Parkinson's treatment revisited to avoid adverse effects

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Parkinson's disease modifies a crucial circuit of the central nervous system in a specific way. This could open up an alternative therapeutic approach that avoids side effects of current therapies.

According to estimates, more than 1.2 million people in Europe are affected by Parkinson's disease. Health costs for the disease amount to €11 billion euros per year. Although a fair number of therapies are available, they have important limitations. There is thus great need to look for better alternative therapies or drugs that can complement the existing ones. Now, the EU-funded REPLACES project, completed in 2013, may have opened the door to potentially new treatments. Project coordinator Monica Di Luca, professor of neuropharmacology at the University of Milan, in Italy, talks to youris.com about a specific way in which Parkinson's disease affects a crucial circuit in the brain.

What are the limits of current therapies for Parkinson's disease?

Today, the available drugs, such as levodopa and so-called dopamine agonists, act on the malfunctioning of nerve signalling through the dopamine receptor in the brain. The problem is that after what we call the honeymoon period, during which they work well, they cause side effects in many patients such as dyskinesia. These are sometimes even more troubling than the symptoms of the disease.

What strategy did you use to overcome such problems?

Everything started few years ago. With my research group, I study a peculiar circuit of the central nervous system, the so-called glutamatergic excitatory system. The connections in this system are highly dynamic: their morphology is completely modified according to the stimulus they receive. Their plasticity is at the base of high and important functions, such as learning and memory.

This circuit is also very significant for Parkinson's disease because its "destination" is one of the brain regions most severely damaged in the pathology. Fabrizio Gardoni, from my lab, discovered that the glutamatergic synapses in Parkinson's disease are completely altered in a peculiar way. Following that finding, we tried to better understand the functioning of the glutamate receptors. And we also focused on how they can be used as a target to modulate the other kind of receptors that go awry in Parkinson's disease, the dopamine receptors.

What did you find?

We did basic research and worked with animal models of Parkinson's disease: mice, rats and monkeys. We also studied tissues of patients affected from the disease coming from a brain bank. What we found is that, with Parkinson's disease, the glutamate receptors are in fact completely altered, as first assumed. Even more important, we found that the modifications are the same in mice, monkeys and people. This means that they really are specific to the disease and constitute a potentially new target for treatment.

Did you test new treatments acting on this region?

We have already experimented with a couple of molecules, small peptides, to try to correct the defective receptors for glutamate. We have tested them on animals: mice and monkeys. And we hope that there will soon be the occasion to start testing their safety in humans.

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