An Accurate Measure of Reaction Time can Provide Objective Metrics of Concussion

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There have been numerous reports of neurological assessments of post-concussed athletes and many deploy some type of reaction time assessment. However, most of the assessment tools currently deployed rely on consumer-grade computer systems to collect this data. In a previous report, we used robotic testing to demonstrate the inaccuracies introduced by typical consumer-grade computer systems (Holden et al, 2020). In that report, we described the accuracy of a tactile based reaction time test (administered with the Brain Gauge) of approximately 0.3 msec and discussed the shortcoming of other methods for collecting reaction time.The consumer-grade systems introduced latencies as high as 400 msec and variabilities as high as 80 msec, which greatly exceeds the control values reported for reaction time (200-220msec) and the control values for reaction time variability (10-20 msec). In this report, we examined the reaction time and reaction time variability from 396 concussed individuals and found that there were significant differences in the reaction time metrics obtained from concussed and non-concussed individuals for 14-21 days post-concussion. A survey of the literature did not reveal comparable sensitivity in reaction time testing in concussion studies using alternative methods. This finding was consistent with the prediction put forth by Holden and colleagues with robotics testing of the consumer grade computer systems that are commonly utilized by researchers conducting reaction time testing on concussed individuals. The significant difference in fidelity between the methods commonly used by concussion researchers is attributed to the differences in accuracy of the measures deployed and/or the increases in biological fidelity introduced by tactile based reaction times over visually administered reaction time tests. Additionally, while most of the commonly used computerized testing assessment tools require a pre-injury baseline test to predict a neurological insult, the tactile based methods reported in this paper did not utilize any baselines for comparisons. The reaction time data reported was one test of a battery of tests administered to the population studied, and this is the first of a series of papers that will examine each of those tests independently.

Citation

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Introduction

Currently, there is no standard, reliable, cost-effective paradigm or methodology for assessing the degree to which the central nervous system (CNS) is impacted by neurological disorders. One of these disorders or systemic central alterations due to trauma is concussion, or mild traumatic brain injury (mTBI). Although awareness of concussion and mTBI is significantly growing in the general public, there is still no standardized, quantitative, biologically based methodology that is effective for assessing the impact of mild neuro-trauma. Current existing methods and products for this need are expensive, extremely slow, and in many cases fail to definitively and quantitatively diagnose the problem. For example, clinical grade medical imaging technologies—though they are able to discern differences in subjects with traumatic brain injury —show few or no differences for mTBI or concussion, are costly (about $1K per scan), are not portable, and are not practical for getting a quick assessment. In fact, no modern medical imaging techniques are as sensitive to subtle alterations in cortical information processing as those detected by sensory percept.While it is unlikely that there will be any medical imaging technologies able to provide such high resolution in the near future, it is even more improbable that such a technology could be widely distributed and used pragmatically and cost effectively on a regular basis.

One of the greatest issues with concussion, or mTBI, is determination of return-to-duty status for the military or return to-play status for athletes at multiple levels of competition (secondary school, college/university, and professional level). Because injury from secondary concussions can be much more serious, if not fatal, during the critical post-concussion recovery period, it is imperative that methods for this determination be developed. Many years ago, we proposed to design and fabricate a noninvasive, portable, sensory-based diagnostic system using state-of-the-art technology to investigate cortical information processing. The first prototype of this device was reported by Tannan et al, 2005 [2] and a second prototype of reported by Holden et al, 2012 [3]. Since that time, we have developed a number of tactile sensory based protocols that target different mechanisms of CNS information processing. Previous reports have demonstrated sensitivity of the methods to concussion. Tommerdahl et al [4] showed that mathematically combining the results from the different measures yielded a unique CNS profile that demonstrated 99% confidence levels for differentiating concussed from non-concussed student-athletes. Additionally, the metric extracted from this CNS profile co-varied consistently with the concussed individual’s symptom score. Expanding on that method, Favorov et al [5], in a study of college students, reported ROC curves for each of the multiple metrics that, although they varied extensively in their ability to assess concussed status, when combined demonstrated very good sensitivity and specificity. The results of that study predicted that the method could prove to be good for tracking an individual’s recovery and could be used as a good quantitative indicator of central nervous system health. Additional reports [6-9] demonstrated the prognostic utility of the method. Demonstrating the sensitivity of the method, Pearce et al [10,11] showed information processing differences between 3 groups of individuals: healthy controls, and symptomatic vs. asymptomatic individuals who had been concussed 3-12 months prior to testing. Taken together, the evidence that has accumulated strongly suggests that the methodology is successful in differentiating concussed vs. non-concussed individuals and more importantly, can be used to track recovery of individuals from concussed to non-concussed status [6]. While the authors view the combination of metrics as critical to obtaining a broader view of overall CNS health, it is important to review each of the measures and the contributions that they make to that profile. In this report, although a battery of tests was administered to the study subjects, only the results from the reaction time test are reported. Subsequent reports will describe the results from each of the other tests that are commonly administered with the Brain Gauge in the sports concussion environment.

Methods

Subjects

Sensory assessments were performed on 793 healthy controls aged 18-22 years old and 440 concussed individuals in the same age range. All participants in the study were student-athletes. All concussed athletes were diagnosed with mTBI in the form of a concussion by a certified athletic trainer and the team physician with the help of the Sport Concussion Assessment Tool 2 (SCAT-2), ImPACT (Immediate Post-Concussion Assessment and Cognitive Test), and, in some cases, the BESS (Balance Error Scoring System). BESS was dropped from several of the participating programs because the health professionals using it deemed it as an ineffective tool for evaluating concussion. Healthy controls had no prior history of concussion or other diagnosed mental health conditions with symptoms similar to concussion. The reported assessments were obtained from concussed individuals at one or more time points ranging from a few hours after concussion to 9 months after concussion. Baseline measures were also collected on each participant prior to beginning the sports season and were used as healthy control data. The experimental procedures were reviewed and approved in advance by an institutional review board.

Sensory Assessment

Somatosensory assessment was performed using a portable vibrotactile stimulation device (Brain Gauge, Cortical Metrics, Carrboro, NC). The device, of similar size and shape as a computer mouse, contains independent, computer-controlled probe tips which can deliver a wide range of sinusoidal vibrotactile stimuli of varying amplitudes and frequencies. All protocols used were originally conducted on a four-site mechanical stimulator (CM4; Cortical Metrics Model #4) which is functionally identical for 2 digits and was previously described in Holden et al. [3] and has been utilized to assess multiple sensory information processing characteristics in a number of subject populations [2,4,5,9,12-21]. Not only do these protocols demonstrate significant sensitivity to alterations in CNS processing, but they are independent of detection thresholds or skin sensitivity [20,22].

Figure 1. *Two point vibro-tactile stimulator.*

During the evaluation session, subjects were seated comfortably in a chair with the right hand resting on the vibrotactile stimulator. In this study, vibrotactile flutter stimulation (25Hz) was delivered via 5mm Delrin probes to the glabrous tips of either, or both, the second (index, D2) and/or the third (middle, D3) digits of the right hand. These digits were chosen as test sites for convenience and comfort and also because of the wealth of neurophysiological data that has provided observations of the associated somatotopic regions in the non-human primate cerebral cortex. The tips of the Brain Gauge device are used both to deliver vibratory stimuli and record subject response. The subject was instructed to press down on the tip to register a response after the vibration had been delivered.

A computer monitor provided visual cueing during each of the experimental runs. The cues indicated when the experimental stimuli would be delivered and when subjects were to respond. Training trials conducted prior to each task familiarized subjects with the test; correct responses on three consecutive training trials were required before the start of each assessment.

A series of sensory perceptual measures were employed to assess tactile information processing ability. In sum, these tests lasted approximately twenty minutes and consisted of sequential evaluations of reaction time (RT), amplitude discrimination (AD), temporal order judgment (TOJ), duration discrimination (DD) and then a second RT task. In this report, only the RT task is described.

Tactile Reaction Time

For the simple tactile reaction time task, a single tap (300µm, 40ms) was delivered to D3 and subjects were instructed to respond by pressing down with D2 as soon as the tap was perceived. A randomized delay ranging from 2 to 7s separated the trials. Response times were recorded for each of the 10 trials. This method was first reported in Zhang et al.[21] and has been reported many times since then [5,10,11,23-38]. The standard deviation of the 10 reaction times was used as a measure of reaction time variability. The reaction time task was completed once at the beginning of the 20-minute battery of testing, and once again at the end.

Results

In an ongoing sports concussion study, observations have been collected from over 400 individuals that were concussed and approximately 800 healthy controls (n for each measure in table below). Reaction times for concussed individuals were significantly slower (i.e., longer) than reaction times healthy controls, and similarly, reaction time variabilities for concussed individuals were higher than were variabilities for non-concussed individuals. Note that p values for comparisons of healthy controls (Contr.) vs. concussed individuals (Conc.) were less than 10^{-15} for reaction time and reaction variability, and this indicates a very significant difference in the data derived from the reaction time task from the two populations.

	RT1 Contr.	**RT1 Conc.**	**RT1 var Contr.**	**RT1 var Conc.**
n	793	440	793	440
mean (msec)	217.8	286.1	17.48	32.88
SEM (msec)	0.97	5.78	0.32	1.34

Table 1. *Average reaction time and reaction time variabilities obtained in the study. Note the significant differences between the control (Contr.) and concussed (Conc.) conditions.*

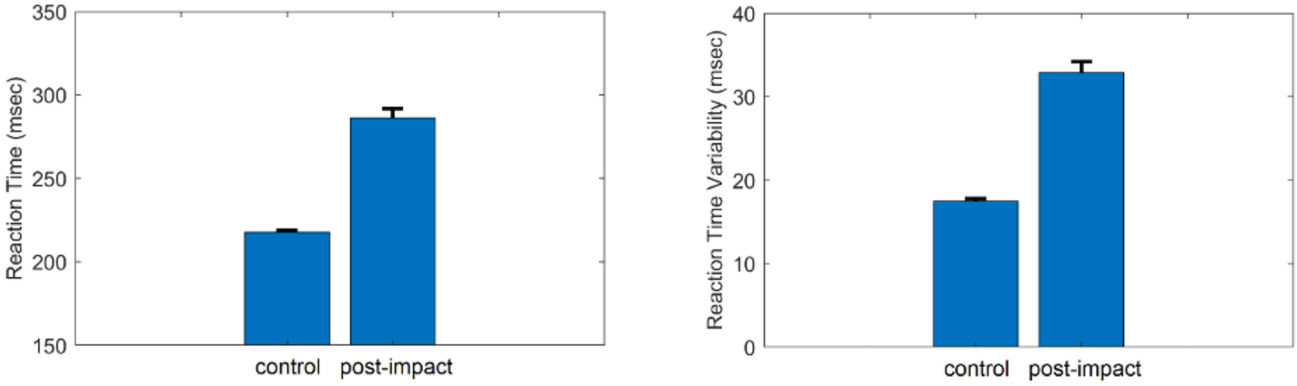

Figure 2. *Left panel: Comparison of reaction time of healthy controls (mean = 218 msec) vs. concussed individuals (mean = 286 msec). Right panel: Comparison of reaction time variability of healthy controls (mean = 17.5 msec) vs. concussed individuals (mean = 33 msec). Note that the difference between controls and concussed individuals is ~31% for reaction time and ~89% for reaction time variability.*

Discussion

The results demonstrate that reaction time and reaction time variability, when collected with an accurate methodology, can be used to significantly differentiate concussed from non-concussed individuals without the use of baseline testing. Although the majority of studies that have investigated sports concussion commonly rely on reaction time as one of their metrics, very few of those studies use accurate reaction time testing methods. Rather, they rely on inferior commercially available online testing methods that are not laboratory grade and are inadequate for any clinical application. Additionally, most of these methods require the use of baseline testing to try to improve the test performance. Baseline testing is the practice of individuals taking a performance-based test before they are injured and subsequently, in the event of an injury, test performance post-injury is compared to the baseline test that was obtained pre-injury. There are obvious disadvantages to relying on baseline testing - not all individuals that become injured and need to be evaluated have the luxury of being part of a sports program that might require baseline testing. Additionally, baselines in collegiate sports programs are typically only collected during participant's freshman year, and this baseline is expected to not change for 3-4 years (a fairly large assumption for any science-based assessment of brain function).

Of particular interest is that while reaction time is typically collected by many assessment tools used to evaluate cognitive status, very few reports demonstrate the degree of difference between concussed and non-concussed individuals as described in the methods of this report. Perhaps the best description of the utility of some of the online cognitive testing methods without baseline testing was provided by Nelson and colleagues [39] (Nelson et al, 2017). In that report, three commonly used online cognitive assessment tools (ANAM, DANA and ImPACT) were used to evaluate concussions in an emergency room setting. Since the individuals under study were first observed in the emergency room, there were no pre-injury baseline tests, and the results of that study demonstrated that there was no difference in reaction time detected. In fact, none of the methods demonstrated overall scores obtained from the injured individuals that were significantly different from healthy controls. If an assessment tool is to be effective, then it should not depend on knowing the performance metric of an individual before they are injured. This problem of depending on baseline testing appears to be resolved when using accurate testing methods such as described in this study. The above-mentioned cognitive assessment tools or online computerized tests that rely on consumer-grade instrumentation introduce significant timing errors to measures such as reaction time (Holden et al, 2020), and this is most likely the reason that differences in reaction time could not be resolved in prior studies without the use of baseline testing.

This is not the first report that demonstrates accurate tactile based reaction time metrics to be sensitive to neurological insult – and more specifically – to concussion. Several studies have reported that accurate tactile based reaction time, collected with the Brain Gauge, successfully differentiates concussed individuals from non-concussed individuals. . Favorov and colleagues demonstrated a 91% and 69% area under the ROC curve for differentiating concussed vs. non-concussed individuals with reaction time variability and reaction time, respectively [5]. Pearce et al [11] showed significant differences between the reaction time and reaction time variabilities of three populations: healthy controls, individuals that had recovered from concussion and individuals that were still asymptomatic. Similar results were also demonstrated in a military population [38].

One of the reasons that there have been so few successful studies that accurately demonstrate differences between concussion and healthy controls without the use of a baseline is because the method commonly used to collect reaction time with commercial methods, such as those in the above-described Nelson study, is a visual reaction time task that relies on inferior consumer-grade equipment. Computer operating systems and hardware introduce significant delays and variability [1] and these delays and variability lead to significant errors. Countless publications have used these visual reaction time tasks, most likely because they are used by commercial systems that rely on inferior methods, and the researchers simply trusted those methods because they were commercially available. Some recent studies have directly compared the visual reaction time tasks that rely on consumer-grade systems with the more accurate Brain Gauge system. Note that, based on robotics testing, without a human element, the accuracy of the visual systems used introduces errors on the order of 80 - 400 msec while the error introduced by the Brain Gauge is approximately 0.3 msec [1]. Pearce and colleagues [11] directly compared reaction time collected with the Brain Gauge and CogState, an online program that administers a visual reaction time task but depends on consumer grade technology. In that study, individuals with post-concussive symptoms (PCS) were evaluated with both the Brain Gauge and CogState. The study demonstrated that individuals with PCS had significantly higher tactile based reaction times and reaction time variabilities, administered with the Brain Gauge, than did healthy controls. The same two groups of individuals were also administered the visually based reaction time task with CogState, and there was no difference observed between the reaction times observed between the two groups with those measures. Additionally, the visually-based reaction time task for the healthy controls was approximately 85 msec slower than the reaction time obtained with the Brain Gauge for the same group of individuals. Since this phase lag is very close to the reaction time measured robotically (i.e., no human timing error) for the same type of computer system used in that study (80 msec; Holden et al [1]), the difference could be considered to be predominantly attributed to a technical instrumentation deficiency and not a biological difference. A subsequent independent study examined differences in reaction time obtained with the Brain Gauge versus a visual task and obtained the same difference, with the visual-based task resulting in the slower reaction time and delayed approximately the same amount of time as in the Pearce study [40]. This further strengthens the argument that the delays observed between visually-based reaction time and the Brain Gauge are technological and not biological. Long before these measures were directly made, Steve Hsiao made the argument that there should not be a significant difference between tasks such as reaction time for visual vs. tactile tasks [41]. Each task (visual vs. tactile) performs object recognition and transmits information to the decision center in the brain that leads to execution of the response task. Thus, both visual- and tactile-based tasks are predicted to take approximately the same amount of time, and any significant difference in visual vs. tactile reaction time would most likely be attributed to technical deficiencies in one or both of the test devices.

Reaction time gets significantly impacted under a number of conditions, and the task has a significant presence in the literature. There are reports on a wide range of topics over many years, such as concussion or TBI [42-55], aging [56-61], sleep deprivation [62], schizophrenia [63], Parkinson's [64,65], acute alcohol use [66], pharmaceuticals [67,68], Tourette's [69], ADD/ADHD [28,70-72], reading disabilities in children [73], and diabetes [74,75]. It is interesting to note that while reaction time has been used to examine a large number of topics, its accuracy has decreased over the past 50 years [1] and this has led to a significant change in the average measured reaction time drifting up 100-200% over that time period [1,76]. In other words, although a wide range of research uses the reaction time task, it is becoming increasingly inaccurate, to the point of being scientifically and clinically useless, because of the expansion of poor research techniques and tools that appear to be becoming more widespread and have come to dominate mainstream research in this area. The ease of using any of a number of commercially available online cognitive testing systems appears to have led to a degree of complacency in some researchers (particularly those without technical backgrounds) to assume that anything that is over-the-counter or involves a "computer" or tablet must have some level of fidelity. The pervasive use of inadequate consumer-grade toys by poorly-trained researchers with no technical background and no understanding of their research tools has the combined effects of (1) delaying and disempowering the use of basic but accurate measures of cognitive function for diagnosis and guidance of treatment of brain injury, and (2) undermining the belief and support of the educated tax-paying public in the enterprise of academic science through waste, and an increasingly self-evident academic scientific culture dominated by a pervasive, ineffective, feckless incompetence.

Conclusion

The use of accurate reaction time methods (e.g., the methods described in this report) can give clear and objective results for assessments of individuals with concussion. Consumer-grade testing devices simply cannot do so. When measured properly, reaction time variability is a more accurate indicator of concussion, and this measure requires high resolution timing accuracy that is only available in laboratory grade equipment and the Brain Gauge.

Notes

Author's note: The results of this study will be continually updated after initial publication with additional analyses and/or data.

Editor's note: The *Journal of Science and Medicine* considers all publications as living documents, and updates are not only allowed, but encouraged.

References

1. Holden J, Francisco E, Tommerdahl A, Lensch R, Kirsch B, Zai L, Dennis D, Tommerdahl M. Accuracy of different modalities of reaction time testing: Implications for online cognitive assessment tools. *BioRXIV.* 2019.
2. Tannan V., Dennis R., Tommerdahl M.. A novel device for delivering two-site vibrotactile stimuli to the skin. *Journal of Neuroscience Methods.* 2005; 147(2)DOI
3. Holden Jameson K., Nguyen Richard H., Francisco Eric M., Zhang Zheng, Dennis Robert G., Tommerdahl Mark. A novel device for the study of somatosensory information processing. *Journal of Neuroscience Methods.* 2012; 204(2)DOI
4. Tommerdahl Mark, Dennis Robert G., Francisco Eric M., Holden Jameson K., Nguyen Richard, Favorov Oleg V.. Neurosensory Assessments of Concussion. *Military Medicine.* 2016; 181(5S)DOI
5. Favorov Oleg V, Francisco Eric, Holden Jameson, Kursun Olcay, Zai Laila, Tommerdahl Mark. Quantification of Mild Traumatic Brain Injury via Cortical Metrics: Analytical Methods. *Military Medicine.* 2019; 184(Supplement_1)DOI
6. King DA, Hume P, Tommerdahl M. Use of the Brain-gauge Somatosensory Assessment for Monitoring Recovery from Concussion: A Case Study. *Journal of Physiotherapy Research.* 2018; 2(1):1-13.
7. King Doug. Use of the King-Devick test and Brain Gauge for the management of concussion. *Journal of Science and Medicine in Sport.* 2018; 21DOI
8. Benham Alex, Powell Dylan, Tommerdahl Mark, King Doug, Godfrey Alan, Stuart Samuel.

Exploratory Analysis of the effects of University Rugby on Brain Health monitored via a Somatosensory Device. *Unpublished.* 2018. DOI

9. Tommerdahl AP, Francisco EF, Lensch R, Holden JK, Favorov OV, Tommerdahl M. Response Time in Somatosensory Discrimination Tasks is Sensitive to Neurological Insult. *Neurology and Neurobiology.* 2019. DOI
10. Pearce Alan J., Tommerdahl Mark, King Doug A.. Neurophysiological abnormalities in individuals with persistent post-concussion symptoms. *Neuroscience.* 2019; 408DOI
11. Pearce Alan J., Kidgell Dawson J., Frazer Ashlyn K., King Doug A., Buckland Michael E., Tommerdahl Mark. Corticomotor correlates of somatosensory reaction time and variability in individuals with post concussion symptoms. *Somatosensory & Motor Research.* 2019; 37(1)DOI
12. Folger Stephen E, Tannan Vinay, Zhang Zheng, Holden Jameson K, Tommerdahl Mark. Effects of the N-methyl-D-Aspartate receptor antagonist dextromethorphan on vibrotactile adaptation. *BMC Neuroscience.* 2008; 9(1)DOI
13. Francisco E., Tannan V., Zhang Z., Holden J., Tommerdahl M.. Vibrotactile amplitude discrimination capacity parallels magnitude changes in somatosensory cortex and follows Weber's Law. *Experimental Brain Research.* 2008; 191(1)DOI
14. Francisco Eric M., Holden Jameson K., Nguyen Richard H., Favorov Oleg V., Tommerdahl Mark. Percept of the duration of a vibrotactile stimulus is altered by changing its amplitude. *Frontiers in Systems Neuroscience.* 2015; 9DOI
15. Tannan V., Dennis R.G., Zhang Z., Tommerdahl M.. A portable tactile sensory diagnostic device. *Journal of Neuroscience Methods.* 2007; 164(1)DOI
16. Tannan Vinay, Holden Jameson K., Zhang Zheng, Baranek Grace T., Tommerdahl Mark A.. Perceptual metrics of individuals with autism provide evidence for disinhibition. *Autism Research.* 2008; 1(4)DOI
17. Tommerdahl M., Tannan V., Cascio C.J., Baranek G.T., Whitsel B.L.. Vibrotactile adaptation fails to enhance spatial localization in adults with autism. *Brain Research.* 2007; 1154DOI
18. Tommerdahl Mark, Tannan Vinay, Zachek Matt, Holden Jameson K, Favorov Oleg V. Effects of stimulus-driven synchronization on sensory perception. *Behavioral and Brain Functions.* 2007; 3(1)DOI
19. Zhang Zheng, Francisco Eric M., Holden Jameson K., Dennis Robert G., Tommerdahl Mark. The impact of non-noxious heat on tactile information processing. *Brain Research.* 2009; 1302DOI
20. Zhang Zheng, Zolnoun Denniz A., Francisco Eric M., Holden Jameson K., Dennis Robert G., Tommerdahl Mark. Altered Central Sensitization in Subgroups of Women With Vulvodynia. *The Clinical Journal of Pain.* 2011; 27(9)DOI
21. Zhang Zheng, Francisco Eric M., Holden Jameson K., Dennis Robert G., Tommerdahl Mark. Somatosensory Information Processing in the Aging Population. *Frontiers in Aging Neuroscience.* 2011; 3DOI
22. Lowe S, Tommerdahl A, Lensch R, Francisco E, Holden J, Tommerdahl M. An Undergraduate Laboratory Exercise that Demonstrates the Difference Between Peripherally and Centrally Mediated Measures. *Journal of Undergraduate Neuroscience Education.* 2016; 15(1):A24-A28.
23. Puts Nicolaas A.J., Edden Richard A.E., Wodka Ericka L., Mostofsky Stewart H., Tommerdahl Mark. 10.1152/jn.00455.2014A vibrotactile behavioral battery for investigating somatosensory processing in children and adults. *Journal of Neuroscience Methods.* 2013; 218(1)DOI
24. Puts Nicolaas A., Wodka Ericka L., Tommerdahl Mark, Mostofsky Stewart H., Edden Richard A.. Reply to Dickinson and Milne. *Journal of Neurophysiology.* 2014; 112(6)DOI
25. Puts Nicolaas A. J., Wodka Ericka L., Tommerdahl Mark, Mostofsky Stewart H., Edden Richard A. E.. Impaired tactile processing in children with autism spectrum disorder. *Journal of Neurophysiology.* 2014; 111(9)DOI
26. Puts Nicolaas A. J., Harris Ashley D., Crocetti Deana, Nettles Carrie, Singer Harvey S., Tommerdahl Mark, Edden Richard A. E., Mostofsky Stewart H.. Reduced GABAergic inhibition and abnormal sensory symptoms in children with Tourette syndrome. *Journal of*

Neurophysiology. 2015; 114(2)DOI
27. Puts Nicolaas A.J., Wodka Ericka L., Harris Ashley D., Crocetti Deana, Tommerdahl Mark, Mostofsky Stewart H., Edden Richard A.E.. Reduced GABA and altered somatosensory function in children with autism spectrum disorder. *Autism Research.* 2016; 10(4)DOI
28. Puts Nicolaas A. J., Harris Ashley D., Mikkelsen Mark, Tommerdahl Mark, Edden Richard A. E., Mostofsky Stewart H.. Altered tactile sensitivity in children with attention-deficit hyperactivity disorder. *Journal of Neurophysiology.* 2017; 118(5)DOI
29. Mikkelsen Mark, He Jason, Tommerdahl Mark, Edden Richard A. E., Mostofsky Stewart H., Puts Nicolaas A. J.. Reproducibility of flutter-range vibrotactile detection and discrimination thresholds. *Scientific Reports.* 2020; 10(1)DOI
30. Nguyen R.H., Ford S., Calhoun A.H., Holden J.K., Gracely R.H., Tommerdahl M.. Neurosensory assessments of migraine. *Brain Research.* 2013; 1498DOI
31. Güçlü Burak, Tanıdır Canan, Çanayaz Emre, Güner Bora, İpek Toz Hamiyet, Üneri Özden Ş., Tommerdahl Mark. Tactile processing in children and adolescents with obsessive–compulsive disorder. *Somatosensory & Motor Research.* 2015; 32(3)DOI
32. Wodka Ericka L., Puts Nicolaas A. J., Mahone E. Mark, Edden Richard A. E., Tommerdahl Mark, Mostofsky Stewart H.. The Role of Attention in Somatosensory Processing: A Multi-trait, Multi-method Analysis. *Journal of Autism and Developmental Disorders.* 2016; 46(10)DOI
33. Bryant Lauren K., Woynaroski Tiffany G., Wallace Mark T., Cascio Carissa J.. Self-reported Sensory Hypersensitivity Moderates Association Between Tactile Psychophysical Performance and Autism-Related Traits in Neurotypical Adults. *Journal of Autism and Developmental Disorders.* 2019; 49(8)DOI
34. Houghton David C., Tommerdahl Mark, Woods Douglas W.. Increased tactile sensitivity and deficient feed-forward inhibition in pathological hair pulling and skin picking. *Behaviour Research and Therapy.* 2019; 120DOI
35. Ruitenberg Marit F. L., Cassady Kaitlin E., Reuter-Lorenz Patricia A., Tommerdahl Mark, Seidler Rachael D.. Age-Related Reductions in Tactile and Motor Inhibitory Function Start Early but Are Independent. *Frontiers in Aging Neuroscience.* 2019; 11DOI
36. Cassady Kaitlin, Ruitenberg Marit F L, Reuter-Lorenz Patricia A, Tommerdahl Mark, Seidler Rachael D. Neural Dedifferentiation across the Lifespan in the Motor and Somatosensory Systems. *Cerebral Cortex.* 2020; 30(6)DOI
37. Rahman Md Shoaibur, Barnes Kelly Anne, Crommett Lexi E., Tommerdahl Mark, Yau Jeffrey M.. Auditory and tactile frequency representations are co-embedded in modality-defined cortical sensory systems. *NeuroImage.* 2020; 215DOI
38. Jorgensen-Wagners K. Brain Gauge: Measuring Brain Health for Concussion Recovery.. *Military Medicine.* 2020; In Review
39. Nelson Lindsay D., Furger Robyn E., Gikas Peter, Lerner E. Brooke, Barr William B., Hammeke Thomas A., Randolph Christopher, Guskiewicz Kevin, McCrea Michael A.. Prospective, Head-to-Head Study of Three Computerized Neurocognitive Assessment Tools Part 2: Utility for Assessment of Mild Traumatic Brain Injury in Emergency Department Patients. *Journal of the International Neuropsychological Society.* 2017; 23(4)DOI
40. Kim J, Francisco E, Holden J, Lensch R, Kirsch B, Dennis R, Tommerdahl M. Visual vs. Tactile Reaction Testing Demonstrates Problems with Online Cognitive Testing. *Journal of Science and Medicine.* 2020; In Press
41. Hsiao S. Similarities between touch and vision. *Advances in Psychology.* 1998; 127(C):131-165. DOI
42. Ruesch Jurgen. Dark Adaptation, Negative After Images, Tachistoscopic Examinations and Reaction Time in Head Injuries. *Journal of Neurosurgery.* 1944; 1(4)DOI
43. van Zomeren A.H., Deelman B.G.. Differential effects of simple and choice reaction after closed head injury. *Clinical Neurology and Neurosurgery.* 1976; 79(2)DOI
44. MacFlynn G, Montgomery E A, Fenton G W, Rutherford W. Measurement of reaction time following minor head injury.. *Journal of Neurology, Neurosurgery & Psychiatry.* 1984; 47(12)DOI
45. Stuss D T, Stethem L L, Hugenholtz H, Picton T, Pivik J, Richard M T. Reaction time after

head injury: fatigue, divided and focused attention, and consistency of performance.. *Journal of Neurology, Neurosurgery & Psychiatry.* 1989; 52(6)DOI

46. Ponsford Jennie, Kinsella Glynda. Attentional deficits following closed-head injury. *Journal of Clinical and Experimental Neuropsychology.* 1992; 14(5)DOI
47. HETHERINGTON C. R., STUSS D. T., FINLAYSON M. A. J.. Reaction time and variability 5 and 10 years after traumatic brain injury. *Brain Injury.* 1996; 10(7)DOI
48. Zahn Theodore P., Mirsky Allan F.. Reaction Time Indicators of Attention Deficits in Closed Head Injury. *Journal of Clinical and Experimental Neuropsychology.* 1999; 21(3)DOI
49. Warden D. L., Bleiberg J., Cameron K. L., Ecklund J., Walter J., Sparling M. B., Reeves D., Reynolds K. Y., Arciero R.. Persistent prolongation of simple reaction time in sports concussion. *Neurology.* 2001; 57(3)DOI
50. Collins Michael W., Iverson Grant L., Lovell Mark R., McKeag Douglas B., Norwig John, Maroon Joseph. On-Field Predictors of Neuropsychological and Symptom Deficit Following Sports-related Concussion. *Clinical Journal of Sport Medicine.* 2003; 13(4)DOI
51. Sarno Stefania, Erasmus Lutz-Peter, Lipp Berthold, Schlaegel Wolfgang. Multisensory integration after traumatic brain injury: a reaction time study between pairings of vision, touch and audition. *Brain Injury.* 2003; 17(5)DOI
52. Willison J, Tombaugh T. Detecting simulation of attention deficits using reaction time tests. *Archives of Clinical Neuropsychology.* 2006; 21(1)DOI
53. Niogi S.N., Mukherjee P., Ghajar J., Johnson C., Kolster R.A., Sarkar R., Lee H., Meeker M., Zimmerman R.D., Manley G.T., McCandliss B.D.. Extent of Microstructural White Matter Injury in Postconcussive Syndrome Correlates with Impaired Cognitive Reaction Time: A 3T Diffusion Tensor Imaging Study of Mild Traumatic Brain Injury. *American Journal of Neuroradiology.* 2008; 29(5)DOI
54. Gould Jennifer A., Ciuffreda Kenneth J., Yadav Naveen K., Thiagarajan Preethi, Arthur Benjamin. The effect of retinal defocus on simple eye-hand and eye-foot reaction time in traumatic brain injury (TBI). *Brain Injury.* 2013; 27(13-14)DOI
55. Eckner James T., Richardson James K., Kim Hogene, Joshi Monica S., Oh Youkeun K., Ashton-Miller James A.. Reliability and Criterion Validity of a Novel Clinical Test of Simple and Complex Reaction Time in Athletes. *Perceptual and Motor Skills.* 2015; 120(3)DOI
56. Benton A. L.. Interactive Effects of Age and Brain Disease on Reaction Time. *Archives of Neurology.* 1977; 34(6)DOI
57. Sherwood DE, Selder DJ. Cardiorespiratory health, reaction time and aging. *Medicine and Science in Sports.* 1979; 11(2):186-189.
58. Fozard J. L., Vercruyssen M., Reynolds S. L., Hancock P. A., Quilter R. E.. Age Differences and Changes in Reaction Time: The Baltimore Longitudinal Study of Aging. *Journal of Gerontology.* 1994; 49(4)DOI
59. Lord Stephen R., Clark Russell D.. Simple Physiological and Clinical Tests for the Accurate Prediction of Falling in Older People. *Gerontology.* 1996; 42(4)DOI
60. Lajoie Y, Gallagher S.P. Predicting falls within the elderly community: comparison of postural sway, reaction time, the Berg balance scale and the Activities-specific Balance Confidence (ABC) scale for comparing fallers and non-fallers. *Archives of Gerontology and Geriatrics.* 2004; 38(1)DOI
61. Der Geoff, Deary Ian J.. Age and sex differences in reaction time in adulthood: Results from the United Kingdom Health and Lifestyle Survey.. *Psychology and Aging.* 2006; 21(1)DOI
62. Lorenzo I, Ramos J, Arce C, Guevara MA, Corsi-Cabrera M. Effect of total sleep deprivation on reaction time and waking EEG activity in man. *Sleep.* 1995; 18(5)
63. Schwartz Fred, Munich Richard L., Carr Arthur, Bartuch Elizabeth, Lesser Barbara, Rescigno Deborah, Viegener Barbara. Negative symptoms and reaction time in schizophrenia. *Journal of Psychiatric Research.* 1991; 25(3)DOI
64. Evarts E. V., Teräväinen H., Calne D. B.. Reaction Time in Parkinson's Disease. *Brain.* 1981; 104(1)DOI
65. Goodrich Susan, Henderson Leslie, Kennard Christopher. On the existence of an attention-demanding process peculiar to simple reaction time: Converging evidence from Parkinson's disease. *Cognitive Neuropsychology.* 1989; 6(3)DOI

66. Hernández Oscar H., Vogel-Sprott Muriel, Huchín-Ramirez Teresita C., Aké-Estrada Fernando. Acute dose of alcohol affects cognitive components of reaction time to an omitted stimulus: differences among sensory systems. *Psychopharmacology.* 2005; 184(1)DOI
67. Edwards Allan E., Cohen Sidney. Visual illusion, tactile sensibility and reaction time under LSD-25. *Psychopharmacologia.* 1961; 2(5)DOI
68. Ancelin Marie L, Artero Sylvaine, Portet Florence, Dupuy Anne-Marie, Touchon Jacques, Ritchie Karen. Non-degenerative mild cognitive impairment in elderly people and use of anticholinergic drugs: longitudinal cohort study. *BMJ.* 2006; 332(7539)DOI
69. Shucard David W., Benedict Ralph H. B., Tekok-Kilic Ayda, Lichter David G.. Slowed reaction time during a continuous performance test in children with Tourette's syndrome.. *Neuropsychology.* 1997; 11(1)DOI
70. Meere Jaap, Vreeling Hendrik Jan, Sergeant Joseph. A Motor Presetting Dtudy in Hyperactive, Learning Disabled and Control Children. *Journal of Child Psychology and Psychiatry.* 1992; 33(8)DOI
71. Tamm Leanne, Narad Megan E., Antonini Tanya N., O'Brien Kathleen M., Hawk Larry W., Epstein Jeffery N.. Reaction Time Variability in ADHD: A Review. *Neurotherapeutics.* 2012; 9(3)DOI
72. Ferraro F Richard. No evidence of reaction time slowing in autism spectrum disorder. *Autism.* 2014; 20(1)DOI
73. Davidson Richard J., Leslie Susan C., Saron Clifford. Reaction time measures of interhemispheric transfer time in reading disabled and normal children. *Neuropsychologia.* 1990; 28(5)DOI
74. Richerson S.J., Robinson C.J., Shum J.A.. A comparative study of reaction times between type II diabetics and non-diabetics. *BioMed Eng OnLine.* 2005; 4(12)DOI
75. Patil S, Phatale S. Auditory and Visual Reaction Time - A Tool for Early Detection of Neuropathy in Diabetics. *Int J Health Sci Res.* 2015; 5(4)
76. Woodley Michael A., te Nijenhuis Jan, Murphy Raegan. Were the Victorians cleverer than us? The decline in general intelligence estimated from a meta-analysis of the slowing of simple reaction time. *Intelligence.* 2013; 41(6)DOI