Promising cell study provides hope of effective treatment of Parkinson's disease

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For the first time, medical doctors and researchers could alleviate serious symptoms of Parkinson's disease, which causes shaking, muscle stiffness and slow movements in those affected. However, before these symptoms appear, and during the course of the disease, many patients experience sleep disorders, gastrointestinal problems, anxiety and depression. Unlike the symptoms in the motor system, there is no effective treatment for these more neglected symptoms.

A team of researchers from Aarhus University has now moved a step closer to understanding how the early symptoms occur—and possibly also how they can be checked. In the study, which has just been published in the scientific journal *EMBO Reports*, the researchers show that in nerve cells with the same type of stress as Parkinson's disease, there is a marked loss of calcium. If the level of calcium decreases, cells cannot function. This is especially true for people at an early stage of Parkinson's disease, because malfunctioning nerve cells can give rise to symptoms such as sleep disorders and anxiety. According to the lead author of the study Cristine Betzer from the brain research centre DANDRITE at Aarhus University, saving calcium-depleted nerve cells indicates that the symptoms can be inhibited.

"The study indicates that the treatment of calcium disturbances is meaningful because the nerve cells are protected. This may help to prevent the disease from developing into such a disabling disease as would otherwise be the case," says Cristine Betzer.

One characteristic symptom of Parkinson's disease is the loss of fine motor control. This happens when protein structures in the brain clump together and kill off nerve cells. By examining brain tissue from mice, pigs and humans, Betzer discovered that the clumped proteins activate a calcium pump. When this happens, the cells cannot function normally and eventually die. The researchers sought to inhibit the activation of the pump in the first place.

In Aarhus, they suppressed the pump in a worm model that was modified to express human genes. "Experiments in the United States with similar models have shown that once the worms with the Parkinson's protein have lived for eight days, their nerve cells begin to die. In our study, we treated the worms with an inhibitor against the calcium pump and then counted the nerve cells in the worms. And there were many cells left, which is a sensational and encouraging result," says Betzer. She emphasises that the result cannot be directly transposed to humans, but it is a positive indication for upcoming studies with mice and rats. "It's a question of regulating calcium in the nerve cells. This is complicated, but also a promising area, as there are already a large number of medications for regulating calcium. It's possible that the knowledge that already exists about the medications can help us make progress quicker in the new area."

She hopes that the study will offer new opportunities for treating Parkinson's disease, particularly for people who suffer from severe sleep disorders and cognitive disorders. "Our study points toward the usefulness of treating patients throughout the whole course of the disease, as the calcium pump will otherwise continue to pump and thus contribute to the patient's symptoms. Perhaps the protection of nerve cells can also mean that the damage caused by Parkinson's disease in the brain does not develop as severely as it otherwise would," says Betzer.

More information: Cristine Betzer et al, Alpha-synuclein aggregates

activate calcium pump SERCA leading to calcium dysregulation, *EMBO reports* (2018). DOI: 10.15252/embr.201744617