Psychiatric Quarterly (2019) 90:793–801
https://doi.org/10.1007/s11126-019-09664-x

REVIEW ARTICLE

Neuropsychiatric Disorders as Erratic Attention Regulation – Lessons from Electrophysiology

Goded Shahaf[1]

Published online: 13 August 2019

Abstract
Attention related electrophysiological waves, such as P300, often deviate from norm in various populations of neuropsychiatric patients. For example, the amplitude is often smaller and the latency is often longer in major depressive disorder, in bipolar disorder and in schizophrenia. On the other hand, in other neuropsychiatric populations, it is often possible to note the opposite phenomena of larger P300 amplitude and shorter latency in comparison with norm, but only for a specific subset of stimuli. This is often reported in various anxiety disorders, substance abuse and various chronic pain syndromes. These findings in the various clinical populations, on their commonalities and differences, are presented in this work. The prevalence of these two types of deviations in the electrophysiological markers of attention, shared by multiple neuropsychiatric populations, raise interesting questions regarding the role of attention deviation and regulation in neuropsychiatry. We present these questions and outline a possible hypothesis in this regard. Furthermore, such potential sensitivity of the attention-related markers to clinical dynamics suggests they could be candidates for monitoring and, potentially, early-sensing of clinical dynamics. Therefore, we discuss the potential usability of such markers.

Keywords Psychopathology · EEG · ERP · Attention

Electrophysiological Markers of Attention Deviate in Neuropsychiatric Patients

Multiple types of electrophysiological markers have been suggested as related to attention processes over decades of research. Some of those markers are based of raw EEG analysis [37, 66], while others are based on measuring the response to stimuli – e.g. in the form of event related potentials (ERP) [63, 64]. Let us take for example the P300 waveform. Indeed, attention is a complex term [55] and, furthermore, various components of the P300 waveform were

✉ Goded Shahaf
godeds@gmail.com

[1] BrainMARC LTD, Yokneam, Israel

associated with somewhat different neuropsychological processes. Nevertheless, for the sake of the current discussion, it seems feasible to relate P300 and attentional processes.

Despite this diversity in attention types and markers, it seems that multiple attention related waves and patterns, often deviate from norm in multiple (if not all) populations of neuropsychiatric patients. For example, P300 amplitude is often smaller and latency is frequently longer in major depressive disorder (MDD) [9, 60], in bipolar disorder [68] and in schizophrenia [71]. On the other hand, in other neuropsychiatric populations, it is often possible to note the opposite phenomena of larger P300 amplitude and shorter latency in comparison with norm. This is often reported in generalized anxiety disorder (GAD) [18], in post-traumatic stress disorder (PTSD) [72], in obsessive compulsive disorder (OCD) [57], in substance abuse [38] and in various pain syndromes such as migraine [19] and fibromyalgia [48].

Furthermore, direct association was demonstrated in multiple neuropsychiatric conditions between clinical severity and the degree of deviation of the attention-related electrophysiological markers. Such association was reported, for example, in MDD [28], in bipolar disorder [68], in schizophrenia [54], in GAD [76], in PTSD [36], in OCD [4] and in multiple other conditions. In-fact, multiple studies in various neuropsychiatric populations demonstrated changes in the attention-related electrophysiological markers, which often precede overt clinical change and thus enable "prediction" of clinical dynamics. For example, this was demonstrated, with both ERP and raw EEG markers, for MDD [9, 27, 65] and in GAD [49]. In other cases, such as migraine, the attention-related electrophysiological changes occur during the prodrome period, a day or two before a pending attack [33, 67] and, thus, "predict" the attack. Taken together, it makes sense to assume that these early "predictive" electrophysiological changes merely represent high sensitivity to clinical dynamics.

Emphasizing the Split – Two Directions of Attention-Related Marker Changes

As was stated above, in various patient groups, attention-related ERP markers are reduced in a rather comprehensive manner, regardless of stimulus type. This was demonstrated for example in MDD [11], bipolar disorder [56], Schizophrenia [74]. However, in other pathologies, attention-related ERP markers are enhanced (e.g. [40] for GAD; [24] for panic disorder). Often, this enhancement is not general for all types of stimuli, but rather selective in response to specific stimuli, which might be threatening or stressing for the specific clinical population (we will use for these stimuli the abbreviation PRS – Pathology Related Stimuli). While for other, more neutral, stimuli the ERP markers are, in-fact, often reduced (we will use for these stimuli the abbreviation GS – General Stimuli) (see for example: [31] for PTSD; [25] for chronic pain; [38] for substance abuse).

Relation of Markers and the Clinical Circle in Pathologies with Selective Enhancement

Three groups of pathologies manifest an enhanced selective attention response to the PRS, while often showing reduced attention response to the GS. These groups are: (1) anxiety disorders [24, 31, 40], where the PRS are anxiety-evoking stimuli [31]; (2) substance abuse disorders, where the PRS are related to the substance [38]; and (3) some chronic pain

pathologies, where the PRS are noxious stimuli [25]. On the other hand, the attention responses are often reduced, in these three groups, following the majority of the other stimuli (GS). Furthermore, this reduced response is also noticeable following stimuli, which may evoke, in normal controls, strong affective response, either positive or negative [17].

Specifically, it should be noted that chronic pain is often the result of tissue injury, but we refer here to conditions in which there is, at-least, major contribution of central nervous system (CNS) processes to the impact of the chronic pain. Thus, we present below, in some detail, migraine as such an example for a chronic pain pathology with major contribution of CNS processes.

Importantly, for these three pathology groups, it seems possible to talk, in many cases, about a clinical cycle. For example, there is a migraine cycle, which is comprised of the migraine attacks themselves, the pre-ictal period (usually, up to 1–2 days before the attack), the post-ictal period (usually, up to 1–2 days after the attack) and the inter-ictal period (some days away from both the previous attack and the next attack) [52]. As another example, for substance abuse we talk about the craving cycle, in which there is growing craving, followed by substance use and then pleasure, to be followed again by growing craving [35]. Furthermore, it seems that anxiety also follows a vicious circle pattern (the anxiety circle), by which preliminary stressors lead to negative thoughts and emotions, which lead to greater anxiety and either avoidance behavior or escalation and an anxiety attack [7]. Of-course, at other times the clinical dynamics might be very rapid – e.g. in response to phobia evoking stimuli. However, all together, it seems that for the three pathology groups, it is possible to describe a clinical cycle of aggravation, which leads to an undesired event (attack, avoidance or substance use) and then a "quieter" period prior to further aggravation.

Interestingly, enhanced attention response to PRS, together with reduced response to GS, seem to show dynamics, which accords with this clinical dynamics of aggravation and reset. For example, in migraine there is reduced attention response to all stimuli during the inter-ictal phase [12, 61, 67], which also manifests as reduced habituation over long exposure to stimuli, due to low level of initial response to begin with [1, 2, 13, 61, 67]. Then, there is increase in attention response to PRS at the pre-ictal and ictal phases, accompanied by reduction in response to GS [12, 33, 34, 61, 67, 70]. Then, there is a global reduction after the attack [12]. Indeed, the repetitive and orderly pattern of the migraine cycle assists in sampling of the dynamics of attention-related electrophysiological markers during the various clinical phases. However, such dynamics of the electrophysiological attention-related markers was also reported with clinical aggravation in anxiety disorders (e.g. with exposure to PRS in phobia – [42]) and in substance abuse disorders (e.g. during abstinence and withdrawal attempts – [50, 51]). Therefore, all 3 groups of pathologies – anxiety disorders, substance abuse disorders and some chronic pain disorders, seem to follow a pattern of selectively enhanced attention-related markers for PRS, with reduced response to GS. For the three pathology groups, this differentiation between the two types of stimuli may increase with clinical aggravation. At times, this dynamics ends with the onset of an undesired event (attack, avoidance or substance use). After this, with return to clinical baseline, the electrophysiological markers for attention also return to their baseline level.

Relation of Markers and Clinical "Rank" in Pathologies with Comprehensive Reduction

In the pathologies, which demonstrate comprehensive reduction in the attention-related marker, MDD, bipolar disorder and schizophrenia, the clinical dynamics, or cycle, is generally

slower. Indeed, we already discussed the relationship between clinical severity and the degree of reduction of the electrophysiological marker and, therefore, we find in these pathologies also an association between the dynamics in clinical status and the electrophysiological deviation [28, 54, 68].

Furthermore, there seems to be a severity rank between and within these pathologies. Thus, several studies have reported that attention reduction is greater in bipolar disorder than in MDD [44], and greater during the manic phase than during the depressive one, and during both the depressive and manic phases the reduction is greater than during the euthymic phase [68]. Notably, in schizophrenia, it appears that the markers are even more reduced, when compared to both MDD and bipolar disorder [8, 71]. Furthermore, during the "negative symptoms" phase in schizophrenia, the reduction of the attention-related markers is mainly limited to frontal regions. However, during the "positive symptoms" psychotic phase, it spreads also posteriorly to the sensory/perceptual cortex [22]. Interestingly, this posterior spread was suggested to be related with the perceptual disturbances of hallucinations and delusions [61], which form the "positive symptoms".

Thus, not unrelated to clinical severity, there is rank between and within MDD, bipolar disorder and schizophrenia with regard to the degree of reduction of the attention-related electrophysiological markers. Such a severity-related rank of the common phenomenon raises a question regarding the possibility of a common underlying mechanism for the various pathologies, which might be invoked, to different degrees, in the different pathologies, and within each pathology, during different phases. However, it is beyond the scope of the current manuscript to suggest such a neurophysiological mechanism (for further discussion, see: [60, 61]).

A Hypothesis on the Role of the Aberrant Attention Regulation in Neuropsychiatry

Notably, this severity-related clinical aggravation, in each of the pathologies, is accompanied by reduction in cognitive abilities, often related to reduced attention, which may (at-least partially) improve with clinical improvement (MDD – [73]; Bipolar disorder – [73]; Schizophrenia – [15]; GAD – [6]; PTSD – [32]; OCD – [47]; substance abuse – [39]; migraine – [10]; fibromyalgia – [23]). Thus, the deviation, which is evident in the electrophysiological markers of attention, is also reported, at-least to a certain extent, by cognitive evaluations.

But, this association of attention and clinical dynamics raises an intriguing question: what is the role of such attention reduction, with or without selective attention enhancement to a subset of the stimuli? Is it merely an epiphenomenon of the neuropsychiatric pathology?

Let us start by noting that clinical aggravation in the various pathologies is often related to either global or specific stress (MDD – [29]; Bipolar disorder – [16]; Schizophrenia – [46]; GAD and PD – [53]; PTSD – [43]; OCD – [20]; substance abuse – [30]; migraine – [58]; fibromyalgia – [75]).

Strong or stressing stimuli drive neuronal systems to explore for effective solutions, simply by activating the involved neuronal networks. When there is stress, or drive, the neuronal system is activated and may generate various responses. However, if one of these responses removes the stress (or drive) it is stabilized as a solution. This is simply because it aborts the drive induced neural activation and further exploration (drive reduction theory – [26; 62]). Indeed, much was learned about the neurophysiological embodiment of this exploration [21]

and stabilization of learning by mechanisms of reward [59]. Yet, the principle of stabilization of solutions, by drive reduction, seems to be an inherent property of any neuronal system, regardless of the precise details of its cell-level implementation.

However, it seems that when effective solutions for the stressors are not found, dysfunctional solutions may form and become stabilized by reducing further exploration. In a sense, these dysfunctional solutions remove the stressing drive internally by regulating attention to it – either by reducing it or by exhausting it. At times, they also reduce the stressing drive, for a while, from the external environment, as demands from the patient are lowered during the clinical aggravation. This is due to the acknowledgement by the patient's social milieu of the overt clinical deterioration and non-functional state and thereby reduction of stressful demands [3, 45, 60, 61, 69]. However, in the longer range this temporary dysfunction may evoke more stress due to social stigma and lack of effective coping with the underlying stressors ([14, 41, 58]; Substance abuse – [69]). Thus, a vicious circle perpetuates.

Possible Utilizations of the Attention-Related Electrophysiological Markers

As was stated above, multiple studies in various neuropsychiatric populations demonstrated changes in the attention-related electrophysiological markers, which often precede overt clinical dynamics and thus enable "prediction" of clinical dynamics [9, 27, 33, 49, 65–67]. Indeed, it makes sense to assume that these early "predictive" electrophysiological changes merely represent high sensitivity to clinical dynamics.

However, as was discussed throughout this work, multiple pathologies would manifest as similar deviations in attention-related electrophysiological markers. Therefore, such markers are not expected to be pathology-specific. Furthermore, as attention is affected by multiple factors, and is highly state dependent [66], the derivation of the marker from a single test is not likely to be predictive. Instead, it is the dynamics between repetitive measures, which is likely to show sufficient sensitivity (e.g. for depression – [27, 65]; for migraine – [67]). Furthermore, as the dynamics of different pathologies evolve over different timescales (e.g. the migraine cycle is often measured in days, while depression often evolves over weeks and months), it is possible to follow the dynamics of attention-related markers with these different timescales, so as to improve specificity, especially when comorbidity is concerned.

However, the utilization of traditional multichannel EEG and ERP tools to extract relevant markers, which are often based on long samples, at the scale of many minutes, might be too cumbersome – rendering it rather impractical for the clinical routine. Therefore, it is of practical importance to develop markers, which could be extracted from easy-to-use headsets, which do not require technical expertise with EEG, and which, furthermore, could be derived from short samples (possibly at the 1-min scale). Recently, such markers are being developed and initial efficacy has been demonstrated in various clinical groups [27, 65–67].

Furthermore, hopefully, it be possible to extract such markers for attention even in real-time, during relevant treatment sessions (e.g. behavioral, such as CBT and electromagnetic, such as TMS) [5, 27]. In which case, it could be possible to tune the treatment in real-time, with the hope of obtaining better clinical outcomes. Altogether, it makes sense to assume, for

example in behavioral therapies, that identification, in real-time, of anxious states, or of depressive and avoidant states, could assist in tuning the treatment. Based on the above, it is not unlikely that such states might manifest in attention-related markers, if these are derived effectively in real-time, at the sub-minute temporal resolution.

Finally, while it is beyond the scope of the current work, we discussed above two general patterns of attention deviation, which seem to be shared by multiple neuropsychiatric pathologies. We also suggested that this similarity might indicate common underlying neurophysiological mechanisms [60, 61]. As a hypothesis, we suggested that the attention deviation may be central to the pathologies, and not merely some epiphenomenon. Thus, it seems of interest to discuss further the neurophysiological modeling of these mechanisms, also as a basis for possible futuristic directed therapies.

Summary

We suggested, in this work, that neuropsychiatric pathologies could be divided to two groups according to the change, in attention-related markers, they display: pathologies, which demonstrate comprehensive reduction of attention and pathologies, which demonstrate reduction of attention to the majority of stimuli, with enhancement of attention to a specific subset of stimuli. We further suggested that each such deviation relates with clinical severity and dynamics, and hypothesized that attention regulation might play a central role in the pathology formation and perpetuation.

The primary purpose of this work was to describe the relevant findings in the literature, and to emphasize the commonalities and differences among neuropsychiatric pathologies. However, we also suggested that effective electrophysiological monitoring of attention might yield important information regarding the clinical dynamics, of the single patient, in the various pathology groups, and might even assist in treatment tuning.

Compliance with Ethical Standards

Conflict of Interests The author is the founder of BrainMARC LTD, which developed the Brain Engagement Index (BEI) – a marker for sustained attention. However, the manuscript is based on literature review of unrelated works. A minority of the studies cited are based on the BEI. However, they serve as a mere example for the larger family of attention-related markers.

Ethical Approval This article does not contain any new studies with human participants or animals performed by the author.

References

1. Afra J, Cecchini AP, De Pasqua V, Albert A, Schoenen J. Visual evoked potentials during long periods of pattern-reversal stimulation in migraine. Brain J Neurol. 1998;121(2):233–41.
2. Afra J, Cecchini AP, Sandor PS, Schoenen J. Comparison of visual and auditory evoked cortical potentials in migraine patients between attacks. Clin Neurophysiol. 2000;111(6):1124–9.
3. Allen NB, Badcock PB. Darwinian models of depression: a review of evolutionary accounts of mood and mood disorders. Prog Neuro-Psychopharmacol Biol Psychiatry. 2006;30(5):815–26.
4. Andreou C, Leicht G, Popescu V, Pogarell O, Mavrogiorgou P, Rujescu D, et al. P300 in obsessive–compulsive disorder: source localization and the effects of treatment. J Psychiatr Res. 2013;47(12):1975–83.
5. Bartur, G., Joubran, K., Peleg-Shani, S., Vatine, J. J., & Shahaf, G. (2017). An EEG tool for monitoring patient engagement during stroke rehabilitation: a feasibility study. BioMed research international, 2017. https://doi.org/10.1155/2017/9071568.

6. Beaudreau SA, O'Hara R. The association of anxiety and depressive symptoms with cognitive performance in community-dwelling older adults. Psychol Aging. 2009;24(2):507–12.
7. Beck AT, Emery G, Greenberg RL. Anxiety disorders and phobias: A cognitive perspective: Basic Books; 2005.
8. Blackwood DH, Whalley LJ, Christie JE, Blackburn IM, St Clair DM, McInnes A. Changes in auditory P3 event-related potential in schizophrenia and depression. Br J Psychiatry. 1987;150(2):154–60.
9. Bruder, G. E., Kayser, J., & Tenke, C. E. (2012). Event-related brain potentials in depression: clinical, cognitive and neurophysiologic implications. The Oxford Handbook of Event-Related Potential Components, 2012, 563–592.
10. Calandre EP, Bembibre J, Arnedo ML, Becerra D. Cognitive disturbances and regional cerebral blood flow abnormalities in migraine patients: their relationship with the clinical manifestations of the illness. Cephalalgia. 2002;22(4):291–302.
11. Cavanagh J, Geisler MW. Mood effects on the ERP processing of emotional intensity in faces: a P3 investigation with depressed students. Int J Psychophysiol. 2006;60(1):27–33.
12. Coppola G, Pierelli F, Schoenen J. Habituation and migraine. Neurobiol Learn Mem. 2009;92(2):249–59.
13. Coppola G, De Pasqua V, Pierelli F, Schoenen J. Effects of repetitive transcranial magnetic stimulation on somatosensory evoked potentials and high frequency oscillations in migraine. Cephalalgia. 2012;32(9):700–9.
14. Cui XJ, Vaillant GE. Does depression generate negative life events? J Nerv Ment Dis. 1997;185(3):145–50.
15. Egeland J, Rund BR, Sundet K, Landrø NI, Asbjørnsen A, Lund A, & Hugdahl K. Attention profile in schizophrenia compared with depression: differential effects of processing speed, selective attention and vigilance. Acta Psychiatr Scand. 2003;108(4):276–284.
16. Ellicott A, Hammen C, Gitlin M, Brown G, Jamison K. Life events and the course of bipolar disorder. Am J Psychiatr. 1990;147(9):1194–8.
17. Engelbregt, H. J., Keeser, D., Promes, V. H., Verhagen-Schouten, S., & Deijen, J. B. (2012). In-vivo EEG changes during a panic attack in a patient with specific phobia. https://doi.org/10.4021/jmc403e.
18. Enoch MA, White KV, Waheed J, Goldman D. Neurophysiological and genetic distinctions between pure and comorbid anxiety disorders. Depress Anxiety. 2008;25(5):383–92.
19. Evers S, Quibeldey F, Grotemeyer KH, Suhr B, Husstedt IW. Dynamic changes of cognitive habituation and serotonin metabolism during the migraine interval. Cephalalgia. 1999;19(5):485–91.
20. Ferrão YA, Shavitt RG, Bedin NR, De Mathis ME, Lopes AC, Fontenelle LF, & Miguel EC. Clinical features associated to refractory obsessive–compulsive disorder. J Affect Disord. 2006;94(1–3):199–209.
21. Ganguly K, & Poo MM. Activity-dependent neural plasticity from bench to bedside. Neuron. 2013;80(3): 729–741.
22. Gerez M, Tello A. Selected quantitative EEG (QEEG) and event-related potential (ERP) variables as discriminators for positive and negative schizophrenia. Biol Psychiatry. 1995;38(1):34–49.
23. Glass JM. Fibromyalgia and cognition. J Clin Psychiatry. 2007;69:20–4.
24. Hanatani T, Sumi N, Taguchi S, Fujimoto O, Nan-No H, Takeda M. Event-related potentials in panic disorder and generalized anxiety disorder. Psychiatry Clin Neurosci. 2005;59(1):83–8.
25. Hermann C, Zohsel K, Hohmeister J, Flor H. Cortical correlates of an attentional bias to painful and innocuous somatic stimuli in children with recurrent abdominal pain. Pain. 2008;136(3):397–406.
26. Hull, C. L. (1943). Principles of behavior: An introduction to behavior theory. New York: Appleton-Century-Crofts.
27. Isserles M, Daskalakis ZJ, George MS, Blumberger DM, Sackeim HA, Shahaf G. Simple electroencephalographic treatment-emergent marker can predict repetitive transcranial magnetic stimulation antidepressant response—A feasibility study. J ECT. 2018;34(4):274–82.
28. Kemp AH, Benito LP, Quintana DS, Clark CR, McFarlane A, Mayur P, et al. Impact of depression heterogeneity on attention: An auditory oddball event related potential study. J Affect Disord. 2010;123(1):202–7.
29. Kendler KS, Karkowski LM, Prescott CA. Causal relationship between stressful life events and the onset of major depression. Am J Psychiatr. 1999;156:837–41.
30. Kilpatrick DG, Acierno R, Saunders B, Resnick HS, Best CL, Schnurr PP. Risk factors for adolescent substance abuse and dependence: data from a national sample. J Consult Clin Psychol. 2000;68(1):19–30.
31. Kimble M, Kaloupek D, Kaufman M, Deldin P. Stimulus novelty differentially affects attentional allocation in PTSD. Biol Psychiatry. 2000;47(10):880–90.
32. Koso M, Hansen S. Executive function and memory in posttraumatic stress disorder: a study of Bosnian war veterans. Eur Psychiatry. 2006;21(3):167–73.
33. Kropp P, Gerber WD. Prediction of migraine attacks using a slow cortical potential, the contingent negative variation. Neurosci Lett. 1998;257(2):73–6.

34. Kropp P, Gerber WD. Slow cortical potentials in migraine. Predictive value and possible novel therapeutic strategies to prevent an attack. Funct Neurol. 2005;20(4):193–7.
35. Lewis M. Memoirs of an addicted brain: A neuroscientist examines his former life on drugs: Public Affairs; 2012.
36. Lobo I, Portugal LC, Figueira I, Volchan E, David I, Pereira MG, et al. EEG correlates of the severity of posttraumatic stress symptoms: a systematic review of the dimensional PTSD literature. J Affect Disord. 2015;183:210–20.
37. Loo SK, Hale TS, Macion J, Hanada G, McGough JJ, McCracken JT, et al. Cortical activity patterns in ADHD during arousal, activation and sustained attention. Neuropsychologia. 2009;47(10):2114–9.
38. Lubman DI, Allen NB, Peters LA, Deakin JW. Electrophysiological evidence that drug cues have greater salience than other affective stimuli in opiate addiction. J Psychopharmacol. 2008;22(8):836–42.
39. Lundqvist T. Cognitive consequences of cannabis use: comparison with abuse of stimulants and heroin with regard to attention, memory and executive functions. Pharmacol Biochem Behav. 2005;81(2):319–30.
40. MacNamara A, Hajcak G. Distinct electrocortical and behavioral evidence for increased attention to threat in generalized anxiety disorder. Depress Anxiety. 2010;27(3):234–43.
41. Mennin DS, Heimberg RG, Turk CL, Fresco DM. Preliminary evidence for an emotion dysregulation model of generalized anxiety disorder. Behav Res Ther. 2005;43(10):1281–310.
42. Michalowski JM, Pané-Farré CA, Löw A, Hamm AO. Brain dynamics of visual attention during anticipation and encoding of threat-and safe-cues in spider-phobic individuals. Soc Cogn Affect Neurosci. 2015;10(9):1177–86.
43. Miller KE, Rasmussen A. War exposure, daily stressors, and mental health in conflict and post-conflict settings: bridging the divide between trauma-focused and psychosocial frameworks. Soc Sci Med. 2010;70(1):7–16.
44. Muir WJ, St Clair DM, Blackwood DH. Long-latency auditory event-related potentials in schizophrenia and in bipolar and unipolar affective disorder. Psychol Med. 1991;21(04):867–79.
45. Newman MG, Llera SJ. A novel theory of experiential avoidance in generalized anxiety disorder: a review and synthesis of research supporting a contrast avoidance model of worry. Clin Psychol Rev. 2011;31(3): 371–82.
46. Nuechterlein KH, Dawson ME. A heuristic vulnerability/stress model of schizophrenic episodes. Schizophr Bull. 1984;10(2):300–12.
47. Olley A, Malhi G, Sachdev P. Memory and executive functioning in obsessive–compulsive disorder: a selective review. J Affect Disord. 2007;104(1):15–23.
48. Ozgocmen S, Yoldas T, Kamanli A, Yildizhan H, Yigiter R, Ardicoglu O. Auditory P300 event related potentials and serotonin reuptake inhibitor treatment in patients with fibromyalgia. Ann Rheum Dis. 2003;62(6):551–5.
49. Park YM, Kim DW, Kim S, Im CH, Lee SH. The loudness dependence of the auditory evoked potential (LDAEP) as a predictor of the response to escitalopram in patients with generalized anxiety disorder. Psychopharmacology. 2011;213(2–3):625–32.
50. Parvaz MA, Moeller SJ, Malaker P, Sinha R, Alia-Klein N, Goldstein RZ. Abstinence reverses EEG-indexed attention bias between drug-related and pleasant stimuli in cocaine-addicted individuals. J Psychiatry Neurosci: JPN. 2017;42(2):78–86.
51. Petit G, Cimochowska A, Cevallos C, Cheron G, Kornreich C, Hanak C, et al. Reduced processing of alcohol cues predicts abstinence in recently detoxified alcoholic patients in a three-month follow up period: an ERP study. Behav Brain Res. 2015;282:84–94.
52. Quintela E, Castillo J, Munoz P, Pascual J. Premonitory and resolution symptoms in migraine: a prospective study in 100 unselected patients. Cephalalgia. 2006;26(9):1051–60.
53. Raskin M, Peeke HV, Dickman W, Pinsker H. Panic and generalized anxiety disorders: developmental antecedents and precipitants. Arch Gen Psychiatry. 1982;39(6):687–9.
54. Renoult L, Prévost M, Brodeur M, Lionnet C, Joober R, Malla A, et al. P300 asymmetry and positive symptom severity: a study in the early stage of a first episode of psychosis. Schizophr Res. 2007;93(1):366–73.
55. Robertson IH, Ward T, Ridgeway V, Nimmo-Smith I. The structure of normal human attention: the test of everyday attention. J Int Neuropsychol Soc. 1996;2(6):525–34.
56. Ryu V, An SK, Jo HH, Cho HS. Decreased P3 amplitudes elicited by negative facial emotion in manic patients: selective deficits in emotional processing. Neurosci Lett. 2010;481(2):92–6.
57. Sanz M, Molina V, Martin-Loeches M, Calcedo A, Rubia FJ. Auditory P300 event related potential and serotonin reuptake inhibitor treatment in obsessive-compulsive disorder patients. Psychiatry Res. 2001;101(1):75–81.
58. Sauro KM, Becker WJ. The stress and migraine interaction. Headache: J Head Face Pain. 2009;49(9):1378–86.

59. Schultz W. Updating dopamine reward signals. Curr Opin Neurobiol. 2013;23(2):229–238.
60. Shahaf, G. (2016a). A possible common neurophysiologic basis for MDD, bipolar disorder, and schizophrenia: lessons from electrophysiology. Front Psychiatry. 7. https://doi.org/10.3389/fpsyt.2016.00094.
61. Shahaf G. Migraine as dysfunctional drive reduction: insight from electrophysiology. Med Hypotheses. 2016b;91:62–6.
62. Shahaf G, & Marom S. Learning in networks of cortical neurons. J Neurosci. 2001;21(22):8782–8788.
63. Shahaf G, Pratt H. Thorough specification of the neurophysiologic processes underlying behavior and of their manifestation in EEG–demonstration with the go/no-go task. Front Hum Neurosci. 2013;7. https://doi.org/10.3389/fnhum.2013.00305.
64. Shahaf G, Fisher T, Aharon-Peretz J, Pratt H. Comprehensive analysis suggests simple processes underlying EEG/ERP–demonstration with the go/no-go paradigm in ADHD. J Neurosci Methods. 2015;239:183–93.
65. Shahaf G, Yariv S, Bloch B, Nitzan U, Segev A, Reshef A, et al. A pilot study of possible easy-to-use electrophysiological index for early detection of antidepressive treatment non-response. Front Psychol. 2017;8:128.
66. Shahaf G, Nitzan U, Erez G, Mendelovic S, Bloch Y. Monitoring attention in ADHD with an easy-to-use electrophysiological index. Front Hum Neurosci. 2018a;12:32.
67. Shahaf G, Kuperman P, Bloch Y, Yariv S, Granovsky Y. Monitoring migraine cycle dynamics with an easy-to-use electrophysiological marker—A pilot study. Sensors. 2018b;18(11):3918.
68. Silva LWDG, Cartier C, Cheniaux E, Novis F, Silveira LA, Cavaco PA, et al. Electrical mapping in bipolar disorder patients during the oddball paradigm. J Psychiatr Res. 2016. https://doi.org/10.1016/j.jpsychires.2015.10.012.
69. Sinha R. How does stress increase risk of drug abuse and relapse? Psychopharmacology. 2001;158(4):343–59.
70. Siniatchkin M, Averkina N, Andrasik F, Stephani U, Gerber WD. Neurophysiological reactivity before a migraine attack. Neurosci Lett. 2006;400(1–2):121–4.
71. Souza VB, Muir WJ, Walker MT, Glabus MF, Roxborough HM, Sharp CW, et al. Auditory P300 event-related potentials and neuropsychological performance in schizophrenia and bipolar affective disorder. Biol Psychiatry. 1995;37(5):300–10.
72. Stanford MS, Vasterling JJ, Mathias CW, Constans JI, Houston RJ. Impact of threat relevance on P3 event-related potentials in combat-related post-traumatic stress disorder. Psychiatry Res. 2001;102(2):125–37.
73. Sweeney JA, Kmiec JA, Kupfer DJ. Neuropsychologic impairments in bipolar and unipolar mood disorders on the CANTAB neurocognitive battery. Biol Psychiatry. 2000;48(7):674–84.
74. Ueno T, Morita K, Shoji Y, Yamamoto M, Yamamoto H, Maeda H. Recognition of facial expression and visual P300 in schizophrenic patients: differences between paranoid type patients and non-paranoid patients. Psychiatry Clin Neurosci. 2004;58(6):585–92.
75. Van Houdenhove B, Egle UT. Fibromyalgia: a stress disorder? Psychother Psychosom. 2004;73(5):267–75.
76. Weinberg A, Olvet DM, Hajcak G. Increased error-related brain activity in generalized anxiety disorder. Biol Psychol. 2010;85(3):472–80.

Goded Shahaf is the founder and technology developer of NeuroIndex LTD and BrainMARC LTD.