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Latest Findings in Alzheimer's Research

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Prof. Ulrich Sprick on Research into Transcranial Pulse Stimulation (TPS) and its Potentials.

"The textbooks say that Alzheimer's disease is a progressive disease that keeps progressing and that it is irreversible. We are about to scratch that irreversibility!"

Mona Elzayat (ME): << Prof. Sprick, you have extensive expertise in the fields of psychiatry, psychotherapy as well as clinical psychology. As head physician of the outpatient services and the day clinics at the Alexius/Josef Hospital, you and your teams ensure the care of people with mental illnesses in the Rhine District of Neuss in Germany for the outpatient and day-care sector. As a lecturer at the Heinrich Heine University in Düsseldorf, you are also involved in research, development and teaching. You are currently researching the effect of transcranial pulse stimulation as a new procedure in the

treatment of Alzheimer's disease. This is the topic we would like to address today. Prof. Sprick, thank you very much for taking the time for our interview today. >>

Prof. Ulrich Sprick (US): << Yes, with pleasure, Ms. Elzayat. >>

ME: <<*Thank you, I'll get right to my first question: what can you think of as neuroplasticity?*>>

US: << Neuroplasticity is the general ability of the brain to respond to appropriate changes. The brain needs neuroplastic processes to represent learning and memory and also to trigger regenerative processes. That is, the growth of neurons, building new synaptic connections, this is called neuronal plasticity.>>

ME: <<*How does neuroplasticity work or what promotes it?*>>.

US: <<Neuroplasticity is first of all the basic prerequisite for us to be able to learn. These are tiny changes in the brain that take place in any learning process. Our brains, if you were to look at it very precisely, are a very little bit different before the interview and after the interview because we have then had certain experiences and that is brought about by neuroplastic processes. The brain is also able to restructure itself, for example after certain diseases, if for example neurodegenerative diseases or inflammations or something like that occur, our brain is able to react to that, for example by triggering certain processes, creating synaptic connections, etc. And one can support this process of neuroplasticity, for example by brain stimulation methods. >>

ME: <<*That is, the activation of neuroplasticity occurs on the one hand through learning and through experience and on the other hand through pulse stimulation?*>>

US: << Yes, of course there are many other things that also trigger neuroplasticity. The brain itself is also capable of triggering neuroplastic processes. In certain diseases, however, this alone is unfortunately not sufficient to compensate for the process of neurodegeneration. Additional support is needed, and this can be achieved through certain procedures - there are drugs that do this - and also brain stimulation, which can provide support here.

ME: << *For example, can you also achieve this with thoughts?*>>

US: << With thoughts you can achieve that insofar as you should use your brain! So that means, if you don't care about these things at all, so you don't do these things at all, you don't allow new experiences at all, also the neuroplasticity has certain limits and insofar certain things should be practiced, as we know it, and through these exercises these neuroplastic processes get going and you can learn again certain abilities quasi anew.>>

ME: << *Professor, what is meant by Transcranial Pulse Stimulation, or TPS for short?*>>

US: << The word 'transcranial' comes from Latin and means 'through the skull'. And pulse stimulation means that we work with mechanical pulses and stimulate the brain. The fact that the whole thing goes through the skull is a special feature, because you can - without having to do an operation, without having to open the head - also reach the brain in depth with this method.

That is already a special feature! There are other procedures that you may be familiar with, where so-called deep brain stimulation is used, where neurosurgeons make a small hole in the skull and then implant an electrode deep into the brain and can then also stimulate there. With TPS, that's not necessary. There are other procedures where that is not required, such as magnetic stimulation. With this, the stimulation also works through the skull.>>

ME: <<*What are the differences between transcranial pulse stimulation and the conventional stimulation techniques used such as ECT, magnetic stimulation and so on?*>>

US: << First of all, you can distinguish three different major types: One is the electro procedures. You had just mentioned ECT, which is an electroconvulsive therapy that is approved for the most severe mental disorders, for example, the most severe depression or schizophrenia. Unfortunately, this procedure is associated with the need for anesthesia so that the patient can tolerate it. There are other electrical procedures that can also be used, but they only reach the surface of the brain, i.e., they do not go into the depths of the brain.

For example, there is direct current therapy and alternating current stimulation, both of which are completely harmless, but cannot reach the deep structures of the brain. Furthermore, there is magnetic stimulation, which works with magnetic waves. Here, one can also reach the deeper regions of the brain, but these applications cannot be carried out very precisely. So, you have relatively large coils and reach a relatively large area of the brain at the same time. And you actually want to set the stimulation very precisely and locally. This is not yet possible with magnetic stimulation. And thirdly, there is mechanotransduction, i.e. working with mechanical waves. Then there is the so-called ultrasound method and there are shock waves.

These differ in that the ultrasound waves of the conventional type are sinusoidal waves, which also reach the depth of the brain, but also generate heat in the depth of the brain. This can be intentional if you want to destroy a deep area of the brain, which is the case, for example, in certain diseases such as tremor disorders, where you can very precisely eliminate a tiny area of the brain, that is, with heat. But we don't want that in Alzheimer's disease, so there we don't want heat to be applied to the brain, and so there we resort to pulse stimulation, where we work with shock waves. >>

ME: <<*What does the patient feel when receiving such therapy?*>>

US: << For the patient, this therapy is largely painless. The patient hears the (acoustic) 'clicks' several times a second and he notices a slight tingling sensation on the skin by the brain. I have heard from some patients, if you apply all the way from the front, that where the nasal sinuses (paranasal sinuses - ed.) are, that is, the large openings for nasal ventilation, there can be unpleasant sensations. But by and large, this treatment with TPS is painless. You get an ultrasound gel in your hair, so that the transmission of the sound waves can take place in a very special way, and afterwards you wash your head and this gel out again. >>

ME: << *That is, because I know this from irradiation, also from head irradiation, there the patients have the feeling of smelling something strong or that they also have unpleasant feelings, and there I would like to ask you whether this is perhaps comparable?*>>

US: <<So, patients reporting to us that they have sensations of smell or taste or anything like that doesn't really happen. What we do see is patients telling us that they get tired after treatment. That's a smaller part, not all patients say, "I get really tired." So that means the intensity of the treatment was such that you realize, yes, this has been a real exercise session for the brain as well. So you can get a little tired, that can be a side effect. Headaches are mentioned in small cases, we are here at five to six percent, but other side effects in the patients we have selected for these treatments are not reported. >>

ME: << *I have a question about what you said earlier, and that is that in certain diseases, areas of the brain can also be destroyed. Is that dangerous, can there also be caught too much and is also artificial intelligence already used in this area?*>>

US: << These are very exciting questions. One is that we have calculated the intensity of our shock waves to be a power of ten below a range that could be dangerous. This means that this is not the case! High-intensity shock waves are even able to break up kidney stones or gallstones, for example.

We are working here in a completely different area, where the intensity of these shock waves has been massively reduced.

It is only in this area that we can induce regenerative or plastic processes. We know that these shock waves do not cause any bleeding or the like, because we take care to limit the intensity precisely. In this procedure, we also work very precisely with the latest MRI images of a patient, because we apply the waves with a so-called neuro-application. This means that we know exactly which intensity and how many pulses have been used at which point.

"For patients, TPS represents a high level of safety."

Prof. Ulrich Sprick

For the patient, this is a high degree of safety, and we can see on our monitor exactly - in real time even! - where and at which point in the brain we are stimulating. And this is a very high level of safety for the patient. The point about AI that you mentioned is particularly exciting from my point of view. We are working with a university that also uses AI. In the future, we will also use AI to be able to accompany diagnostic processes, so that the software can tell us after a short time whether we are seeing effects or not. For patients, this can be done in a very simple way, for example by reading out certain things.

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Just by reading it out, the software is able to tell in a few seconds whether the dementia process has spread further, whether it has stayed that way, or whether it has even improved. And the special thing about the shock wave procedure - and I would like to emphasize this again at this point - is that we don't just want to achieve the effect of maintaining the status. This is the primary goal.

"We've seen in our patients, even in a larger number, that improvements have been shown with TPS, which is totally atypical in Alzheimer's disease!"

Prof. Ulrich Sprick

However, we have seen in some of our patients, even in a larger number, that there have even been improvements, which is completely atypical in Alzheimer's disease! Normally, with treatments, also with pharmacotherapy, also with these new immunotherapeutic interventions, which create a flattening of the curve and the performances become successively less - this does not happen in such a short time.

But the fact that this disease process remains the same and, above all, can be topped in some cases and functions improve through TPS therapy - that is something absolutely new, which we also have to deal with. This is not what the textbooks say! The textbooks say that Alzheimer's disease is a progressive disease that keeps progressing and that it is irreversible. And we are in the process of scratching away at this irreversibility!

So that means that we see significant improvements in our patients in some cases, I have to emphasize this again, not in all cases. For example, in the so-called executive functions: What are executive functions? Here, it is the case that one plans certain things, then implements them, and this can also be measured with various test procedures, and here, interestingly enough, we already see considerable improvements after a very short time.

ME: << *That's nice! Does that mean now that the Alzheimer's patients have to come regularly for these therapies? Is this a lifelong accompanying measure now for them or can one say, it has improved at some point so far that one does not need the therapy anymore?>>*

US: << There are several things to say about this: On the one hand, we start with an intensive therapy over a period of two weeks, where six treatments take place, and after that we do so-called booster treatments in a period of four or six or eight weeks. But then you only need one treatment at a time! Unfortunately, you can't do without those booster sessions. We see, especially when we have seen improvements, that these improvements are lost if you don't do booster sessions. So that means - it's also easy to imagine - if you take a certain drug and then you leave that drug out, that the effect of that drug then also diminishes over time. That's clear.

"Our TPS method supports the effect of the drugs quite massively. Drugs that didn't work on their own can have an effect all at once together with TPS."

Prof. Ulrich Sprick

Speaking of medication: It is also very important to me to say that patients who come to us and take medication for Alzheimer's disease are asked by us to continue taking this medication without fail. Why is that? Because our TPS method massively supports the effect of the medication. With shock wave therapy, we are able to make certain areas of the brain significantly more sensitive and receptive to pharmacotherapy, and it is often the case that a medication alone has not had any effect at all, but together with TPS it suddenly has an effect. Therefore, if one has these medications, we strongly recommend continuing to take them.>>

ME: << *That was a very important statement, Professor. This means, the combination develops thereby a better effectiveness?>>*

US: << Exactly.>>

ME: << *My last question: What are you currently researching and what will the future bring? What can we hope for?>>*

US: << Yes, the last part of your question, what the future will bring, is of course difficult to answer. But it is the case that there are various research groups around the world working on the TPS method.

We are in the process of further researching the mechanisms of action of TPS because we don't yet know exactly where the optimal level is, that is, how to set the appropriate parameters such as pulse rates, frequencies, and so on. We also do not yet know exactly what the optimal booster intervals are. It may also be that we will actually combine this method with other stimulation methods so that you can achieve even more with it. And we are also in the process of researching the mechanisms of action.

"There are quite a few mechanisms of action of TPS that are being further explored in global research groups."

Prof. Ulrich Sprick

The mechanisms of action of TPS are highly exciting. It's not just the point, as I just said, that certain areas of the brain become more receptive to drugs, but it's now also known that TPS treatment releases growth factors. That is, there it is that in the brain neurons start to grow, to sprout, that's what it's called, and to make new connections via certain trophic factors, so growth factors. Another point is that the vessels start to form again, in part, so that areas of the brain that were not so well supplied with blood suddenly become better supplied with blood. Vessels dilate, which is also known as a mechanism of action, and certain neurotransmitter levels in the brain are changed, which has also been measured in the meantime with this method.

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So you see, there are many different mechanisms of action and we would like to know how they interact. And I would also like to point out that the corresponding treatment with pulse waves is something new for the brain, but that this has been used for a long time, for example in dermatology, where severe ulcers can be treated, for example. This is so that a massive ulcer in the leg can be treated with shock waves and then it is so that these ulcers in the course of time or very, very quickly again zugranulieren. This is something that can also happen in the brain, of course, and that we want to use for our patients. I would also like to point out that there is also further research currently being done, for example by cardiologists, especially cardio surgeons, who are using the same procedure on the heart! This is currently still being done on the open heart, but it may soon also be possible to do it transthoracically, so that it no longer requires an operation.

These are all research procedures that show the effects of shock waves in other areas as well. Therefore, I am very positive that TPS will also prove to be effective in the future. But we need more studies, especially larger studies, where you also have placebo-controlled groups that you can compare to prove this effect scientifically. >>

ME: << *Professor, thank you very much for this wonderful interview. I wish you very, very great research results and that you can help many more people with your knowledge and creativity. Thank you very much, goodbye.>>*

US: << Likewise, thank you very much, goodbye.>>

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