The Brain Gauge and Some of the Science from Behind the Scenes

There are currently quite a few Brain Gauges in use today (over 1000 in the field, at last count) and we often get questions from end-users about what the scores mean. After getting many of the same questions about the scores, our answers started to get a bit more focused as we realized that if we could explain the science behind the scores, or the science behind what the scores measured, then people could make more informed decisions. And with that realization, we started writing a blog, with each blog post targeting some aspect of either the Brain Gauge scores, the science behind the scores, or things that impact Brain Gauge scores. This book is a collection of the descriptions of the individual Brain Gauge tests, some of the science behind them and some of the things that impact those scores.

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Introduction: The Brain Gauge is a Functional Measure

A functional measure simply tells you how well something works. In the physical world, there are lots of functional measures. How fast can you run a mile? How much weight can you lift? How fast can you swim across the pool? Can you run up 2 flights of stairs without getting out of breath? These measures tell you something about performance and how well your body functions when it tries to do something - when it is stressed or pushing the envelope.

Why are functional measures important? After all, I can get my resting blood pressure and heart rate without doing anything - and those measures are pretty close to identical to what they were when I was in college. But I promise that I can't swim a mile or run a mile as fast as I could when I was in college. So if my resting blood pressure and heart rate are the same as they were 4 decades ago, does that mean I am in good physical shape?

As I mentioned, we had to take the physicals before our training started, so some of us were not in the best of shape and we all passed the test with flying colors. Except for one guy – one of the upperclassmen that the freshmen (that's what I was at the time) were supposed to look up to. When the nurse was not looking, he held his breath and did jumping jacks for about 90 seconds – plenty of time to NOT have a reasonable blood pressure and heart rate reading. The nurse almost had a heart attack and he ended up having to stay at the infirmary for quite a while. Anyway, it was pretty funny but it does demonstrate vividly the difference between a static measure versus a functional measure. Of course, the nurse had no idea what he had done, so she thought he was about to have a heart attack even though his measures would have been considered normal for the activity he had just done. You need to test the system to see if it is working properly and that is just what functional measures do.

Most people go through life without really thinking about being in good physical or mental shape. If you're reading this, you're probably not in that group. It's easy to tell if you are in good physical shape because there are so many functional measures for that. But how do you tell if you are in good mental shape? Well, the answer is NOT getting your brain imaged or scanned. That will tell you if you have a tumor, but without some relatively large aberration to physically view in the image, it won't provide you with an indicator that your brain function is altered. You could use the world's best imaging device and not see any difference before and after taking a dozen shots of expresso – but I guarantee that you will feel difference and you'll definitely score differently on a properly executed functional test. FYI, the Brain Gauge is pretty sensitive to caffeine, and you can read about that in here.

So what can you do with a functional brain measure like the Brain Gauge? Everyone has a different use. If you are recovering from concussion, when is it safe to return to play? After all, the ct scan is the standard of care for evaluating a concussion, but it does not detect the concussion. It just tells you if there is something worse than the concussion that you need to worry about. Many people worry about degenerative aging and you have probably read about so-called breakthroughs in Alzheimer's where researchers have detected amyloid plaques with imaging - but that's a bit too late in the process – you really need a functional measure to detect that problem long before that happens so you can hopefully reverse the trend. Many people are on medications or therapies for some neurological disorder and want

to know if they are working. And many are on medications that are non-neurological (such as heart medications) and would like to know if those meds are impacting their brain function. Are your supplements working? Lots of advertisements and blogs out there say that they do, but how much data have you seen from bio-hackers? In short, the Brain Gauge is the ideal tool for someone that wants to track their progress and observe what impacts their brain function.

What if I don't like my scores?

Believe it or not, we've heard this quite a bit. But to me, that's a bit like saying, what if I don't like how long it takes me to run a mile? About a year ago, I decided to try to get back in shape, so I just went out for a run. I was so slow that buzzards were circling around me. I did not bother looking at my watch – it was that bad. And I am not joking about the buzzards. The next week I did a bit better and got down to one buzzard. And then the next week I was even better and started to glimpse at the time it took me. Still pretty awful, but I slowly got better. Having trained for many decades in a wide variety of sports taught me to be patient and that it takes time to crawl out of that below normal hole. At first it feels impossible, but eventually you can recover. I spent the better part of 5 decades as a competitive swimmer, and just about everyone I knew in the sport had a pretty good idea about what they needed to do (or not do) to optimize their performance – and we're talking about very minor fluctuations – in the neighborhood of 1 to 3%. The key ingredient? Measuring your performance.

Why not apply the same strategy to brain function?

We have seen the same type of training progression with many Brain Gauge users and in particular, with some that were recovering from what appeared to be really bad scores for a variety of reasons. The main point is to not get discouraged – there are a lot of good clinicians and researchers that are starting to give very good advice for how to improve brain health, and now you can track your progress as you search for what works for you.

It appears, that in this arena, trained athletes are a lot smarter than academic nerds. But researchers might eventually be catching up. Whereas a decade or two ago the notion that we just keep losing brain cells as we get older and never re-generate them was seemingly gospel, it now appears that we constantly re-wire and re-grow a lot of stuff in our brains. If you want to read about stroke and neuroplasticity, take a look at Bob Dennis' book "Stroke of Luck".

The Reaction Time Measure

Reaction time has been used since the mid-1800s to assess cognitive function, and it is still useful for that today. The reaction time test has been used for a really long time to investigate nervous system function. Papers written as early as the mid 1800's describe the reaction time test and since that time, most papers focused on differences in reaction time and other populations. In other words, most of these papers demonstrated comparisons that were made between healthy control populations and populations of individuals that had some condition that impacted brain health. A few papers describe the reaction time of the same population of healthy controls before and after some other condition (e.g., taking reaction time test before and after a medication, before or after caffeine, before or after exercise, or in the presence of a threat/punishment if you are too slow). Below is a list of conditions or disorders that have been shown in publications to have had an impact on reaction time. Obviously, if your reaction time is slower than normal it does not mean that you have any (or all) of these conditions. Not only that, it would be difficult to have all of these conditions, if not impossible! Additionally, if you go into depth in the literature, you will find that there are subtle nuances to different conditions. For example, as you might predict, sleep deprivation has a negative impact on reaction time and caffeine has been shown to have a positive impact. Does that mean caffeine will counter-act fatigue and/or sleep deprivation? Actually, the answer is that it depends on the level of sleep deprivation. At 72 hours of sleep deprivation, caffeine actually has a null or negative impact on reaction time, but at much milder levels of sleep deprivation, it appears to have some positive impact and has a lot to do with individual tolerances.

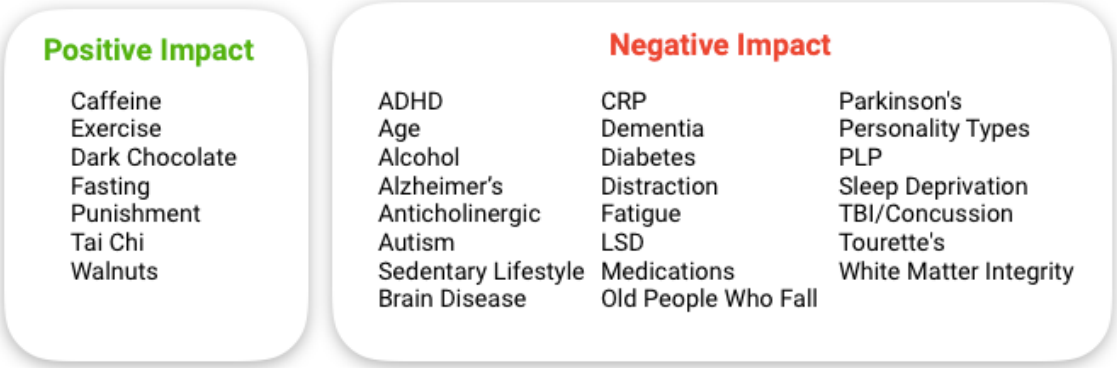
Some of the papers that these findings were extracted from were quite old (hence the "brain disease" reference was from a paper written when political correctness was not common) but the findings of those papers should not be discounted. We have not physically evolved in the past 150 years to the point where reaction time comparisons such as these would not be valid. For example, we noticed that a 2016 paper demonstrating that caffeine had a positive impact on reaction time did not cite a 1934 paper that demonstrated the same finding. The more recent paper did have a larger cohort, but it should not take all the credit for the "discovery" (the reason we bring this up is because this happens quite frequently – authors of papers like these need to do a thorough review of the literature!).

One the more interesting papers (and an example of the type of research that probably would not be allowed now) was a 1965 paper that found that negative reinforcement (an electric shock) had a positive impact on reaction time. I suppose that if I were shocked every time I was slow, I would make an enormous effort to react as quickly as possible! The important point of that story though is that effort on reaction time is important. Trying to do well on the reaction time test (whether or not you have the threat of a punishment if you do poorly; we do not recommend that you shock yourself if you are slow!) is an important part of the task performance. And probably most importantly, effort on the task should be equal on each testing session.

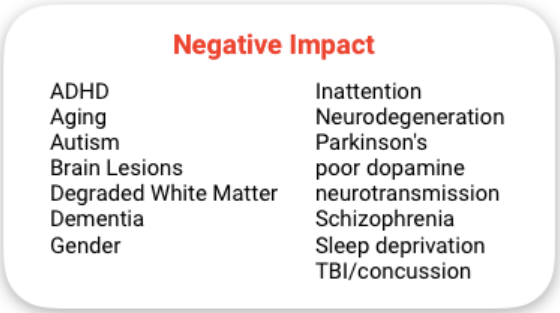
For more reading on the topic, Robert J. Kosinski of Clemson posted a very nice review of reaction time.

The take-away message on reaction time is that faster (or lower) RTs are better and this is inversely correlated with your Speed metric (100% is the best you can do on Speed – that means you are equal to

or better than the norm). When checking your score, take note of the RT value to determine if you are doing better than the norm (~200msec). Best scores to date are in the 140 msec range, and you don't get extra credit for being faster than the norm (i.e., 100% is the best you can do on Speed).
There are many things that can impact your Reaction Time:



And also your Reaction Time Variability:

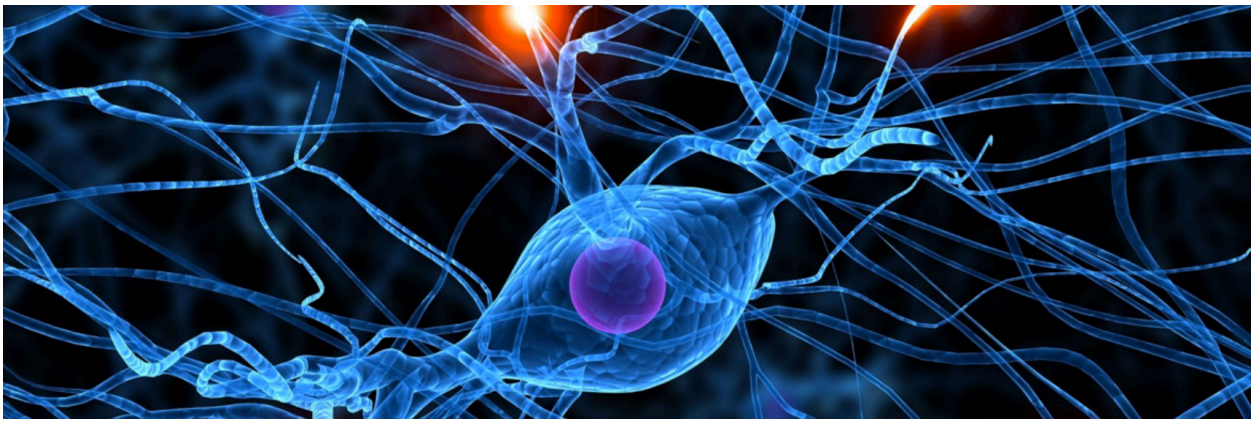


Note that there are not nearly as many indications listed for reaction time variability as there are for reaction time. This is because of the necessity of laboratory grade research tools to get accurate measures of reaction time variability (the Brain Gauge is the only commercially available lab grade research tool that has the accuracy necessary to obtain this measure).
How does reaction time variability differ from reaction time?

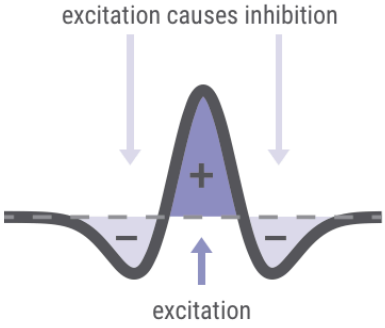
Just like reaction time, lower values for reaction time variability are better. This indicates how consistent you were while taking the test. In other words, did you have trouble focusing on the task? Note that adolescents with ADHD generally have a pretty poor reaction time variability. But if you do poorly on this test, it does not mean that you are an adolescent with ADHD! Alterations in the score can be indicative of long-term or short-term changes.

Typically, healthy control adults score in the 5-22 msec range for reaction time variability (that would generate a 100% score on Focus metric; lower reaction time variability values lead to higher or better Focus score). Keep in mind that this is all research, but Reaction time variability appears to be more sensitive to CNS insult than reaction time. If you want to baseline yourself, figure out what your best reaction time variability score is, and just for fun, see how it changes under different conditions (fatigue, caffeinated, etc.).

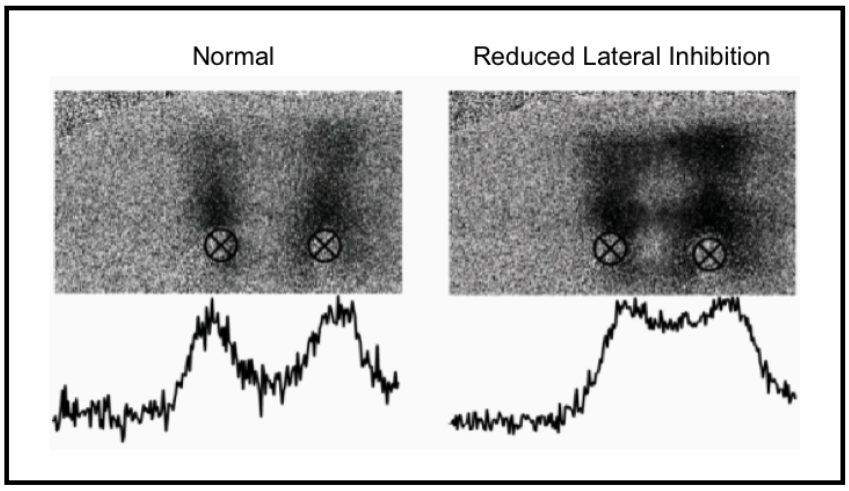
The Accuracy Measure



Lateral inhibition is the brain's way of improving contrast between adjacent or near-adjacent cortical areas. In the 1960s, Nobel prize winner Georg Von Bekesy postulated the idea of lateral inhibition. The basic idea was that when you deliver a stimulus, brain activity will be correlated with the stimulus site, and the surrounding areas will be inhibited or turned off. Long story short, Von Bekesy's predictions, which were based on sensory testing, turned out to be true. If you stimulate a single place on the skin repetitively, you will enhance a focused area of brain activity through lateral inhibition – the areas surrounding excited areas will be inhibited or suppressed. In this manner, the brain efficiently processes inputs. Much less energy is needed to turn things off than is needed to turn things on, and turning down the noise from areas surrounding the areas of interest increases the signal to noise ratio extremely rapidly.

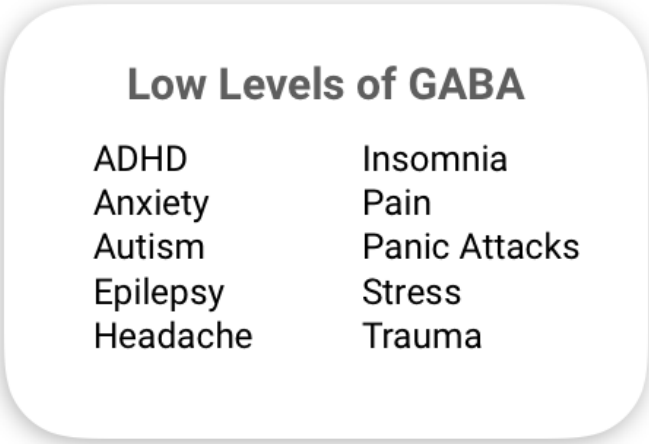


Fast forward to more modern neuroscientific techniques, and we can actually observe changes in lateral inhibition. The image below is a set of images that depict a slice of brain (cortex) tissue stimulated at two sites ("x" marks the spot). The dark areas show where the cortex is activated.



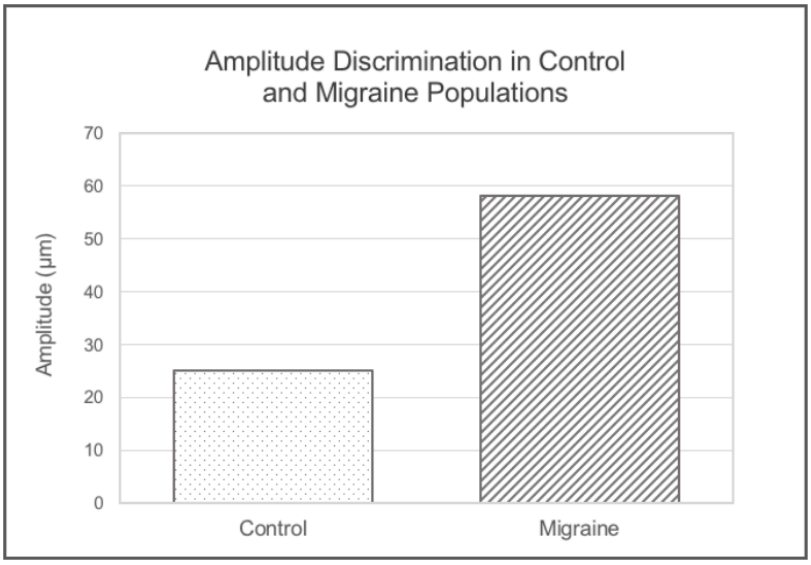
The difference between the conditions in the two images displayed above is that a drug has been administered on the right side that blocks inhibition (this is actually what is called a GABA antagonist; GABA is the predominant inhibitory neurotransmitter in the brain). This is done in order to mimic neurological disorders that are consistent with low or below normal GABA conditions. If the balance between excitation and inhibition is normal, then the brain can process inputs rapidly and fairly easily. If the balance is disrupted, then it becomes difficult to contrast-enhance these inputs.
Looking at the graphs below each of the cortex images, it is easy to see that the contrast between the two sites is lowered (or made worse) when the inhibition is lowered. Thus, you would predict that neurological conditions that have lower than normal GABA levels, GABA receptors that are not operating efficiently or some other condition that impacts GABA transmission/reception would have lower than normal contrast in information processing.

You might be wondering which populations would have lower than normal GABA. Low levels have been associated with the following things:



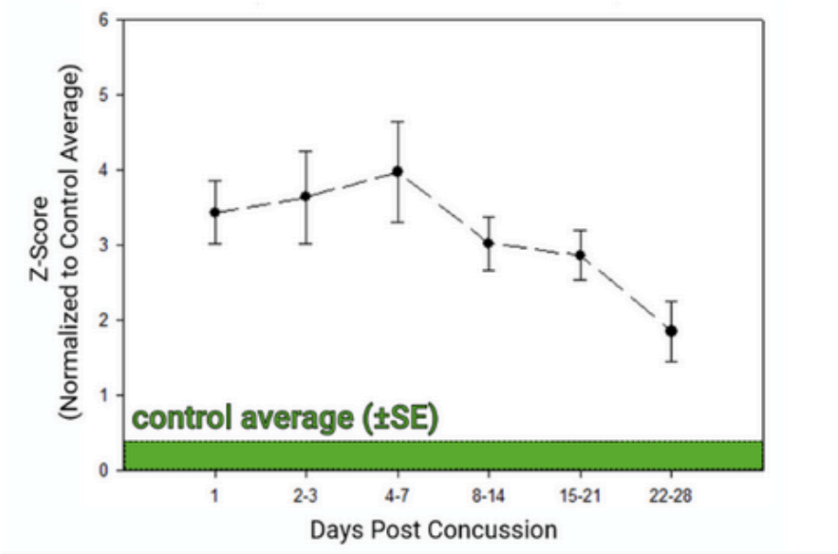
Too much GABA can cause problems as well. Too much, and you'll probably go into a coma. Take a lot on a regular basis, like alcoholics do (alcohol is a GABA agonist) and you might go into alcohol withdrawal delirium when you try to quit drinking. In alcoholism, the withdrawal delirium tremens (DTs) result because the body quits making its own GABA. As a result of this, there is not enough inhibition when the alcoholic tries to "dry out" (to prevent the DTs, GABA agonists are often prescribed).
Some neurohacker's claim that over-the-counter GABA supplements have a calming effect, but GABA does not cross the blood-brain barrier (unless it's leaky, which is another topic).

How to measure lateral inhibition with Brain Gauge: Amplitude Discrimination
The easiest way to tell if lateral inhibition is intact (and/or if there is a good balance between excitation and inhibition in the brain) is to use the amplitude discrimination task. Two stimuli of different amplitudes are delivered to the finger tips. These two places on the skin project to two places in the brain that are side by side. When two stimuli are delivered by the Brain Gauge at the same time (simultaneously, or, as we refer to it, "ADsimult"), a subject will have a difficult time telling the stimuli apart if lateral inhibition is below norm (which could be due to impaired GABA). If they are not delivered at the same time but one after the other (sequentially, or, as we refer to it, "ADseq"), then, unless something else is malfunctioning, they should not have any trouble telling the two stimuli apart from each other. In both cases, the amplitude discrimination task is performed, and the subject has to determine which of two stimuli are larger. If there is a significant difference between the two metrics (i.e., AD simult >> ADseq) then we can tell that lateral inhibition is impaired, meaning that there is either too much excitation or not enough inhibition.



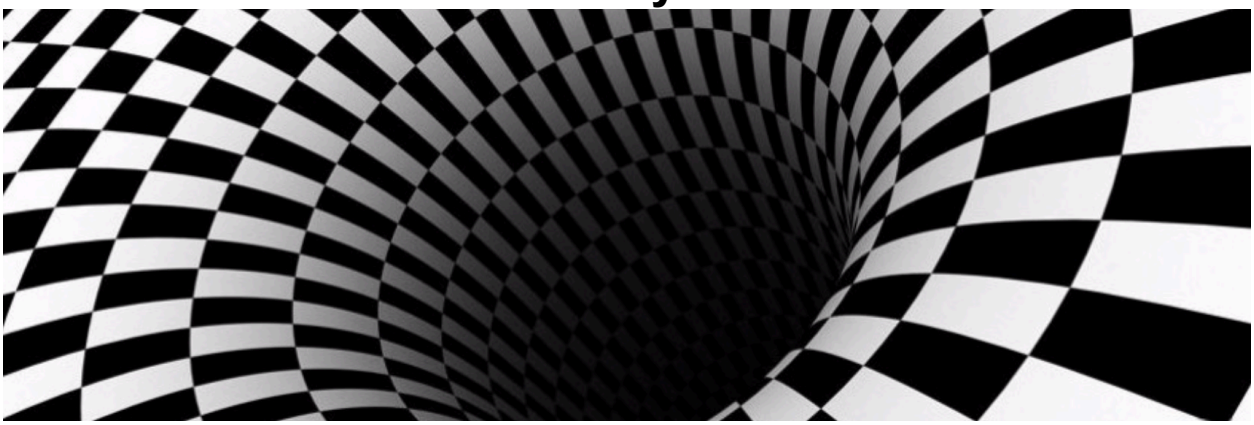
The graph above shows sample results from a headache and a concussion study. Amplitude Discrimination (AD) data were collected from healthy controls and individuals with migraines. The average DLs or raw scores of ADsimult for the two groups is plotted at right (Note that smaller numbers indicate better performance). In this study, only ADsimult was collected from controls and individuals that had chronic headache conditions. Lower difference limens (DLs) on the AD tests indicate better or higher accuracy scores. Many studies (including our own) demonstrate that there are lower than normal GABA levels in this population, and some of the drug treatments that are used for headache sufferers are GABA agonists (one example is Topiramate).

Note that when doing a population study, the goal is simply to demonstrate differences between populations and doing only the simultaneous AD test is adequate. However, if you want to increase accuracy and sensitivity of the lateral inhibition measure, you need to compare the ADsimult score to the ADseq score. Subtle differences between individuals to perform the AD tasks can be taken into account if the both AD tests are administered. A recent concussion study that we performed tracked the results of over 200 student athletes post-concussion, and the lateral inhibition metric is plotted below. Note that with increased time post-concussion, the lateral inhibition metric (plotted as a z score) begins to approach the normative values, and this is consistent with the time course that has been observed in animal studies of concussion.

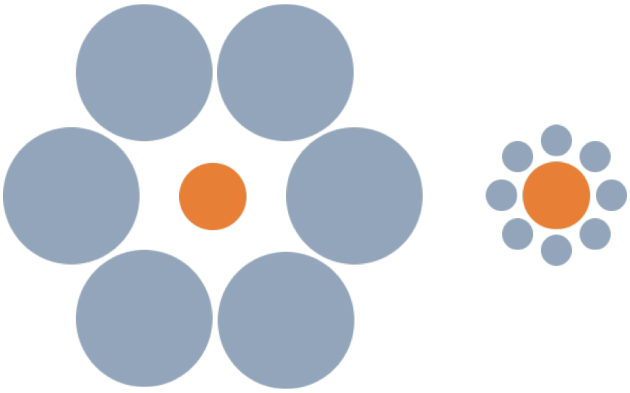


If you're interested in reading further on this topic, a good description of the metrics of lateral inhibition can be found here. You can read more about the headache study mentioned in this post here. To read further about the original idea of lateral inhibition, take a look at Von Bekesy's book "Sensory Inhibition".

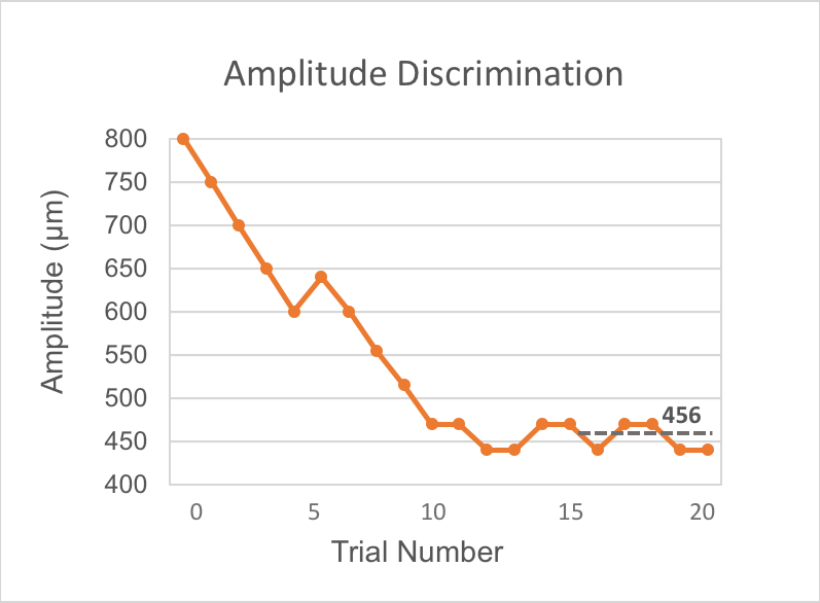
The Plasticity Measure



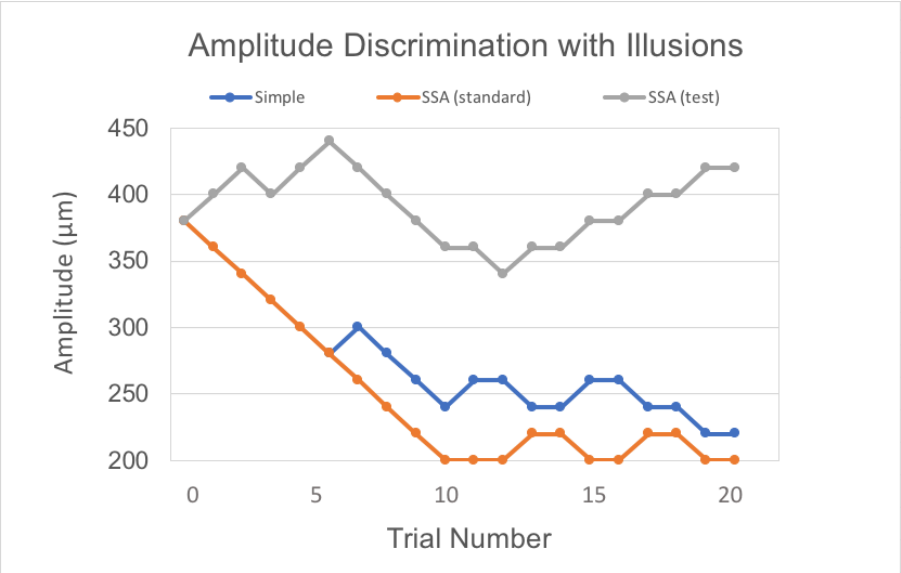
Most people are familiar with optical illusions. For example, the one shown here is a context dependent illusion. Glancing at the two sets of circles, it appears that the center circle of the cluster on the left is smaller than the center circle of the cluster on the right. But in fact, the two center circles are of equal size. Why does the brain trick you into thinking this? Part of the answer is that your brain quickly evaluates the center circle in the context of its surroundings, and the result is that the two center circles appear to be different sizes. Cortical circuitry is ideally suited for contrast enhancement, and to navigate the real-world environment, we process an enormous number of images at literally lightning speed. If something goes wrong with the circuitry, the illusions will no longer appear. Many individuals with autism are not impacted by illusory stimuli such as these – they immediately recognize the pattern without the contextual evaluation and perform better at evaluating the comparison of the two center circles.

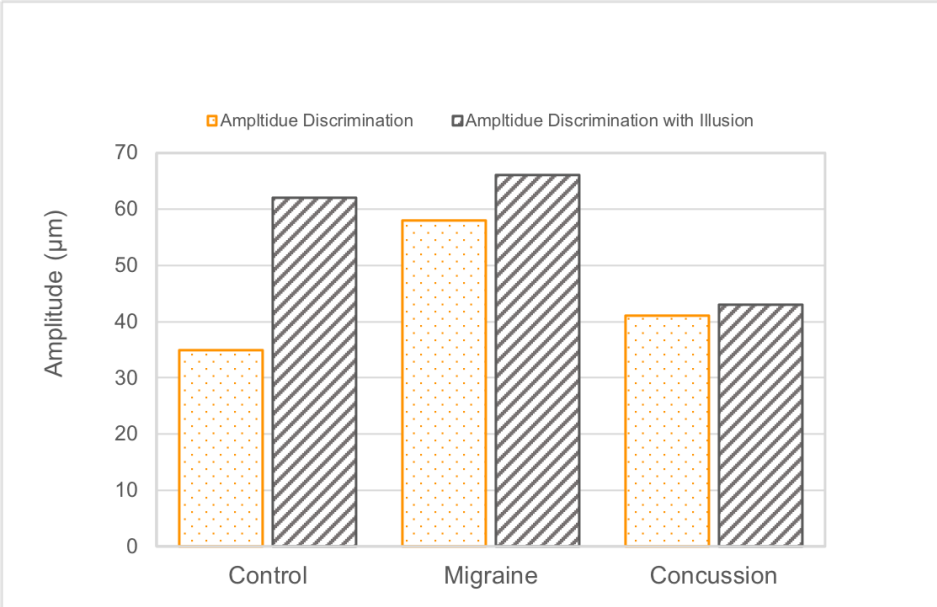


Delivery of tactile illusions to the skin is a way that we can evaluate how well the cortex is processing inputs. One of the simplest examples of this utilizes the amplitude discrimination task. In this task, the subject is queried about which of two stimuli are larger. Each time the answer is correct, the difference between the amplitudes of the stimuli in the subsequent tests get smaller. At some point, the values of the amplitudes oscillate around what is referred to as their difference limen.



This amplitude discrimination task, as described above, was done without any illusory confounds. But what if we added a conditioning stimulus? Specifically, suppose we deliver a half second (500 msec) stimulus to the skin site where the larger of the two subsequent stimuli will be delivered? The result, normally, is for the perception of the larger stimulus to be much smaller (think of this as an adaptive response – after you feel something for a long time, you start to ignore it). When this happens, you effectively have created an illusion – a larger stimulus now feels smaller, and a comparison of the two stimuli on the amplitude discrimination task is now much more difficult. The percept of the larger stimulus is now smaller, so the difference between the percepts of the two stimuli are much smaller and more difficult to evaluate. With the illusion in place, the scores get worse, but plasticity scores get better. In other words, the illusory conditioning stimulus is supposed to make you worse (usually about 30%). The terminology in cortical metrics is that single site adaptation (SSA) will be high when plasticity is high and low when plasticity is low.





There are different features of adaptation, and in particular, how it relates to repetitive stimulation. In general, one of the main features of a repetitive stimulus (even though its only 500 msec long, it does have that effect) is that the cortical activity that relates to the skin site being stimulated (i.e., the fingertip representation in the brain) actually goes down with repeated stimulation, and this change in activity level is roughly correlated with the percept of intensity. Another feature of adaptation with repetitive stimulation is that there is an increase in contrast enhancement, but that will be the subject of another report. Multiple mechanisms are involved in adaptation, but a predominant one is feedback circuitry that is highly influenced by the balance of excitation and inhibition in the brain. If there is not enough inhibition (or too much excitation), then adaptation will be suppressed, and the plasticity score will be low. This is discussed in more detail than most people would like to read about, but here are a list of papers that demonstrate neurological disorders with lower than normal plasticity scores:

- Autism (Tommerdahl 2006, Tannan 2008, Puts 2014)
- Chronic alcohol use (Nguyen 2013)
- Pain (Zhang 2011, Nguyen 2013)
- Concussion (Tommerdahl 2015)
- OCD (Guclu 2015)
- Tourette's (Puts 2015)
- Acute DXM / NMDAr antagonist (Folger 2009)
- Degenerative Disorders / Parkinson's (Kursun 2013)

A comprehensive discussion on cortical dynamics and the scientific basis of plasticity can be found here.

The Temporal Order Judgement (TOJ) Measure

One of the cortical metrics that you get is called “TOJ” which stands for Temporal Order Judgement. This test delivers two taps, one to each of the two fingers positioned on the Brain Gauge, and queries “which came first?”. The test starts out easy (taps are initially 150 msec apart) and gets harder each time you get the question right (sort of like reading an eye chart – it gets more difficult the farther you progress). If you look at your TOJ raw score (on the bottom right hand side of the analysis page next to the label “TOJ”) you will most likely see a number in the range of 20-40. This is in milliseconds (msec) and is your raw score. Remember that the initial test (during training) was set at 150 msec, and the number that you see is what you tracked to. If your raw score was 30, that means that you started getting the TOJ query wrong around 30 msec. The final value is the average of the last several trials since most people track down and then oscillate around their actual best performance (this is called the difference limen). The lower the TOJ raw score, the better that you did. However this differs from the TOJ value that is presented on the bar graph or radar plot. That value is scaled to normative values – if you scored in the normative range, then you scored 100%. If you scored 0%, that means you were very far below the normative range. These scores do not go above 100% or below 0%, so if you are tracking yourself over a period of time (days, weeks, months) and your score is well above the norm or well below the norm, then it pays to note the raw score values. This is often the case for super-testers who do extremely well on this task: they might have a TOJ raw score of 30 msec (which would be 100% of the norm) that goes down to 15 msec after they have done something to improve their performance (nootropics, exercise, etc.). Significant neurological insult can make it very difficult for some people to score in the scaled TOJ graph range, but with recovery, we have seen many individuals progress from well out of range to normative values.
There have been lots of papers that used TOJ to measure differences between subjects with or without some condition. From these papers (a few of them are from research that we participated in) we can list some things that published research has demonstrated to have an impact on TOJ:

Impact on TOJ

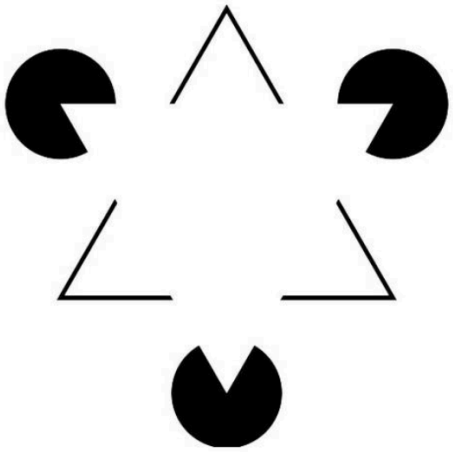
ADHD	Head trauma
Aging	Pain
Autism	Parkinson’s
Botox injections	Schizophrenia
Crossing your hands	Sleep Deprivation
Dystonia	

Note that if your TOJ scores are below normal, then it does not mean that you just had a botox injection to your forehead! This goes for everything else in the list – poor performance does not mean that you are in one of those categories. It just means that those populations do more poorly on TOJ than healthy control populations. And also note that just because it's published, you might disagree with the publication. For example, stating that aging contributes to poor TOJ scores can be disputed – what really matters is whether or not the older cohort tested was healthy or not. Many studies do not exclude any neurological conditions when they do an aging study (this would be comparison of young adults to older adults). The point is, as people age, a larger portion of those people have more and more things that are neurologically non-optimal. For example, a much higher percentage of people in their 60s have chronic pain than do people in their 20s, and chronic pain significantly impacts tests such as TOJ. We have observed many healthy people in their 80s with above normative scores on all tests; it just depends on the overall neurological status.

How is TOJ and its meaning studied? There have been a wide range of studies that target identification of the network involved for TOJ. These include imaging studies of healthy controls performing the TOJ task, studies of individuals with known anatomical deficits and studies of neurological disorders (i.e., somewhat identifiable deficits). Taken together, it appears that parietal and temporal lobes are involved, and there is also evidence for frontal areas to be involved. From our own observations of concussed individuals, it appears that concussions that have impact to the front part of the head have the largest impact on TOJ while insults to the back of the head have much less impact (but these injuries tend to impact timing perception, which will be the topic of another report).

Temporal Order Judgement with a Confound (The Connectivity Measure)

In our discussion of the Plasticity measure we mentioned how an illusory conditioning stimulus could be context dependent and that frequently delivering repetitive stimuli has the effect of suppressing the percept of a stimulus. Repeat a stimulus many times (the conditioning stimuli that are delivered by the Brain Gauge are typically sinusoidal at a frequency that delivers many repeats to the same place on the finger tip) and the effect is that stimuli feel much smaller. Are there other illusions? The obvious answer is yes, since we're writing this report. The illusion in the figure below appears to have multiple triangles drawn. However, if you inspect it carefully, there are actually no triangles in the image. This is a good example of the brain literally "connecting the dots" in order to make a coherent pattern that makes sense. This is a property of the neural network – cortical assemblies coordinate their activity and optimize connections so that we can navigate the environment in the most efficient manner. Computational neural networks have been built to detect sparse information embedded in very noisy fields using some of the principles that have been learned from evaluating the brain's neural network (but this will be the subject of another report).



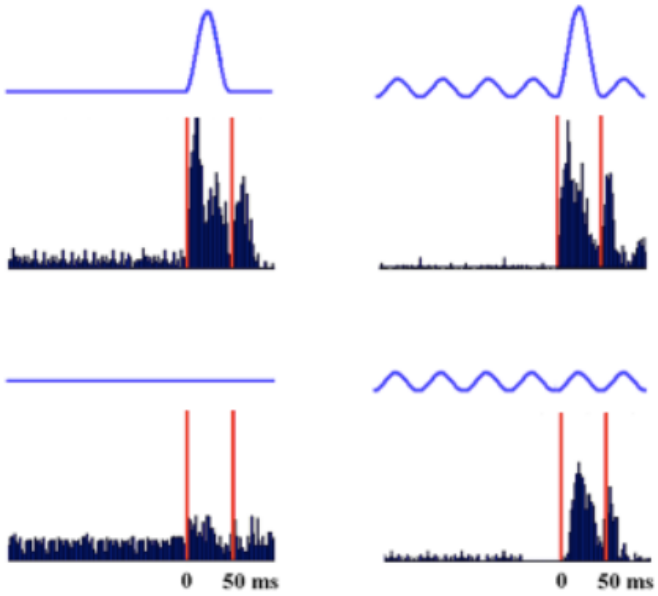
So how could we evaluate an illusion that connects the dots with a well-controlled tactile stimulus, such as the Brain Gauge is capable of delivering? Perhaps the best way to explain this is to go through the logic that I went through when designing the original experiment.

First, the fingers have independent sensation. You can tell when one finger is tapped and identify it from its neighbor. Tap two fingers, one after the other, and you can reliably tell which finger was tapped first, as long as there is a sufficient separation in the timing of the taps. But what happens when you use your

fingers together? Anytime you grab and object, you don't consciously think about coordinating the movements of the fingers – it is done automatically. In similar fashion, when we observed responses to repetitive sinusoidal stimuli (this was a couple of decades ago) in the brain, we discovered that groups or assemblies of cortical neurons would start working together and synchronize (or coordinate) their response activity. Stimulate two places on the skin together (or two fingers at the same time) and within about 130 milliseconds, activity of the two cortical regions that are associated with those two fingers becomes unified. That coordinated activity (that only occurs under normal healthy conditions) would predict that if we delivered conditioning stimuli that are identical (i.e., two repetitive sinusoids to two fingertips) then it would make the two fingers perceive a unified or coordinated response. This is how we set up the connectivity test the first time that we did it – we delivered two identical conditioning stimuli (which we now call illusory conditioning) to two fingers and then performed the temporal order judgement (TOJ) task. TOJ is the test where you are queried as to which of two taps came first. The timing between taps is varied and you get a score that reflects the shortest interval that you were able to reliably perceive the order of the taps. Comparison of the TOJc (TOJ with conditioning stimulation) and TOJ showed that TOJc was significantly more difficult (i.e., got a worse score) than TOJ.

You might think that a robust finding like that would be easy to publish and for reviewers to accept, but we knew that would not be the case. So we went ahead and did a couple of other experimental conditions that demonstrated that this phenomenon of TOJc >> TOJ only occurred with conditioning stimuli that were identical (synchronized and periodic). Randomly delivered (aperiodic) stimuli of even greater magnitude did not have any impact and resulted in TOJc = TOJ. Delivery of TOJ and TOJc to fingers on opposite hands resulted in TOJc=TOJ, so that demonstrated that the cortical regions needed to be in close proximity (we later did experiments to demonstrate that cortical distance between finger representations could be correlated to the impact that conditioning has on TOJc). This idea was still met with a bit of resistance with a grumpy reviewer (the idea ran counter to some long-held beliefs about how the cortex was organized), but the editor thought it was pretty compelling evidence and published it anyway. We subsequently did other experiments that demonstrated the underlying neurophysiological evidence as well as published findings that demonstrated that in populations that have disrupted cortical connectivity, TOJc==TOJ. These populations, in general, have lower than normal global functional connectivity which is a measure obtained with fMRI (fMRI does not have the capability to examine local functional connectivity, which is what the Brain Gauge does with TOJc/TOJ comparison). We believe that global functional connectivity is dependent on local functional connectivity (a belief widely held by many other researchers but still debated).

The take away message from those findings on populations with different neurological disorders is that disrupted connectivity (this can be functional or anatomical) results in a lower than normal impact of the illusory condition stimulus on TOJ. If TOJc >> TOJ, then connectivity is probably intact (TOJc>>>>TOJ is something we are still investigating as it may indicate other problems) and the connectivity score will be high. If TOJc is approximately equal to TOJ, then the connectivity score will be low.



What happens when 2 finger tips are conditioned and a tap is delivered to one of them? The figure above shows the neurophysiological response to finger tips receiving a tap in the absence (2 left panels) and presence (2 right panels) of conditioning stimuli. The top left panel shows a signficant cortical response to a tap on one finger (D2) while the bottom left panel shows very little response at the adjacent finger (D3) cortical site. However, with a conditioning stimulus delivered to both fingers (right hand panels) both places in the brain that correspond to the adjacent finger tips respond to the single tap, and this demonstrates the coordinated response of the cortex to the simple tap.

Let's demonstrate changing the connectivity score with a published intervention on human subjects. Aimee Nelson and colleagues did an elegant experiment demonstrating that disruption of cortical circuitry resulted in the TOJc score actually improving. Subjects took the TOJc test (all had scores that reflected TOJc>>TOJ) before getting a dose of theta-burst TMS over the somatosensory cortex, and then tested until the effects of the TMS wore off. While the TMS burst was effective, TOJc was approximately equal to TOJ (unless they received sham TMS, which was ineffective at changing it). That study demonstrated the sensitivity of the metric.

The TOJ connectivity score is currently only recommended with the Brain Gauge Pro because the sensors in the Pro model provide feedback to the user that they are pressing the probe tips down too hard (this happens with about 10% of all users). If the probe tips are actively pressed down, then there is no guarantee that the two conditioning stimuli will be equal and the result will be an inaccurate connectivity score.

Scientific publications are available for further reading on the following topics:

- Autism *original paper referenced in this post
- Transcranial Magnetic Stimulation
- Temporal Order Judgement
- Concussion
- Migraine

The Timing Perception Measure

Timing perception is derived from your duration discrimination task. This is the test that asks “Which stimulus lasted longer?” The first trial of the task (during training) delivers a 650 msec duration stimulus to one finger and subsequently a 500 msec duration stimulus to the other (a 150 msec difference). Each time the person taking the test identifies the finger that received the longer stimulus correctly, the difference between the two durations on the next trial is reduced. Most people track down to a difference limen of 35-60 msec, and this results in a 100% score for timing perception. If the raw score for DD (on the bottom right hand list of scores on the analysis page) is above that, then the timing perception score will be less than 100%.

The ability to perceive the difference in two stimuli is a network function that relies heavily on the cerebellum. The cerebellum plays a role in accurate timing of events and coordinating many functions including walking, balance and posture. It accomplishes this contribution by organizing inputs from many parts of the brain (including sensory systems) and integrating them to fine tune motor control. Intuitively, it makes sense that the region of the brain that performs these types of time dependent tasks would also play an important role in timing perception.

There were several different research groups that studied timing perception and the role that the cerebellum played in that function. Each of the groups, even though they used different sensory modalities (each group used either tactile, auditory or visual stimuli) blocked activity in the cerebellum and demonstrated that timing perception capacity was greatly diminished. This is also consistent with timing perception results that were obtained from populations with neurological disorders or insults that involve damage or degeneration to the cerebellum. And it is also consistent with our own observations in concussion that when an individual receives a blow to the back of the head (where the cerebellum is located), timing perception is usually diminished.

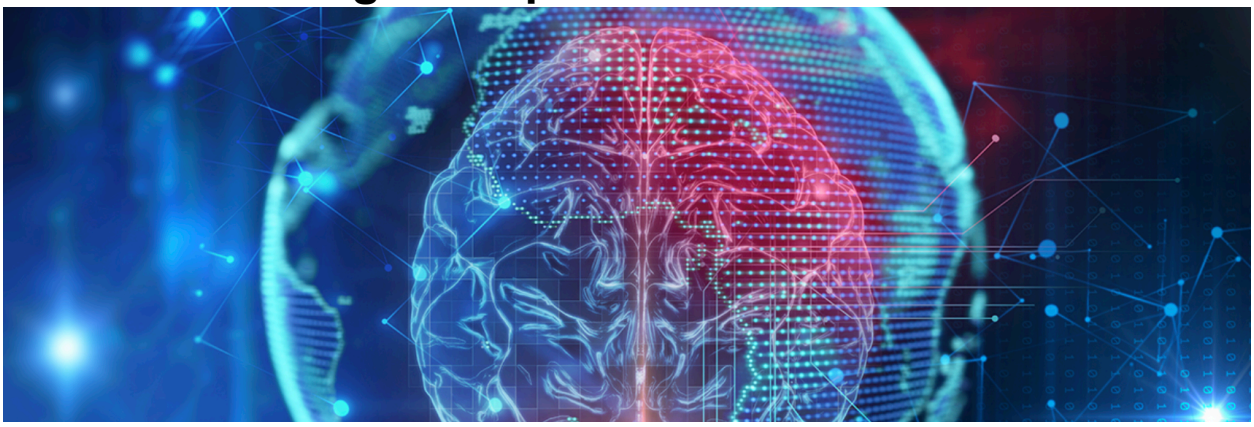
A note of interest on this topic is that in sports concussion studies, balance is probably one of the most over-rated measures routinely collected. There have been no studies that demonstrated that balance was a problem in the majority of concussed individuals in any reported study. In our own study (200 concussed individuals who were balance tested as well as tested with the Brain Gauge), individuals tested, on average, 13% better 2 days after becoming concussed than they were at baseline (i.e., better than normal!). This compares to 99% of the individuals testing worse than normative values post-concussion with the Brain Gauge. Loss of balance is one of the symptoms that can occur with concussion, but there are many symptoms that result from concussion. Measuring the degree of one possible symptom is a bit like measuring the force from a sneeze to determine if someone has a cold: it might be related, but it probably is not. Measuring the underlying cause of a symptom is much more effective. If timing perception is off, then there is very high probability that timing circuitry involved in the cerebellum (which plays a role in balance) could be damaged. Sometimes the insult to this timing circuitry will result in the loss of balance, and sometimes it won’t. In our current TBI work (which includes more than 300 concussions), it appears that timing perception is usually disrupted in certain conditions, such as when the back of the head is impacted significantly (but this is still a topic of research) or when the blow to the head is significant enough to cause deficits in all of the Brain Gauge scores. If the frontal and pre-

frontal cortices are impacted significantly, then your ability to make decisions – regardless of what the decisions are about – will make it difficult to perform any of the tests.

There are a number of papers in the literature that document different neurological disorders that have a degenerative or negative impact on timing perception. If your timing perception is poor, it does not mean that you have one of these conditions! Also note that there are different degrees of poor timing perception. Someone that is mildly sleep deprived will do moderately poorly, someone with migraines will do worse, and individuals with Parkinson's typically do very poorly.

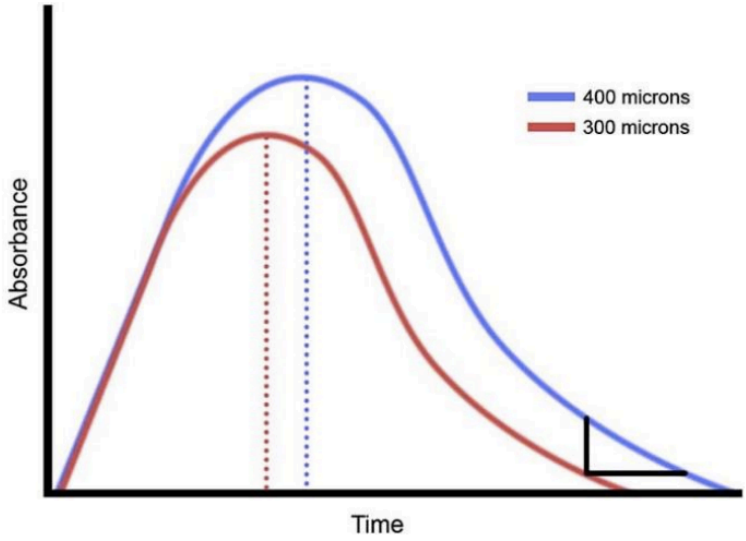
- Alzheimer's
- ADHD
- Parkinson's
- Lesions to the cerebellum
- Acute TMS to the cerebellum (TMS used to turn off cerebellum)
- Schizophrenia
- Migraine
- THC
- Sleep deprivation
- Huntington's disease
- Haloperidol

Timing Perception with a Confound



The Timing Perception measure (or Duration Discrimination) comes from the test that asks you “which stimulus lasted longer?”. This score is useful on its own, but you can gain even more insight into your brain health by comparing it to your Duration Discrimination with confound score. The difference between these two scores is based on a brain illusion - a mistake that your brain makes when comparing two sensations. But don't worry - if your brain is making this mistake, it means that it's healthy!

How the illusion is created
Check out the graph below, which shows how a single location in the brain reponds to a simple stimulus (like a finger tap). Time is plotted on the x-axis and absorbance is plotted on the y-axis. Absorbance reflects the activity levels of both neurons and neuroglia, non-neuronal cells of the central nervous system that provide support and protection for the brain's neurons. When the stimulus is stronger (the 400 micron plot), the glial and neural cells in your brain take longer to return to baseline activity levels.



Now let’s see what happens in the same brain location if we use an extracellular electrode to measure the neural activity. This technique is not affected by the activation or inhibition of the glial cells.
When a stimulus is delivered, there is activity at that location in the brain. But unlike the first plot, there is zero activity when the stimulus ends, regardless of how strong the stimulus is.
The difference between these two graph allows us to design tests to measure impaired glial activity.

Applying the illusion to Brain Gauge tests
If we increase the strength of a Brain Gauge test stimulus by a tiny amount (not enough for a human to notice a difference), a healthy person's brain will perceive that the duration of that stimulus increased.

Therefore, when we increase the intensity on one of the stimuli during the Timing perception test, healthy controls tend to perform poorly. Healthy brains misinterpret the increased intensity as an increased duration. If this illusion disappears, and the patient has no problem identifying the durations of different stimuli regardless of their intensity - it means that neuron-glial interactions have been disrupted. This condition often emerges after brain injuries that cause neuroinflammation.

The intensity-duration illusion allows us to identify the presence of neuroinflammation in patients suffering from concussions and mTBI. We've also seen cases where the illusion was restored after certain treatments - quantifiable evidence of a healing brain.

Illusion confusion
Illusion-based neuroscience can be tricky. Currently, we only offer this test on request since it requires some clinical experience to interpret the results.

The intensity-duration illusion can also be absent even in patients suffering severe brain injuries. If timing perception is altered - maybe from a localized blow to the head - then patients might have trouble identifying duration differences at all.

In other conditions, such as chronic pain, the inflammation can be isolated; neuron-glial interactions are only disrupted in the brain hemisphere on the opposite the side of the pain site (pain in the left leg = inflammation in the right brain hemisphere). Patients suffering from localized chronic pain usually have wide variability in their scores on different hands.

Although the illusion measure is not currently one of the scores, you can investigate it manually in the Brain Gauge app. On the Analyze results page, look at the Raw scores box in the lower right-hand corner. Compare your Duration Discrimination (Dur. Discrim.) score to your Duration Discrimination confound (Dur. Discrim. confound) score : Duration Discrimination with confound should be about 30% greater than Duration Discrimination.

To read our paper about the Duration Discrimination measure, click here.

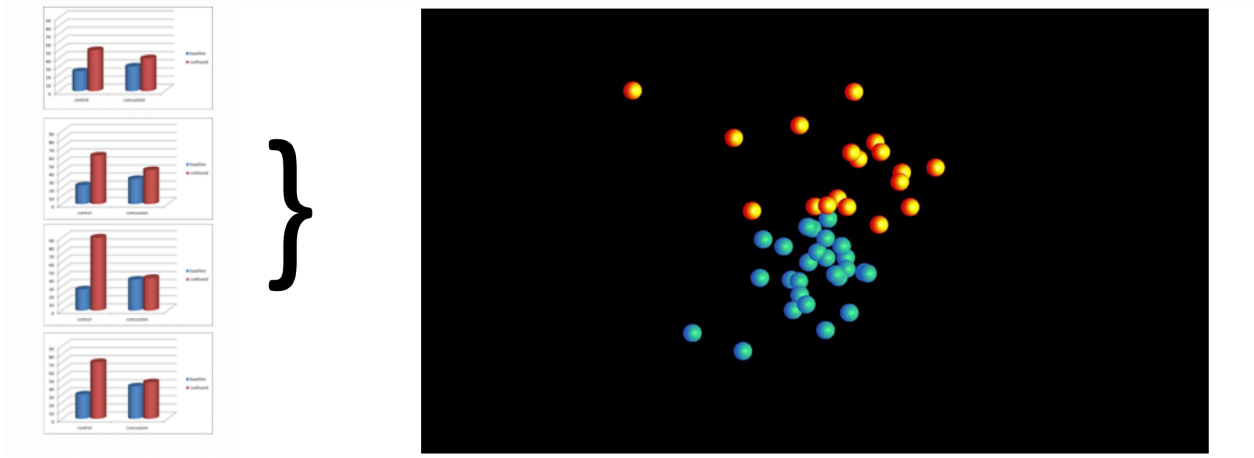
The Cortical Metric

If you are a Brain Gauge user, you've probably noticed the overall corticalmetric score. This comprehensive measure is calculated from all the tests that were taken in a single test session. If that is a sufficient explanation, then read no further.

When we first started developing cortical metrics – all the different measures collected by the Brain Gauge (and also the name of the company... we realize that can be confusing!) – we wanted to create a unique metric that could summarize the brain profile of each individual. We believe that it takes multiple measures to accurately assess brain health; no single test could describe a person's entire range of cognitive functions. For example, if you go to a clinic and say that you have a headache, the physician will not immediately suggest a remedy or just write you a prescription (at least we would hope that is not the case!). Before a treatment protocol can be established, you would be asked about to describe specific symptoms and when they started and how long they last and what your sleep habits are and what if anything has changed in your life and about three dozen other questions that probably won't do your headache much good (at least not at that time). Your responses help the doctor narrow down the possible causes of your headache, allowing them to create a treatment plan that will target the underlying mechanism.

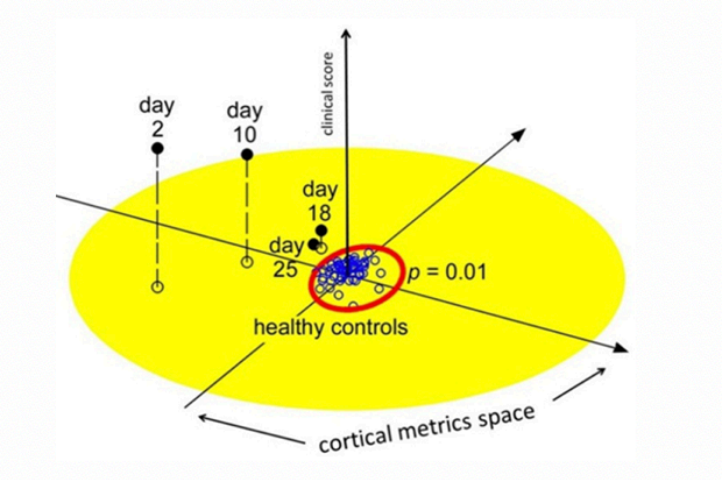
We take the same approach when designing with tests to be delivered by the Brain Gauge. Each Brain Gauge test targets a different mechanism of information processing. From looking at your scores from every test, we develop a "brain health profile" - consisting of your corticalmetrics scores like Speed, Fatigue, and Plasticity - that gives clinicians an idea of where to begin searching for things that could be affecting your brain health.

We collect a variety of measures in a single test session, and then we convert those measures into your overall corticalmetric. For the sake of simplicity, we'll do an example without too many data points.

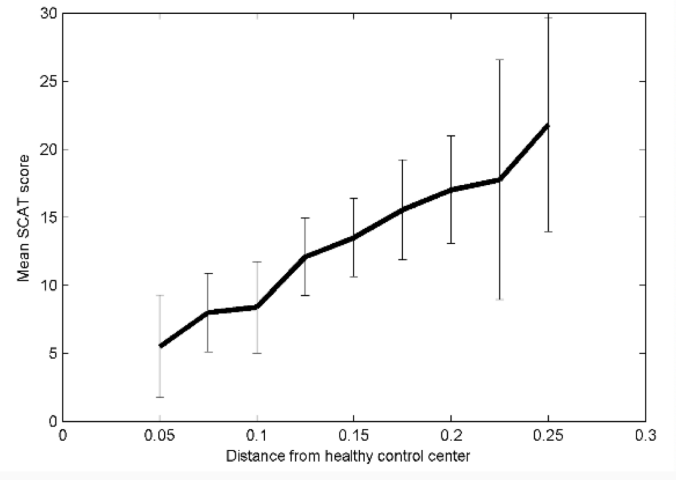


First, we combine all n-measures into an n-dimensional space; if there are 6 measures, then we plot the data into a vector with 6 coordinates. Each data point has a particular magnitude and direction. We then apply a technique known as principle component analysis (PCA), which shows us the scores that have the greatest effect on your corticalmetric. When we plot that data healthy controls tend to cluster in the center while non-healthy individuals shift to different locations. The plot above shows a 2D rendition of an 8-dimensional dataset.

Now let's examine how a concussed individual compares to healthy controls in just 2 dimensions of the corticalmetrics space. The graph below plots the multi-dimension corticalmetric on the x-y axes and the clinical severity score (the number of concussive symptoms) on the z-axis. Note that healthy controls cluster around the center point while concussed individuals (points labeled with #-days post-concussion) move closer to the center as they recover from concussion.



If we look at multiple individuals in this study and just look at distance from the center, corticalmetric scores correlate very well with the number of concussive symptoms.



The distance described above is equivalent to your corticalmetric score from each Brain Gauge test session. However, if you shorten the battery by only taking one or two of the tests (which is perfectly fine to do – there are lots of good reasons for taking that approach), it just reports the average for those select tests. Those measures cannot be compared accurately to a corticalmetric that is collected from all eight of our measures. One advantage of the method for research purposes is that implementation of the multi-dimensional method allows you to compare different populations. Note that when you use the full

implementation of the method mathematically, different populations separate by orientation, not just distance. Note the plots below that show the differences between people with migraine vs. controls, people with concussion vs. controls and migraine vs. concussion. We don't expect anyone to try to figure out if their headache is from getting concussed or some other neurological reason, but it is an area of research that will be interesting to pursue.