

#### RESEARCH REPORT

Effects of the AVACEN Treatment Method on the Brain and Microcirculation of Participants with Type 2 diabetes:
Pilot study

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#### Goal and

This is a pilot project to examine differences in brain mapping and microcirculation of 6 participants with type 2 diabetes before and after a treatment with the AVACEN device.

#### Statement of Work

Brain mapping scans were performed on 6 participants with type 2 diabetes using a 19 channels neuro-imaging system (Appendix D) before and after a 20-minute session with the AVACEN device

#### **Participants**

Participants were 6 people between 18 and 75 years old with a clear medical diagnostic of type 2 diabetes from a physician. Recruitment of participants was done using electronic marketing, asking health practitioners in private practice and by word of mouth.

#### The inclusion criteria are:

- Medical diagnostic of type 2 diabetes
- Between 18 and 75 years old
- Must have all 10 fingers (have short nails, no artificial nails; this is to perform GDV scans)

#### The exclusion criteria are:

- Pregnancy
- Diagnostic of mental disorder within the past 2 years
- o Taking medication for blood pressure or cardiovascular problems
- Taking any painkiller medication (prescribed or over the counter)
- Smoking, vaping, consumption alcohol (less than 24 hours before the session), or any other intoxicant such as recreational drugs, marijuana, CBD



- Simultaneously participating in any other research project
- o Consumption of caffeine or other stimulants within 2 hours prior to a visit
- Exercising 24 hours or less before each visit

#### **Summary and conclusion**

All six participants experienced an improvement in brain function after the AVACEN treatment. All of them also showed an increase in bioenergy. In light of these positive results, the fact that only 2 participants showed a change in cardiovascular function (one an improvement while the other experienced a degradation) is an indication that the impact of AVACEN on the cardiovascular system is likely a long-term effect and so a longitudinal study, where people are followed for longer period of time, is the only way to know the impact of AVACEN technology on the cardiovascular system.

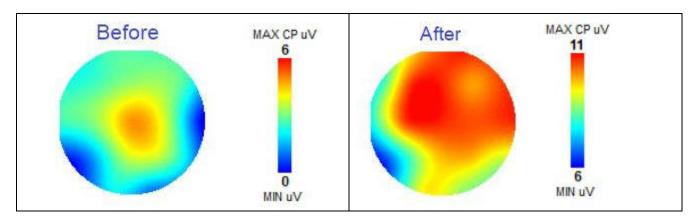
#### Results

#### **Brain Mapping**

#### Participant 1

Male, 70, expert in marketing. Before the AVACEN Treatment, he indicated that he feels relaxed and that he had some of his muscles feeling sore. There was tightness and lack of flexibility mainly in the hips and thighs. The VAS pain scale indicated low pain at about 0.5 on a scale from 0 to 10. After the treatment, he indicated that he was more relaxed and that he felt a mild change in his muscles throughout the entire body. The VAS pain scale still indicated 0.5 but he commented "Great Time!".

#### Scalp Topography Map

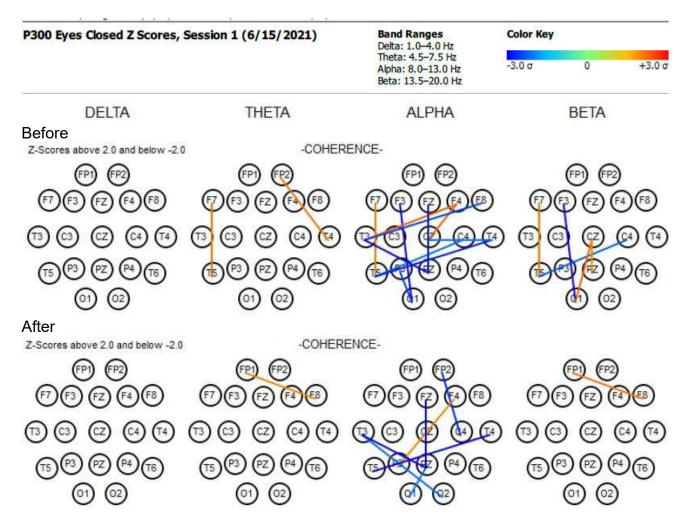


These scalp topographical maps were computed from the 19 EEG channels recorded by the brain mapping system (frontal part of the brain at the top and back of the head at the bottom of each circle). These maps show the amplitude of the P300 recording for each channel (in



microvolts or  $\mu V$ ) using a color-coding scale presented on the right side of each topographical map (notice the scale is different before vs. after; red is for the maximum amplitude and dark blue for the minimum amplitude). It can be noted that when he came in, his brain was calm and became very active after the session (the max of the scale before the AVACEN treatment is the minimum on the scale after the treatment).

#### <u>Coherence</u>



The coherence diagrams above show a perspective where we are looking down at the top of the head from above (FP1 and FP2 are on the forehead while O1 and O2 are at the back of the head). EEG coherence can be defined as the normalized cross-power spectrum per frequency of two signals recorded simultaneously at different sites of the scalp. It is a measure of the synchronization between the two signals and may be interpreted as an expression of their functional interaction (1). Coherence reflects how stable the phase relationship is between two electrode sites. Coherence quantifies the degree of interaction or communication, shared information, between brain sites. Hypercoherence is when brain sites are not functioning in efficient interdependent fashion, they have too much "cross-talk", they are overly connected or locked together. Hypocoherence is called poor inter-site



interaction and is associated with diminished cognitive efficiency (2). The red lines between two sites indicate hypercoherence (orange lines represent mild hypercoherence) while blue lines represent hypocoherence. Note that when there is no line between sites, the coherence level between those sites is in the normal range. Beta brain waves are normally dominant in a person awake, alert, with normal level of consciousness and brain function. Theta brain waves show up in deep relaxation, meditation and mental imagery (3).

Participants were awake with eyes closed during their brain scans and so the most relevant results are those presented in the Alpha (relaxation) band. As expected, Alpha was dominant since this participant had his eyes closed. He was calm, aware, and quietly alert. What is of note here is that Participant 1 had about half of his brain sites in hypocoherence in the Alpha band before the AVACEN treatment and that improved with less brain sites in hypocoherence after the treatment. This result suggests an improvement in cognitive efficiency.

#### **Screening Scores**

Assessment Scores	Session 1 (6/15/2021)	Session 2 (6/15/2021)	Target Range
Performance Assessments			
Physical Reaction Time	372 (±87) ms	450 (±128) ms	273-393 ms
Trail Making Test A	60 sec	67 sec	73-123 sec
Trail Making Test B	99 sec	96 sec	69-135 sec
Evoked Potentials			
Audio P300 Delay	356 ms	432 ms	300-390 ms
Test/Retest Change		u u	±11 ms
Audio P300 Voltage	4.9 µV	11.3 µV	6-15 µV
Test/Retest Change		7	±2 μV
State			
CZ Eyes Closed Theta/Beta (Power)	2.0	1.8	0.6-1.5
F3/F4 Eyes Closed Alpha (Magnitude)	1.0	1.5	0.9-1.1

The goal is for each screening score to be inside the target range. If a score is below or above the target range it is considered abnormal (too fast if below or too slow if above the target time). An explanation of each screening score result follows.

#### Physical Reaction time

It is a measure of functional speed in response to an audible odd tone. This relies on different pathways than the Auditory P300, so physical reaction time may be different than the brain speed and more connected to brain/body communication speed. Physical Reaction Time became slow after the treatment, probably due to increased relaxation as the participant mentioned greater relaxation after the AVACEN treatment.



#### Trail Making

A standard measure of brain function and includes measures of psychomotor and visual scanning. For this participant, Trail Making Test A was faster than the target range and stayed faster after the treatment. Trail Making B was in the normal range before and after the treatment. This participant has excellent visual/psychomotor coordination which stays excellent even while relaxed.

#### Evoked Potentials - Auditory P300 Delay

Auditory P300 is a measure of brain response speed and attentional resources. P300 slowing and/or a reduction in voltage may signal changes in cognitive function. Participant 1 presents an increase in the Auditory P300 delay and an increase in voltage increased after the treatment. The voltage range was too low before the treatment and in the normal range after the treatment indicating and improvement in cognitive function. For more information on P300, see https://en.wikipedia.org/wiki/P300 (neuroscience) and the references section.

#### State - CZ Theta/Beta

Theta and Beta frequency bands are affected by cortical arousal and can give insight into how the brain functions. In some people high Theta/Beta ratios at CZ may present as inattention, while others may benefit from cortical arousal. Because of the initial high Theta/Beta ratio at CZ that decreased after the treatment, the participant's brain's cortical arousal decreased to some extent, again indicating better attention.

Researchers have shown that calculating the relative power ratio Theta/Beta at CZ can be used to determine slow-wave disorders, ADHD, interpersonal detachment with qualitative aspects of autistic or Asperger's behavior (3, 4, 5).

#### State - F3/F4 Alpha

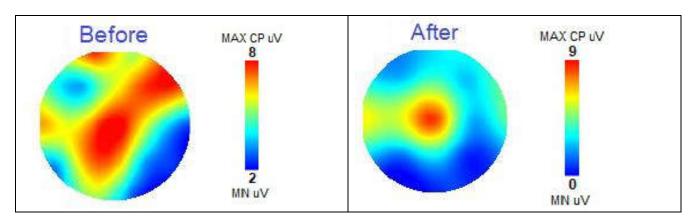
Researchers discovered that calculating F3/F4 relative power ratio in the Alpha band means processing information in a positive way for an increase while a decrease in the ratio indicated a more negative processing mode (6, 7). The present substantial increase likely means that a more positive way of processing information after the treatment.

In conclusion, Participant 1 brain was activated in a way that it was not overwhelming and that did not prevent the brain from improving its functioning, instead improving alertness and its cognitive functions. His brain processed information in a much more positive way after the AVACEN treatment.



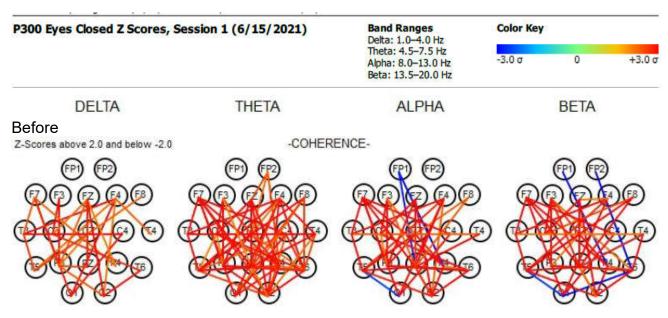
Female, 74. This participant indicated that she takes medformin for her diabetes and levothyroxine for her thyroid. Before the AVACEN Treatment, she indicated that she feels relaxed and that she had no pain.

#### Scalp Topography Map



These scalp topographical maps were computed from the 19 EEG channels recorded by the brain mapping system (frontal part of the brain at the top and back of the head at the bottom of each circle). These maps show the amplitude of the P300 recording for each channel (in microvolts or  $\mu V$ ) using a color-coding scale presented on the right side of each topographical map (notice the scale is different before vs. after; red is for the maximum amplitude and dark blue for the minimum amplitude). It can be noted that when she came in, her brain was quite activated and became calmer after the session (the scale of the maps is almost the same before and after the treatment).

#### Coherence





# After z-scores above z.0 and below -z.0 -COHERENCE FP) FP2 FP3 FP4 F8 F7 FP4 F8 F

The coherence diagrams above show a perspective where we are looking down at the top of the head from above (FP1 and FP2 are on the forehead while O1 and O2 are at the back of the head). EEG coherence can be defined as the normalized cross-power spectrum per frequency of two signals recorded simultaneously at different sites of the scalp. It is a measure of the synchronization between the two signals and may be interpreted as an expression of their functional interaction (1). Coherence reflects how stable the phase relationship is between two electrode sites. Coherence quantifies the degree of interaction or communication, shared information, between brain sites. Hypercoherence is when brain sites are not functioning in efficient interdependent fashion, they have too much "cross-talk", they are overly connected or locked together. Hypocoherence is called poor inter-site interaction and is associated with diminished cognitive efficiency (2). The red lines between two sites indicate hypercoherence while blue lines reflect hypocoherence. Beta brain waves are normally dominant in a person awake, alert, with normal level of consciousness and brain function. Theta brain waves show up in deep relaxation, meditation and mental imagery (3). Participants were awake with eyes closed during their brain scans and so the most relevant results are those presented in the Alpha (relaxation) and Beta (normal brain activity) bands.

Before the AVACEN treatment, the brain of this participant was in extreme hypercoherence involving most of the brain sites measured and for all frequency bands. The brain was so much in hypercoherence that there was no clear dominance of any frequency band. After the treatment, the brain became hypocoherent, allowing the brain to calm down. Hypocoherence was a bit more pronounced in the Alpha and Theta band an indication of brain relaxation. This enormous change in brain coherence suggests an improvement in cognitive efficiency and attention.



#### **Screening Scores**

Assessment Scores	Session 1 (6/22/2021)	Session 2 (6/22/2021)	Target Range
Performance Assessments			
Physical Reaction Time	471 (±155) ms	364 (±81) ms	280-404 ms
Trail Making Test A	90 sec	90 sec	80-136 sec
Trail Making Test B	173 sec	134 sec	77-149 sec
Evoked Potentials			
Audio P300 Delay	240 ms	484 ms	308-400 ms
Test/Retest Change		¥	±11 ms
Audio P300 Voltage	7.6 µV	9.1 µV	6-14 µV
Test/Retest Change	2	<u>=</u>	±2 μV
State			
CZ Eyes Closed Theta/Beta (Power)	1.8	0.8	0.6-1.5
F3/F4 Eyes Closed Alpha (Magnitude)	0.4	1.1	0.9-1.1

The goal is for each screening score to be inside the target range. If a score is below or above the target range it is considered abnormal (too fast if below or too slow if above the target time). An explanation of each screening score follows.

#### Physical Reaction time

It is a measure of functional speed in response to an audible odd tone. This relies on different pathways than the Auditory P300, so physical reaction time may be different than the brain speed and more connected to brain/body communication speed. Physical Reaction Time was slow before the treatment and went into the normal range after the session, indicating an improvement in physical reaction time.

#### <u>Trail Making</u>

A standard measure of brain function and includes measures of psychomotor and visual scanning. For this participant, Trail Making Test A was in the low side of the normal range before and after the treatment (there was no change at all, staying at 90 sec). Trail Making B was slower than normal before the treatment and went into the normal range after the treatment. This participant's visual/psychomotor coordination improved after the AVACEN treatment.

#### Evoked Potentials - Auditory P300 Delay

Auditory P300 is a measure of brain response speed and attentional resources. P300 slowing and/or a reduction in voltage may signal changes in cognitive function. Participant 1 presents an increase in the Auditory P300 delay and an increase in voltage increased after the treatment. The Audio P300 Delay was too low before the treatment, an indication of faster than normal reaction, and went into the normal range after the treatment indicating



and improvement in cognitive function. For more information on P300, see <a href="https://en.wikipedia.org/wiki/P300">https://en.wikipedia.org/wiki/P300</a> (neuroscience) and the references section.

#### State - CZ Theta/Beta

Theta and Beta frequency bands are affected by cortical arousal and can give insight into how the brain functions. In some people high Theta/Beta ratios at CZ may present as inattention, while others may benefit from cortical arousal. Because of the initial high Theta/Beta ratio at CZ that decreased after the treatment, the participant's brain's cortical arousal decreased to some extent, indicating better attention.

Researchers have shown that calculating the relative power ratio Theta/Beta at CZ can be used to determine slow-wave disorders, ADHD, interpersonal detachment with qualitative aspects of autistic or Asperger's behavior (3, 4, 5).

#### State - F3/F4 Alpha

Researchers discovered that calculating F3/F4 relative power ratio in the Alpha band means processing information in a positive way for an increase while a decrease in the ratio indicated a more negative processing mode (6, 7). The present substantial increase likely means that a more positive way of processing information after the treatment.

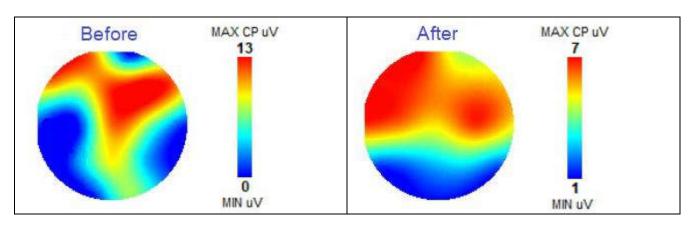
In conclusion, Participant 2 brain was in overdrive and inefficient before the AVACEN treatment and improved tremendously in cognitive function and in visual/psychomotor coordination. It also processed information in a much more positive way after the AVACEN treatment.

#### Participant 3

Male, 64. His highest level of education is at the doctorate level, and he works as a consultant. He indicated that he experiences problems or pain in his bones, joints, or muscles as well as back or neck discomfort and that he is under the care of a healthcare professional for other health/medical problems. Before the AVACEN Treatment, he indicated that he feels relaxed and that he had pain in all body parts. He did not fill the VAS so his level of pain is unknown. He indicated that he sustained injuries as a strongman.

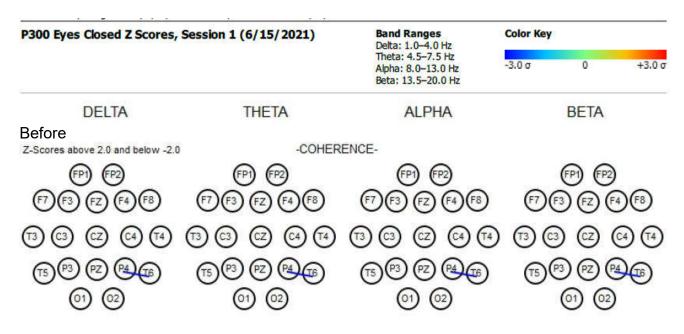


#### Scalp Topography Map



These scalp topographical maps were computed from the 19 EEG channels recorded by the brain mapping system (frontal part of the brain at the top and back of the head at the bottom of each circle). These maps show the amplitude of the P300 recording for each channel (in microvolts or  $\mu V$ ) using a color-coding scale presented on the right side of each topographical map (notice the scale is different before vs. after; red is for the maximum amplitude and dark blue for the minimum amplitude). It can be noted that when he came in, his brain was somewhat activated and became less active after the session (note that the max of the scale after is almost half of the max of the scale before).

#### **Coherence**





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The coherence diagrams above show a perspective where we are looking down at the top of the head from above (FP1 and FP2 are on the forehead while O1 and O2 are at the back of the head). EEG coherence can be defined as the normalized cross-power spectrum per frequency of two signals recorded simultaneously at different sites of the scalp. It is a measure of the synchronization between the two signals and may be interpreted as an expression of their functional interaction (1). Coherence reflects how stable the phase relationship is between two electrode sites. Coherence quantifies the degree of interaction or communication, shared information, between brain sites. Hypercoherence is when brain sites are not functioning in efficient interdependent fashion, they have too much "cross-talk", they are overly connected or locked together. Hypocoherence is called poor inter-site interaction and is associated with diminished cognitive efficiency (2). The red lines between two sites indicate hypercoherence while blue lines reflect hypocoherence. Beta brain waves are normally dominant in a person awake, alert, with normal level of consciousness and brain function. Theta brain waves show up in deep relaxation, meditation and mental imagery (3). Participants were awake with eyes closed during their brain scans and so the most relevant results are those presented in the Alpha (relaxation) and Beta (normal brain activity) bands.

Before the AVACEN treatment, the brain of this participant was in normal coherence involving one line of hypocoherence for all brain frequencies (Beta, Alpha, Theta and Delta). most of the brain sites measured and for all frequency bands. There was no clear dominance oat any frequency band. After the treatment, the brain became hypocoherent, allowing the brain to become calmer. After the treatment, hypocoherence was quite similar at all frequency bands. This enormous change in brain coherence suggests a relaxation of the brain.



#### **Screening Scores**

Assessment Scores	Session 1 (8/20/2021)	Session 2 (8/20/2021)	Target Range
Performance Assessments			
Physical Reaction Time	395 (±105) ms	385 (±133) ms	264-380 ms
Trail Making Test A	68 sec	78 sec	63-107 sec
Trail Making Test B	82 sec	86 sec	60-117 sec
Evoked Potentials			
Audio P300 Delay	■ 240 ms	292 ms	289-375 ms
Test/Retest Change	1275		±11 ms
Audio P300 Voltage	<b>■</b> 12.8 μV	6.7 µV	6-15 µV
Test/Retest Change		( <b>*</b>	±2 μV
State			
CZ Eyes Closed Theta/Beta (Power)	■ 2.3	1.2	0.7-1.6
F3/F4 Eyes Closed Alpha (Magnitude)	1.0	1.2	0.9-1.1

The goal is for each screening score to be inside the target range. If a score is below or above the target range it is considered abnormal (too fast if below or too slow if above the target time). An explanation of each screening score follows.

#### Physical Reaction time

It is a measure of speed in response to an audible odd tone. This relies on different pathways than the Auditory P300, so physical reaction time may be different than the brain speed and more connected to brain/body communication speed. Physical Reaction Time was slow before the treatment and improved a tiny bit after the treatment, possibly due to increased relaxation.

#### Trail Making

A standard measure of brain function and includes measures of psychomotor and visual scanning. For this participant, these measures are in the target range before and stayed in that range after the treatment. This participant has normal visual/psychomotor coordination.

#### Evoked Potentials - Auditory P300

Auditory P300 is a measure of brain response speed and attentional resources. P300 slowing and/or a reduction in voltage may signal changes in cognitive function. Here we have that the Auditory P300 Delay was too fast before the treatment and slowed down to be in the normal range after the treatment, an indication of brain relaxation. At the same time the Audio P300 voltage decreased by almost a factor of 2 after the treatment, again indication of brain relaxation. There was clearly a change in cognitive function for the better.



#### State - CZ Theta/Beta

Theta and Beta frequency bands are affected by cortical arousal and can give insight into how the brain functions. In some people high Theta/Beta ratios at CZ may present as inattention, while others may benefit from cortical arousal. Because of the initial very high Theta/Beta ratio at CZ that decreased by almost a factor of 2 after the treatment, the participant benefited from a relaxation effect already mentioned with other parameters.

Researchers have shown that calculating the relative power ratio Theta/Beta at CZ can be used to determine slow-wave disorders, ADHD, interpersonal detachment with qualitative aspects of autistic or Asperger's behavior (3, 4, 5).

#### State - F3/F4 Alpha

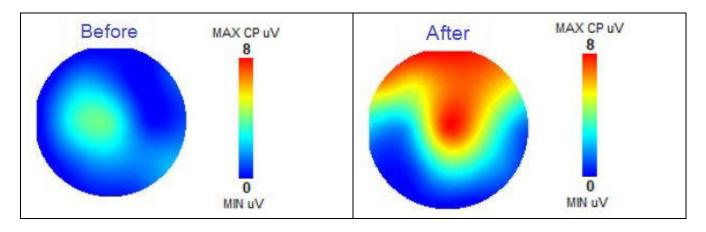
Researchers discovered that calculating F3/F4 relative power ratio in the Alpha band means processing information in a positive way for an increase while a decrease in the ratio indicated a more negative processing mode (6, 7). The present increase likely means that a more positive way of processing information after the treatment.

In conclusion, the brain of Participant 3 was in active mode before the AVACEN treatment and improved in cognitive function and processed information in a more positive way after the AVACEN treatment.

#### Participant 4

Female, 47 working in sales She indicated that in the past 12 months, she was told by a healthcare professional that she has an elevated cholesterol level or abnormal lipid profile. She also indicated that she has high blood pressure and an elevated blood glucose level. Before the AVACEN treatment she indicated that she feels relaxed and that she has no pain.

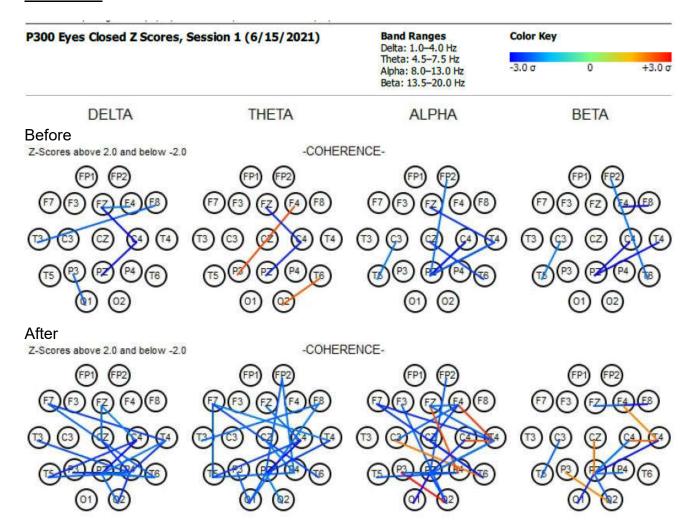
#### Scalp Topography Map





These scalp topographical maps were computed from the 19 EEG channels recorded by the brain mapping system (frontal part of the brain at the top and back of the head at the bottom of each circle). These maps show the amplitude of the P300 recording for each channel (in microvolts or  $\mu V$ ) using a color-coding scale presented on the right side of each topographical map (notice the scales are the same before vs. after; red is for the maximum amplitude and dark blue for the minimum amplitude). It can be noted that when she came in, her brain was not only calm but maybe hypo-functioning and became active after the treatment. That was more specially the case for the frontal part of the brain.

#### Coherence



The coherence diagrams above show a perspective where we are looking down at the top of the head from above (FP1 and FP2 are on the forehead while O1 and O2 are at the back of the head). EEG coherence can be defined as the normalized cross-power spectrum per frequency of two signals recorded simultaneously at different sites of the scalp. It is a measure of the synchronization between the two signals and may be interpreted as an expression of their functional interaction (1). Coherence reflects how stable the phase relationship is between two electrode sites. Coherence quantifies the degree of interaction



or communication, shared information, between brain sites. Hypercoherence is when brain sites are not functioning in efficient interdependent fashion, they have too much "cross-talk", they are overly connected or locked together. Hypocoherence is called poor inter-site interaction and is associated with diminished cognitive efficiency (2). The red lines between two sites indicate hypercoherence while blue lines reflect hypocoherence. Beta brain waves are normally dominant in a person awake, alert, with normal level of consciousness and brain function. Theta brain waves show up in deep relaxation, meditation and mental imagery (3). Participants were awake with eyes closed during their brain scans and so the most relevant results are those presented in the Alpha (relaxation) and Beta (normal brain activity) bands.

Before the AVACEN treatment, the brain of this participant was mainly in normal coherence, there are very few lines of hypocoherence for all brain frequencies (Beta, Alpha, Theta and Delta) and only 2 lines of mild hypercoherence in the Theta band (orange lines). After the treatment there was a clear increase in hypocoherence in Alpha, Theta and Delta bands and a bit of increase in hypercoherence in Beta and Alpha. It can be concluded that the brain relaxed after the treatment.

#### **Screening Scores**

Assessment Scores	Session 1 (9/28/2021)	Session 2 (9/28/2021)	Target Range
Performance Assessments			
Physical Reaction Time	372 (±47) ms	316 (±63) ms	251-361 ms
Trail Making Test A	37 sec	28 sec	43-74 sec
Trail Making Test B	58 sec	50 sec	45-87 sec
Evoked Potentials			
Audio P300 Delay	244 ms	296 ms	261-339 ms
Test/Retest Change	•	<b>T</b>	±11 ms
Audio P300 Voltage	3.9 µV	7.7 µV	8-19 μV
Test/Retest Change	620 C	21	±2 μV
State			
CZ Eyes Closed Theta/Beta (Power)	1.3	0.9	0.8-1.9
F3/F4 Eyes Closed Alpha (Magnitude)	1.2	1.0	0.9 - 1.1

The goal is for each screening score to be inside the target range. If a score is below or above the target range it is considered abnormal (too fast if below or too slow if above the target time). An explanation of each screening score follows.

#### Physical Reaction time

It is a measure of speed in response to an audible odd tone. This relies on different pathways than the Auditory P300, so physical reaction time may be different than the brain speed and more connected to brain/body communication speed. The Physical Reaction



Time was too slow before the treatment and came to the normal range after, probably due to increased relaxation.

#### Trail Making

A standard measure of brain function and includes measures of psychomotor and visual scanning. For this participant, Trail Making A was faster than normal and became still faster after the treatment, while Trail Making B was in the normal range at the start and stayed in the normal range after the treatment. This participant has excellent visual/psychomotor coordination.

#### Evoked Potentials - Auditory P300

Auditory P300 is a measure of brain response speed and attentional resources. P300 slowing and/or a reduction in voltage may signal changes in cognitive function. Participant 4 started with a very fast Audio P300 Delay that went to the normal range after the treatment. The Audio P300 Voltage was too low to start with and went into the normal range after the treatment. Both results are probably an indication of a more relaxed state.

#### State - CZ Theta/Beta

Theta and Beta frequency bands are affected by cortical arousal and can give insight into how the brain functions. In some people high Theta/Beta ratios at CZ may present as inattention, while others may benefit from cortical arousal. Both the initial and final values were in the normal range with a notable decrease after the treatment, again probably an effect of relaxation.

Researchers have shown that calculating the relative power ratio Theta/Beta at CZ can be used to determine slow-wave disorders, ADHD, interpersonal detachment with qualitative aspects of autistic or Asperger's behavior (3, 4, 5).

#### State - F3/F4 Alpha

Researchers discovered that calculating F3/F4 relative power ratio in the Alpha band means processing information in a positive way for an increase while a decrease in the ratio indicated a more negative processing mode (6, 7). The present small decrease to come down to the normal range likely means very little change in the way the brain is processing information after the treatment.

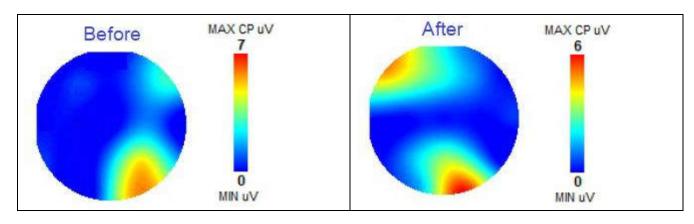
In conclusion, the brain of Participant 4 was rather inactive before the AVACEN treatment and became more active and relaxed probably showing an improved alertness of the brain after the AVACEN treatment.



# Non-Invasive Scanning and Subtle Energy Testing Lab Participant 5

Female, 71, retired computer programmer. Before the AVACEN Treatment, she indicated that she has some unexplained dizziness or fainting and that she has difficulty breathing at night, except in an upright position. She also indicated that she has high blood pressure and that she was told by a healthcare professional that she has an elevated fasting blood glucose level. She is also under the care of a healthcare professional for other health/medical problems. She indicated before the treatment that she feels relaxed and that she had a little bit of back pain. She indicated on the VAS pain scale a level of "1".

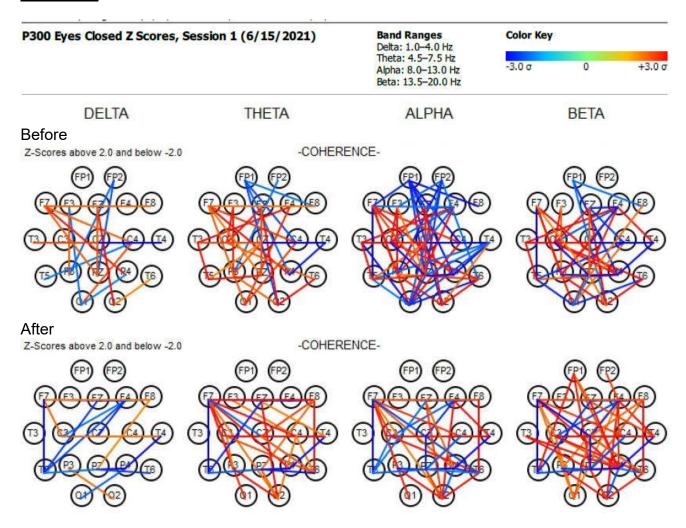
#### Scalp Topography Map



These scalp topographical maps were computed from the 19 EEG channels recorded by the brain mapping system (frontal part of the brain at the top and back of the head at the bottom of each circle). These maps show the amplitude of the P300 recording for each channel (in microvolts or  $\mu V$ ) using a color-coding scale presented on the right side of each topographical map (notice the scales are almost the same with before max being only one point higher than after). It can be noted that when she came in, her brain was not only calm but maybe hypo-functioning (except for the lower occipital area) and became more active after the treatment. That was more specially the case for the left frontal and right occipital parts of the brain.



#### Coherence



The coherence diagrams above show a perspective where we are looking down at the top of the head from above (FP1 and FP2 are on the forehead while O1 and O2 are at the back of the head). EEG coherence can be defined as the normalized cross-power spectrum per frequency of two signals recorded simultaneously at different sites of the scalp. It is a measure of the synchronization between the two signals and may be interpreted as an expression of their functional interaction (1). Coherence reflects how stable the phase relationship is between two electrode sites. Coherence quantifies the degree of interaction or communication, shared information, between brain sites. Hypercoherence is when brain sites are not functioning in efficient interdependent fashion, they have too much "cross-talk", they are overly connected or locked together. Hypocoherence is called poor inter-site interaction and is associated with diminished cognitive efficiency (2). The red lines between two sites indicate hypercoherence while blue lines reflect hypocoherence. Beta brain waves are normally dominant in a person awake, alert, with normal level of consciousness and brain function. Theta brain waves show up in deep relaxation, meditation and mental imagery (3). Participants were awake with eyes closed during their brain scans and so the



most relevant results are those presented in the Alpha (relaxation) and Beta (normal brain activity) bands.

As expected, Alpha was dominant both in hyper and hypo-coherence since this participant had her eyes closed. This means the brain was not only attentive but hypervigilant before the AVACEN treatment. After the treatment the vigilance decreased and for most bands except the Beta, where there was a slight increase in hypercoherence in the frontal parts of the brain. These results suggest an improvement in brain relaxation and cognitive efficiency.

#### **Screening Scores**

Assessment Scores	Session 1 (9/30/2021)	Session 2 (9/30/2021)	Target Range
Performance Assessments			
Physical Reaction Time	489 (±78) ms	407 (±53) ms	275-395 ms
Trail Making Test A	76 sec	77 sec	74-127 sec
Trail Making Test B	68 sec	74 sec	71-138 sec
Evoked Potentials			
Audio P300 Delay	■ 396 ms	N/A	302-393 ms
Test/Retest Change		5	±11 ms
Audio P300 Voltage	<b>■</b> 7.1 μV	1.4 µV	6-14 µV
Test/Retest Change	•	2	±2 μV
State			
CZ Eyes Closed Theta/Beta (Power)	■ 1.2	1.2	0.6-1.5
F3/F4 Eyes Closed Alpha (Magnitude)	0.5	1.3	0.9-1.1

The goal is for each screening score to be inside the target range. If a score is below or above the target range it is considered abnormal (too fast if below or too slow if above the target time). An explanation of each screening score follows.

#### Physical Reaction time

It is a measure of speed in response to an audible odd tone. This relies on different pathways than the Auditory P300, so physical reaction time may be different than the brain speed and more connected to brain/body communication speed. The Physical Reaction Time was too slow before the AVACEN treatment and came to be almost in the normal range after, probably due to increased relaxation of the brain resulting in more efficient physical reactions.

#### Trail Making

A standard measure of brain function and includes measures of psychomotor and visual scanning. For this participant, Trail Making A was on the fast side of the normal range at the start and stayed the same after the treatment. Trail Making B was also faster than normal



and went into the fast normal range after the treatment. This participant has excellent visual/psychomotor coordination.

#### Evoked Potentials - Auditory P300

Auditory P300 is a measure of brain response speed and attentional resources. P300 slowing and/or a reduction in voltage may signal changes in cognitive function. Participant 5 started with a very slightly Audio P300 Delay that could be considered normal. Unfortunately, there was no value presented after the treatment, so we do not know if the Audio P300 Delay improved or not. The Audio P300 Voltage went down from the normal range to low, an indication of changes in cognitive function, probably an indication of a more relaxed state.

#### State - CZ Theta/Beta

Theta and Beta frequency bands are affected by cortical arousal and can give insight into how the brain functions. In some people high Theta/Beta ratios at CZ may present as inattention, while others may benefit from cortical arousal. Both the initial and final values were the same and in the normal range, indicating little change in arousal or attention level.

Researchers have shown that calculating the relative power ratio Theta/Beta at CZ can be used to determine slow-wave disorders, ADHD, interpersonal detachment with qualitative aspects of autistic or Asperger's behavior (3, 4, 5).

#### State - F3/F4 Alpha

Researchers discovered that calculating F3/F4 relative power ratio in the Alpha band means processing information in a positive way for an increase while a decrease in the ratio indicated a more negative processing mode (6, 7). The present substantial increase, from below the normal range to above the normal range, likely means that the brain is processing information in a much more positive way after the AVACEN treatment.

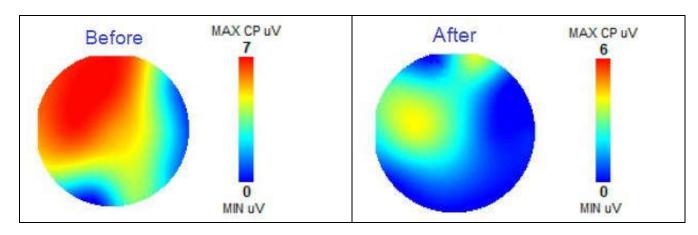
In conclusion, the brain of Participant 5 was rather in an inefficient state before the AVACEN treatment and became more efficient and processed information in a much more positive way after the AVACEN treatment.

#### Participant 6

Female, 71. Before the AVACEN Treatment, she indicated that she has high blood pressure and that she was is experiencing problems or pain in her bones, joints, or muscles that maybe aggravated with exercise. She also indicated that she feels in between relaxed and stressed and that she has pain in her hip and neck. She indicated on the VAS pain scale a pain level of "2" out of 10.

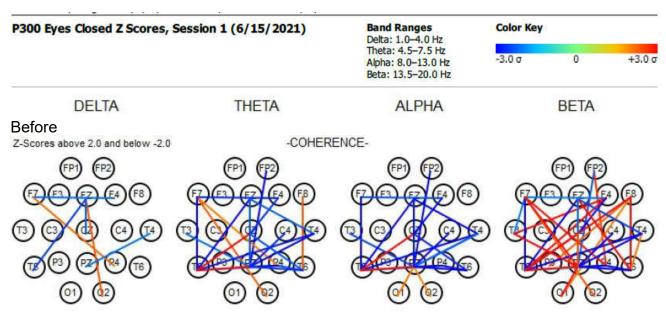


#### Scalp Topography Map



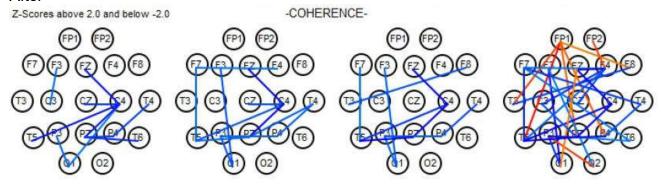
These scalp topographical maps were computed from the 19 EEG channels recorded by the brain mapping system (frontal part of the brain at the top and back of the head at the bottom of each circle). These maps show the amplitude of the P300 recording for each channel (in microvolts or µV) using a color-coding scale presented on the right side of each topographical map (notice the scale is slightly different before vs. after, the max of the scale is 7 before and 6 after the treatment; red is for the maximum amplitude and dark blue for the minimum amplitude). It can be noted that when she came in, her brain was somewhat activated and became less active after the session.

#### Coherence





#### After



The coherence diagrams above show a perspective where we are looking down at the top of the head from above (FP1 and FP2 are on the forehead while O1 and O2 are at the back of the head). EEG coherence can be defined as the normalized cross-power spectrum per frequency of two signals recorded simultaneously at different sites of the scalp. It is a measure of the synchronization between the two signals and may be interpreted as an expression of their functional interaction (1). Coherence reflects how stable the phase relationship is between two electrode sites. Coherence quantifies the degree of interaction or communication, shared information, between brain sites. Hypercoherence is when brain sites are not functioning in efficient interdependent fashion, they have too much "cross-talk", they are overly connected or locked together. Hypocoherence is called poor inter-site interaction and is associated with diminished cognitive efficiency (2). The red lines between two sites indicate hypercoherence while blue lines reflect hypocoherence. Beta brain waves are normally dominant in a person awake, alert, with normal level of consciousness and brain function. Theta brain waves show up in deep relaxation, meditation and mental imagery (3). Participants were awake with eves closed during their brain scans and so the most relevant results are those presented in the Alpha (relaxation) and Beta (normal brain activity) bands.

Unexpectedly, Beta was dominant in hypercoherence before the AVACEN treatment. This participant's brain looks more like someone processing information with open eyes. After the treatment the Beta hypercoherence decreased markedly, indicating a more relaxed and efficient brain.



#### Screening Scores

Assessment Scores	Session 1 (9/29/2021)	Session 2 (9/29/2021)	Target Range
Performance Assessments			
Physical Reaction Time	318 (±50) ms	325 (±36) ms	275-395 ms
Trail Making Test A	95 sec	93 sec	74-127 sec
Trail Making Test B	239 sec	170 sec	71-138 sec
Evoked Potentials			
Audio P300 Delay	332 ms	344 ms	302-393 ms
Test/Retest Change	•		±11 ms
Audio P300 Voltage	7.3 µV	3.9 µV	6-14 µV
Test/Retest Change		-	±2 μV
State			
CZ Eyes Closed Theta/Beta (Power)	0.7	■ 0.7	0.6-1.5
F3/F4 Eyes Closed Alpha (Magnitude)	2.2	1.2	0.9-1.1

The goal is for each screening score to be inside the target range. If a score is below or above the target range it is considered abnormal (too fast if below or too slow if above the target time). An explanation of each screening score follows.

#### Physical Reaction time

It is a measure of speed in response to an audible odd tone. This relies on different pathways than the Auditory P300, so physical reaction time may be different than the brain speed and more connected to brain/body communication speed. The Physical Reaction Time was in the normal range before the AVACEN treatment and remain in the normal range after the treatment, an indication of normal level of physical reaction time processing.

#### Trail Making

A standard measure of brain function and includes measures of psychomotor and visual scanning. For this participant, Trail Making A was in the normal range before the treatment and stayed in the normal range after the treatment. Trail Making B was much too slow before the treatment and decreased to come closer to the normal range after the treatment. This is an indication of improvement in visual/psychomotor coordination after the AVACEN treatment.

#### Evoked Potentials - Auditory P300

Auditory P300 is a measure of brain response speed and attentional resources. P300 slowing and/or a reduction in voltage may signal changes in cognitive function. Participant 6 started in the normal range and stayed in the normal range after the treatment, having changed very little. On the other hand, the Audio P300 Voltage went down from the normal



range to low, an indication of changes in cognitive function, probably an indication of a more relaxed state.

#### State - CZ Theta/Beta

Theta and Beta frequency bands are affected by cortical arousal and can give insight into how the brain functions. In some people high Theta/Beta ratios at CZ may present as inattention, while others may benefit from cortical arousal. Both the initial and final values were the same and in the normal range, indicating little change in arousal or attention level.

Researchers have shown that calculating the relative power ratio Theta/Beta at CZ can be used to determine slow-wave disorders, ADHD, interpersonal detachment with qualitative aspects of autistic or Asperger's behavior (3, 4, 5).

#### State - F3/F4 Alpha

Researchers discovered that calculating F3/F4 relative power ratio in the Alpha band means processing information in a positive way for an increase while a decrease in the ratio indicated a more negative processing mode (6, 7). The present substantial decrease, from way above to almost in the normal range likely means that the brain is processing information in a much less super positive way to a normal positive way after the AVACEN treatment.

In conclusion, the brain of Participant 6 was rather in an inefficient state before the AVACEN treatment, probably because Participant 6 was a bit anxious maybe because of the unknown nature of the experiment (she indicated that she feels in between relaxed and stressed before the treatment). She relaxed and her brain became somewhat more efficient after the AVACEN treatment.