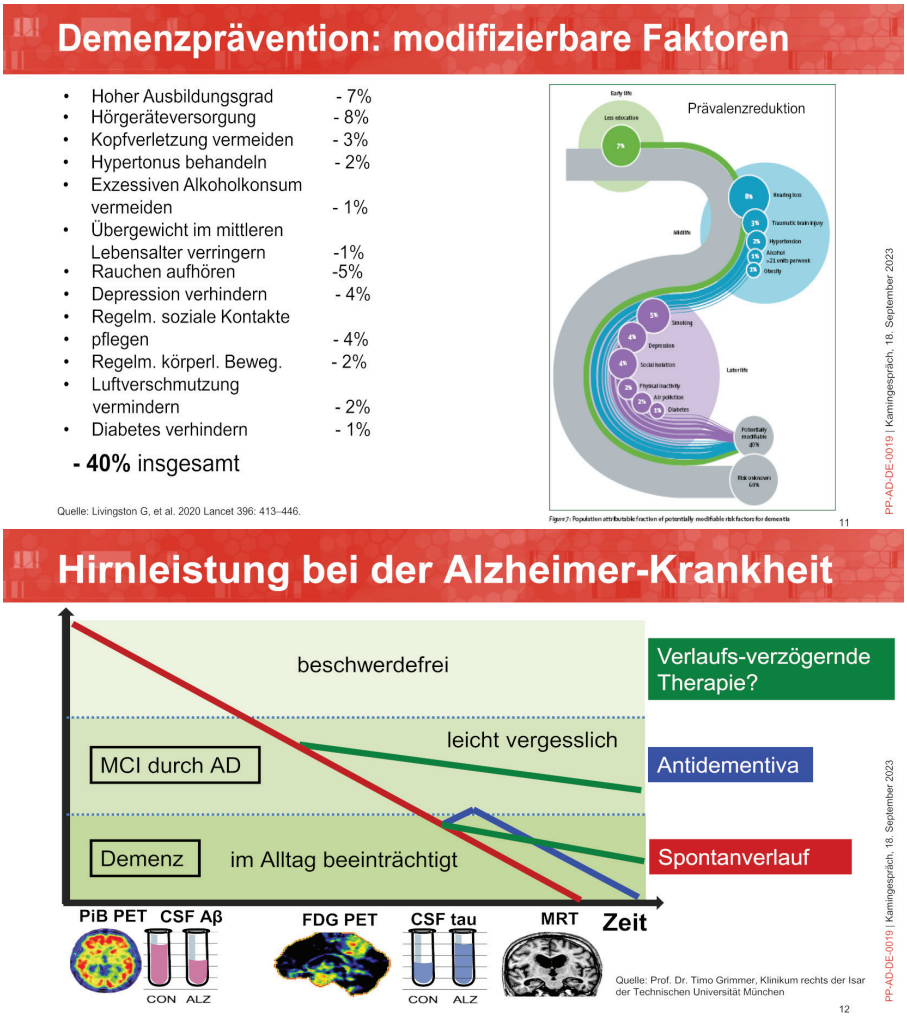


Fig. 2: Lilly background talk „Care of Alzheimer's disease“, lecture „Alzheimer's disease: importance of early diagnosis and possibilities for early detection“; Prof. Dr. med. Timo Grimmer (Technical University of Munich), 2023. *Leg: PET = positron emission tomography.

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